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Understanding Lower Limb Amputation: A Review of the Strategies for Healthcare Improvement, Prevention, and Management

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ABSTRACT

INTRODUCTION: Lower limb amputation (LLA) is a global health issue affecting millions of people worldwide. Factors such as diabetes, peripheral vascular disease, infections, and improper medical practices also contribute to Lower limb amputation. The personal, family, and socio-economic costs associated with amputation are substantial, emphasizing the need for preventive measures, improved healthcare resources, and support for amputees.

METHODS: A literature review of Lower limb amputation and its associated risk factors, which focuses on hypertension, hypercholesterolemia, smoking, diabetic complications, Indigenous ethnicity, and foot infections.

RESULTS: It was revealed that the socio-economic impact of Lower limb amputation includes job loss and financial burdens. Also, access to rehabilitation services, stigma, and marginalization further complicate the lives of amputees. Furthermore, peripheral vascular disease is a significant risk factor, and chronic hyperglycemia in diabetes leads to diabetic foot syndrome and subsequent amputations. Lower limb amputation has a profound impact on quality of life and psychological well-being, particularly in rural areas where manual labor is prevalent. Strategies to address Lower limb amputation include prevention and management of diabetes-related complications, improved healthcare access, and awareness programs. Public health initiatives, health education campaigns, early detection, and affordable healthcare are also crucial in reducing amputation rates. Specific interventions for diabetic foot care, timely surgical intervention, and preserving limb length and function are important considerations.

CONCLUSION: Multifaceted strategies are necessary for the effective management and prevention of lower limb amputation.

Keywords: Lower-limb, Amputation, Improvement, Prevention, Management, Multidisciplinary approach

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INTRODUCTION

Globally, it is estimated that 65 million people live with limb amputations, and 1.5 million people undergo amputations every year, with 60% being Lower limb amputations (LLA)[1]. Also, two-thirds of people with amputation live in low-resourced settings [1], and it is estimated that 5 million of the amputee population live in Africa, of which around 75% are lower limb amputees [1]. LLA does not only disfigure but also renders people less mobile and may lead to loss of Independence [2,3] Reported that people with LLA often withdraw from social activities owing to their physical limitations, perceived body image, and lack of disability-supported facilities.

Amputation is one of the oldest and most commonly performed surgical procedures. The first written surgical description of lower limb amputation was written by Hippocrates (460-377 BC). The earliest known case was reported to have been performed in Borneo 31,000 years ago [4].

Lower limb amputation is defined as a complete loss in the transverse anatomical plane of any part of the lower extremity for any reason [5]. Lower limb Amputation is among the most acquired disabilities, with a global prevalence ranging from 3.6 to 68.4 per 100,000 population [6]. There are 30,000- 40,000 amputations performed annually in the United States, with an estimated 1.6 million amputees worldwide in 2005, and this figure is expected to rise to 3.6 million by 2050 [7]. Also, LLA accounted for 3.08% of operations done at the University Hospital of Butare, Rwanda [8]. According to the Uganda national population census of the year 2014, the prevalence of limb disability increases with age, varying from .5% in children through 7.5% in teenagers to 16.5% in adults, of whom 5% have difficulty walking. LLA occurs as a result of a wide range of diseases and trauma. It is attributed to significant morbidity, disability, and mortality. An amputation is not merely limb loss as it can mean disability, joblessness, high insurance payments, depression and poor quality of life [9]. Lower-limb amputation is attributed to a number of complications, which include: infection, phantom limb sensation and pain, residual limb pain, painful neuroma, depression, and heterotopic ossification [9].

Indications for LLA are generally considered as the 3Ds: Dead limb, Deadly limb, and Damn nuisance of a limb. In high income countries, peripheral vascular disease ranks first as the major cause of amputation, while trauma, infection, complications of Diabetes Mellitus, and malignancy are the indications for Amputation in Low-to middle-income countries-Uganda not left out [10,11]). Subsequently, it has been reported that trauma is the leading cause of LLA followed by Diabetes, neoplasms, and peripheral vascular Disease in Uganda [12]. LLA is often performed as a lifesaving procedure, usually done when the limb is deemed non-salvageable following severe injury (e.g., road traffic accident, war injuries), when there is tissue loss due to vascular occlusive disease or to control/ stop infection progress [13].

LLA is performed at different anatomical levels based on the need and reason for the amputation, namely: Toe-ectomy – removal of single or multiple

Table 1: Summary of the lower limb amputation; the prevalence across different regions

Region	Prevalence of lower limb amputation (LLA)
Global	Estimated 65 million individuals worldwide [14]
High-Income Countries	Relatively lower compared to low- and middle-income countries. Decreased prevalence in the United States from 8.2 per 1,000 individuals in 2000 to 4.4 per 1,000 individuals in 2008 [27,28]
Low- and Middle-Income Countries	Higher prevalence, particularly in sub-Saharan Africa (Uganda, Kenya, Nigeria) due to limited access to healthcare resources, inadequate infrastructure, and high prevalence of risk [16–18]
Specific Regions	Higher prevalence observed in South Africa, India, and Bangladesh due to factors like trauma, diabetes-related complications, peripheral vascular [21]
Risk Factors	Diabetes, peripheral vascular disease, infections, trauma, and inadequate medical practices contribute to the prevalence of LLA globally [23]

toes at the level of the metatarsophalangeal joints, transmetatarsal – amputation through the shafts of metatarsals, Mid-tarsal (Chopart/ Lisfranc) – amputation through the tarsal bones, Through-ankle (Symes) – amputation of the foot at the ankle joint with retention of the plantar heel and removal of the malleoli, below-knee – a leg amputation 11-12cm distal to the knee, through knee – the knee joint is disarticulated leaving the patient to weight bear on condyles, above knee – amputation through the femur, ideal length of 25-30 cm from the greater trochanter, hip disarticulation – the femur is disarticulated from the acetabulum and hind quarter – the side of the brim of the pelvis is removed.

PREVALENCE OF LOWER LIMB AMPUTATION

The prevalence of lower limb amputation (LLA) varies around the world due to differences in

Table 2: Incident rate of lower limb amputation across different region

Aspect	Findings	References
Global LLA incidence	173 per 105 population	Hennis et al 2004
Global amputee population	Estimated 65 million people	Liao et al., 2020
Global annual amputations	Approximately 1.5 million people	Liao et al., 2020
Global amputees in low-resourced settings	Two-thirds of amputees, including Uganda	Liao et al., 2020
African amputee population	Estimated 5 million	Liao et al., 2020
European Union LLA incidence trends	Increasing trend observed between 1990 and 2017; highest incidences in Australia (male: 37.8 per 100,000; female: 31.4)	LEA study group, 2020
LLA demographics in Uganda	Unknown trend due to lack of past data and amputee registry	Kenney et al., 2019
Functional difficulties in Uganda	Approximately 12.5% of the population with walking or sensory disabilities	Uganda Bureau of Statistics, 2018, 2019
Prevalence of major limb loss in Acholi	11,400 people out of 1.9 million in the Acholi sub-region of Uganda	Atim et al., 2020
Causes of LLA	Diabetes complications, peripheral vascular disease, trauma, malignancy, infection, congenital defects, and others	Engstrom et al., 1993; Van Houtum et al., 1996, etc.
Factors associated with higher LLA incidence	Geographical location, male gender, diabetes duration, co-morbidities, lack of education	Wrobel et al., 2001; Resnick et al., 2004, etc.
Trauma-related LLA in Uganda	Highest number of incidents in referral hospitals; causes include road accidents, violence, fire, occupational accidents, etc.	Muhumuza & Bangirana, 2015; Kenney et al., 2019
Costs of amputation in KwaZulu-Natal, SA	Personal, family, and socio-economic costs estimated at $290,000 per amputee; additional annual cost of $359,779,298.28	Journal of Endocrinology, Metabolism, and Diabetes of South Africa, 2020

risk factors, healthcare systems, and population characteristics. This section will provide a detailed explanation of the prevalence of LLA in different regions, supported by relevant references.

