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Offloading for the Treatment of the Diabetic Foot - A Systematic Review

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Offloading for the Treatment of the Diabetic Foot

A Systematic Review

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Abbreviation List

ABD – An Bord Altranais
ABI – Ankle Brachial Index
BMI – Body Mass Index
CCGO – Cochrane Collaboration Glossary Online
CI – Confidence Interval
CTF – Custom Therapeutic Footwear
DF – Diabetic Foot
DFU – Diabetic Foot Ulcers
DEAG – Diabetes Expert Advisory Group
DM – Diabetes Mellitus
DoHC – Department of Health and Children
EBP – Evidence-based Practice
FU – Foot Ulcers
HSE – Health Service Executive
IDF – International Diabetes Federation
iTCC – instant Total Contact Cast
IWGDFG – International Working Group on the Diabetic Foot Guidelines
LR – Literature Review
MD – Mean Difference
NIDDK – National Institute of Diabetes and Digestive and Kidney Diseases
PAD – Peripheral Arterial Disease
PVD – Peripheral Vascular Disease
QoL – Quality of Life
RCC – Removable Contact Cast
RCT – Randomised Control Trial
RCW – Removable Cast Walker
RR – Risk Ratio
SMC – Shoe Model Cast
SR – Systematic Review
SSD – Significant Statistical Difference
TCC – Total Contact Cast
TePO₂ – Transcutaneous Oximetry
TDT – Traditional Dressing System
UTDFWCS – University of Texas Diabetic Foot Wound Classification System
VPT – Vibration Perception Threshold
WHO – World Health Organisation
Abstract

Aim: To compare the strengths and limitations of different offloading devices in the treatment of diabetic foot ulcers.

Method: Systematic review.

Background: Diabetes is a chronic disease where neuropathy and peripheral vascular disease, associated with foot deformity, trauma and high plantar pressures contribute to the development of foot ulceration. For those with existing ulcers, if the foot is subject to continuous high pressures, tissue damage persists and healing will be impaired. Therefore, the use of offloading devices becomes fundamental for the treatment of these ulcers.

Findings: Following a systematic search of the literature, 14 studies were included in this review. Healing rates, healing times and reduction in ulcer size were improved with the use of total contact casting, compared with other offloading devices. The main adverse effects associated with use of the device were infection, maceration and abrasion. Cost, compliance and quality of life issues were rarely included within the studies.

Conclusion: Offloading is a key treatment strategy for the management of diabetic foot ulceration and total contact casts were found to be the most effective devices to achieve ulcer healing. However, they are not without complications and further, their impact on cost, compliance and quality of life is not well understood.
Chapter 1. Background

1.1. Introduction

This chapter will give an international and national overview of the incidence and prevalence of diabetes mellitus (DM). Then it will focus on diabetic foot ulcers (DFUs) characteristics, incidence, costs and complications. Finally, the chapter will analyse offloading for the treatment of DFUs.

1.2. DM: an overview

Diabetes is a chronic disease (International Diabetes Federation (IDF) 2012a) and according to IDF (2012b) projections in 2011 the prevalence of DM in the world was of 8.3% and it will increase to 9.90% by 2030. Furthermore, in 2011 the number of deaths related to DM was of 4,593,109 people (IDF 2012b). Focusing on Irish figures, in 2011 the national prevalence of DM was 6.07%, and by 2030 it will rise to 7.49%, the number of deaths in the population between 20-79 years of age was 1,457 deaths in 2011 (IDF 2012b). Additionally, the mean diabetes expenditure per person with diabetes in 2011 was €6,629.00 (IDF 2012b). It is clear that the prevalence of people with DM in the world and, more specifically, in Ireland is growing and this growth impacts negatively on the economy, society, healthcare services, and mainly on the individual.

Diabetes occurs when the pancreas cannot produce insulin or its production is impaired (IDF 2012a, World Health Organization (WHO) 2012). This hormone is important for the body to function, as it allows glucose to enter the cells and be used as energy (IDF 2012a). However, if the body lacks insulin, high levels of glucose in the blood will
occur and overtime these will promote tissue damage at the microvascular and macrovascular level (IDF 2012a, WHO 2012). At the microvascular level the damage occurs in the small blood vessels and can lead to complications like retinopathy, nephropathy and neuropathy. In terms of macrovascular damage, this occurs in larger blood vessels and can lead to complications like cardiovascular disease and peripheral vascular disease (PVD) (IDF 2012a, WHO 2012). From the many complications that can arise, neuropathy and PVD alone or in conjunction can, with the influence of other factors, lead to the development of DFUs, and if untreated, can lead to amputation, both of which have a negative impact on the individual.

1.3. Diabetic Foot Ulcers

DFUs are lesions characterised by a skin break involving loss of epithelium, which can extend through the dermis and deeper tissue, and in some cases involve muscle and even bone (Reiber et al. 1998, Boulton 2004b). Although, neuropathy and PVD are the primary factors for the presentation of DFUs, other risk factors play an important role in the development, aggravation and healing outcomes of DFUs (Boyko et al. 1999, Reiber et al. 1999, Merza and Tesfaye 2003, Boulton 2004b, Lavery et al. 2008, Wu and Armstrong 2005).

1.3.1. DFU: Neuropathy and PVD

Neuropathy results from continued peripheral nerve damage of motor, sensory and autonomic fibres, that affect sensation, innervation of the muscles of the foot and its circulation (Reiber et al. 1998, Jeffcoate and Harding 2003, Merza and Tesfaye 2003, Boulton 2004b, National Institute of Diabetes and Digestive and Kidney Diseases
Motor neuropathy causes muscle wasting, atrophy and weakness which leads to foot deformities, such as claw and hammer toe that in turn predispose the individual to restricted joint mobility, balance problems and gait instability (Reiber et al. 1998, Merza and Tesfaye 2003, Boulton 2004b, Cavanagh et al. 2005, Singh et al. 2005). Sensory neuropathy leads to decreased or loss of protective sensation to pain, pressure and loss of proprioception (inability to recognize the feet position) (Reiber et al. 1998, Merza and Tesfaye 2003, Boulton 2004b, van Deursen 2004). The loss of protective sensation places the individual at risk of continuously harming the foot without realising it (Laing 1998, Wu and Armstrong 2005). Autonomic neuropathy refers to altered microvascular blood flow that results in warm feet, and decreased sweat production, resulting in dry skin, predisposing callus formation, which is hyperkeratosis that develops around the ulcer, and skin breakdown (Reiber et al. 1998, Merza and Tesfaye 2003, Boulton 2004b, Lavery et al. 2008).

PVD causes reduced blood supply in the lower extremities and consequently poor foot perfusion (Boyko et al. 1999, Spencer 2008). The individual with PVD presents a cool, red shiny and dry foot (Elkles and Wolfe 1991, Jeffcoate and Harding 2003). The presence of PVD contributes to DFUs formation and delayed healing as it influences the ability to fight infection because, poor perfusion adversely impacts on the ability of cells, necessary for wound repair, to reach the wounded area. Further, the delivery of nutrients, antibiotics and oxygen are compromised (Reiber et al. 1998, Boyko et al. 1999, Merza and Tesfaye 2003, Boulton 2004b).
In a study by Reiber et al. (1999) where the causal pathways for the incidence of DFUs were analysed (n=148), in 78% of the subjects neuropathy was the most common cause of ulceration, while PVD (ischemia) represented 35% of cases. Another study by Oyibo et al. (2001) (n=194), 67% of FU s were neuropathic, 26.3% were mixed aetiology and just 1.0% were ischaemic. The study by Pompers et al. (2007) reported, in a cohort of 1,229 subjects, that PVD was present in 49% of the subjects whereas neuropathy was diagnosed in 86%. Finally in the study by Lavery et al. (2008) of 87 subjects with a total of 103 ulcers, 92.2% were neuropathic and 23.3% were ischaemic. These figures support the fact the neuropathy and PVD are the main precursors of DFUs. Nevertheless, other factors also play an important role in the development of FU s.

1.3.2. DFU: Other Causal Pathways

Within the research (Reiber et al. 1998, Boyko et al. 1999, Reiber et al. 1999, Merza and Tesfaye 2003, Boulton 2004b, Wu and Armstrong 2005, Lavery et al. 2008) it is well established that other risk factors such as foot deformities, trauma, callus, pressure, inappropriate footwear and oedema also contribute to DFUs development, aggravation and healing outcomes. Furthermore, infection, being one of the possible consequences of DFUs, also has a negative impact in healing outcomes particularly when associated with PVD, due to poor perfusion of the lower limb (Pompers et al. 2008).

In a study by Reiber et al. (1999), (n=148), trauma and foot deformities where present in 77% and 63% of the subjects, respectively. In the same study oedema was present in 37% of the subjects and callus in 30%. Another study by Lavery et al. (2008), of 87 subjects with 103 ulcers identified, deformity was present in 63.1% of the subjects,
callus in 60.2% and high pressures in 52.4%, whilst inappropriate footwear and trauma were the contributing factors in 19.4% and 10.7% of the subjects.

From the contributing factors mentioned, foot deformity is influenced by changes due to motor neuropathy that causes atrophy of the intrinsic muscles of the foot, which in turn will pull the toes out of shape leading to hammer/claw toes, which are rigid contractures of the toes (Reiber et al. 1999, Merza and Tesfaye 2003, Lavery et al. 2008). Oedema is related to cardiac and venous disorders that promote fluid accumulation in the lower limbs and feet (Reiber et al. 1998). In relation to callus formation this is influenced by increased vertical and shear stresses, and dry skin (Reiber et al. 1998, Reiber et al. 1999). Overall, these structural changes of the foot, together with neuropathy, PVD and the action of pressure, trauma and inappropriate footwear will predispose the individual to the formation and poor healing of DFUs.

1.3.3. DFUs: Prevalence, Incidence and Cost

With respect to prevalence and incidence, it is estimated that the incidence of DFUs in the USA is between 2-3% and the point prevalence is around 5-7% (Posnett et al. 2009). In relation to Europe it is suggested that between 1.0-1.4million people have a DFUs at any time (Posnett et al. 2009). The prevalence of DM is expected to rise from 8.3% in 2011 to 9.90% by 2030 (IDF 2012b) increasing the number of cases of DFUs. In Ireland according to the HSE (2009) it is estimated that there are 20,470-41,020 cases of DFUs and around 5234 cases were treated in 2003 in Irish hospitals.

In terms of costs with DFUs in a 2003-2004 study in 14 DF centres in 10 European countries the authors concluded that, for the treatment of DFUs the average direct and
indirect cost was around €10,000, based on the data from 821 patients from the participating countries (Pompers et al. 2008). In the USA in 2001, the cost of DFUs and amputations was 10.1 billion dollars and in the same year in the UK the annual cost, of diabetes foot related complications (excluding amputations), was £252 million pounds (Boulton et al. 2005). In a 2001-2002 Irish audit of 30 patients admitted with DFUs, with an average hospitalization of 20-30 days, the net in hospital cost was €704,689 with an average €23,489.63 per patient (Smith et al. 2004).

This data shows that DFUs are an increasing health problem that impacts greatly on economy and society.

1.3.4. DFUs: Amputation and QoL

Individuals with DM are at risk of developing DFUs and around 15% of these if untreated, or poorly managed, can result in limb amputation, which has a mortality rate of around 30-80% (McDermott-Scales et al. 2009). Amputation involves the surgical removal of a non-viable part of the limb (Boulton 2004b). According to a study by Pecoraro et al. (1990) of 80 subjects requiring first time amputation, the main factors leading to limb amputation were failure of wound healing in 81% of cases, infection and gangrene were associated with 42% of cases, trauma that resulted in ulceration accounted for 72% of the cases, neuropathy was found to be present in 82% of cases and PVD in 46% of cases. These figures show that individuals often present with more than one confounding factor predisposing ulceration and influencing wound healing.

Following a more detailed analysis, PVD emerges as the only independent cause that led to amputation of the limb. Moreover, in a French incidence study by Fosse et al. (2009), 95% of amputations were preceded with ulceration confounded by PVD and
neuropathy. In a study by Vamos et al. (2010), in the UK between, 2004-2008 49,487 non-traumatic amputations were performed from which 51% occurred in diabetic patients. Of these 59.6% were minor amputation and 42.6% were major amputations. Thus, if poorly managed DFUs increase the incidence of non-traumatic amputations, raising the costs associated with DFUs not only at an economic level but also at a social and human level (Margolis et al. 2005).

In relation to the impact that both DFUs and amputation have on the individual, an Irish study of 38 subjects identified that depression, anxiety, social discomfort and body image were the main issues identified as having the greatest impact in the individuals quality of life (QoL) (Coffey et al. 2009). Focusing on DFUs, in the study by Brod (1998), mobility issues were identified by subjects as having the greatest impact on participants QoL. Additionally, Brod (1998) identified frustration and anger as feelings that emerged due to mobility issues. Vileikyte (2001) and Vileikyte et al. (2004) reported in their review that individuals identified mobility difficulties as having an impact in their daily activities, which in turn affected their professional and social life, creating anxiety and poor QoL. Furthermore, Vileikyte (2001) mentions that individuals also experienced fear of developing new ulcers.

DFUs are an important health issue that needs to be addressed. It is fundamental to implement prevention and treatment practices that will improve individuals QoL and bring better cost-effectiveness for the health services.
1.4. Offloading the Diabetic Foot

DFUs develop due to a combination of different physiological, structural and environmental factors. When these factors are combined they promote skin tear and the progression of a small break into a possible deep and large ulcer that if untreated can lead to infection and gangrene, rendering the limb unviable and amputation as the only solution (Laing 1998, Merza and Tesfaye 2003, Boulton 2004b, Leung 2007). Thus, prevention, early recognition and treatment are fundamental to salvage the limb and to allow individuals to have a better QoL (Brod 1998, Boulton 2004a, Bakker et al. 2011).

Neuropathy, PVD, pressure, foot deformities, oedema, trauma and callus all play a major role in the development and maintenance of DFUs (Boulton 2004b, Cavanagh et al. 2005, Wu and Armstrong 2005, Lavery et al. 2008). Although, there is a bigger emphasis around neuropathic foot ulcers, as these are more common (Cavanagh et al. 2005), ischaemic ulcers are also a reality (Laing 1998, Boulton 2004b, Bakker et al. 2012).

In relation to neuropathic ulcers, these develop because the foot is subject to high pressures, due to loss of sensation and unperceived mechanical load, that with time or with the help of callus, foot deformities and minor trauma will result in an ulcer (Laing 1998, Boulton 2004a, Boulton 2004b, Cavanagh et al. 2005). Ischaemic ulcers form due to continuous low pressures applied over time, in a dry, cold foot (Laing 1998). These ulcers are also precipitated by new footwear, minor trauma and foot deformities and once they have formed they are difficult to heal because, the foot needs a good blood supply, which is impaired in individuals with PVD (Laing 1998, Bakker et al. 2012). Neuroischaemic ulcers have characteristics of both neuropathic and ischaemic ulcers,
however it is important to establish which condition is more predominant (Laing 1998) so that a more focused treatment may be planned and implemented.

Pressure plays a central role in the development of DFUs and its management becomes essential not only to prevent the development of new ulcers but also to allow the healing process to take place (Caravaggi et al. 2000, Armstrong et al. 2001, Reiber et al. 2002, van Deursen 2004, Piaggesi et al. 2007, Faglia et al. 2010).

Pressure results from mechanical loading of the feet when the individual engages in activities like walking and standing, exposing the plantar surface of the feet to reaction forces that act upon the foot tissue causing compression and sometimes shear stress (van Deursen 2004). This pressure and stress is aggravated by foot deformities like hammer and claw toes, prominence of metatarsal heads, hallux valgus and limited joint mobility (Boulton 2004a, van Deursen 2004). For these reasons, offloading the foot and accommodating its deformities with the use of appropriate footwear is essential for the treatment of DFUs (van Deursen 2004).