Global Prevalence: LLA is a significant health issue globally, affecting millions of people. According to the International Society for Prosthetics and Orthotics, an estimated 65 million individuals are living with limb amputations worldwide [14]. This figure underscores the substantial burden of LLA on individuals, families, and society as a whole.

High-Income Countries: In high-income countries, such as the United States and those in Western Europe, the prevalence of LLA is relatively lower compared to low- and middle-income countries. This is attributed to better healthcare resources, advanced medical interventions, and preventive measures. For example, in the United States, the prevalence of major non-traumatic lower extremity amputations among adults with diabetes decreased from 8.2 per 1,000 individuals in 2000 to 4.4 per 1,000 individuals in 2008 [15].

Low- and Middle-Income Countries: LLA is more prevalent in low- and middle-income countries, where access to healthcare resources and preventive measures may be limited. For instance, in sub-Saharan Africa, LLA is a significant health concern. Studies conducted in countries like Uganda, Kenya, and Nigeria have reported a high burden of LLA, particularly among individuals with diabetes and those affected by trauma [16–18].

Specific Regions: The prevalence of LLA may vary within specific regions. For example, studies have highlighted a higher prevalence of LLA in certain areas, such as South Africa, where a combination of factors, including trauma, diabetes-related complications, and peripheral vascular disease, contribute to the burden of LLA [19,20]. In Southeast Asia, countries like India and Bangladesh have also reported a high prevalence of LLA, primarily due to diabetes-related complications [21]. Several risk factors contribute to the prevalence of LLA globally. Diabetes is a major risk factor, with diabetic foot ulcers and complications being a leading cause of LLA [22,23]. Other risk factors include peripheral vascular disease, infections, trauma (such as road

Table 3: Associated risks factors associated with lower limb amputation

Risk Factors for Lower Limb Amputation	References
Viability of soft tissues for bone coverage	Molina & Faulk (2021)
Presence of femoral pulse, gangrene, and necrotizing soft tissue infection	Molina & Faulk (2021)
Removal of diseased tissue, prosthetic fit, tapering bone ends, edema control, pain control	Schnur & Meier (2014)
Hypertension, hypercholesterolemia, raised serum creatinine, history of smoking	Lazzarini et al. 2012
Diabetic retinopathy, CABG surgery, Charcot's foot, Indigenous ethnicity	Ndip et al. (2010)
Diabetic neuropathy, dyslipidemia, CABG surgery	Al-Ani et al. (2011)
Prevalence and ulcer severity among African American cohorts	Lavery et al. (2010)
Indigenous ethnicity	Rodrigues et al. (2016)
Charcot's arthropathy, history of osteomyelitis, severity of foot infection or cellulitis	Korzon-Burakowska & Dziemidok (2011); Wukich et al. (2013)
Glycemic control (HbA1c levels)	Ndip et al. (2010); Winkley et al.
Socio-economic impact: job loss, financial demands, difficulties in returning to work	Burger & Marincek (2007)
Inaccessible and inappropriate rehabilitation services, stigma, marginalization	Okello et al. (2019)
High mortality rates among people with LLA in Johannesburg, South Africa	Godlwana et al. (2007)
Overweight or obesity status, lower education levels, urban settings among individuals with diabetes	Stanifer et al. (2016)

traffic accidents and violence), and inadequate medical practices [24–26]

EPIDEMIOLOGY OF LOWER LIMB AMPUTATION

The global incidence of lower limb amputation (LLA) has been reported to be 173 per 105 population, with an estimated 65 million people living with limb amputations worldwide[29,30]. It is estimated that 1.5 million people undergo amputations each year, and two-thirds of people with amputations reside in low-resourced settings, including Uganda [30]. In Africa, it is estimated that 5 million of the amputee population live on the continent [30]. The Lower Extremity Amputation (LEA) study group reported an increasing trend in the incidence of LLA among 15 European Union countries between 1990 and 2017. The highest incidences were observed in Australia, with rates of 37.8 per 100,000 for male patients and 31.4 per 100,000

Table 4: Outcomes of lower limb amputation among patients in some regions

Study	Outcomes	Findings
McEwen et al. (2013)	Increased Risk of Adverse Outcomes	Peripheral Vascular Disease (PVD) significantly increases the risk of adverse outcomes, such as amputation and mortality, among individuals with diabetes.
Sutkowska (2012)	Chronic Complications and Reduced Quality of Life	Chronic hyperglycemia in poorly controlled diabetes leads to organ and system damage, resulting in long-term complications, reduced quality of life, and death. Common complications include diabetic foot, peripheral neuropathy (7.28%), calluses (35.37%), foot deformities (24.2%), and arterial vessel pathologies (17.39%).
Zhang et al. (2020)	Diabetic Foot Syndrome and Amputation	Diabetic foot syndrome can lead to lower-extremity amputation. Globally, approximately 131 million people (1.8% of the population) had diabetes-related lower-extremity complications, resulting in 6.8 million amputations in 2016.
Lazzarini et al. (2011)	Diabetic Foot Syndrome and Amputation	Diabetes accounts for 60-70% of all lower-extremity amputations (LEA), contributing significantly to the global disability burden and impacting the cost of illness and quality of life. Post-amputation, patients have a decreased quality of life compared to the general population.
Sahu et al. (2016)	Psychiatric Disorders and Pain:	Among individuals with diabetes in India, there is a high prevalence of psychiatric disorders, including depression (10.4% to 63%) and posttraumatic stress disorder (3.3% to 56.3%). Phantom limb pain and residual stump pain are also common issues.
Gurney et al. (2018)	Increased Mortality Rates:	Lower-extremity amputations in patients with diabetes are associated with significant short-term and long-term postoperative mortality rates. In New Zealand, over 11% of patients died within 30 days, and nearly 18% died within 90 days after major amputations.
De Godoy et al. (2002)	Psychological and Emotional Effects:	Limb amputation not only leads to physical disability but also has profound psychological and emotional effects, resulting in feelings of worthlessness and a loss of independence. In Uganda, where subsistence farming is prevalent, lower-limb amputations contribute to poverty and a diminished quality of life.

for female patients, increasing to 41.9 and 34.8 per 100,000, respectively, in 2017 (LEA study group, 2020). LLA is commonly observed in males, individuals with diabetes, and those residing in rural settings [16,31,32]. However, the trend of LLA in Uganda is currently unknown due to the lack of past data and the absence of an amputee registry [33]. Functional difficulties related to walking and sensory impairments have been measured in Uganda, with approximately 12.5% of the population experiencing at least one form of walking or sensory disability (Uganda Bureau of Statistics, 2018, 2019) [34]. The prevalence of major upper and/or lower limb loss was estimated to be 11,400 people out of 1.9 million in the Acholi sub-region of Uganda.

LLA can result from various causes, including diabetic complications (neuropathic foot and ischemic foot), peripheral vascular disease (PVD), trauma, malignancy, infection, congenital lower limb defects, burns, rhabdomyolysis, sepsis, cellulitis, improper intravenous therapy practices [35–37]. Factors such as geographical location, male gender, duration of diabetes, presence of co-morbidities, and lack of high school education have been associated with a higher incidence of LLA [38–40]. Trauma has been identified as a significant cause of limb amputations in Uganda, with studies indicating that it accounts for the highest number of incidents in referral hospitals [33]. Road traffic accidents, violence, fire, occupational accidents, congenital limb loss, illness (leading to gangrene and malignancy), and improper intravenous therapy practices are among the main contributors to trauma-induced limb loss. The personal, family, and socio-economic costs associated with amputation are substantial. A study conducted in the KwaZulu-Natal province of South Africa estimated costs exceeding $290,000 per amputee, resulting in an additional cost of $359,779,298.28 per year to the region (Journal of Endocrinology, Metabolism, and Diabetes of South Africa, 2020).

THE RISK FACTORS ASSOCIATED WITH LOWER LIMB AMPUTATION

The level of amputation depends on the viability of the soft tissues used for bone coverage [35]. Preservation of functional limb length is essential for post-operative functionality [35]. Principles of amputation surgery include removing diseased tissue, providing a residual limb for prosthetic fit, tapering bone ends, controlling edema, and optimizing pain control [41].