Offloading is both a treatment and prevention intervention which relieves, reduces or redistributes plantar pressure to avoid the concentration of high pressures in DFUs, in the diabetic ulcer free foot and also to protect pressure points in the foot (Burden et al. 1983, Cavanagh et al. 2000, Cavanagh et al. 2005, Leung 2007, Edmonds et al. 2008: 85). Besides managing plantar ulcers, offloading is also important when the ulcer is located on the heel and on the lateral aspect of the midfoot and forefoot (Cavanagh et al. 2005).
Offloading is a central intervention in the treatment and management of DFUs (Reiber et al. 2002, Armstrong et al. 2005, Katz et al. 2005, Piaggesi et al. 2007, Faglia et al. 2010). Indeed, a wide variety of offloading devices have been compared and evaluated to try to bring a better understanding on their efficacy and to identify which device has better healing outcomes. Although, the most effective approach is total offloading/non-weight bearing, this practice is often impractical so the use of devices to achieve the maximum pressure relief possible are often standard practice (Cavanagh et al. 2005).

1.4.1. Offloading Devices

In terms of offloading devices there is a great variety available that can be used when there is an active ulcer or only when pressure redistribution is necessary. Some of the devices available are included in the following categories casts, therapeutic shoes, orthoses, felt padding and foam (see appendix 1 for list of devices in each category) (Edmonds et al. 2008, Spencer 2008).

The different offloading devices available are all important for the treatment of DFUs. However, total contact cast (TCC) is considered the most effective device, as it cannot be removed easily by the individual allowing for better compliance (Caravaggi et al. 2000, Armstrong et al. 2001, Reiber et al. 2002, Jeffcoate and Harding 2003, Beuker et al. 2005, Leug 2007, Faglia et al. 2010).

Nonetheless, the consensuses around the best way of offloading DFUs is not well established yet as various authors recommend different devices for offloading DFUs (Caravaggi et al. 2000, Armstrong et al. 2001, Armstrong et al. 2005, Katz et al. 2005, Piaggesi et al. 2007, Faglia et al. 2010). Thus, for the purpose of this systematic review
the writer wishes to explore the following question: What is the impact of offloading in the treatment of DFUs?

Taking this into account the aim of this review is to compare the strengths and limitations of different offloading devices in the treatment of DFUs.

The objectives of this review are to:

- Identify the most effective offloading device in the treatment of the DFUs.
- Identify the strengths and limitations of the different offloading devices in the studies reviewed.
- Determine the impact that offloading devices have in patients QoL, in the studies reviewed.

1.5. Summary

Around 6% of the Irish population has DM and its prevalence is growing. As the number of people suffering from diabetes increases the incidence of its complications also increases. Diabetes causes tissue damage in the small and large bloods vessels that with time can develop PVD and neuropathy that play a primary role in the development of DFUs. Neuropathy is characterised by nerve damage causing loss of protective sensation in the foot, whilst PVD leads to an impaired blood supply of the foot. These two risk factors in combination with trauma, foot deformities, callus, oedema, inappropriate footwear and/or pressure can contribute to skin breakdown and the development of FUs. Although, all these factors play an important role in the DFU causal pathway, pressure is a factor always present in the development or maintenance of DFUs whether they are neuropathic, ischaemic or mixed aetiology. Pressure results in the mechanical loading of the foot’s surface, though this concentrates more in the
plantar aspect of the foot. Taking into account, that in order for DFUs to heal it is fundamental to minimize mechanical loading, offloading is a key intervention for both prevention and treatment of DFUs, as it will allow for the redistribution and relief of pressure in the feet. To achieve this various offloading devices, insoles, orthoses and casts, can be used. From these TCCs appear in the literature as the “gold standard” for the treatment of DFUs. However, it is important to analyse the research around offloading for the treatment of DFUs to gain a better understanding of the effectiveness of the various devices.

1.6. Conclusion

DFUs are a complex and debilitating complication of DM. Although, various interventions are essential for the treatment of these ulcers, offloading, by alleviating and redistributing pressure, is crucial for this treatment to be effective.
Chapter 2. Methodological Issues in Systematic Reviews

2.1. Introduction

Initially this chapter will explore the concept of research particularly in nursing and how this is important for evidence-based practice (EBP). Subsequently, it will analyse, in greater depth, the concept of systematic review (SR) and its importance and role as a research method.

2.2. Nursing Research and EBP

An Bord Altranais (ABA) (2007) main focus is in promoting and assuring high standards of nursing practice, education, training and professional conduct. For this objective to be attained research, which is an integral part of education, training and professional development, becomes cornerstone for nursing development as a profession and science.

Since 1980, that the Working Party on General Nursing considered nursing research essential for the continuous development of this profession due to its growing complexity (Department of Health and Children (DoHC) 2003), and in 2003 the DoHC issued a final report, which states that knowledge acquisition is necessary for the development of any profession. Thus, it is clear that research is needed to create new knowledge and re-validate the existing knowledge. Therefore, research is a crucial link between knowledge acquisition and practice development (DoHC 2003). Furthermore, it is important to recognise that research, and more specifically nursing research, aims at ‘solving clinical problems, evaluating practice, evaluating policy and generating and testing theory’ (Watson et al. 2008: 4). Ultimately, research will promote nurses
knowledge and enhance their practice, enabling them to provide evidence-based, and efficient healthcare services to society (ABA 2007: 6).

According to Watson et al. (2008), there is primary and secondary research, the first is used when data pertaining to a certain question, that arises from practice, is being explored either through qualitative or quantitative methods. The second relates to research based on data that is brought together through, for example, a SR. Independently of the type of research being used this will allow nurses to integrate EBP into their care and to use it in their clinical decision-making (Sackett et al. 1996, Upton 1999, Holland and Watson 2012). Evidence-based practice, involves using up-to-date evidence, based on current research, in clinical decision making (Sackett et al. 1996) as experience alone is not enough to reach high standards of clinical practice, knowledge and professional development. EBP is paramount not only to integrate the highest quality research for best practice but also to allow for best clinical decision-making, where the nurse is certain to be delivering the utmost care to their patients (Sackett et al. 1996).

EBP phases can be summarised as follows (Upton 1999: 549, Gerrish and Lacey 2010: 495, Holland and Watson 2012: 104):

1. Identifying a clinical problem,
2. Formulating a question regarding the problem identified,
3. Identifying the evidence,
4. Critically assessing the evidence,
5. Develop a strategy for implementing the evidence into clinical practice,
6. Evaluate the impact and results of intervention applied.
This process is central to gather quality research and to examine its strengths and limitations not only in terms of the appropriateness of the methods employed but also in terms of the validity of its conclusions (Evans 2003, Holland and Watson 2012). Conversely, it is important to determine which evidence is the best evidence (Evans 2003, Holland and Watson 2012). Sackett et al. (1996) argues that the best evidence accurately informs and answers clinical questions, being RCTs and SRs of RCTs the ‘gold standard’ and when these are not available one must follow a hierarchy and find the next best evidence. Evans (2003) adds that to determine best evidence, the focus should include the appropriateness (psychosocial aspects of the intervention) and feasibility (the impact of the evidence and how this would be implemented) of the evidence and not exclusively its effectiveness (whether an intervention works as anticipated) (Evans 2003:79). These dimensions evaluate in a broad and complete way how research was conducted and if it achieved what it set to achieve. Furthermore, these dimensions give some insight into the person, how the research affected the person and if it is suitable and relevant for the wider community. Ultimately, it assesses if the research can be used for future decision making in terms of cost-effective practices, implementation of new policies and particularly professional practice actualisation and development.

2.3. SRs: rationale and methodological issues

2.3.1. Rationale for conducting SRs

SRs play a central role in EBP and, to bring together valid and reliable information that can be used to allow informed clinical decision-making which, in turn, will support policymakers in the development of cost-effective and best evidence guidelines that will

Mulrow (1994), grounds the basis for conducting SRs in a number of principles some of which pertain to research in general and others focus more in the SR of quantitative research. The first reason is related to the fact that today around 20,000 journals publish an estimated two million articles every year (Mulrow 1994, O’Mathúna 2010) rendering it impossible for nurses to take in all the available research information produced. Therefore, SRs help reduce the amount of information available (Mulrow 1994). Another rationale is the fact that, professionals and decision makers will use the information in SRs to identify and justify hypothesis through which guidelines and policies can be produced (Mulrow 1994). Moreover, SRs are a research technique that: follows a rigorous method; allows for generalizability; assesses the reliability of primary research; identifies any gaps or contradictory information in data (Mulrow 1994). Consequently, SRs can be a mean of shaping the way qualitative and quantitative research are used and brought together, for nurses to base their practice and contribute not only for the production of guidelines and management change but also for the highest standards of care for patients, their family and the community (Mulrow 1994, O’Mathúna 2010).

2.3.2. SR: its’ background and definition

New demands in healthcare practices where decisions have to be based on the best evidence available and the fact that research data is constantly growing (Egger et al.
2001, Centre for Reviews and Dissemination (CRD) (2008) has made SRs fundamental for healthcare professionals to have up-to-date evidence and also to find where evidence is lacking (Egger et al. 2001). However, this need for SRs has been part of the research community for some time.

An important pioneer was Archie Cochrane, an epidemiologist, who argued that healthcare professionals did not have ‘...access to reliable reviews of the available evidence’ (Egger et al. 2001: 449) making it difficult to practice and make decisions based on best evidence (Egger et al. 2001). Cochrane conducted a SR of RCT’s where steroids had been used by women in premature births and its’ conclusion was that there was a reduction of babies deaths of up to 50% (Egger et al. 2001, Watson et al. 2008, Moore 2012). From this SR, Cochrane identified that it was fundamental to undertake SRs and to make them available for healthcare professionals, and in 1993 the Cochrane Collaboration in the UK was launched (Egger et al. 2001, Watson et al. 2008, Moore 2012). Besides the Cochrane Collaboration there are other organisations committed in the development and publishing of SRs like the Joanna Briggs Institute, the National Institute of Health and Clinical Excellence, the EBP Centre Program and the International Campbell Collaboration (Fineout-Overholt et al. 2008, Smith et al. 2011)

A SR is a research method that objectively and rigorously retrieves, summarizes, critically interprets and evaluates all the available published and unpublished primary research relating to a specific subject/healthcare problem (Bero and Jadad 1997, Cook et al. 1997, Mulrow et al. 1997, National Health and Medical Research Council (NHMRC) 2000, Magarey 2001, White and Schmidt 2005, Fineout-Overholt et al. 2008, O’Mathúna 2010, McGowan 2012). It is possible to understand that, SRs follow a
very strict method in order to acquire and gather the utmost level of evidence, where the quality of the research being summarised is key for the quality of the review (Cook et al. 1997, Watson et al. 2008, Higgins and Green 2011). In fact, not every literature review is systematic and there are differences that have to be recognised so that nurse’s practice is only evidence based (Holland and Watson 2012).

Literature reviews (LR) are normally conducted by experts of a particular area, who summarise articles in a subjective way that is supportive of the reviewer opinion and is not representative of all the evidence available (Magarey 2001, Lipp 2007, Watson et al. 2008, McGowan 2012). Furthermore, LRs do not follow a scientific method, do not report how the selection and analysis of the articles was done, and lack quality appraisal of the included articles (Magarey 2001, Whitney 2004, Watson et al. 2008, McGowan 2012). This leads to a biased LR, as the reviewer opinions are often part of the review and there is no clarity of the method by which the LR was conducted, limiting the confidence that the reader can have in its results (Cook et al. 1997, Lipp 2007, Watson et al. 2008). Thus, the difference between SRs and LRs is that the first is comprehensive, takes into consideration studies quality and follows a transparent and rigorous method (Victor 2008). All these characteristics are crucial for the results and evidence obtained to be rigorous, valid and reliable (Victor 2008). In terms of rigour, this will measure the strength of the SR ensuring that all the steps for conducting the review were followed, that any confounding factors were eliminated and that the reader thrusts the results and conclusions (Gerrish and Lacey 2010). In relation to reliability, this will look into the consistency of the review and validity will allow the reader to be sure that the SR answers the question it set to answer and the methods employed in its
process are without bias, making sure the SR is trustworthy (Watson et al. 2008, Gerrish and Lacey 2010).

Therefore, the difference between a LR and a SR is that, a SR has to follow a rigorous protocol which sets the steps that have to be followed, in a systematic way, so that the conclusions obtained are best evidence and allow for its application in practice. Being a research method, SRs will follow the same steps of any other primary research method (NHMRC 2000).

2.3.3. Steps in SR

To conduct a SR it is necessary to establish a protocol that has a thorough description of the methods that will be used (Victor 2008). Although the process is the same, different authors identify a different number of steps for conducting SRs. McGowan (2012), Magarey (2001) and Fineout-Overholt (2008) mention seven steps; White and Schmidt (2005) identify three steps; NHMRC (2000), Victor (2008), Whitney (2004), Khan et al. (2003) and Lavis et al. (2005) indicate five steps; and the CRD (2008) mentions nine steps. Bringing all the different number of steps suggested it is possible to enumerate the steps to conduct a SR as the following (NHMRC 2000, Egger et al. 2001, Magarey 2001, Khan et al. 2003, Whitney 2004, Lavis et al. 2005, White and Schmidt 2005, CRD 2008, Fineout-Overholt 2008, Victor 2008, McGowan 2012):

- Background,
- Research question formulation,
- Identification of inclusion and exclusion criteria,
- Search strategy,
- Study selection,
2.3.3.1. Background

The background is an important component as this will provide the reasons for undertaking the SR around a particular topic and will allow the reader to have a better view of the current knowledge around that topic (CRD 2008, Watson et al. 2008). For example in a SR by Happell and Gaskin (2012: 148) entitled, The attitudes of undergraduate nursing students towards mental health nursing: a systematic review, a summary of their background is given.

2.3.3.2. Research question formulation

Framing the question for the SR is an important step, as through this, the problem of focus in the review can be identified (Magarey 2001, Khan et al. 2003, Whitney 2004, Holland and Watson 2012). The research question should be clear and well structured (Khan et al. 2003), and should include four components ‘...patient group being investigated, intervention, comparative interventions and the outcomes used to measure the effect.’ (Magarey 2001: 377, Whitney 2004). Furthermore, to the components mentioned above the CRD (2008) explores the PICOS formula where P stands for participants, I for intervention, C for comparators, O for outcomes and S for study design. This formula allows the reviewer to establish the inclusion and exclusion criteria for the review (CRD 2008).
In their review Happell and Gaskin (2012: 148-149) report on two research questions and, identify the aim and objectives of their SR.

2.3.3.3. Identification of inclusion and exclusion criteria

Another important aspect of the SR process is to determine the inclusion/exclusion criteria, which will further aid in the selection of appropriate studies. This should not be too narrow, as it may miss important research, nor too broad that the research retrieved is disparate and as a consequence difficult to compare (White and Schmidt 2005, CRD 2008). Examples of inclusion/exclusion criteria are the study design, the intervention and the outcomes (White and Schmidt 2005).

In the review by Happell and Gaskin (2012: 149-150) the inclusion and exclusion criteria is identified.

2.3.3.4. Outline of the search strategy

The search strategy is a core step because through it the reviewer will gain access to the information from which the evidence and recommendations are drawn (Smith et al. 2011). To retrieve all the pertinent articles, the search strategy needs to be extensive, comprehensive, but sensitive so that the maximum of articles are retrieved (White and Schmidt 2005, Smith et al. 2011). Moreover, it is necessary that the reviewer clearly states the search strategy in terms of databases searched, search terms used, so that bias can be avoided, to allow for search strategy replication and for the retrieval of all published and unpublished studies pertaining to the topic, as much as possible (Magarey 2001, Watson et al. 2008). In terms of unpublished literature, often termed as grey literature, this is literature publicly available through special channels and is not part of
the normal systems of publication (Benzies et al. 2006). Grey literature can include theses, government reports, and, conference abstracts, and the majority is not peer-reviewed (Magarey 2001, Benzies et al. 2006). Peer-reviewing consists in giving the research to a group of experts that will evaluate if it followed the protocol flawlessly, if every step was conducted appropriately and if it reports what it intended to report (Watson et al. 2008).

The review by Happell and Gaskin (2012: 150), reports a detailed search strategy. It is also important to provide a detail of the results of the search strategy before and after limits were applied, as these limitations can lead to the exclusion of valuable studies (Smith et al. 2011, Holland and Watson 2012).

2.3.3.5. Study selection

Study selection is done taking into account the inclusion/exclusion criteria and this can be a difficult process because the reviewers need to screen all the articles retrieved and access those relevant for the topic being researched (Smith et al. 2011). Study selection involves a few steps, first the titles and abstracts are read and any duplicates are identified, after selecting the relevant articles full text copies are obtained for data extraction and critical appraisal in terms of their quality is done (CRD 2008, Smith et al. 2011). Happell and Gaskin (2012) do not clearly report study selection in their review.

2.3.3.6. Data extraction

After choosing the studies for inclusion in the SR, it is necessary to data extract as this will allow the reviewer to have a concise picture of the studies characteristics (Magarey
2001, White and Schmidt 2005, Victor 2008). For data extraction various templates are available and the data to be extracted includes:

- Authors,
- Date of study and geographical location,
- Study setting,
- Inclusion/exclusion criteria,
- Sample size,
- Study design,
- Intervention details,
- Outcome measures,
- Analysis,
- Results,
- Conclusions,
- Recommendations.

This is just an example of the information that can be extracted and this will vary according to the template being used. Furthermore, it is recommended that data extraction is done by the reviewers of the studies independently, as they might interpret the results differently (White and Schmidt 2005).

In the SR of Happell and Gaskin (2012) a table of data extraction pertaining to survey studies obtained and one pertaining to the quasi-experimental studies obtained was included.
2.3.3.7. Quality Appraisal

Quality appraisal is a core step when undertaking a SR, as it will allow the reviewer to have access to the best evidence available (Victor 2008). Only by thoroughly evaluating the quality of the studies included in the review will the review originate reliable evidence based information that can be used by nurses in their practice (Victor 2008, Smith et al. 2011). According to the CRD (2008) research studies can vary greatly in terms of their methodological thoroughness, and if a study is not conducted properly or if deviations from the established protocol happen without being reported, bias can occur and the results and effects of interventions of the study can be questioned.

To be able to evaluate the findings of the research to be included in a review it is paramount to quality assess (White and Schmidt 2005: 57, CRD 2008: 33):

- Suitability of study design to the research question, aims and objectives,
- Assess the presence or potential risk of bias,
- Outcomes measures,
- Quality of the intervention,
- Quality of reporting.

2.3.3.7.1. Suitability of study design to the research question, aims and objectives

When assessing the quality of a study it is essential to evaluate if the study design chosen is appropriate from the point of view of the research question, the aims and objectives proposed (CRD 2008). For example, if an intervention is being assessed but it is unethical to randomly assign participants to a particular group, then another type of design should be used (CRD 2008). It is important to be knowledgeable of study
designs in quantitative and qualitative research so that an appropriate method can be employed.

2.3.3.7.2. Assess the presence or potential risk of bias

Bias is a systematic deviation from the truth and is a consequence of poorly conducted research that can enhance results and the true value of the findings, which could ultimately lead to bad decisions in practice (CRD 2008: 34). There are various types of bias: publication bias, time-lag bias, citation bias, language bias, outcome reporting bias, selection bias, performance bias, detection bias, and attrition bias (Egger et al. 2001, Magarey 2001, Moore 2012).

Publication bias relates to the publication of studies, with the same type of data, depending on the results favourability, this can influence the conclusions of the SR as it could support a beneficial treatment or fail to identify an adverse effect of a treatment (Egger et al. 2001, Moore 2012).

Time-lag bias impacts in the way the strength of evidence for or against a particular intervention is determined (Moore 2012) thus, influencing the results of SRs because positive results will dominate the research literature, before the, also important, negative results are published (Egger et al. 2001).

Citation bias is related to the way authors of a study conveniently include or exclude research articles for citation and, this is influenced by the trend of the results (Egger et al. 2001, Moore 2012). This will affect the SR as only positive results will be part of the
research being summarized, moreover the actual SR could be biased if it manipulates its inclusion/exclusion criteria to obtain, previously known, positive articles.

Language bias refers to the inclusion of research articles from a particular language and the consequent exclusion of potential significant research from other languages (Egger et al. 2001, Moore 2012). Language bias occurs when the search strategy is limited to a language of interest to the reviewer. However, it is necessary to note that in some cases there is a lack of access to translation services, and financial funds to pay for the translation (Smith et al. 2011, Moore 2012). Nevertheless, the reviewer should acknowledge this limitation and report the difference in the number of articles retrieved with and without language limits. This type of bias can affect the consistency of the SR as only part of the body of evidence is being assessed and summarised.

Outcome reporting bias occurs when the researchers overlook the results of some of the outcome measures and decide not to report them, thus reporting the more positive results and conclusions (Egger et al. 2001, Moore 2012). This will consequently influence the results and outcomes of the SR.

Selection bias is related to the method used to allocate the participants to the treatment or control group (Magarey 2001). To avoid selection bias, concealment and blinding are two necessary methods. Concealment means that the researchers do not know to which of the groups the participants will be allocated to and blinding means that the researchers do not know which treatment the participants will receive (Magarey 2001).
Performance bias occurs if there is external or internal factors that cause a difference in the interventions being researched, modifying it, and thus influencing the results obtained (Magarey 2001).

Detection bias relates to the process of appraising the results of the outcomes, as this has to be conducted in the same way for the treatment and control group (Magarey 2001).

Attrition bias happens when there are dropouts, as this will influence the number of participants and cause a difference between study groups (Magarey 2001). Taking into account that these dropouts could be due to the interventions being studied it is imperative that the reasons for the dropouts are reported (Magarey 2001).

2.3.3.7.3. Outcome measures
According to the CRD (2008) assessing outcome measures is related to the assessment of the reliability and validity of the outcome measures being used. This means that the study, established outcome measures that are attainable and relevant, according to the research question and objectives of the study, and that they will help to understand the effect of the intervention being study (CRD 2008).

2.3.3.7.4. Quality of the intervention
When assessing the quality of the intervention(s) proposed in the study it is necessary to evaluate if these where used properly, if they were implemented has described in the protocol, if the participants received the intervention as planned and if it was
consistently applied for every participant (CRD 2008). This is an important aspect of the study because if the interventions are changed or flawed the results obtained might not represent reality, thus, influencing the quality of the study in general.

2.3.3.7.5. Quality of reporting

Quality of reporting is related to whether the study reports and identifies methodological issues such as allocation concealment and details about the intervention being studied (CRD 2008). Moreover, the CRD (2008) mentions that this type of quality assessment is not representative of the general quality of the study being reviewed. Besides assessing studies quality it is also important and necessary that the quality of the SR process is, in itself, assessed (Victor 2008). Happell and Gaskin (2012) did not report on quality appraisal or bias analysis.

2.3.3.8. Data Analysis and Synthesis

After quality appraising the studies included in the SR, these can be analysed and then synthesised. Depending on the type of studies included data analysis and synthesis will be conducted using quantitative or qualitative methods (Magarey 2001). For analysis and synthesis of quantitative research meta-analysis is used when only trials are being analysed and synthesised (Watson et al. 2008). If other types of quantitative study designs are being reviewed (such as quasi-experimental studies) a narrative form of synthesis should be used (Victor 2008). For analysis and synthesis of qualitative research meta-synthesis or thematic analysis and synthesis can be used (Lipp 2007, Victor 2008).
In the study by Happell and Gaskin (2012), meta-analysis was not practical, and although the authors do not explicitly report the type of data analysis and synthesis that was done, the only conclusion plausible from examining the study is that a narrative summary was conducted.

2.3.4. SR of Quantitative Research: meta-analysis

Quantitative research is a method to collect data that can be translated into numerical data and through its measurements, tries to explain the information obtained, to describe variables and to predict and examine relationships of cause and effect (Watson et al. 2008). Quantitative research methods can include RCTs, quasi-experimental and observational studies (CRD 2008, Watson et al. 2008). An example of a quantitative research study is the study by Gethin and Cowman (2008) where the method used was a prospective, open label, multicentre randomised control trial.

Meta-analysis is a ‘...specific methodological and statistical technique for combining quantitative data’ (Mulrow et al. 1997: 389). In meta-analysis, to combine different data it is necessary that the individual studies, that will be systematically reviewed, have similar clinical problems and research methodologies (Moore 2012). Meta-analysis is an important method as it increases the power of the study, which is ‘...the probability that a trial will detect, as statistically significant, an intervention effect of a specified size’ (Cochrane Collaboration Glossary Online (CCGO) 2011).

Due to the fact that similar studies are combined, the sample size also increases which further increases the power of the review. Conducting meta-analysis also influences the precision of the review (Moore 2012), which is in statistical terms ‘A measure of the likelihood of random errors in the results of a study, meta-analysis or measurement’
Another advantage of conducting meta-analysis is the fact that new problems and questions that arise from the combined studies can be answered, contributing to the body of knowledge and to EBP (Moore 2012). Furthermore, meta-analysis contributes for the proposal of new hypotheses and can help in solving differences in studies results (Moore 2012).

Before, conducting meta-analysis it is essential to ascertain the studies homogeneity as only studies with comparable problems, participants and methods, can be combined, because the summary of disparate data can yield misleading results and conclusions that will impact negatively in clinical practice (Moore 2012). Besides assessing data heterogeneity, it is fundamental to assess for bias in the study as this can alter significantly the results of the review.1

According to Moore (2012) there are three types of data relevant for conducting meta-analysis. These are dichotomous or binary data, continuous data and survival or time to event data (Watson et al. 2008, Moore 2012). According to the CCGO (2011) dichotomous data is ‘Data that can take one of two possible values, such as dead/alive...’ In terms of continuous data, this is ‘Data with a potentially infinite number of possible values within a given range’ for example, height (CCGO). Relatively to time to event data, this is ‘A description of the data in studies where the analysis relates not just too whether an event occurs but also when’ (CCGO 2011).

Thus, it is important to highlight that meta-analysis besides combining similar data from research, aims at determining the general treatment effect of all included research and is

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1 Refer to sub-heading Quality Appraisal, for further detail on types of bias.
conducted in two steps (Watson et al. 2008, Moore 2012). The first step is to determine a summary statistics that in terms of dichotomous data is reported as the odds ratio or relative risk and in continuous data is reported as the weighted mean difference (Watson et al. 2008). The second step is to determine the overall treatment effect based on the summary statistics (Watson et al. 2008).

Meta-analysis is an important method for the SR of quantitative data, and if properly conducted can provide essential information to practice in terms of the validity of the evidence.

2.3.5. SR of Qualitative Research

Qualitative research gathers verbal and observational data to understand, interpret and describe participant’s life experiences of a certain phenomenon (Watson et al. 2008: 17). Some of its methodologies include ethnography, phenomenology, and grounded theory (Gerrish and Lacey 2010). Moreover, qualitative research includes different designs such as structured or semi-structured interviews (CRD 2008). The choice of the design will depend on the methodology used. An example of a qualitative research study is the study by Hynes et al. (2010) where a qualitative exploratory approach was used through semi-structured interviews.

SRs focus has been mainly in summarising evidence from RCTs (Evans and Pearson 2001). However, qualitative research has become more prominent and its data can complement quantitative research as it gathers important information from patient, professionals and care givers experiences, about a certain treatment or intervention, that ultimately can help improve practice and add to the body of knowledge, necessary for

Qualitative research review, occurs through the use of meta-synthesis which is ‘...the critical review, analysis, interpretation and comparison or integration of findings, or processed data, from primary qualitative studies’ (Jones 2004). The CRD (2008), reports other methods that can be used for the synthesis of qualitative research, such as meta-ethnography, thematic analysis/synthesis and content analysis. The choice of method will depend on the research question of the studies included and the methodology used in the primary study (CRD 2008).

Quality assessment of primary qualitative studies for inclusion in SR is an important step as the data as to be of high standards so the evidence summarised can inform clinical practice, and will also highlight the strengths and limitations of the evidence being synthesised (CRD 2008). A few appraisal tools exist including the Critical Appraisal Skills Programme and the Quality Framework (CRD 2008), yet the quality assessment criteria proposed by Popay et al. (1998) cited by Horsburgh (2003) will be analysed in more detail. According to these authors there are three criteria for assessing the quality of qualitative research: interpretation of subjective meaning, description of social context and attention to lay knowledge.
Interpretation of subjective meaning is concerned with assuring that only the participant’s interpretation and description of what is being researched is the core of the researcher analysis and interpretation (Popay et al. (1998) cited by Horsburgh 2003, Holland and Watson 2012). Description of social context, is concerned with the clear report of the environment where the participants were at the time of research, has this can influence easing or constraining the participants actions and the way they share information (Popay et al. (1998) cited by Horsburgh 2003, Holland and Watson 2012). Finally, attention to lay knowledge means that it is necessary that the participant’s points of view and knowledge are given the same value, of those of specialists or professionals in the area being researched (Popay et al. (1998) cited by Horsburgh 2003, Holland and Watson 2012). This is important because the accuracy and the process of assessing the information will influence the credibility of the studies (Holland and Watson 2012).

2.4. Summary

The development of nursing as a profession and a science is essential and can be attained through research. Additionally, research is a process that will allow professionals to base their practice in the best evidence available. Therefore, EBP is crucial for safe clinical practice and patient and community satisfaction.

SRs are at the top of the hierarchy of evidence as they summarise, analyse, interpret and report the results of research in the same topic, either from qualitative or quantitative research. Being a research method it has to follow a protocol that will inform on the key steps that have to be included for a reliable and valid SR, some of these are: research question formulation, data extraction, quality appraisal, data analysis and synthesis.
Although, all steps are important, quality appraisal is fundamental because if in the studies included the research design is not appropriate and if bias is identified this can influence negatively the results of the review, which in turn will have a damaging impact on clinical practice.

SRs from qualitative research are summarised through meta-synthesis and quantitative data through meta-analysis as these combine and interpret studies which have similar designs, participants and interventions, thus augmenting the credibility of the results in favour or against the intervention under research.

2.5. Conclusion

It is possible to conclude that SRs are an essential research method in an environment where studies are constantly being published and nurses are not able to keep up with the evidence. So, SRs by employing accurate research methods and by consistently and deeply analysing research evidence from both qualitative and quantitative research will allow nurses to access best evidence information that can not only allow for EBP, but also for evidence based clinical decisions that are crucial for the quality of nursing care.
Chapter 3. Methods of this SR

3.1. Introduction

This chapter will describe the methods by which this SR was conducted. It will focus on the objectives and outcome measures of the review, identifying the target population and interventions being researched, as well as the inclusion criteria of the studies in the review. Further, it will report on the search strategy identifying the databases searched and search terms used. Finally this chapter will report on how the data were collected and how they were analysed.

3.2. Objectives and Outcome Measures of the Review

3.2.1. Objectives

The purpose of this SR was to understand the impact that offloading has in the treatment of DFUs.