Various risk factors contribute to lower limb amputation (LLA). LLA patients have significant risk factors such as hypertension, hypercholesterolemia, raised serum creatinine, and a history of smoking, necessitating extended medical follow-ups and incurring heavy medical costs[42]. Factors like diabetic retinopathy, CABG surgery, Charcot's foot, and Indigenous ethnicity have been identified to significantly contribute to LLA [43]. Emphasis on the association of diabetic neuropathy and dyslipidemia with an increased risk of LLA was made [12]. There exists a significant difference in prevalence and ulcer severity contributing to LLA among African American cohorts [44]. It has been established that Indigenous ethnicity to be a strong contributing factor to LLA, possibly due to genetic predisposition or late presentation for clinical care.[45]

Other risk factors for LLA include Charcot's arthroplasty, a history of osteomyelitis, and severity of foot infection or cellulitis [46]. Glycemic control is important for healing and reducing mortality, although studies have reported increased amputation risk with HbA1c levels above 7.5% [44].

The socio-economic impact of amputations is significant, leading to job loss, financial demands, and difficulties in returning to work [47]. Amputees in Northern Uganda face challenges with inaccessible and inappropriate rehabilitation services, stigma, and marginalization [12]. Mortality rates among people with LLA in Johannesburg, South Africa, are among the highest globally [48].

In a study conducted in the Kilimanjaro region of Tanzania, it was discovered that overweight or obesity status had an independent prevalence risk ratio for glucose impairment, and individuals with diabetes had lower education levels and were more likely to live in urban settings [49].

THE OUTCOME OF LOWER LIMB AMPUTATION AMONG PATIENTS

Peripheral vascular disease, or PVD, has been identified with an increased risk of adverse outcomes, which labels it as a causal factor for amputation and mortality amongst people with diabetes [50].

Pathologies that are risk factors for the occurrence of a diabetic foot occur quite common in diabetic

patients, e.g., in a study conducted in Wroclaw (Poland), it was found that 7.28% of diabetic patients have peripheral neuropathy; 35.37%, calluses; 24.2%, foot deformities; and 17.39%, features of the pathology of arterial vessels [51]
A study revealed that diabetic foot syndrome may result in lower-extremity amputation [52]. According to the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD), in 2016, about 131 million people (1.8% of the global population) had diabetes-related lower-extremity complications, including 6.8 million amputations [52] revealed that cases with diabetes account for 60-70% of all lower-extremity amputations (LEA). Diabetes-related lower-extremity complications are a large and growing contributor to the disability burden worldwide. Lower limb amputation concurrently leads to an increase in illness-related costs and a huge change in the quality of life and function of the patient. After LEA, patients have a diminished quality of life compared to the general population [53].
A review of studies from India indicates that there is an increased prevalence of psychiatric disorders among this group of patients, which account for 32% to 84%, including depression rates of 10.4%–63% and posttraumatic stress disorder of 3.3%–56.3%. Another problem to consider in this population is the incidence of phantom limb pain and residual stump pain [54].
Lower-extremity amputations are also related to significant early and long-term postoperative mortality. In a national study performed in New Zealand on individuals diagnosed with diabetes, more than 11% of patients who underwent major amputation died within 30 days, whereas nearly 18% died within 90 days [55].
Amputation of a limb does not only leave a physical disability on an individual but also leads to psychological and emotional effects, thus feeling useless because of the inability to do anything, lowering their quality of life [56].

MANAGEMENT STRATEGIES FOR LOWER LIMB AMPUTATION: PREVALENCE, RISK FACTORS, AND OUTCOMES

Epidemiological Survey: Epidemiological studies and national databases play a crucial role in understanding the prevalence of lower limb amputation in different populations and regions. These studies provide valuable insights into the burden of amputation and aid in planning appropriate healthcare resources. Researchers analyzed data from the National Health Interview Survey and estimated that approximately 1.6 million people were living with limb loss in the United States in 2005. Among them, lower limb amputations accounted for the majority[7].
Another analysis was conducted using data from the National Diabetes Audit. The study estimated that the prevalence of major lower limb amputation among individuals with diabetes in England was 1.0 per 1,000 people with diabetes [57]. This finding highlighted the substantial burden of lower limb amputation among the diabetic population.

Implementation of Public Health Initiatives: Implementing public health initiatives aimed at preventing or reducing the occurrence of conditions that lead to lower limb amputation is crucial in addressing this significant healthcare issue. Health education programs on the knowledge, attitude, and practice of diabetic foot care among individuals with diabetes have been implicated to have a significant improvement in participants' knowledge and practice of foot care, [58]. Also, investigation of the effectiveness of a screening program has shown a significant reduction in the incidence of foot ulcers and subsequent amputations among individuals with diabetes, emphasizing the importance of early detection and intervention in preventing amputation [59]. It was found that states that expanded Medicaid experienced a significant reduction in diabetes-related amputations compared to non-expansion states, highlighting the positive effect of improved healthcare access on preventing amputations [60].

Comprehensive Assessment of Individual Risk Factors: Comprehensive assessment of individual risk factors is crucial in managing lower limb amputation. It has been revealed that better glycemic control was associated with a lower risk of amputation, emphasizing the importance of diabetes control in preventing amputations [61]. Investigating the association between PVD and adverse outcomes in individuals with diabetes showed that PVD significantly increased the risk of amputation and mortality [62]. The role of peripheral neuropathy has been implicated as a contributing factor to foot ulcers and subsequent

amputations, underscoring the need for its assessment in risk stratification [63]. Studies have examined the association between foot deformities and diabetic foot complications, which highlighted the significance of foot deformities in predicting the risk of ulcers and subsequent amputations, emphasizing the importance of assessing and managing deformities in at-risk individuals [46,60]. There is a significant reduction in ulcer recurrence rates following callus removal, emphasizing the importance of callus assessment and management in preventing amputations. This demonstrated a. Arterial vessel pathologies, including peripheral artery disease, can compromise blood flow to the lower extremities and increase the risk of amputation [64]. Also, the significant impact of arterial vessel pathologies on amputation risk, emphasizing the importance of their assessment in managing at-risk individuals, has been established [65]. Therefore, a comprehensive assessment of individual risk factors is essential in managing lower limb amputation.

Adopting a Multidisciplinary Approach: Adopting a multidisciplinary approach that involves various healthcare professionals is crucial in the management of lower limb amputation. Collaboration among endocrinologists, vascular surgeons, podiatrists, orthopedic surgeons, wound care specialists, and rehabilitation therapists facilitates comprehensive evaluation, treatment, and management of risk factors, ultimately aiming to prevent or delay the need for amputation. Endocrinologists play a key role in preventing diabetic foot complications, including amputation, through comprehensive diabetes care and patient education [66]. Vascular surgeons provide expertise in diagnosing and treating arterial and venous circulation disorders [67]. Podiatrists are essential in foot care and the prevention of foot ulcers, a precursor to lower limb amputation. They conduct foot examinations, manage foot deformities, provide wound care, and offer guidance on appropriate footwear [68]. Orthopedic surgeons may be involved in the management of severe foot and ankle deformities that pose a risk of ulceration and amputation. They provide expertise in surgical interventions, including corrective procedures and salvage operations [69]. Wound care specialists help facilitate wound healing and prevent amputations in patients with diabetic foot ulcers [70]. Rehabilitation therapists, including physical therapists and occupational therapists, play a vital role in the postoperative care and rehabilitation of individuals who undergo lower limb amputation. They provide support in optimizing wound healing, pain management, gait training, prosthetic fitting, and functional recovery [71]. The collaboration among endocrinologists, vascular surgeons, podiatrists, orthopedic surgeons, wound care specialists, and rehabilitation therapists enables comprehensive evaluation, treatment, and management of risk factors, contributing to the prevention or delay of amputation.