Besides this main objective, this SR was also concerned with:

- Identifying the most effective offloading device in the treatment of the DFUs.
- Identifying the strengths and limitations of the different offloading devices.
- Determining the impact that offloading devices have in the QoL of the patient.

3.2.2. Outcome Measures

The primary outcome measure of this SR was ulcer healing rate in terms of percentage of ulcers healed, healing time and reduction in ulcer size. The secondary outcome measures were: adverse effects, such as infection, or any other effect that can be attributed to the use of the offloading device, compliance, cost and QoL.
3.3. Criteria for Inclusion of studies in the Review

All studies, in English or Portuguese, where different types of casts, therapeutic shoes and other orthotic devices have been compared and analysed in adult patients with only DFUs were included. Studies where participants are reported to have foot deformities and arthropathies were excluded.

3.4. Search Strategy

For the purpose of this SR a search strategy was established, so that the writer could access the available primary and secondary research relating to offloading for the treatment of DFUs.

For the search strategy of this review, the following search terms were used:

- Diabetic Foot,
- Orthosis/Orthotic Devices/Orthoses,
- Foot Orthosis/Foot Orthoses,
- Casts/Plaster Cast/Surgical Cast,
- Shoes.

The variance noted in some of the terms is due to differences in the MeSH tool of each database searched. All the terms used in the search strategy were MeSH terms.

In terms of the databases searched these included CINAHL, Medline, Embase, Cochrane Library and Web of Knowledge, refer to appendix 2 to 6 for a detailed summary of the search strategy in each data base.
According to the different databases searched, different limits had to be applied since some limits were not available in some of the databases. In general the limits applied were: research article and language – English or Portuguese. Only the search conducted in Medline the type of studies to be retrieved was limited to: control clinical trial, RCT, meta-analysis.

Besides searching the databases, the reference list of the chosen articles were also analysed and any relevant research articles were retrieved. The manual _Diabetic Foot Care_ by Edmonds _et al._ (2008), more specifically the reference list of chapter 4 was analysed and some articles retrieved.

No contact was made with authors or any other industry for published and/or unpublished work.

### 3.5. Data Extraction, Analysis and Synthesis

For the purpose of this SR data from the retrieved research articles was extracted using the data extraction table provided by the RCSI for all the studies retrieved (see appendix 7) except for the SRs. For these a table adapted from the table “*Characteristic of Included Reviews*” from the Cochrane Handbook was used (Higgins and Green 2011) (see appendix 8). Specifically, the following data were extracted from all studies except SRs: author, date of study, title, source, study geographical location, research question/aim/objectives, care setting, type of wound, inclusion/exclusion criteria, sample size, patient characteristics, design details, study type, allocation, intervention details, outcome measures, analysis, results, conclusions and recommendations. Relatively to the SRs the following data were extracted: review author, date of review,
source, geographical location, population, interventions and comparison interventions, outcomes for which data was reported.

For quality appraisal this was undertaken using the risk of bias assessment from RevMan 5.2 tool (The Cochrane Collaboration 2013) for all RCTs retrieved. The EBL Critical Appraisal Checklist (see appendix 9) was used for any other quantitative studies retrieved. For the SRs retrieved quality appraisal was done assessing if all steps, as described in The Cochrane Handbook (Higgins and Green 2011), that have to be followed for conducting a SR were reported (see appendix 10).

Following data extraction, a narrative summary was undertaken this, included a general description of the characteristics of the retrieved studies, followed by a description of the individual interventions under investigation in each study. This was followed by quality analysis of the RCTs, the SRs and the other quantitative studies. Data synthesis was narratively done for each individual study as each study compared different interventions, making it impossible to undertake meta-analysis. However, in all RCTs dichotomous data was analysed in terms of risk ratio (RR) and continuous data was analysed in terms of mean differences (MD) and were presented in a forest plot.

### 3.6. Summary

The purpose of this SR was to understand the impact that offloading has in the treatment of DFUs. Its primary outcome measure was healing rates, in terms of healing times and reduction in ulcer size. Its secondary outcomes were adverse effects, cost, compliance
and QoL issues. The search strategy was conducted in CINAHL, Medline, Embase, Web of Knowledge and Cochrane Library databases, using diabetic foot, orthosis/orthotic devices/orthoses, foot orthosis/foot orthoses, cast/plaster cast/surgical cast, shoe as MeSH terms. All articles retrieved in English or Portuguese were analysed and those were patients had foot deformities and arthropathies were excluded. Data extraction was done using data extraction tables. For quality analysis according to the type of study different tools were used. For RCTs risk of bias was assessed, for other qualitative studies the EBL appraisal checklist was used and SRs were quality appraised assessing if they reported all the steps for conducting SRs. Data was then synthesised generally and then in relation to each individual intervention identified. Results for RCTs were presented in terms of RR or MD depicted in forest plots. All studies were narratively synthesised.

### 3.7. Conclusion

This SR has as its main objective to understand the impact that offloading has in the treatment of DFUs. For this a search strategy was conducted and the quantitative studies and SRs retrieved, were data extracted, quality appraised and analysed in order to access the results of the studies and comprehend how well these relate to current practice in the treatment of DFUs.
Chapter 4. Results

4.1. Introduction

This chapter will give a detailed description of the results obtained from the search strategy in terms of number of articles retrieved for this SR. This will be followed by a general description of the studies obtained in terms of study designs, geographical location, study settings, populations, sample size and interventions. In relation to the interventions explored for this review, these will be described individually. Finally, this chapter will appraise the quality of the studies retrieved and summarise the results taking into account the outcome measures of interest for this SR.

4.2. Search Strategy: Results

For the purpose of this SR a search strategy was conducted and its details were described in the previous chapter. From the search strategy (see Figure 1) 289 records were identified in the databases and an additional 6 records were obtained. Two of these records were retrieved from the reference list of grey literature, more specifically the manual Diabetic Foot Care by Edmonds et al. (2008), in particular chapter 4. The remaining four were retrieved after screening the reference lists of articles used for preparing chapter 1 of this SR. After removal of duplicates, the titles of the remaining articles were read, yielding a total of 102 for further screening. The abstracts of these records were read and the full-text of 25 records was retrieved. From these 25 articles, 14 met the inclusion criteria and as such formed the base for this review. These records will be narratively summarised and analysed.
Records identified through database searching (n = 289)

Additional records identified through other sources (n = 6)

Records after duplicates removed (n = 179)

Records screened (n = 102)

Records excluded (n = 77)

Full-text articles assessed for eligibility (n = 25)

Studies included in qualitative synthesis (n = 0)

Studies included in quantitative synthesis (n = 12) of which 9 allow meta-analysis

Studies included systematic reviews (n = 2)

**Figure 1:** Search Strategy Flow Diagram  Adapted from Prisma 2009 Flow Diagram
4.3. Included and Excluded Studies

From the 25 articles retrieved 14 were included (see appendix 11), for data extraction, data analysis and quality appraisal, and 11 were excluded, see appendix 12 for exclusion reasons.

4.4. Description of Studies

4.4.1. Study Design


4.4.2. Geographical Location

In terms of the geographical location of the studies, 5 were carried out in the USA (Mueller et al. 1989, Armstrong et al. 2001, Birke et al. 2002, Armstrong et al. 2005, Katz et al. 2005), 3 in Italy (Caravaggi et al. 2000, Piaggesi et al. 2007, Faglia et al. 2010), 2 in the UK (Mason et al. 1999, Spencer 2008), 2 in The Netherlands (Nabuurs-Franssen et al. 2005, Van de Weg et al. 2008), 1 study was conducted between Belgium and France (Dumont et al. 2009) and 1 was conducted in Germany (Zimny et al. 2003).
4.4.3. Study Settings

With regard to study settings where the participants of the studies were recruited and where the studies were carried out, 4 studies did not mention the type of setting (Caravaggi et al. 2000, Armstrong et al. 2001, Armstrong et al. 2005, Nabuurs-Franssen et al. 2005), 2 studies were conducted in diabetic foot clinics (Katz et al. 2005, Piaggesi et al. 2007) 1 study was conducted in a clinic, but the type or description of the clinic was not given (Zimny et al. 2003), 1 study was conducted between seven specialist units (Dumont et al. 2009), 1 was carried out in a health sciences centre diabetes foot program (Birke et al. 2002), 1 study was conducted in two centres specialised in DFUs management (Faglia et al. 2010), 1 was conducted in a diabetic foot clinic and physical therapy department (Mueller et al. 1989) and 1 study was conducted in a rehabilitation department of two hospitals (Van de Weg et al. 2008).

4.4.4. Populations

All participants were either adult men or women with an age ≥ 18 years old, all had type 1 or type 2 DM and all presented with a DFUs. Besides this general information about the population in the studies, each study collected different population characteristics that are recorded in the detailed data extraction tables that can be found in appendix 13 to 25.

4.4.5. Sample Size

The mean sample size was 65 participants, the smallest sample was 40 participants (Mueller et al. 1989, Piaggesi et al. 2007) and the biggest sample was 135 participants (Dumont et al. 2009).
4.4.6. Interventions

4.4.6.1. TCC vs. RCW vs. Half-Shoe

In the first study, by Armstrong et al. (2001), a TCC, a RCW and half-shoes were compared in terms of their effectiveness to heal neuropathic DFUs (see appendix 13). All participants were followed-up on a weekly basis for ulcer care and debridement, and device inspection. In terms of TCCs these were changed on a weekly basis or whenever it was clinically necessary. These were applied according to a technique by Kominsky that was modified by the authors of the study, which included the use of a cast boot instead of the rubber cast walker and a plywood platform. Relatively to the RCWs and half-shoes these were applied according to packaging instructions and participants were advised to use them at all times. The authors do not describe in detail how the casts were applied or the characteristics of the half-shoe.

4.4.6.2. iTCC (“instant” TCC) vs. RCW

In the second study, by Armstrong et al. (2005), an iTCC and a RCW were compared to assess their effectiveness in healing neuropathic DFUs (see appendix 14). All participants were followed on a weekly basis for ulcer care and debridement, and device inspection. The iTCC is a RCW rendered irremovable by wrapping it in a cohesive bandage. However, the authors do not describe how the casts were applied and refer it to another article where the characteristics of this application are explained.

4.4.6.3. TCC, Accommodative Dressing, Healing Shoe, Walking Splint, Other

The third study was a retrospective analysis, by Birke et al. (2002), where a TCC, an accommodative dressing, a healing shoe, a walking splint and other devices were
compared to assess their effectiveness in terms of healing time in days and percentage of healed forefoot nonsurgical DFUs (see appendix 15). In this study, 120 medical records were revised and diabetic patients that were referred for nonsurgical treatment of neuropathic foot ulceration during a 30 month period were included in this analysis. For devices characteristics see appendix 26.

4.4.6.3.1. Accommodative Dressing

Dry dressings were used and these were revised and changed on a weekly basis.

4.4.6.3.2. Healing Shoe

Patients in this group were instructed in daily dressing changes and were followed-up weekly for reassessment and ulcer debridement as needed.

4.4.6.3.3. Walking Splint

Patients in this group were instructed in daily dressing changes with moisture retentive dressings and were followed at 1 to 2 week intervals to observe the progress of wound healing, for ulcer debridement as needed and reassessment.

4.4.6.3.4. TCC

Ulcers in the TCC group were dressed with dry dressings and TCCs were changed at 1 to 2 week intervals, depending on the amount of drainage.
4.4.6.3.5. Combination of devices

In this group how the combination of the devices was determined and what was used, was not clearly described by the authors.

4.4.6.4. Therapeutic Shoe vs. Fiberglass Cast

In the fourth study, by Caravaggi et al. (2000), a therapeutic shoe and a fiberglass cast were compared to assess their effectiveness in the rate of neuropathic plantar ulcers surface area reduction (see appendix 16). All participants changed dressings every two days, ulcers were debrided and medicated with paraffin gauze. For devices characteristics see appendix 27.

4.4.6.5. Ransart Boot

The fifth study was an observational study, by Dumont et al. (2009), where the effectiveness of the Ransart Boot for the management of DFUs was analysed (see appendix 17). All participants were followed on a weekly basis for ulcer care and debridement, and for device inspection. The dressings used were chosen by the supervising clinician. For device characteristics see appendix 28.

4.4.6.6. TCC vs. Stabil-D

In the sixth study, by Faglia et al. (2010), a TCC and Stabil-D were compared in terms of their effectiveness to heal plantar DFUs (see appendix 18). All participants were followed-up on a weekly basis for ulcer care and debridement, photograph and
measurement using the Visitrak® system. Dressings were done with paraffin gauze and covered with sterile gauze. For device characteristics see appendix 29.

4.4.6.7. TCC vs. iTCC

In the seventh study, by Katz et al. (2005), a TCC and an iTCC were compared in terms of their effectiveness in healing neuropathic plantar DFUs (see appendix 19). All participants were followed on a weekly basis for ulcer care and debridement (by a clinician), for photograph and measurement on acetate sheet, and for device inspection.

The TCCs were applied in a standard fashion by either a cast technician or certified pedorthodist. The iTCCs were applied by placing the patient in the DH Walker RCW in the manner recommended by the manufacturer. After the wound was treated additional padding was placed on the leg, to match treatment with patients in the TCC group. The iTCCs were then wrapped circumferentially with a single roll of fiberglass casting material, thus rendering them “irremovable”. The authors do not describe in detail how the TCC was fabricated and applied.

4.4.6.8. TCC vs. Traditional Dressing Treatment (TDT)

In the eighth study, by Mueller et al. (1989), a TCC and a TDT were compared in terms of their management of plantar DFUs (see appendix 20). In the TCC group, casts were applied by a physical therapist on the initial visit. If there were no complications, the cast was reapplied and changed every 2-3 weeks until the ulcer was completely healed. For the TDT group participants were followed at least every 2-4 weeks for routine wound care and debridement. For devices characteristics see appendix 30.
4.4.6.9. TCC, RCC (Removable Contact Cast), SMC (Shoe Model Cast)

In the ninth study, by Nabuurs-Franssen et al. (2005), a TCC, RCC and a SMC were used (see appendix 21). Cats were fabricated and applied using a modification of the technique described by Kominsky however the authors do not explain how this was done. Nonetheless, they mention that felt was applied around the ulcer to reduce peak pressure. Patients with a removable cast were instructed to remove the device only during wound care. At every visit, necrotic tissue and callus were surgically debrided. TCCs were renewed every 1–2 weeks, and RCC and SMC devices were modified if necessary. Cast treatment was terminated when there was no reduction in wound size or depth during 4 consecutive weeks.

4.4.6.10. TCC vs. Optima Diab Walker

In the tenth study, by Piaggesi et al. (2007), a TCC and Optima Diab Walker were compared in terms of their effectiveness, safety and cost-effectiveness in the management of DFUs (see appendix 22). All patients were followed-up weekly, ulcers were debrided, measured, photographed, and dressed with paraffin gauze and a layer of sterile gauze, and a new cast was then manufactured by the same certified podologist. For devices characteristics see appendix 31.

4.4.6.11. TCC vs. Custom Therapeutic Footwear (CTF)

In the eleventh study, by Van de Weg et al. (2008), a TCC and CTF were compared in terms of their effectiveness to heal neuropathic DFUs (see appendix 23). Prior to device application all participants had ulcer care and debridement (by a podiatrist), and device
inspection. Authors do not mention periodicity of visits only mention that out-patient visits were regular. For devices characteristics see appendix 32.

4.4.6.12. Felted Foam vs. Half-Shoe

In the twelfth study, by Zimny et al. (2003), felted foam and a half-shoe were compared in terms of their effectiveness to heal DFUs (see appendix 24). The authors do not mention the characteristics of the half-shoe or how ulcers in this group were managed. In the felted foam group, ulcers were thoroughly debrided, with removal of necrotic tissue and wound margins were traced at entry and at each follow-up with an indelible marker for subsequent calculation of the wound area. For device characteristics see appendix 33.