Specific Interventions for Diabetic Foot Care: Specific interventions for diabetic foot care are essential in preventing complications that may lead to lower limb amputation. These interventions include regular foot examinations, proper footwear, foot hygiene, wound management, and patient education. By implementing these strategies, healthcare providers aim to identify early signs of foot problems, prevent foot ulcers, and promote overall foot health in individuals with diabetes.
Regular foot examinations are a fundamental component of diabetic foot care. These examinations involve assessing the skin, nails, sensation, and vascular status of the feet. They help in identifying potential risk factors and early signs of foot complications. A systematic review emphasized the importance of regular foot examinations in preventing diabetic foot ulcers and subsequent amputations [72]. Proper footwear plays a crucial role in reducing the risk of foot ulceration and amputation. Individuals with diabetes should wear well-fitting shoes that provide adequate support and protection. Customized footwear and orthotics may be necessary for individuals with foot deformities or high-risk feet. Appropriate footwear and hygiene significantly reduced the incidence of foot ulcers in individuals with diabetes [73]. Foot hygiene helps reduce the risk of foot complications in individuals with diabetes, and wound management is critical in preventing the progression of foot ulcers and avoiding amputations [74,75]. Specialized wound care interventions, such as offloading devices and advanced dressings, effectively promoted wound healing and reduced the risk of amputation [76]. Providing individuals with diabetes with comprehensive education on foot care practices, self-monitoring, early recognition of foot problems, and the importance of regular follow-up can

empower them to take an active role in preventing complications. A randomized controlled trial demonstrated that patient education interventions significantly reduced the risk of foot ulcers and amputations in diabetic individuals [75,77]. These interventions aim to identify early signs of foot problems, prevent foot ulcers, and promote foot health in diabetic individuals.

Timely and Appropriate Surgical Intervention: When lower limb amputation is deemed necessary, timely and appropriate surgical intervention by experienced surgeons is crucial. The selection of the level of amputation considers the patient's functional status, vascular supply, and potential for prosthetic fitting. This ensures optimal outcomes and the best possible functional and prosthetic rehabilitation for the individual. Patients who underwent amputation performed by experienced surgeons had lower mortality rates and shorter hospital stays compared to those operated on by less experienced surgeons. The goal is to preserve as much functional ability as possible while addressing the underlying condition necessitating the amputation. Preservation of a functional residual limb allows for better mobility, potential for prosthetic fitting, and improved overall quality of life [78]. Considering functional status in the decision-making process for lower limb amputation, vascular supply for adequate blood flow is very important, the latter being necessary for wound healing and successful rehabilitation [79]. Vascular evaluation, prosthetic fitting, and rehabilitation potential are important when selecting the level of amputation, which is important in lower limb amputation procedures. The aim is to provide individuals with the opportunity to regain mobility and function through the use of prosthetic devices [80]. The selection of the level of amputation considers the patient's functional status, vascular supply, and potential for prosthetic fitting. This comprehensive approach ensures optimal outcomes, functional rehabilitation, and improved quality of life for individuals undergoing lower limb amputation [81].

Comprehensive Postoperative Care: Comprehensive postoperative care plays a crucial role in optimizing outcomes following lower limb amputation. It involves various aspects, such as wound management, pain management, physical therapy, and rehabilitation services. These interventions aim to promote wound healing, facilitate functional recovery, and support the adaptation to prosthetic devices. Effective wound care practices contribute to better healing outcomes and reduce the risk of secondary complications [82]. Pain management is important to ensure the comfort and well-being of individuals undergoing lower limb amputation. Adequate pain control not only improves patient satisfaction but also facilitates participation in rehabilitation and functional recovery. Various pain management strategies, including pharmacological and non-pharmacological approaches, can be employed based on the individual's needs and preferences [83]. Physical therapy and rehabilitation services are crucial for optimizing functional recovery and promoting adaptation to prosthetic devices. These interventions include exercises to improve strength, range of motion, balance, and gait training. Physical therapists play a key role in guiding individuals through the rehabilitation process, providing individualized treatment plans, and monitoring progress. [84] Prosthetists work closely with individuals to ensure proper alignment, comfort, and functionality of the prostheses. Ongoing prosthetic rehabilitation is necessary to address any challenges, make necessary adjustments, and optimize the individual's ability to use the prosthetic limb effectively [85].

Recognizing and Addressing the Psychosocial Impact: Recognizing and addressing the psychosocial impact of lower limb amputation is a vital component of comprehensive care for individuals undergoing amputation. The emotional distress, body image concerns, and changes in quality of life that can arise following amputation necessitate appropriate support and interventions to promote psychological well-being and adjustment. Counseling, support groups, and psychological interventions are effective strategies for addressing these psychosocial challenges. Counseling and therapy provide individuals with a safe and supportive environment to express their emotions, process grief and loss, and develop coping strategies. Mental health professionals, such as psychologists or counselors, can offer individual counseling sessions tailored to the specific needs of the patient. These sessions can address emotional distress, body image issues, self-esteem concerns, and adjustment difficulties [86]. Support groups bring together individuals

who have experienced or are undergoing lower limb amputation, providing a platform for mutual support, shared experiences, and learning from one another. Psychological interventions, such as mindfulness-based stress reduction and acceptance and commitment therapy, can be beneficial in helping individuals adjust to life after amputation. These interventions focus on building resilience, acceptance of physical changes, and the development of adaptive coping mechanisms [86]. Mindfulness-based interventions improved psychological well-being, acceptance of disability, and adjustment to limb loss in individuals with lower limb amputation [87]. It is important for healthcare professionals to recognize the psychosocial impact of amputation and proactively address these issues throughout the treatment process. By providing appropriate counseling, facilitating access to support groups, and incorporating psychological interventions into care plans, healthcare providers can support patients in navigating the emotional and psychological challenges associated with lower limb amputation.

Establishing Long-term Follow-up Care: Establishing long-term follow-up care is crucial in the management of individuals who have undergone lower limb amputation. This ongoing care aims to monitor wound healing, prevent recurrent ulcers, manage comorbidities, and address any complications or prosthetic-related issues that may arise over time. By providing regular and comprehensive follow-up, healthcare providers can ensure the long-term well-being and functional outcomes of amputees. Monitoring wound healing is an important aspect of long-term follow-up care. Regular assessment of the residual limb's condition allows for early detection and prompt management of any issues, such as infection, delayed wound healing, or skin breakdown. Timely intervention can prevent complications and optimize the healing process [88]. Regular foot checks and preventive strategies reduced the incidence of foot ulcers in individuals with diabetes and a history of amputation [89]. Managing comorbidities is essential in the long-term care of individuals with lower limb amputation. Many amputees have underlying conditions such as diabetes, peripheral vascular disease, or cardiovascular disorders that require ongoing management. Regular monitoring, appropriate medication management, and lifestyle modifications are necessary to control these comorbidities and minimize their impact on overall health and well-being. There is a need for integrated care that addresses both amputation-related needs and the management of comorbid conditions in optimizing long-term outcomes. Addressing complications and prosthetic-related issues is another critical aspect of long-term follow-up care. Prosthetic devices may require adjustments, repairs, or replacements over time, and individuals may experience functional limitations or discomfort related to their prostheses. Regular follow-up visits allow for assessment of the prosthetic fit, function, and comfort and enable necessary modifications to optimize mobility and quality of life. Additionally, addressing any complications that arise, such as skin breakdown, socket-related issues, or pain, is crucial in ensuring optimal prosthetic use [90,91].

In summary, pidemiological studies and national databases provide crucial insights into the burden of this condition, allowing for more targeted resource allocation and healthcare planning. The prevalence estimates from studies like the National Health Interview Survey and the National Diabetes Audit underscore the substantial impact of lower limb amputation on both the general population and individuals with diabetes. The implementation of public health initiatives aimed at prevention and early intervention in conditions leading to lower limb amputation is paramount. Initiatives such as health education programs, screening programs, and improved healthcare access have demonstrated significant potential in reducing the incidence of amputations. The comprehensive assessment of individual risk includes glycemic control, peripheral vascular disease, peripheral neuropathy, foot deformities, and callus assessment. These risk factors are essential for effective risk stratification, prevention, and management of lower limb amputation.