4.4.7. Characteristics of Included SRs

One of the SRs addressed various types of treatment modalities for DFUs (Mason et al. 1999) and the other SR focused on pressure relief interventions for prevention and treatment of DFUs (Spencer 2008), only the data relevant for the present SR were considered and analysed (see appendix 25).

In both SRs the target populations had to have type 1 or 2 DM, but Spencer (2008) adds that patients had to have DFUs. Both reviews mention casts as a treatment (Mason et al. 1999) and as a pressure relieving intervention for the treatment (Spencer 2008) of DFUs. In both reviews only one RCT (Mueller et al. 1989) was found and analysed pertaining to the role of offloading devices in the treatment of DFUs.
In the SR by Spencer (2008), and taking into account the outcomes of interest, the study by Mueller et al. (1989) only reported on one outcome – healing rate. Accordingly, Mason et al. (1999) analysed the same study in terms of healing rates, although this is not clearly identified as an outcome of the review.

4.4.8. Quality Appraisal of Included Studies

4.4.8.1. Quality Appraisal of included RCTs: Risk of Bias

This SR analysed data from 9 RCTs for the risk of bias using the RevMan 5.2 tool (The Cochrane Collaboration 2013).

4.4.8.1.1. Selection Bias (Randomisation)

All the studies report that a randomisation sequence was developed showing that participants were randomly assigned to one of the treatment options (see appendix 34). However, in two studies (Armstrong et al. 2001, Armstrong et al. 2005) the randomisation was undertaken after initial screening.

4.4.8.1.2. Selection Bias (allocation)

In relation to allocation sequence and concealment the studies report different types of methods used for allocation sequence, however one study does not report the method of allocation sequence (Zimny et al. 2003) and it is no clear if there was concealment of allocation or not. Only two studies (Armstrong et al. 2005, Van de Weg et al. 2008) make reference to some degree of allocation concealment (see appendix 35).
4.4.8.1.3. Performance Bias

In terms of performance bias, only the study by Van de Weg et al. (2008) reports the difficulty and even impossibility in blinding participants to the treatment, as offloading devices cannot be masked, and also the difficulty of blinding the investigator to the treatment as some patients made comments on the type of device they were using. All the other studies may have come across the same issues but it is not clear how they dealt with performance bias (see appendix 36).

4.4.8.1.4. Detection Bias

With regards to detection bias only the study by Van de Weg et al. (2008) reports that investigators were not involved in the treatment. In the other studies it is not clear if investigators had knowledge of the allocated interventions or if they had any direct participation in the interventions being studied (application of casts, ulcer care). In one study (Zimny et al. 2003) it is reported that the observer was not blinded to treatment group when measuring ulcer size. In the study by Faglia et al. (2010), Mueller et al. (1989) and Piaggesi et al. (2007), casts were applied by technicians but it is not clear if investigators were present and if they were involved in ulcer care. Katz et al. (2005) report that a clinician managed ulcer care and a cast technician or pedorthodist applied the casts however, it is not clear if the investigators add any involvement. Armstrong et al. (2001), Armstrong et al. (2005) and Caravaggi et al. (2000) do not mention if there was involvement of the investigators in the treatment (see appendix 37).
4.4.8.1.5. Attrition Bias

In relation to attrition bias only three studies (Caravaggi et al. 2000, Zimny et al. 2003, Piaggesi et al. 2007) did not report any dropouts or losses to follow-up. In the other studies there are some issues in terms of incomplete data reporting that might influence the results in favour or against the interventions being studied (see appendix 38).

4.4.8.1.6. Reporting Bias

All RCTs analysed reported data on the outcomes that were under investigation therefore, not demonstrating any issues relating to selective data reporting (see appendix 39).

Some of the studies, present bias issues that could potentially influence the validity and applicability of the results obtained from the interventions studied.

4.4.8.2. Quality Appraisal of other included quantitative studies

Quantitative studies were quality appraised using the EBL Critical Appraisal check list. If the overall validity of the study (Yes/Total) is ≥75% or ((No+Unclear)/Total) is ≤25% then the study is valid.

In the study by Birke et al. (2002) the overall validity was 60% (see appendix 40), in the Dumont et al. (2009) study the overall validity was 53% (see appendix 41) and in the Nabuurs-Franssen et al. (2005) study the overall validity was 68.4% (see appendix 42).
The overall validity of the studies, previously mentioned, show that conclusions are not widely generalizable to the general population.

4.4.8.3. Quality Appraisal of SRs

Taking into account that SRs are a research method, these have to follow a protocol identifying the steps taken to conduct a quality and reliable study (NHMRC 2000). For this reason the two SRs included in this study were quality appraised from the point of view of the steps that needed to be taken to conduct a SR.

The SR by Mason et al. (1999) reports most of the steps needed to conduct a SR (see appendix 43). The SR by Spencer (2008) reports most of the steps however it fails to mention the research question and the aim of the review (see appendix 44).

4.5. Results of Outcomes of interest for this review

All the studies were analysed in terms of outcomes reported. Taking into account that no one study compared exactly the same intervention, it is impossible to synthesise the studies in terms of outcomes. Therefore, outcomes are presented individually for each intervention. Detailed tables relating to all studies, except the SRs, can be found in appendix 45 to 56.
4.5.1 How the results are presented and how to interpret the analysis

The RevMan 5.2 tool (The Cochrane Collaboration 2013) was used for data analysis of all RCTs retrieved. For the remaining studies a narrative analysis of the results was undertaken. In relation to data analysed using the RevMan tool, dichotomous data was analysed in terms of RR and continuous data was analysed in terms of MD and were presented in a forest plot.

Forest plots (see Figure 2) are graphics used to depict results of meta-analysis (Akobeng 2005, Ried 2006). In this SR, although meta-analysis was not conducted, data analyses is displayed, were possible, using forest plots and instead of comparing studies only the groups in each study are compared. The square represents the RR or MD and is in line with the outcome value (Ried 2006). The size of the squares is related to the weight of the study, however if meta-analysis was being conducted different sized squares could be found and these would represent the weight given to each study (Ried 2006, Callcut and Branson 2009). The line through the square represents the Confidence Interval (CI) and the longer the line the less precise the study results are (Ried 2006). The 95% CI is the estimate of the range within which there is 95% certainty “…that the true population treatment effect will lie” (Akobeng 2005). The vertical line of the graphic represents the line of no effect (Akobeng 2005, Ried 2006). The value of this line is 1 for RR and 0 for MD (Ried 2006). The X axis is where outcomes are situated (Callcut and Branson 2009).

The last element of the graphic is the diamond and this demonstrates the overall result/effect of the comparison between the two groups (Ried 2006). The middle of the
diamond represents the estimate treatment effect (RR or MD) and the horizontal tips represent the 95% CI (Akobeng 2005, Ried 2006). If the diamond touches the line of no effect there is no significant statistical difference (SSD) among the groups being compared (Akobeng 2005, Ried 2006).

Data in this SR was analysed in terms of RR and MD. RR looks at the proportion of participants who experience an event in the intervention group compared to the proportion in the control group (Gerrish and Lacey 2011). If the RR is equal to 1 then there is no difference among the groups (Ried 2006). In relation to MD this measures the “…absolute difference between the mean values in the experimental and control groups…” (Watson et al. 2008: 105). If the MD is equal to 0 then there is no difference among the groups (Ried 2006).
4.5.2. Primary Outcomes

4.5.2.1. Healing Rate

4.5.2.1.1. TCC vs. RCW vs. Half-Shoe

In the study by Armstrong et al. (2001), healing rates were 89.5% (n=17) for the TCC, 65% (n=13) for the RCW and 58.3% (n=14) for the half-shoe group.

Comparing healing rates between the TCC and the RCW p=0.08. This means that there is no SSD in the healing rate between the TCC and the RCW. The overall effect in terms of RR is 1.38 and the 95% CI is 0.96 to 1.97. Despite this, the graphic confirms that more ulcers healed in the TCC group as the diamond lies to the right of the line of no effect (see figure 3).

In terms of healing rates between the TCC and the half-shoe there is a SSD between the two devices as p=0.02. The overall effect in terms of RR is 1.53 and the 95% CI is between 1.06 and 2.22 (see figure 4).

Figure 3: Forest plot 1 – TCC vs. RCW (healing rates)
Regarding the healing rates between the RCW and the half-shoe there is no SSD between the two devices as p=0.65. The overall effect in terms of RR is 1.11 and the 95% CI is between 0.70 and 1.78 (see figure 5).

![Figure 4: Forest Plot 2 – TCC vs. Half-Shoe (healing rates)](image)

![Figure 5: Forest Plot 3 – RCW vs. Half-Shoe (healing rates)](image)

**4.5.2.1.2. iTCC vs. RCW**

In the study by Armstrong *et al.* (2005), healing rates at 12 weeks were 82.6% (n=19) for the iTCC and 51.9% (n=14) for the RCW group. Forest plot 4 shows that there is a SSD between the two groups as p=0.03. The overall effect in terms of RR is 1.59 and the 95% CI ranges from 1.06 to 2.40. In this intervention it is clear from the position of the diamond on the plot that more episodes of the outcome of interest happen in the iTCC group (see figure 6).
4.5.2.1.3. **TCC, Accommodative Dressing, Healing Shoe, Walking Splint, Other**

In this retrospective study (Birke *et al.* 2002) from a total of 120 participants, only 113 were accounted for, healing rates at 12 weeks was 81%. In terms of healing rates for the individual devices, 92% of ulcers healed in the TCC group (n=13), 93% healed in the accommodative dressing group (n=26), 81% healed in the healing shoe group (n=57), 83% healed in the walking splint group (n=18) and of the 6 participants in the group were a combination of the aforementioned devices was used no healing rates were reported. It is clear that a higher percentage of ulcers healed in the TCC and accommodative dressing group, however the number of participants in each group is to disparate to allow comparisons. Furthermore the participants in the accommodative dressing used a modified surgical shoe in conjunction with the dressing.

4.5.2.1.4. **Therapeutic Shoe vs. Fiberglass Cast**

In the study by Caravaggi *et al.* (2002), at the end of the 30 days follow-up, 5 ulcers had healed in the therapeutic shoe group and 13 in the fiberglass group. Forest plot 5 shows a p=0.05 and the diamond being on the left side indicating that more episodes (ulcer healing) happened in the fiberglass cast group. There is a certain SSD in the healing rates between the groups (p=0.05) (see figure 7).
4.5.2.1.5. Ransart Boot

In this study (Dumont et al. 2009), only the Ransart Boot was used by the 135 participants and from these only 117 were analysed as 22 underwent amputations. From the 117 participants only 70.1% (n=82) of the ulcers healed. Statistical analysis is not appropriate as there is no comparator group.

4.5.2.1.6. TCC vs. Stabil-D

In the study by Faglia et al. (2010), its healing rates at 90 days were 73.9% (n=17) for the TCC and 72.7% (n=16) for the Stabil-D group. It is possible to see in forest plot 6 that p=0.93 which means that there is no SSD in the healing rate between the TCC and the Stabil-D. The 95% CI is between 0.71 and 1.45, and the overall effect in terms of RR is 1.02 (see figure 8).
4.5.2.1.7. TCC vs. iTCC

In the study by Katz et al. (2005), the mean healing rate at 12 weeks was 74% (n=15) for the TCC and 80% (n=17) for the iTCC group. From forest plot 7 it is possible to see that p=0.47 which means that there is no SSD in the healing rate between the TCC and the iTCC. The 95% CI is between -7.40 and 3.40, and the overall effect in terms of MD, the influence that each device has in the overall result, is -2.00 (see figure 9).

![Figure 9: Forest Plot 7 – TCC vs. iTCC (healing rates)](image)

If the participants lost to follow-up are not included in the analysis there still is no SSD between the two groups, p=0.48 (see figure 10).

![Figure 10: Forest Plot 8 – TCC vs. iTCC (healing rates loss to follow-up data not included)](image)

4.5.2.1.8. TCC vs. TDT

In the study by Mueller et al. (1989), the percentage of ulcers healed was 90% (n=19) in the TCC group and 32% (n=6) in the TDT group. Forest plot 9 shows that there is a SSD between the two types of devices as p=0.002, the diamond lies on the right of the
line of no effect showing that more ulcers healed on the TCC group. The overall effect
in terms of RR is 2.87, and the 95% CI is between 1.46 and 5.63 (see figure 11).

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>TCC Events</th>
<th>TDC Events</th>
<th>Risk Ratio</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mueller et al 1989</td>
<td>19</td>
<td>21</td>
<td>2.87</td>
<td>[1.46, 5.63]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>21</td>
<td>19</td>
<td>2.87</td>
<td>[1.46, 5.63]</td>
</tr>
</tbody>
</table>

Total events: 19 6
Heterogeneity: Not applicable
Test for overall effect: Z = 3.05 (P = 0.002)

Figure 11: Forest Plot 9 – TCC vs. TDT (healing rates)

4.5.2.1.9. TCC, RCC, SMC

In the study by Nabuurs-Franssen et al. (2005), although the 98 participants used
different devices, the healing rate is not given for the individual devices. In general 76%
(n=74) ulcers healed. The healing rates in this study are also given in terms of groups of
patients with PAD and infection. Thus 90% of ulcers healed where there was no PAD
and no infection; where there was only infection 87% healed; where only PAD was
present 69% healed and where both PAD and infection were present only 36% of the
ulcers healed. The authors give no indication of which device participants with PAD
and/or with infection were using.

4.5.2.1.10. TCC vs. Optima Diab Walker

In the study by Piaggesi et al. (2007), the percentage of ulcers healed was 95% (n=19)
on the TCC group and 85% (n=17) in the Optima Diab Walker. Forest plot 10 shows
that there is no SSD between the two types of devices as p=0.30 and because the
diamond is touching the line of no effect. The overall effect in terms of RR is 1.12, and the 95% CI is between 0.91 and 1.38 (see figure 12).

4.5.2.11. TCC vs. CTF

In the study by Van de Weg et al. (2008), the number of ulcers healed was 6 in the TCC group and 6 in the CTF group. Forest plot 11 shows that there is no SSD between the two types of devices as p=0.78 and because the diamond is touching the line of no effect. The overall effect in terms of RR is 0.87, and the 95% CI is between 0.33 and 2.27 (see figure 13).

4.5.2.12. Felted Foam vs. Half-Shoe

No healing rates reported (Zimny et al. 2003).
4.5.2.1.3. Results from SRs

In the review by Mason et al. (1999) and Spencer (2008) only the study by Mueller et al. (1989) was analysed. This study compares a TCC and a TDT which has already been analysed in the present review.

4.5.2.2. Healing Time

4.5.2.2.1. TCC vs. RCW vs. Half-Shoe

In the study by Armstrong et al. (2001), healing times were expressed in terms of mean days to heal. In the TCC group the ulcer took 33.5 days to heal, in the RCW group it took 50.4 days to heal and in the half-shoe group it took 61.0 days to heal.

Comparing the healing times between the TCC and the RCW in terms of MD, it is clear in forest plot 12 that there is a SSD amongst the two groups p<0.00001, that favours the TCC group. The 95% CI is between -21.02 and -12.78, and the overall effect in terms of MD is -16.90 (see figure 14).

Figure 14: Forest Plot 12 – TCC vs. RCW (healing times)
In relation to the healing times between the TCC and the half-shoe forest plot 13 shows that there is a SSD between the two groups with a p<0.00001, that favours the TCC group. The 95% CI is between -31.21 and -23.79, and the overall effect in terms of MD is -27.50 (see figure 15).

Comparing the healing times between the RCW group and half-shoe group forest plot 14 indicates that there is a SSD between the two groups with a p<0.00001, but in this case the RCW is favoured. The 95% CI is between -14.69 and -6.51, and the overall effect in terms of MD is -10.60 (see figure 16).

4.5.2.2. iTCC vs. RCW

In the study by Armstrong et al. (2005), in the iTCC group the ulcers took 41.6 days to heal and in the RCW group they took 58.0 days to heal. From forest plot 15 it is
possible to see that $p=0.0008$ which means that there is a SSD in the healing times between the iTCC and RCW, being the iTCC favoured. The 95% CI is between -25.95 and -6.85, and the overall effect in terms of MD is -16.40 (see figure 17).

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>iTCC Mean</th>
<th>SD</th>
<th>Total</th>
<th>RCW Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Armstrong et al 2006</td>
<td>41.6</td>
<td>18.7</td>
<td>23</td>
<td>58.5</td>
<td>15.2</td>
<td>27</td>
<td>1.000%</td>
<td>-16.40 [-25.95, -6.85]</td>
<td>-16.40 [-25.95, -6.85]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>41.6</td>
<td>18.7</td>
<td>23</td>
<td>58.5</td>
<td>15.2</td>
<td>27</td>
<td>1.000%</td>
<td>-16.40 [-25.95, -6.85]</td>
<td>-16.40 [-25.95, -6.85]</td>
</tr>
</tbody>
</table>

Heterogeneity: Not applicable
Test for overall effect: $Z = 3.86$ ($P = 0.0008$)

Figure 17: Forest Plot 15 – iTCC vs. RCW (healing times)

4.5.2.2.3. TCC, Accommodative Dressing, Healing Shoe, Walking Splint, Other

In this retrospective study (Birke et al. 2002) the healing times were given for the individual devices. In general, all ulcers took a mean healing time of 45.5 days. In the TCC group the mean healing time was 47.7 days, in the accommodative dressing group it was 36.1 days, in the healing shoes it was 41.4 days, in the walking splint it was 50.5 days and in the group where a combination of these devices were used healing times were not reported. From this data it appears that the accommodative dressing was more effective and ulcers healed quicker, however is important to note that participants that used the accommodative dressing were additionally fitted with a modified surgical shoe which could have influenced healing times.

4.5.2.2.4. Therapeutic Shoe vs. Fiberglass Cast

No healing times reported (Caravaggi et al. 2000).
**4.5.2.2.5. Ransart Boot**

In this study where all participants used the same offloading device the median healing time was 60 days (Dumont et al. 2009).

**4.5.2.2.6. TCC vs. Stabil-D**

In the study by Faglia et al. (2010), in the TCC group ulcers took 35.3 days to heal and in the Stabil-D group they took 39.7 days to heal. From forest plot 16 p<0.00001, this means that there is a SSD among the two groups being the TCC more effective. The 95% CI is between -6.56 and -2.24, and the overall effect in terms of MD is -4.40 (see figure 18).

![Figure 18: Forest Plot 16 – TCC vs. Stabil-D (healing times)](image)

**4.5.2.2.7. TCC vs. iTCC**

In the study by Katz et al. (2005) in the TCC group ulcers took 5 weeks to heal and in the iTCC group they took 4 weeks to heal.

**4.5.2.2.8. TCC vs. TDT**

In the study by Mueller et al. (1989), in the TCC group ulcers took 42 days to heal and in the TDT group they took 65 days to heal. When analysing the results in terms of MD...
p=0.01 which means that there is a SSD in the healing times between the two groups, being the TCC favoured. The 95% CI is between -41.00 and -5.00, and the overall effect in terms of MD is -23.00 (see figure 19).

**Figure 19: Forest Plot 17 – TCC vs. TDT (healing times)**

### 4.5.2.9. TCC, RCC, SMC

In the study by Nabuurs-Franssen *et al.* (2005), healing times are not reported for the individual devices. In general the median time for ulcers to heal was 33 days. Healing times in this study are also given in terms of groups of patients with PAD and infection. Thus, where there was no PAD and no infection ulcers took 18 days to heal; where there was only infection ulcers healed in 29 days; where only PAD was present ulcers healed in 42 days and where both PAD and infection were present, authors report that a minority of ulcers healed being the numbers too small to calculate time to heal. Moreover the authors give no indication of which device participants with PAD and/or with infection were using.

### 4.5.2.10. TCC vs. Optima Diab Walker

In the study by Piaggesi *et al.* (2007), in the TCC group ulcers took 6.5 weeks to heal and in the Optima Diab Walker group they took 6.7 weeks to heal. From forest plot 18 it
is possible to see that there is no SSD between the groups as $p=0.87$. This suggests that both devices are equally effective in terms of time to heal. The 95% CI is between -2.64 and 2.24, and the overall effect in terms of MD is -0.20 (see figure 20).

![Figure 20: Forest Plot 18 – TCC vs. Optima Diab Walker (healing times)](image)

### 4.5.2.11. TCC vs. CTF

In the study by Van de Weg et al. (2008), in the TCC group ulcers took 59 days to heal and in the CTF group they took 90 days to heal. In forest plot 19 $p=0.0003$, which means that TCC is more effective as this value shows a SSD between the two devices. The 95% CI is between -47.78 and -14.22, and the overall effect in terms of MD is -31.00 (see figure 21).

![Figure 21: Forest Plot 19 – TCC vs. CTF (healing times)](image)

### 4.5.2.12. Felted Foam vs. Half-Shoe

In the study by Zimny et al. (2003), in the felted foam group ulcers took 75.2 days to heal and in the half-shoe group they took 85.2 days to heal.
4.5.2.2.13. Results from SRs

In the review by Mason et al. (1999) only the study by Mueller et al. (1989) was analysed and this has already been analysed in the present review. In the review by Spencer (2008) no healing times are mentioned.

4.5.2.3. Reduction in Ulcer Size

4.5.2.3.1. Therapeutic Shoe vs. Fiberglass Cast

The authors only present a graphic in relation to ulcer area reduction, but do not explain it (Caravaggi et al. 2000).

4.5.2.3.2. TCC vs. Stabil-D

In the study by Faglia et al. (2010), the percentage of reduction in ulcer size was 73.6% (n=17) in the TCC group and 90% (n=20) in the Stabil-D group. In forest plot 20 p=0.14, which means that there is no SSD between the TCC and the Stabil-D. The 95% CI is between 0.62 and 1.07, and the overall effect in terms of RR is 0.81 (see figure 22).

![Figure 22: Forest Plot 20 – TCC vs. Stabil-D (reduction in ulcer size)](image-url)
4.5.2.3.3. TCC vs. CTF

In the study by Van de Weg et al. (2008) in terms of reduction in ulcer size, at the end of the 16 weeks follow-up both ulcers had a median size of 0.4cm$^2$, from an initial 3.6 cm$^2$ in the TCC group and 1.9 cm$^2$ in the CTF group. The authors report on ulcer reduction at 2, 4, 8 and 16 weeks, however the number of participants analysed, varies in the different weeks.

4.5.2.3.4. Felted Foam vs. Half-Shoe

In the study by Zimny et al. (2003), reduction in ulcer size was expressed in terms of mean radius reduction per week. In the felted foam group there was a reduction of 0.48mm per week in ulcer radius and in the half-shoe group there was a reduction of 0.39mm per week in ulcer radius. Forest plot 21 shows the mean area reduction after 10 weeks, and it is possible to see that there is a SSD between the two groups, with p<0.00001. The 95% CI is between -7.15 and -3.25, and the overall effect in terms of MD is -5.20 (see figure 23).

Figure 23: Forest Plot 21 – Felted Foam vs. Half-Shoe (reduction in ulcer size)
4.5.2.3.5. Results from SRs

The systematic review by Mason et al. (1999) only reports on the study by Mueller et al. (1989) and this study did not analyse reduction in ulcer size. Spencer (2008) does not have reduction in ulcer size as an outcome measure.


4.5.3. Secondary Outcomes

4.5.3.1. Adverse Effects

4.5.3.1.1. iTCC vs. RCW

In the study by Armstrong et al. (2005), the adverse effects reported were maceration and infection. The percentage of participants with maceration and infection in the iTCC group were 37.5% (n=8) and 27.3% (n=6), respectively. In the RCW group the percentage of participants with maceration and infection, was 68.2% (n=18) and 41.7% (n=11), respectively.

In relation to maceration there is no SSD between the two groups with p=0.07 (see figure 24).
With regard to infection there is also no SSD between the two groups with p=0.29 (see figure 25).

**Figure 24: Forest Plot 22 – iTCC vs. RCW (maceration)**

4.5.3.1.2. Therapeutic Shoe vs. Fiberglass Cast

In the study by Caravaggi et al. (2000), the adverse effect reported was increase in ulcer size. This happened in 2 participants of the therapeutic shoe group. Forest plot 24 shows that there is no SSD between the two groups with p=0.27. The overall effect in terms of RR is 5.40, with a 95% CI between 0.27 and 107.09 (see figure 26).

**Figure 26: Forest Plot 24 – Therapeutic Shoe vs. Fiberglass Cast (increase in ulcer size)**
4.5.3.1.3. Ransart Boot

In the study by Dumont et al. (2009), the adverse effects reported were: abrasion in the instep (n=8); redness on the 5\textsuperscript{th} metatarsal head (n=2) and blister on the heel (n=1). The authors report that after modifications were made to the Ransart Boot, complications healed.

4.5.3.1.4. TCC vs. Stabil-D

In the study by Faglia et al. (2010), the adverse effects reported were itching in the TCC group and maceration in the Stabil-D group.

In relation to itchiness there is no SSD between the two groups with p=0.51 (see figure 27).

![Figure 27: Forest Plot 25 – TCC vs. Stabil-D (itchiness)](image)

With regard to maceration there is also no SSD between the two groups, p=0.48 (see figure 28).

![Figure 28: Forest Plot 26 – TCC vs. Stabil-D (maceration)](image)
4.5.3.1.5. TCC vs. iTCC

In the study by Katz et al. (2005), in the TCC group the percentage of participants who developed adverse effects were as follows: maceration 35%, second ulcer 10%, abrasion 10%, toe amputation 5%, oedema 5%, kissing ulcer 5% and falls 0%. In the iTCC group the percentage of participants who developed adverse effects were as follows: maceration 29%, second ulcer 5%, abrasion 0%, toe amputation 5%, oedema 0%, kissing ulcer 0% and falls 5%.

In terms of maceration, from forest plot 27, it is possible to see that there is no SSD between the two groups with p=0.66 (see figure 29).

![Forest Plot 27 – TCC vs. iTCC (maceration)](image)

Figure 29: Forest Plot 27 – TCC vs. iTCC (maceration)

In terms of second ulcer development, from forest plot 28 it is possible to see that there is no SSD between the two groups with p=0.53 (see figure 30).

![Forest Plot 28 – TCC vs. iTCC (second ulcer)](image)

Figure 30: Forest Plot 28 – TCC vs. iTCC (second ulcer)
In terms of abrasion, from forest plot 29, it is possible to see that there is no SSD between the two groups with \( p=0.28 \) (see figure 31).

![Figure 31: Forest Plot 29 – TCC vs. iTCC (abrasion)](image)

In terms of toe amputation, from forest plot 30, it is possible to see that there is no SSD between the two groups with \( p=0.97 \) (see figure 32).

![Figure 32: Forest Plot 30 – TCC vs. iTCC (toe amputation)](image)

In terms of oedema, from forest plot 31, it is possible to see that there is no SSD between the two groups with \( p=0.48 \) (see figure 33).

![Figure 33: Forest Plot 31 – TCC vs. iTCC (oedema)](image)
In terms of development of a kissing ulcer, from forest plot 32, it is possible to see that there is no SSD between the two groups with $p=0.48$ (see figure 34).

![Figure 34: Forest Plot 32 – TCC vs. iTCC (kissing ulcer)](image)

In terms of falls, from forest plot 33, it is possible to see that there is no SSD between the two groups with $p=0.51$ (see figure 35).

![Figure 35: Forest Plot 33 – TCC vs. iTCC (falls)](image)

4.5.3.1.6. TCC vs. TDT

In the study by Mueller et al. (1989), the adverse effect reported was infection. This happened in 5 participants of the TDT group, 2 of which required forefoot amputation. From forest plot 34, it is possible to see that there is no SSD between the two groups with $p=0.08$ (see figure 36).
4.5.3.1.7. TCC, RCC, SMC

In the study by Nabuurs-Franssen et al. (2005), adverse effects were not reported for the individual devices. In general from the 98 participants: 9 developed infection of which 6 required hospitalisation for antibiotics and 3 were amputated; 2 needed revascularisation; 3 needed a free-flap transplantation and 7 stopped using the cast due to discomfort. New ulcers developed in 9% of the participants, but healed in 13 days with a revised cast. There were also pre-ulcerative lesions of which 28% resolved in a few days after minor adaptations in the cast. There were 8% of patients with chafed skin and 7% with joint problems.

4.5.3.1.8. TCC vs. Optima Diab Walker

In the study by Piaggi et al. (2007), the adverse effects reported in the TCC group were maceration and infection in 4 and 1 participants respectively. In the Optima Diab Walker group maceration occurred in 2 participants, infection, paraesthesia and haematoma occurred in 1 participant.

In terms of maceration, from forest plot 35, it is possible to see that there is no SSD between the two groups with p=0.39 (see figure 37).
In terms of infection, from forest plot 36, it is possible to see that there is no SSD between the two groups with \( p=1.00 \) (see figure 38).

![Figure 38: Forest Plot 36 – TCC vs. Optima Diab Walker (infection)](image)

In terms of paraesthesia from forest plot 37, it is possible to see that there is no SSD between the two groups with \( p=0.49 \) (see figure 39).

![Figure 39: Forest Plot 37 – TCC vs. Optima Diab Walker (paraesthesia)](image)
In terms of haematoma development in the calf, from forest plot 38, it is possible to see that there is no SSD between the two groups with p=0.49 (see figure 40).

![Figure 40: Forest Plot 38 – TCC vs. Optima Diab Walker (haematoma)](image)

**4.5.3.1.9. TCC vs. CTF**

In the study by Van de Weg et al. (2008), in the TCC group complications (not specified) were reported in 5 participants, from which 2 had to discontinue treatment. In the CTF group abrasion occurred in 2 participants.

In terms of complications, from forest plot 39, it is possible to see that there is no SSD between the two groups with p=0.12 (see figure 41).

![Figure 41: Forest Plot 39 – TCC vs. CTF (complications)](image)

In terms of abrasion, from forest plot 40, it is possible to see that there is no SSD between the two groups with p=0.25 (see figure 42).
4.5.3.10. Felted Foam vs. Half-Shoe

In the study by Zimny et al. (2003), the adverse effect reported was infection in 25% (n=6) of the participants in the felted foam group, and in 23% (n=7) of the participants in the half-shoe group. From forest plot 41 it is possible to see that there is no SSD between the two groups, with p=0.89 (see figure 43).

![Forest Plot](forest_plot.png)

**Figure 43**: Forest Plot 41 – Felted Foam vs. Half-Shoe (infection)

4.5.3.11. Results from SRs

In the review by Mason et al. (1999) only the study by Mueller et al. (1989) is analysed and this has already been analysed in the present review. In the review by Spencer (2008) the complications found in the studies reviewed (Mueller et al. 1989 was the only study significant for the present review) were considered to be reported insufficiently, so the author does not make any analysis in terms of adverse reactions.
Only two studies (Armstrong et al. 2001, Birke et al. 2002) did not report on adverse effects.