The involvement of a multidisciplinary healthcare team, which places emphasis on collaboration among various specialists, is essential in ensuring comprehensive evaluation, treatment, and management of risk factors, as it contributes significantly to the prevention or delay of amputations. Specific interventions for diabetic foot care, including regular foot examinations, proper footwear, foot hygiene, wound management, and patient education, are fundamental in preventing complications that may lead to lower limb

amputation.

When lower limb amputation is necessary, timely and appropriate surgical intervention is essential. Skilled surgeons play a critical role in selecting the appropriate level of amputation, considering the patient's functional status, vascular supply, and potential for prosthetic fitting. Comprehensive postoperative care encompasses wound management, pain control, physical therapy, and prosthetic rehabilitation. Effective postoperative care can reduce the risk of complications and improve the overall quality of life for individuals who have undergone lower limb amputation. The psychosocial impact of lower limb amputation is a significant concern, and recognizing and addressing these challenges is a vital component of comprehensive care. Counseling, support groups, and psychological interventions are effective strategies in helping individuals adjust to life after amputation.

Establishing long-term follow-up care to monitor wound healing, prevent recurrent ulcers, manage comorbidities, and address prosthetic-related issues over time ensures the well-being and functional outcomes of individuals who have undergone lower limb amputation.

Finally, the systematic review provides a comprehensive overview of the multifaceted strategies necessary for the effective management and prevention of lower limb amputation. These strategies encompass epidemiological research, public health initiatives, risk factor assessment, multidisciplinary care, specific interventions, surgical intervention, postoperative care, psychosocial support, and long-term follow-up.

REFERENCES

1. Morgado Ramirez, D.Z.; Nakandi, B.; Ssekitoleko, R.; Ackers, L.; Mwaka, E.; Kenney, L.; Holloway, C.; Donovan-Hall, M. The Lived Experience of People with Upper Limb Absence Living in Uganda: A Qualitative Study. African Journal of Disability 2022, 11, doi:10.4102/ajod.v11i0.890.

2. Amoah, V.M.K.; Anokye, R.; Acheampong, E.; Dadson, H.R.; Osei, M.; Nadutey, A. The Experiences of People with Diabetes-Related Lower Limb Amputation at the Komfo Anokye Teaching Hospital (KATH) in Ghana. BMC Res Notes 2018, 11, 66, doi:10.1186/s13104-018-3176-1.

3. Godlwana, L.; Stewart, A.; Musenge, E. The Effect of a Home Exercise Intervention on Persons with Lower Limb Amputations: A Randomized Controlled Trial. Clin Rehabil 2020, 34, 99–110, doi:10.1177/0269215519880295.

4. Maloney, T.R.; Dilkes-Hall, I.E.; Vlok, M.; Oktaviana, A.A.; Setiawan, P.; Priyatno, A.A.D.; Ririmasse, M.; Geria, I.M.; Effendy, M.A.R.; Istiawan, B.; et al. Surgical Amputation of a Limb 31,000 Years Ago in Borneo. Nature 2022, 609, 547–551, doi:10.1038/s41586-022-05160-8.

5. Ang, Y.; Yap, C.W.; Saxena, N.; Lin, L.-K.; Heng, B.H. Diabetes-Related Lower Extremity Amputations in Singapore. Proceedings of Singapore Healthcare 2017, 26, 76–80, doi:10.1177/2010105816663521.

6. Moxey, P.W.; Gogalniceanu, P.; Hinchliffe, R.J.; Loftus, I.M.; Jones, K.J.; Thompson, M.M.; Holt, P.J. Lower Extremity Amputations - a Review of Global Variability in Incidence: Lower Extremity Amputations-a Global Review. Diabetic Medicine 2011, 28, 1144–1153, doi:10.1111/j.1464-5491.2011.03279.x.

7. Ziegler-Graham, K.; MacKenzie, E.J.; Ephraim, P.L.; Travison, T.G.; Brookmeyer, R. Estimating the Prevalence of Limb Loss in the United States: 2005 to 2050. Archives of Physical Medicine and Rehabilitation 2008, 89, 422–429, doi:10.1016/j.apmr.2007.11.005.

8. Ssebuufu, R.; Murwanashyaka, E.; Kyamanywa, P. Prevalence, Indications, Levels and Outcome Limb Amputations at University Teaching Hospital-Butare in Rwanda | East and Central African Journal of Surgery Available online: https://www.ajol.info/index.php/ecajs/article/view/97357 (accessed on 23 October 2023).

9. Francis, B.; Dionizi, M.; Fredrick, M. Outcomes of Major Lower Limb Amputation among Patients at a Refferal Hospital. Journal of Clinical Research 2022, 6, 167, doi:0.37421/2795-6172.2022.6.167.

10. Wong, I.; Lee, D.; Thompson, D. Lower Limb Ulcerations in Older People in Hong Kong. Journal of Clinical Nursing 2005, 14, 118–119, doi:10.1111/j.1365-2702.2004.00947.x.

11. Dunbar, G.L.; Hellenberg, D.A.; Levitt, N. Diabetes Mellitus and Non-Traumatic Lower Extremity Amputations in Four Public Sector Hospitals in Cape Town, South Africa, during 2009 and 2010. S Afr Med J 2015, 105, 1053, doi:10.7196/SAMJ.2015.v105i12.9276.

12. Okello, T.R.; Magada, S.M.; Atim, P.; Ezati, D.; Campion, A.; Moro, E.B.; Huck, J.; Byrne, G.; Redmond, A.; Nirmalan, M. Major Limb Loss (MLL): An Overview of Etiology, Outcomes, Experiences and Challenges Faced by Amputees and Service