### 4.5.3.2. Cost

#### 4.5.3.2.1. TCC vs. Stabil-D

In relation to cost-effectiveness the study by Faglia et al. (2010), reports on the cost of both devices. Relatively to the TCC this costs €73.5, although there is an increase to €89.5 for obese patients, as these require extra bandages. For a total of 91 casts, taking into account that these had to be changed, the cost was €6,688.50. Regarding the Stabil-D device this costs €130 plus €20 for the Modus sole. In total €3,300.00 were spent in this device for 22 participants. It is possible to see that the Stabil-D is more cost-effective allowing for savings of up to €3,388.50.

#### 4.5.3.2.2. TCC vs. iTCC

In the study by Katz et al. (2005), cost is reported in terms of materials per week and then the direct cost of treatment. For the TCC group the cost of the materials per week was $38.36 and the cost of treatment was $210.67, which makes a total of $670.99. For the iTCC group the cost of the materials per week was $14.70 plus once the cost of the device $89.95 and the cost of treatment was $158.47, which makes a total of $424.82. It is possible to see that the iTCC is more cost-effective allowing for savings of up to €246.17 per patient per week.
4.5.3.2.3. TCC vs. Optima Diab Walker

In the study by Piaggesi et al. (2007), cost was reported in terms of mean cost per cast and per patient in both groups. In the TCC group the mean cost per cast was €110.5, and €727.29 per patient. In relation to the Optima Diab Walker, the device cost was €130, and the mean cost per patient was €162.5. From forest plot 42, in terms of cost per patient there is a SSD between the two devices with a p<0.00001. The 95% CI is between 348.01 and 781.57, and the overall effect in terms of MD is 564.79. It is possible to see that the cost per patient is lower in the Optima Diab Walker device (see figure 44).

Figure 44: Forest Plot 42 – TCC vs. Optima Diab Walker (cost)

4.5.3.2.4. Results from SRs


4.5.3.3. Compliance

4.5.3.3.1. Therapeutic Shoe vs. Fiberglass Cast

In the study by Caravaggi et al. (2000), compliance was analysed in terms of device acceptance using a visual analogue scale ranging from 1 to 100. In the therapeutic shoe group the mean acceptance value was 91.15 and in the fiberglass cast group the mean acceptance value was 88.33. Forest plot 43 shows that there is no SSD in the acceptance of the devices, p=0.48. The 95% CI is between -4.92 and 10.56, and the overall effect in terms of MD is 2.82 (see figure 45).

![Figure 45: Forest Plot 43 – Therapeutic Shoe vs. Fiberglass Cast (device acceptance)](image)

4.5.3.3.2. Ransart Boot

In the study by Dumont et al. (2009), the authors report that 9.6% of participants (n=13) were judged non-compliant, as according to the authors of the study these participants were not using their devices as instructed.

4.6.3.3.3. TCC vs. Optima Diab Walker

In the study by Piaggesi et al. (2007), compliance was analysed in terms of device acceptance using a visual analogue scale ranging from 0 to 10. In the TCC group the mean acceptance value was 6.85 and in the Optima Diab Walker group the mean acceptance value was 8.45. Forest plot 44 shows that there is a SSD in the acceptance of
the devices $p=0.02$. The 95% CI is between -2.91 and -0.29, and the overall effect in terms of MD is -1.60 (see figure 46).

![Forest Plot 44 - TCC vs. Optima Diab Walker (device acceptance)](image)

**Figure 46: Forest Plot 44 – TCC vs. Optima Diab Walker (device acceptance)**

### 4.5.3.3.4. Results from SRs

The SR by Mason *et al.* (1999) and Spencer (2008) do not report on compliance relating to offloading.


### 4.5.3.4. Quality of Life

No QoL issues were identified as an outcome of all the studies included in this SR. Only the SR by Spencer (2008) looks at patient satisfaction and QoL but analysis is in relation to one study that does not look at offloading.
4.6. Summary

From the search strategy 25 full text articles were retrieved, from which 11 were excluded and 14 were further included. From these 9 were RCTs, 2 were SRs, one was an observational study, one a retrospective study and one was a prospective data collection. From all the studies the samples sizes varied from 40 to 135 participants. Some studies did not report on the study setting, whereas others did, and care settings varied between diabetic foot clinics and hospitals. Geographically the locations were spread between America and Europe. The interventions under investigation in the different studies were analysed individually comparing the characteristics of the devices used. In terms of study analysis the 9 RCTs presented a few issues relating to bias, the SRs failed to report on some of the steps for conducting SRs, and the other 3 studies presented validity issues. All the studies reported one or more of the outcome measures of interest for this SR however these were analysed individually for every intervention, as these were not comparable. It was possible to see that a few of the outcomes presented SSDs, whereas others did not.

From the results the TCC shows better healing rates and healing times, followed by the iTCCs and the RCWs. The remaining devices mainly the therapeutic shoes, felted foam and CTF show worst results when compared with casts. In terms of adverse reactions infection and maceration were the most predominant amongst devices, and all devices were responsible for the development of one or more adverse reactions. With regard to cost very few studies reported on the costs associated with devices and the studies that undertook cost-analysis show higher costs with the TCC when compared with RCWs. In relation to compliance few studies reported on compliance assessment. The studies where compliance was analysed, this was related with device acceptance and there was
no SSD in terms of device acceptance. QoL issues were not analysed in any of the studies.

4.7. Conclusion
Casts allow for better healing rates when compared with other devices like therapeutic shoes and accommodative dressings. From these, TCCs show better results followed by iTCCs and RCWs for the treatment of DFUs.
Chapter 5. Discussion

5.1. Introduction

This chapter will give a succinct summary of the key findings of this SR. It will also
discuss the methodological issues of the included studies in this SR. Additionally, this
chapter will discuss the findings in terms of primary and secondary outcomes and
analyse them in terms of what is already know, if the studies bring new information for
clinical practice or education and if further research is needed in the area. Finally this
chapter will analyse the strengths and limitations of this SR and discuss its overall
contribution to health and social gain.

5.2. Summary of the key findings of this SR

The key findings from the SR of the included studies are:

- Offloading is an important strategy for the treatment of DFUs.
- A variety of removable (therapeutic shoes) and irremovable (TCC) devices are
  being used worldwide for the treatment of DFUs.
- Healing rates were in general higher with the TCC however the iTCC and RCWs
  when compared with the TCC did not show SSD in healing rates, showing that
  these devices are also effective in the treatment of DFUs.
- Healing times were higher with the TCC. However when healing time with the
  TCC was compared with the Optima Diab Walker there was no SSD.
- Reduction in ulcer size was reported in three studies (Zimny et al. 2003, Van de
  Weg et al. 2008, Faglia et al. 2010) but no SSD was found among devices
  compared.
- The most reported adverse effects were infection and maceration.
• Cost analysis was reported in three studies, and the TCC had higher costs when compared with an iTCC, Stabil-D and Optima Diab Walker.

• The studies where compliance was analysed, this was related with device acceptance and there was no SSD in terms of device acceptance.

• No QoL assessment was undertaken in the studies included for this SR.

5.3. Methodological issues of included studies

5.3.1. Study Design

The design of the studies, included in a SR, will impact on the reliability of the results of those studies and also in the validity of the effects relating to the study design (CRD 2008). Further, it is important to recognise that some study designs are more robust than others (CRD 2008). For this SR, two SRs and twelve quantitative studies were included.

From the three quantitative studies, one was a retrospective analysis (Birke et al. 2002), one an observational study design (Dumont et al. 2009) and the final a prospective data collection (Nabuurs-Fransen et al. 2005). Retrospective analysis is a type of design that, although of value, is subject to recall bias (Watson et al. 2008) as the authors may select cases, which show more positive results enhancing or devaluing the interventions being analysed. This, in consequence, will limit the applicability of the results to other populations (CRD 2008). The observational study design cannot be generalised to the general population as participants are not randomly selected (CRD 2008). In terms of prospective data collection, this design brings together data as it is produced making it a more reliable method (Watson et al. 2008). However, in the study included (Nabuurs-
Fransen et al. (2005) the results within the individual groups, using different types of casts, were not compared and results were expressed in general for the total amount of participants, this does not allow for a better understanding of the individual efficacy of the different devices that were used (CRD 2008). Although of value, the designs mentioned do not allow for conclusions to be applied to the wider population (CRD 2008, Higgins and Green 2011).

The SR by Mason et al. (1999) analysed various methods for the treatment of DFUs, including casting, and only identified one RCT, which does not allow for firm conclusions or recommendations for practice to be made. Moreover this SR did not report a detailed search strategy, making it difficult to be replicated (Magarey 2001, Watson et al. 2008). The SR by Spencer (2008) focuses on prevention and treatment of DFUs. It only reports on one RCT where offloading was used for the treatment of DFUs. This does not allow for firm conclusions to be reached as more studies are needed for comparisons to be made, in terms of which are the best devices for the treatment of DFUs (Cook et al. 1997, Muir Gray 1997 cited in Gerrish and Lacey 2010). The findings of the SRs did not bring new information to the present SR.

Regarding the RCTs retrieved, this type of design is extremely important, as it allows for the random allocation of subjects into the experimental and control group (Watson et al. 2008). This random allocation will avoid any bias that could devalue the findings (Watson et al. 2008). The RCTs analysed, compared different offloading devices so that results could allow for healthcare professionals to have a better understanding of which devices have better outcomes for patients (Mueller et al. 1989, Caravaggi et al. 2000,
Armstrong et al. 2001, Zimny et al. 2003, Armstrong et al. 2005, Katz et al. 2005, Piaggesi et al. 2007, Van de Weg et al. 2008, Faglia et al. 2010). Although, RCTs are considered the gold standard, through the use of controlled methods, random allocation of participants and concealment of which participants are assigned to the experimental or control group, this method is still subject to systematic errors, that can enhance or devalue the true effect of an intervention (CCGO 2013), potentially rendering the results invalid and unfit for generalisation.

5.3.2. Sampling

Sampling is a necessary method used in research as the sample will represent a subset of the population being investigated (Gerrish and Lacey 2010). Furthermore, it is important to obtain the correct sample size so that results obtained can be generalised back to the population of interest, and that a SSD may be detected, should one exist (Watson et al. 2008), for this to happen power analysis is necessary (Watson et al. 2008) and important for the calculation of the adequate sample size, which will influence the estimated expected difference to be found between the interventions being compared among the groups.

From the studies included, two (Piaggesi et al. 2007, Faglia et al. 2010) did not report power analysis in their methods. The studies by Mueller et al. (1989), Zimny et al. (2003), Katz et al. (2005) and Van de Weg et al. (2008) aimed for p values < 0.05 and CI of 95%, this means that there is 95% probability of finding a difference between the groups if one exists. Nonetheless, none of the previously mentioned studies elaborate if their sample sizes are sufficiently large for the aimed power to be achieved and for a true SSD to be observed among the groups. From the remaining studies (Caravaggi et
sample sizes were calculated for the study to have a certain power and to find a possible SSD between groups.

Although, sample sizes of these studies appear to be small, when compared with other RCTs, they were calculated to have a power between 80% and 95%. This will yield an 80-95% probability of detecting a real difference between groups. Sample size calculation is important as it will influence the real significance and power of the results obtained, thus influencing the strength of the study as a whole.

5.3.3. Sequence Generation

Sequence generation is related to whether adequate methods, like randomisation, were used for the generation of the allocation sequence (Moore 2009). For example, the use of a table of random numbers is considered to be an adequate method of sequence generation whereas using case record numbers is considered to be an inadequate method (Higgins and Green 2011). All RCTs report that randomisation was done using a table/list of random numbers or a computer random number generator. Only Mueller et al. (1989) and Zimny et al. (2002) did not specify the method used for randomisation. Sequence generation prevents the occurrence of selection bias allowing balanced intervention groups and assuring that participants with the same characteristics receive each intervention (Higgins and Green 2011). This way the researchers of the study do not know which participants were attributed to which group preventing them from choosing a participant with particular characteristics, such as a smaller ulcer, that with a particular device could enhance its properties and result in better outcomes from that device.
5.3.4. Allocation Concealment

Allocation concealment is another method to prevent selection bias. With this method researchers will not know how the randomisation sequence was generated (Moore 2009) and will not be able to alter it, to benefit a particular intervention. Allocation concealment will prevent results from having a weight that can be attributed, not to the interventions being studied, but to the changes that could have been made in the allocation of participants (Higgins and Green 2011). In the studies reviewed allocation concealment was done in the study by Van de Weg *et al.* (2008) through opaque sealed envelopes. In the study by Armstrong *et al.* (2005) allocation was provided to the treating clinician by a single study coordinator via telephone. This creates a risk of selection bias (Higgins and Green 2011), as both the clinician and a study coordinator are aware of the participants’ allocation and, although this was done via telephone there is no guarantee that changes were made to the allocation.

5.3.5. Blinding

Blinding will ensure that the allocation is not known for the participants, the healthcare professionals, the outcome assessors, and also data analysts and manuscript writers (Moore 2009, Higgins and Green 2011). The lack of blinding can magnify the estimate effect of the interventions under investigation thus, magnifying the effect of the results obtained (Higgins and Green 2011). Inadequate blinding can create performance bias, or detection bias (Higgins and Green 2011). In the studies reviewed only Van de Weg *et al.* (2008) address the impossibility of blinding the participants of each group to the devices being used. This is due to the fact that TCC and other devices cannot be masked and the participants are able to see its application. Although, blinding would be impractical in all the studies reviewed, it is important that researchers acknowledge this
fact and give some rational regarding any risk of bias that can arise. Even though, in some cases, blinding is not always achievable because of obvious differences of the interventions in each group (Moore 2009) it is important to consider how knowing the intervention can impact on behavioural outcomes (Higgins and Green 2011).

In relation to blinding of outcome assessment, in the studies reviewed only Van de Weg et al. (2008) acknowledge that the researchers were not involved in the treatment/interventions studied. The study by Mueller et al. (1989), Katz et al. (2005), Piaggesi et al. (2007) and Faglia et al. (2010) report that other professionals such as certified cast technicians were involved in the fabrication of the casts, however it is not clearly stated that researchers were not involved in the treatment, cast application and/or ulcer care. No study addressed the risk of detection bias in its discussion.

5.3.6. Outcome Assessment

5.3.6.1. Incomplete Outcome Data
Incomplete outcome data is related to missing data due to dropouts, such as losses to follow-up (Moore 2009, Higgins and Green 2011), this can create biased effect estimates, possibly compromising the true value of the results obtained. Linked to incomplete outcome data, is intention-to-treat analysis (ITT). ITT allows for low bias occurrence when estimating the intervention effects in RCTs (Higgins and Green 2011) as all the participants are analysed in the groups where they were originally assigned (Moore 2009). In the studies reviewed only three (Caravaggi et al. 2000, Zimny et al. 2003, Piaggesi et al. 2007) did not report any dropouts. From the remaining six studies only one (Armstrong et al. 2005) reported the inclusion of dropouts in the ITT. The remaining studies report dropouts but do not include them in the ITT, except for one
cross-over participant, in Van de Weg *et al.* (2008), who was analysed in the original group they were allocated to. The studies where dropouts were not included in the ITT may be at risk of attrition bias that could alter the true estimate effect of the intervention and thus the results obtained, which in turn will limit its application to practice. Additionally, studies should have given more insight into how they dealt with missing data and how this might have affected results.

### 5.3.6.2. Selective Outcome Reporting

Selective outcome reporting is related to the deliberate exclusion of data derived from the primary or secondary outcomes of the study (Moore 2009). In this case researchers might decide to report only the significant statistical results obtained, creating a false estimate of the effect of the intervention (Moore 2009), which will further weaken a possible generalisation of the results to the wider population. In all the studies reviewed data were reported relating to primary and secondary outcomes.