Providers in the Post-Conflict Period in Northern Uganda. Journal of Global Health Reports 2019, 3, e2019018, doi:10.29392/joghr.3.e2019028.
13. Abe, M.; Fujii, H.; Funakoshi, S.; Satoh, A.; Kawazoe, M.; Maeda, T.; Tada, K.; Yokota, S.; Yamanokuchi, T.; Yoshimura, C.; et al. Comparison of Body Mass Index and Waist Circumference in the Prediction of Diabetes: A Retrospective Longitudinal Study. Diabetes Ther 2021, 12, 2663–2676, doi:10.1007/s13300-021-01138-3.
14. ISPO 17th World Congress Abstract Book. Prosthet Orthot Int 2019, 43, 1–600, doi:10.1177/0309364619883197.
15. Sauter, C.N.; Pezzin, L.E.; Dillingham, T.R. Functional Outcomes of Persons Who Underwent Dysvascular Lower Extremity Amputations: Effect of Postacute Rehabilitation Setting. American Journal of Physical Medicine & Rehabilitation 2013, 92, 287–296, doi:10.1097/PHM.0b013e31827d620d.
16. Owolabi, E.O.; Adeloye, D.; Ajayi, A.I.; McCaul, M.; Davies, J.; Chu, K.M. Lower Limb Amputations among Individuals Living with Diabetes Mellitus in Low- and Middle-Income Countries: A Systematic Review Protocol. PLoS ONE 2022, 17, e0266907, doi:10.1371/journal.pone.0266907.
17. Oyibo, S.O.; Jude, E.B.; Tarawneh, I.; Nguyen, H.C.; Harkless, L.B.; Boulton, A.J.M. A Comparison of Two Diabetic Foot Ulcer Classification Systems. Diabetes Care 2001, 24, 84–88, doi:10.2337/diacare.24.1.84.
18. Hall, V.; Thomsen, R.W.; Henriksen, O.; Lohse, N. Diabetes in Sub Saharan Africa 1999-2011: Epidemiology and Public Health Implications. a Systematic Review. BMC Public Health 2011, 11, 564, doi:10.1186/1471-2458-11-564.
19. Mtshali, S.; Mahomed, O. Patient-Level Predictors of Diabetes-Related Lower Extremity Amputations at a Quaternary Hospital in South Africa. PLoS ONE 2020, 15, e0240588, doi:10.1371/journal.pone.0240588.
20. knadmin Lower Limb Amputations: Epidemiology and Assessment. PM&R KnowledgeNow 2017.
21. Amalraj, M.J.; A, A.R.; Viswanathan, V. A Study on Positive Impact of Intensive Psychological Counseling on Psychological Well-Being of Type 2 Diabetic Patients Undergoing Amputation. IJPC 2017, 9, 10–16, doi:10.5897/IJPC2016.0461.
22. McDermott, K.; Fang, M.; Boulton, A.J.M.; Selvin, E.; Hicks, C.W. Etiology, Epidemiology, and Disparities in the Burden of Diabetic Foot Ulcers. Diabetes Care 2023, 46, 209–221, doi:10.2337/dci22-0043.
23. Welcome to IDF | International Diabetes Federation Available online: https://idf.org/# (accessed on 23 October 2023).
24. Kim, J.; Jeon, Y.S.; Cho, S.G.; Hong, K.C.; Park, K.-M. Risk Factors of Amputation in Lower Extremity Trauma with Combined Femoropopliteal Arterial Injury. VSI 2019, 35, 16–21, doi:10.5758/vsi.2019.35.1.16.
25. Davidovic, L.B.; Cinara, I.S.; Ille, T.; Kostic, D.M.; Dragas, M.V.; Markovic, D.M. Civil and War Peripheral Arterial Trauma: Review of Risk Factors Associated with Limb Loss. Vascular 2005, 13, 141–147, doi:10.1258/rsmvasc.13.3.141.
26. Barth, C.A.; Wladis, A.; Blake, C.; Bhandarkar, P.; Perone, S.A.; O'Sullivan, C. Retrospective Observational Study of Characteristics of Persons with Amputations Accessing International Committee of the Red Cross (ICRC) Rehabilitation Centres in Five Conflict and Postconflict Countries. BMJ Open 2021, 11, e049533, doi:10.1136/bmjopen-2021-049533.
27. Girijala, R.L.; Bush, R.L. Review of Socioeconomic Disparities in Lower Extremity Amputations: A Continuing Healthcare Problem in the United States. Cureus 2018, doi:10.7759/cureus.3418.
28. Goldberg, J.B.; Goodney, P.P.; Cronenwett, J.L.; Baker, F. The Effect of Risk and Race on Lower Extremity Amputations among Medicare Diabetic Patients. Journal of Vascular Surgery 2012, 56, 1663–1668, doi:10.1016/j.jvs.2012.05.100.
29. Hennis, A.J.M.; Fraser, H.S.; Jonnalagadda, R.; Fuller, J.; Chaturvedi, N. Explanations for the High Risk of Diabetes-Related Amputation in a Caribbean Population of Black African Descent and Potential for Prevention. Diabetes Care 2004, 27, 2636–2641, doi:10.2337/diacare.27.11.2636.
30. Liao, C.; Seghers, F.; Savage, M.; Fineberg, A.; Goedde, B.; Austin, V.; Holloway, C.; Oldfrey, B. Product Narrative: Prostheses. A Market Landscape and Strategic Approach to Increasing Access to Prosthetic Devices and Related Services in Low- and Middle-Income Countries. 2020.
31. Alvarsson, A.; Sandgren, B.; Wendel, C.; Alvarsson, M.; Brismar, K. A Retrospective Analysis of Amputation Rates in Diabetic Patients: Can Lower Extremity Amputations Be Further Prevented? Cardiovasc Diabetol 2012, 11, 18, doi:10.1186/1475-2840-11-18.
32. Peacock, J.M.; Keo, H.H.; Duval, S.; Baumgartner, I.; Oldenburg, N.C.; Jaff, M.R.; Henry, T.D.; Yu, X.; Hirsch, A.T. The Incidence and Health Economic

Burden of Ischemic Amputation in Minnesota, 2005-2008. Prev Chronic Dis 2011, 8, A141.
33. Kenney, L.; Ssekitoleko, R.; Chadwell, A.; Ackers, L.; Donovan Hall, M.; Morgado Ramirez, D.; Holloway, C.; Graham, P.; Cockcroft, A.; Deere, B.; et al. Prosthetics Services in Uganda: A Series of Studies to Inform the Design of a Low Cost, but Fit-for-Purpose, Body-Powered Prosthesis Available online: https://apps.who.int/iris/bitstream/handle/10665/330372/9789240000261-eng.pdf#page=422 (accessed on 24 October 2023).
34. Atim, P.; Loum, C.S.; Okello, T.R.; Magada, S.M.; Yagos, W.O.; Abelle, P.; Moro, E.B.; Huck, J.J.; Redmond, A.; Nirmalan, M. A Cross-Sectional Study of Prevalence and Spatial Patterns of Major Limb Loss in the Acholi Sub-Region of Uganda; Scientific Communication and Education, 2020;
35. Molina, C.S.; Faulk, J. Lower Extremity Amputation. In StatPearls; StatPearls Publishing: Treasure Island (FL), 2023.
36. Meffen, A.; Pepper, C.J.; Sayers, R.D.; Gray, L.J. Epidemiology of Major Lower Limb Amputation Using Routinely Collected Electronic Health Data in the UK: A Systematic Review Protocol. BMJ Open 2020, 10, e037053, doi:10.1136/bmjopen-2020-037053.
37. Lazzarini, P.A.; O'Rourke, S.R.; Russell, A.W.; Clark, D.; Kuys, S.S. What Are the Key Conditions Associated with Lower Limb Amputations in a Major Australian Teaching Hospital? J Foot Ankle Res 2012, 5, 12, doi:10.1186/1757-1146-5-12.
38. Chernev, I.; Chernev, A. Education Level Among Patients with Major Limb Amputation. Cureus 2020, doi:10.7759/cureus.7673.
39. Heikkinen, M.; Saarinen, J.; Suominen, V.P.; Virkkunen, J.; Salenius, J. Lower Limb Amputations: Differences between the Genders and Long-Term Survival. Prosthetics & Orthotics International 2007, 31, 277–286, doi:10.1080/03093640601040244.
40. Fanaroff, A.C.; Yang, L.; Nathan, A.S.; Khatana, S.A.M.; Julien, H.; Wang, T.Y.; Armstrong, E.J.; Treat-Jacobson, D.; Glaser, J.D.; Wang, G.; et al. Geographic and Socioeconomic Disparities in Major Lower Extremity Amputation Rates in Metropolitan Areas. JAHA 2021, 10, e021456, doi:10.1161/JAHA.121.021456.
41. Schnur, D.; Meier, R.H. Amputation Surgery. Physical Medicine and Rehabilitation Clinics of North America 2014, 25, 35–43, doi:10.1016/j.pmr.2013.09.013.
42. Lim, T.S.; Finlayson, A.; Thorpe, J.M.; Sieunarine, K.; Mwipatayi, B.P.; Brady, A.; Abbas, M.; Angel, D. OUTCOMES OF A CONTEMPORARY AMPUTATION SERIES. ANZ Journal of Surgery 2006, 76, 300–305, doi:10.1111/j.1445-2197.2006.03715.x.
43. Lavery, L.A.; Hunt, N.A.; Ndip, A.; Lavery, D.C.; Van Houtum, W.; Boulton, A.J.M. Impact of Chronic Kidney Disease on Survival after Amputation in Individuals with Diabetes. Diabetes Care 2010, 33, 2365–2369, doi:10.2337/dc10-1213.
44. Lavery, L.A.; Hunt, N.A.; LaFontaine, J.; Baxter, C.L.; Ndip, A.; Boulton, A.J.M. Diabetic Foot Prevention. Diabetes Care 2010, 33, 1460–1462, doi:10.2337/dc10-0310.
45. Rodrigues, B.T.; Vangaveti, V.N.; Malabu, U.H. Prevalence and Risk Factors for Diabetic Lower Limb Amputation: A Clinic-Based Case Control Study. Journal of Diabetes Research 2016, 2016, 1–7, doi:10.1155/2016/5941957.
46. Wukich, D.K.; Armstrong, D.G.; Attinger, C.E.; Boulton, A.J.M.; Burns, P.R.; Frykberg, R.G.; Hellman, R.; Kim, P.J.; Lipsky, B.A.; Pile, J.C.; et al. Inpatient Management of Diabetic Foot Disorders: A Clinical Guide. Diabetes Care 2013, 36, 2862–2871, doi:10.2337/dc12-2712.
47. Burger, H.; Marinček, Č. Return to Work after Lower Limb Amputation. Disability and Rehabilitation 2007, 29, 1323–1329, doi:10.1080/09638280701320797.
48. Godlwana, L.; Nadasan, T.; Puckree, T. Global Trends in Incidence of Lower Limb Amputation: A Review of the Literature. South African Journal of Physiotherapy 2008, 64, 8–12, doi:10.4102/sajp.v64i1.93.
49. Stanifer, J.W.; Cleland, C.R.; Makuka, G.J.; Egger, J.R.; Maro, V.; Maro, H.; Karia, F.; Patel, U.D.; Burton, M.J.; Philippin, H. Prevalence, Risk Factors, and Complications of Diabetes in the Kilimanjaro Region: A Population-Based Study from Tanzania. PLoS ONE 2016, 11, e0164428, doi:10.1371/journal.pone.0164428.
50. McEwen, B.; Morel-Kopp, M.-C.; Chen, W.; Tofler, G.; Ward, C. Effects of Omega-3 Polyunsaturated Fatty Acids on Platelet Function in Healthy Subjects and Subjects with Cardiovascular Disease. Semin Thromb Hemost 2013, 39, 025–032, doi:10.1055/s-0032-1333309.
51. Sutkowska, E.E.; Sokołowski, M.; Zdrojowy, K.; Dragan, S. Active Screening for Diabetic Foot — Assessment of Health Care Professionals' Compliance to It. Clinical Diabetology 2016, 5, 83–87, doi:10.5603/DK.2016.0014.
52. Zhang, Y.; Lazzarini, P.A.; McPhail, S.M.; Van Netten, J.J.; Armstrong, D.G.; Pacella, R.E. Global

Disability Burdens of Diabetes-Related Lower-Extremity Complications in 1990 and 2016. Diabetes Care 2020, 43, 964–974, doi:10.2337/dc19-1614.
53. Sinha, R.; Van Den Heuvel, W.J.; Arokiasamy, P. Factors Affecting Quality of Life in Lower Limb Amputees. Prosthetics & Orthotics International 2011, 35, 90–96, doi:10.1177/0309364610397087.
54. Sahu, A.; Sagar, R.; Sarkar, S.; Sagar, S. Psychological Effects of Amputation: A Review of Studies from India. Ind Psychiatry J 2016, 25, 4, doi:10.4103/0972-6748.196041.
55. Gurney, J.K.; Stanley, J.; York, S.; Rosenbaum, D.; Sarfati, D. Risk of Lower Limb Amputation in a National Prevalent Cohort of Patients with Diabetes. Diabetologia 2018, 61, 626–635, doi:10.1007/s00125-017-4488-8.
56. De Godoy, J.M.P.; Braile, D.M.; Buzatto, S.H.G.; Longo, O.; Fontes, O.A. Quality of Life after Amputation. Psychology, Health & Medicine 2002, 7, 397–400, doi:10.1080/1354850021000015212.
57. Papoutsi, C.; Hargreaves, D.; Hagell, A.; Hounsome, N.; Skirrow, H.; Muralidhara, K.; Colligan, G.; Vijayaraghavan, S.; Greenhalgh, T.; Finer, S. National Diabetes Audit Data Tables. In Group clinics for young adults living with diabetes in an ethnically diverse, socioeconomically deprived population: mixed-methods evaluation; National Institute for Health and Care Research, 2022.
58. Yazdanpanah, L.; Shahbazian, H.; Nazari, I.; Arti, H.R.; Ahmadi, F.; Mohammadianinejad, S.E.; Cheraghian, B.; Latifi, S.M. Prevalence and Related Risk Factors of Diabetic Foot Ulcer in Ahvaz, South West of Iran. Diabetes & Metabolic Syndrome: Clinical Research & Reviews 2018, 12, 519–524, doi:10.1016/j.dsx.2018.03.018.
59. Prompers, L.; Schaper, N.; Apelqvist, J.; Edmonds, M.; Jude, E.; Mauricio, D.; Uccioli, L.; Urbancic, V.; Bakker, K.; Holstein, P.; et al. Prediction of Outcome in Individuals with Diabetic Foot Ulcers: Focus on the Differences between Individuals with and without Peripheral Arterial Disease. The EURODIALE Study. Diabetologia 2008, 51, 747–755, doi:10.1007/s00125-008-0940-0.
60. Barshes, N.R.; Sigireddi, M.; Wrobel, J.S.; Mahankali, A.; Robbins, J.M.; Kougias, P.; Armstrong, D.G. The System of Care for the Diabetic Foot: Objectives, Outcomes, and Opportunities. Diabetic Foot & Ankle 2013, 4, 21847, doi:10.3402/dfa.v4i0.21847.
61. Mc Sharry, J.; Moss-Morris, R.; Kendrick, T. Illness Perceptions and Glycaemic Control in Diabetes: A Systematic Review with Meta-analysis. Diabetic Medicine 2011, 28, 1300–1310, doi:10.1111/j.1464-5491.2011.03298.x.
62. McEwen, L.N.; Ylitalo, K.R.; Herman, W.H.; Wrobel, J.S. Prevalence and Risk Factors for Diabetes-Related Foot Complications in Translating Research Into Action for Diabetes (TRIAD). Journal of Diabetes and its Complications 2013, 27, 588–592, doi:10.1016/j.jdiacomp.2013.08.003.
63. Hicks, C.W.; Selvin, E. Epidemiology of Peripheral Neuropathy and Lower Extremity Disease in Diabetes. Curr Diab Rep 2019, 19, 86, doi:10.1007/s11892-019-1212-8.
64. Bakker, K.; Apelqvist, J.; Lipsky, B.A.; Van Netten, J.J.; on behalf of the International Working Group on the Diabetic Foot (IWGDF) The 2015 IWGDF Guidance Documents on Prevention and Management of Foot Problems in Diabetes: Development of an Evidence-based Global Consensus. Diabetes Metabolism Res 2016, 32, 2–6, doi:10.1002/dmrr.2694.
65. Adams, O.P.; Herbert, J.R.; Unwin, N.; Howitt, C. Peripheral Arterial Disease Prevalence in a Population-Based Sample of People with Diabetes on the Caribbean Island of Barbados. VHRM 2022, Volume 18, 387–395, doi:10.2147/VHRM.S364993.
66. Handelsman, Y.; Anderson, J.E.; Bakris, G.L.; Ballantyne, C.M.; Beckman, J.A.; Bhatt, D.L.; Bloomgarden, Z.T.; Bozkurt, B.; Budoff, M.J.; Butler, J.; et al. DCRM Multispecialty Practice Recommendations for the Management of Diabetes, Cardiorenal, and Metabolic Diseases. Journal of Diabetes and its Complications 2022, 36, 108101, doi:10.1016/j.jdiacomp.2021.108101.
67. Conte, M.S.; Pomposelli, F.B.; Clair, D.G.; Geraghty, P.J.; McKinsey, J.F.; Mills, J.L.; Moneta, G.L.; Murad, M.H.; Powell, R.J.; Reed, A.B.; et al. Society for Vascular Surgery Practice Guidelines for Atherosclerotic Occlusive Disease of the Lower Extremities: Management of Asymptomatic Disease and Claudication. Journal of Vascular Surgery 2015, 61, 2S-41S.e1, doi:10.1016/j.jvs.2014.12.009.
68. Blanchette, V.; Brousseau-Foley, M.; Cloutier, L. Effect of Contact with Podiatry in a Team Approach Context on Diabetic Foot Ulcer and Lower Extremity Amputation: Systematic Review and Meta-Analysis. J Foot Ankle Res 2020, 13, 15, doi:10.1186/s13047-020-0380-8.
69. Kavarthapu, V. Is There a Need for Diabetic Foot Orthopaedic Surgery as a Sub-Specialty? Journal of

Clinical Orthopaedics and Trauma 2021, 17, 72–73, doi:10.1016/j.jcot.2021.02.004.
70. Lim, J.Z.M.; Ng, N.S.L.; Thomas, C. Prevention and Treatment of Diabetic Foot Ulcers. J R Soc Med 2017, 110, 104–109, doi:10.1177/0141076816688346.
71. Hijmans, J.M.; Dekker, R.; Geertzen, J.H.B. Pre-Operative Rehabilitation in Lower-Limb Amputation Patients and Its Effect on Post-Operative Outcomes. Medical Hypotheses 2020, 143, 110134, doi:10.1016/j.mehy.2020.110134.
72. Amini, M.R.; Sanjari, M.; Mohajeri Tehrani, M.R.; Nasli, E.; Yazdanpanah, L.; Mousavi, Z.; Forghan, F.; Valizadeh, N.; Gozashti, M.H.; Afkhami-Ardekani, M.; et al. Evaluation of Foot Self-Care Status and Foot Screening Problems in Patients with Diabetes in Iran: A National Multicenter Study. BMC Endocr Disord 2023, 23, 178, doi:10.1186/s12902-023-01401-7.
73. Pérez-Panero, A.J.; Ruiz-Muñoz, M.; Cuesta-Vargas, A.I.; Gónzalez-Sánchez, M. Prevention, Assessment, Diagnosis and Management of Diabetic Foot Based on Clinical Practice Guidelines: A Systematic Review. Medicine 2019, 98, e16877, doi:10.1097/MD.0000000000016877.
74. Shavelson, D. The Diabetic Foot. In Principles of Diabetes Mellitus; Poretsky, L., Ed.; Springer International Publishing: Cham, 2016; pp. 1–23 ISBN 978-3-319-20797-1.
75. Pickles, S.; McAllister, E.; McCullagh, G.; Nieroba, T. Quality Improvement Evaluation of Postoperative Wound Dressings in Orthopaedic Patients. International Journal of Orthopaedic and Trauma Nursing 2022, 45, 100922, doi:10.1016/j.ijotn.2022.100922.
76. Lazzarini, P.A.; Jarl, G.; Gooday, C.; Viswanathan, V.; Caravaggi, C.F.; Armstrong, D.G.; Bus, S.A. Effectiveness of Offloading Interventions to Heal Foot Ulcers in Persons with Diabetes: A Systematic Review. Diabetes Metabolism Res 2020, 36, e3275, doi:10.1002/dmrr.3275.
77. Alshammari, L.; O'Halloran, P.; McSorley, O.; Doherty, J.; Noble, H. The Effectiveness of Foot Care Educational Interventions for People Living with Diabetes Mellitus: An Umbrella Review. Journal of Tissue Viability 2023, 32, 406–416, doi:10.1016/j.jtv.2023.06.001.
78. Lavery, L.A.; Wunderlich, R.P.; Tredwell, J.L. Disease Management for the Diabetic Foot: Effectiveness of a Diabetic Foot Prevention Program to Reduce Amputations and Hospitalizations. Diabetes Research and Clinical Practice 2005, 70, 31–37, doi:10.1016/j.diabres.2005.02.010.
79. Leong, J.; Parzer, P.; Perteneder, F.; Babic, T.; Rendl, C.; Vogl, A.; Egger, H.; Olwal, A.; Haller, M. proCover: Sensory Augmentation of Prosthetic Limbs Using Smart Textile Covers. In Proceedings of the Proceedings of the 29th Annual Symposium on User Interface Software and Technology; ACM: Tokyo Japan, October 16 2016; pp. 335–346.
80. Dillingham, T.R.; Pezzin, L.E.; MacKenzie, E.J. Limb Amputation and Limb Deficiency: Epidemiology and Recent Trends in the United States. Southern Medical Journal 2002, 95, 875–884.
81. Czerniecki, J.M.; Gitter, A.J. Gait Analysis in the Amputee: Has It Helped the Amputee or Contributed to the Development of Improved Prosthetic Components? Gait & Posture 1996, 4, 258–268, doi:10.1016/0966-6362(96)01073-9.
82. Nelissen, E.; Ersdal, H.; Mduma, E.; Evjen-Olsen, B.; Twisk, J.; Broerse, J.; Van Roosmalen, J.; Stekelenburg, J. Clinical Performance and Patient Outcome after Simulation-Based Training in Prevention and Management of Postpartum Haemorrhage: An Educational Intervention Study in a Low-Resource Setting. BMC Pregnancy Childbirth 2017, 17, 301, doi:10.1186/s12884-017-1481-7.
83. Krishnan, S.H.; Gilbert, L.A.; Ghoddoussi, F.; Applefield, D.J.; Kassab, S.S.; Ellis, T.A. Addition of Buprenorphine to Local Anesthetic in Adductor Canal Blocks after Total Knee Arthroplasty Improves Postoperative Pain Relief: A Randomized Controlled Trial. Journal of Clinical Anesthesia 2016, 33, 432–437, doi:10.1016/j.jclinane.2016.04.021.
84. Marasco, P.D.; Hebert, J.S.; Sensinger, J.W.; Shell, C.E.; Schofield, J.S.; Thumser, Z.C.; Nataraj, R.; Beckler, D.T.; Dawson, M.R.; Blustein, D.H.; et al. Illusory Movement Perception Improves Motor Control for Prosthetic Hands. Sci. Transl. Med. 2018, 10, eaao6990, doi:10.1126/scitranslmed.aao6990.
85. Hafner, B.J.; Spaulding, S.E.; Salem, R.; Morgan, S.J.; Gaunaurd, I.; Gailey, R. Prosthetists' Perceptions and Use of Outcome Measures in Clinical Practice: Long-Term Effects of Focused Continuing Education. Prosthetics & Orthotics International 2017, 41, 266–273, doi:10.1177/0309364616664152.
86. Lombard-Vance, R.; O'Keeffe, F.; Desmond, D.; Coen, R.; Ryall, N.; Gallagher, P. Comprehensive Neuropsychological Assessment of Cognitive Functioning of Adults With Lower Limb Amputation in Rehabilitation. Archives of Physical Medicine and Rehabilitation 2019, 100, 278-288.e2,

doi:10.1016/j.apmr.2018.07.436.
87. Schrier, E.; Geertzen, J.H.B.; Scheper, J.; Dijkstra, P.U. Psychosocial Factors Associated with Poor Outcomes after Amputation for Complex Regional Pain Syndrome Type-I. PLoS ONE 2019, 14, e0213589, doi:10.1371/journal.pone.0213589.
88. Poehler, D.; Czerniecki, J.; Norvell, D.; Henderson, A.; Dolan, J.; Devine, B. Comparing Patient and Provider Priorities Around Amputation Level Outcomes Using Multiple Criteria Decision Analysis. Annals of Vascular Surgery 2023, 95, 169–177, doi:10.1016/j.avsg.2023.05.026.
89. Waaijman, R.; Keukenkamp, R.; De Haart, M.; Polomski, W.P.; Nollet, F.; Bus, S.A. Adherence to Wearing Prescription Custom-Made Footwear in Patients With Diabetes at High Risk for Plantar Foot Ulceration. Diabetes Care 2013, 36, 1613–1618, doi:10.2337/dc12-1330.
90. Fortington, L.V.; Geertzen, J.H.B.; Van Netten, J.J.; Postema, K.; Rommers, G.M.; Dijkstra, P.U. Short and Long Term Mortality Rates after a Lower Limb Amputation. European Journal of Vascular and Endovascular Surgery 2013, 46, 124–131, doi:10.1016/j.ejvs.2013.03.024.
91. Khetarpaul, V.; Kirby, J.P.; Geraghty, P.; Felder, J.; Grover, P. Socioecological Model-Based Design and Implementation Principles of Lower Limb Preservation Programs as Partners for Limb-Loss Rehabilitation Programs— A Mini-Review. Front. Rehabilit. Sci. 2022, 3, 983432, doi:10.3389/fresc.2022.983432.