### 5.3.7. Heterogeneity of Studies

Heterogeneity is related to the variability among studies that are included in a SR (Higgins and Green *et al.* 2011). This variability can be related to study design, participants, interventions and outcomes (Higgins and Green *et al.* 2011). From the studies included in this SR, heterogeneity is present in terms of study design, and in terms of interventions under investigation, as all studies compared different devices to ascertain the efficacy of offloading for the treatment of DFUs. Relating to participants, their demographic profile was similar across studies. In relation to outcomes, this varied amongst studies although the majority include healing rates, healing times and reduction
in ulcer size as primary outcomes. The results that arise from this comparability cannot be combined because all studies used different devices, making it impossible to conduct meta-analysis. Taking into account that the studies are not homogenous combining them would bring meaningless results and thus rendering any conclusions and recommendations unfit for EBP.

5.4. Discussion on Outcomes of this SR

5.4.1. Primary Outcomes

The primary outcomes of this SR were healing rates, healing times and reduction in ulcer size. From the analysis of the results obtained it is possible to say that offloading is effective for the treatment of DFUs. However, it is necessary to highlight that in the studies all participants had neuropathy alone, and only the study by Nabuurs-Franssen et al. (2005) also included participants with PVD. Nonetheless, due to the fact that offloading devices are sometimes irremovable and stay in place for periods of at least one week, patients with impaired circulation should be continuously monitored when and if using offloading (Leung 2007).

In the studies included, devices differed from self-applied, such as therapeutic shoes, to TCCs where trained technicians are needed for cast application. Furthermore, devices also varied in terms of removability where TCC and iTCC are known as irremovable whereas a half-shoe is removable. Additionally, dressings and felted foam were also used, and are considered offloading devices as they allow for pressure relief in the ulcerated area however they should be used in combination with a therapeutic shoe (Edmonds et al. 2008). In three studies (Mueller et al. 1989, Birke et al. 2002, Zimny et
al. 2003) devices were used in combination with therapeutic shoes, which could act as a confounding factor, so the outcomes of these devices, in the mentioned studies, cannot be attributed to the device alone.

From all the devices analysed TCCs have better outcomes in terms of ulcer healing, followed by the iTCC and RCWs. The higher efficacy of the TCC and iTCC is due to the fact that both devices are irremovable enforcing compliance, not only in terms of device use but also in clinic follow-up (Armstrong et al. 2001, Edmonds et al. 2008).

It is important to emphasise that offloading is cornerstone for DFU healing regardless of the device used, as long as one is appropriately used (Bakker et al. 2012). Nonetheless, it is necessary to highlight that casts are, of all, the best devices and should be used as a first choice, because of their higher healing rates (Bakker et al. 2012). Other devices such as therapeutic shoes, accommodative dressings or modified insoles, should be used as a second line intervention when the ulcer is healed and pressure relief is necessary to prevent recurrence or, they may be used as a way to prevent ulcers in diabetic patients where neuropathy has been diagnosed (Cavanagh et al. 2000, Boulton 2004a, Cavanagh et al. 2005, Leung 2007).

5.3.2. Secondary Outcomes

5.3.2.1. Adverse Effects

Offloading is an important treatment strategy (Boulton 2004b), however depending on the device used adverse effects might develop. The most common adverse effects
mentioned in the literature are the development of new ulcers, oedema, infection and maceration (Boulton 2004a, Boulton 2004b, Cavanagh et al. 2005).

From the analysis of the adverse effects reported in the studies included for this SR, infection and maceration where the most common adverse effects observed (Mueller et al. 1989, Zimny et al. 2003, Armstrong et al. 2005, Katz et al. 2005, Nabuurs-Franssen et al. 2005, Piaggesi et al. 2007, Van de Weg et al. 2008, Faglia et al. 2010). These adverse effects occurred equally among the devices studied. Taking into account that, exudate might have been present, that casts could have been too tight and rubbed against the limb and due to the fact that participants were followed on a weekly basis, unless any discomfort symptoms became unbearable, this could have influenced the development of infection and maceration (Caravaggi et al. 2000, Jeffcoate and Harding 2003, Edmonds et al. 2008). However, it is interesting to see that no SSD was found between devices in terms of adverse effects and all devices actually caused an adverse effect. Nonetheless, it is important to reduce the occurrence of adverse effects, particularly infection because if left unnoticed or improperly treated it could aggravate and result in limb amputation (Svensson et al. 2011, Schaper et al. 2012). One action that could decrease adverse effect rates is a more regular follow-up (Mueller et al. 1989). Although, adverse effects are an issue of concern they should not be a reason to discontinue offloading, as this is key in the treatment of DFUs, a strategy that could be used is to change to a different device from the one the patient is currently using or doing modifications to the device being used (Dumont et al. 2009).
**5.4.2.2. Cost**

In a period of challenging economic background, the reduction of health resources is a reality and policymakers and managers look for more cost-effective practices that can accompany the current economic climate (DoHC 2012). It is important to highlight that the expenditure with health services is expected to be reduced by €1.1 billion (DoHC 2012) which will greatly affect the care delivered and will therefore, affect the patient. Placing this reality into context, it is clear that the most cost-effective offloading device is going to be the primary choice for the treatment of DFUs because, resources are scarce in today’s economic climate and because policy makers need to measure and compare the cost of a treatment with the consequences it brings (Drummond et al. 2005).

From the studies included and, where cost analysis was undertaken, TCCs are the most costly devices not only due to fact that materials cannot be reused, but also because they need to be applied by qualified professionals, which adds extra cost to the treatment (Katz et al. 2005, Piaggesi et al. 2007, Faglia et al. 2010). However, one may argue that although, TCCs are more expensive they have proven to have better healing rates than RCWs (Caravaggi et al. 2000, Armstrong et al. 2005, Katz et al. 2005, Piaggesi et al. 2007, Faglia et al. 2010). Therefore, if ulcers heal better and faster when TCCs are used, this means that the consequences of the treatment (shorter healing time and high healing rates) overcome the costs (Drummond et al. 2005), making the TCC more cost-effective. Another, discussion point is the fact that, it is becoming current practice to use RCWs and rendering them irremovable through the application of fiberglass cast material, these become iTCCs and because the cast is re-usable, the cost decreases (Katz et al. 2005). Nevertheless, if devices are used based only on their cost, in the scenario where a patient is having his device continuously changed because ulcer healing is not
being achieved the cost will undoubtedly increase, whereas if a TCC or even a iTCC are
used in the first place real savings might be achieved and most importantly ulcer healing
will occur.

5.4.2.3. Compliance

Individuals behave in a way that allows them to detect and prevent any health issues and
reach maximum well-being (Conner and Norman 2005). Compliance with therapeutic
regimens is a health behaviour that can affect patients’ health (Conner and Norman
2005). Compliance describes patients’ behaviours in relation to prescribed regimens,
which are seen by healthcare professionals as paramount for patients to be healthy
(German 1988, Murphy and Canales 2001). Compliance is the extent to which patients’
behaviours follow medical advice (Murphy and Canales 2001). However this definition
puts the patient in a spectator position disregarding the way these regimens may affect
their lives and bringing paternalism back to healthcare services (German 1988, Murphy
and Canales 2001).

Offloading is a regimen that aims at helping patients to achieve well-being by healing
DFUs. However, if patients do not see that offloading is improving their well-being and
health, because of mobility restrictions and discomfort using the device (Brod 1998,
Armstrong et al. 2001) they will behave in a way to avoid the treatment and will be seen
by healthcare providers as noncompliant (German 1988, Murphy and Canales 2001). To
overcome this negative connotation it is important that nurses understand how
offloading affects patients’ lives and if they have the necessary environmental and
psychological support to deal with the difficulties inherent to offloading (German 1988,
Murphy and Canales 2001). Furthermore, in collaboration with the patient and family,
nurses need to give a clear explanation on how offloading might help patients restore
their health and well-being, so that patients perceive themselves as part of the process of decision making and that there is a joint responsibility in this process (German 1988, Murphy and Canales 2001).

From the included studies, only three analysed compliance in terms of device acceptance (Caravaggi et al. 2000, Piaggesi et al. 2007, Dumont et al. 2009).

5.4.2.4. QoL

QoL is the way individuals see and assess the impact that their physical, psychological, social, and economic well-being has in their life, and it is dependent on the way each domain influences each other (WHO 1997). Currently research is mainly focused in treatment efficacy and cost-effectiveness (Moore 2009). However, it is important to understand patient’s experience of the treatment (Moore 2009), in this case offloading and also the impact that DFUs have in their life, in order to develop a better and more focused delivery of care.

QoL issues were not addressed in any of the studies reviewed. According to other qualitative studies (Brod 1998, Vileikyte 2001, Vileikyte et al. 2004) DFUs affect patients QoL mainly in terms of mobility, which further impacts patients’ daily activities. Therefore, from the lack of results it is possible to recommend that future studies include QoL assessment for a better understanding of the impact that DFUs and offloading devices have on patient’s life. Additionally, one may deduce that if offloading and DFUs affect QoL this might influence compliance rates, thus affecting treatment outcomes, however, research is need to support this.
5.5. Summary and Conclusion

In terms of the methodological issues in the studies included, these were mainly related with risk of bias. In relation to outcome measures analysed in this SR it is possible to conclude that offloading is an effective method for the treatment of DFUs. From the devices available TCCs seem to be the most effective in terms of healing rates, times and reduction in ulcer size, closely followed by iTCCs and RCWs. However, these can cause adverse effects mainly infection and maceration. Moreover, although devices, especially TCCs, seem to be costly for the current economic climate, in the long term, due to their high efficacy, costs might be reduced as more ulcers are healed in a shorter period of time. Besides cost issues, compliance and QoL are two variables also important for offloading to be acceptable for patients. However, these were rarely alluded to in the studies. Thus, more research relating to cost analysis, compliance and QoL is needed.

5.6. Strengths and Limitations of this SR

This SR followed and reported on all the steps necessary to conduct a SR as highlighted in appendix 57. Furthermore, it thoroughly reported on the search strategy implemented so that it can be replicated. However, in its search strategy, this SR focused on studies in English and/or Portuguese as these were the only languages known by the writer. This can be identified as language bias, because other important studies written in other languages could have been included and may have brought new information or evidence to the current body of knowledge around offloading for the treatment of DFUs. However, the writer did not have financial support for conducting this SR, which, if available, could have been used for the translation of research studies in other
languages. Another limitation of this SR is the fact that it was not possible to conduct meta-analysis as the RCTs retrieved were too disparate.

5.7. Contributions of this SR

This SR had the objective of identifying the most effective offloading device in the treatment of DFUs, identifying the strengths and limitations of the different offloading devices in the studies reviewed and to determine the impact that offloading devices have in the patient QoL. From what has been reviewed it is possible to say that TCC is the most effective offloading device in terms of percentage of ulcers healed and time to heal. However, other offloading devices like iTCCs and RCWs are also effective in the treatment of DFUs. This is corroborated by the IWGDF guidelines (2012) that recommend the use of TCCs and other casts for the treatment of DFUs. Nonetheless, they add that the use of these casts should be done when ulcers are present in the plantar aspect of the foot. In the studies reviewed the majority of the ulcers were plantar.

Although this SR has not unearthed new evidence relating to offloading for the treatment of DFUs, it has showed and confirmed that casting is the first line of choice for the treatment of DFUs; that other devices such as therapeutic shoes, orthoses and felted foam are also of value, but might be more effective as a prevention measure. Furthermore, this SR showed that few RCTs and SRs of RCTs have been conducted to analyse and compare the effectiveness of offloading devices for the treatment of DFUs. Moreover, studies need to address other factors such as cost, compliance and QoL. These factors are of importance not only for clinical practice and management, but also for patients.
Research is fundamental for health and social gain so that a better understanding of the factors that influence changes in social structures that in turn will promote healthier environments for the population, is gained (DoHC 2003). DFUs as a consequence of diabetes are a health problem that hinders peoples’ health, QoL, social activity and financial stability. Through this SR, it is apparent that offloading as a treatment strategy needs to be put into practice. Nurses need to be aware of best practice in terms of the treatment of DFUs, so that they can refer their patients to specialist services which in turn will provide patients with best clinical practice. Further, it is important that on referral, such modalities are available for the management of DFUs. If best practice is implemented then patients can expect that all negative factors derived from DFUs that might impact on their life will be addressed, thus promoting better life conditions allowing patients to have a healthier and enhanced QoL.
Chapter 6. Summary and Conclusion of this SR

6.1. Introduction

This chapter will present an overall summary and conclusion of this SR.

6.2. Summary and Conclusion

Diabetes is a chronic disease, its prevalence in the Irish population is around 6% and it is growing (IDF 2012b). As the number of people suffering from diabetes increases the incidence of its complications also increase (IDF 2012a, WHO 2012). Diabetes causes tissue damage in the small and large blood vessels that with time can develop into PVD, neuropathy and other complications (IDF 2012a, WHO 2012). Neuropathy and PVD play a primary role in the development of DFUs, another complication of diabetes (Laing 1998, Reiber et al. 1998, Boulton 2004b, Cavanagh et al. 2005). Neuropathy is characterised by nerve damage causing loss of protective sensation in the foot, whilst PVD leads to an impaired blood supply of the foot (Laing 1998, Boulton 2004a, Bakker et al. 2012). These two risk factors, in combination with trauma, foot deformities, callus, oedema, inappropriate footwear or pressure will contribute to skin breakdown and the progression of a small wound to a wider and deeper ulcer (Reiber et al. 1998, Boulton 2004b, Lavery et al. 2008). Although these factors are all important, pressure is a factor always present and will promote the development or maintenance of DFUs (van Deursen 2004). Pressure results in the mechanical loading of the foot in its entire surface, though this pressure concentrates more in the plantar aspect of the foot (van Deursen 2004). Therefore, offloading is a treatment intervention that will promote the redistribution of pressure in the feet. To achieve this various offloading devices can be used from orthoses, therapeutic shoes and casts. From these TCC appears in the literature as the “gold standard” for the treatment of DFUs (Boulton 2004a).
In order to analyse the efficacy of offloading devices for the treatment of DFUs and determine which device has better outcomes, a SR was conducted. This method was chosen because it is at the top of the hierarchy of evidence, as SRs summarise, analyse, interpret and report the results of a group of research in the same topic, either from qualitative or quantitative research (Cook et al. 1997, Mulrow et al. 1997, Watson et al. 2008, McGowan 2012). This type of research is key as it will allow nurses to access best evidence information that can not only allow for EBP, but also for evidence based clinical decisions that are crucial for the quality of nursing care (Sackett et al. 1996, ABA 2007, Holland and Watson 2012).

From the analysis of the studies retrieved for this SR it is evident that TCC is the best offloading device for the treatment of DFUs, followed by iTCCs and RCWs. It was not possible to conduct meta-analysis of the nine RCTs retrieved, because their methods and interventions were not similar. The results of the SR will inform clinical practice providing nurses with the evidence to develop guidelines and awareness through educational practices in their clinical area. Through this diabetic patients, in any service, that are identified as having a DFU can be promptly referred to a specialist nurse and offloading can be initiated to help in the treatment and management of DFUs. Furthermore, although this SR has not unearthed new information, it gives a clear insight into the need of conducting RCTs that address the risk of bias with more care, as this can hinder the quality of the study and consequently the results (Higgins and Green 2011).

It is already well established that offloading is an important strategy for the treatment of DFUs however it is necessary to develop more research around the impact that this
method has on health related QoL and compliance. These two domains will influence the impact of offloading in the treatment of DFUs (Armstrong et al. 2003). Further, such research can help to understand how patients view this treatment which could, in turn, allow for the development of new devices that will consider and address the restrictions that the current devices impose on patients.
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Appendices
Appendix 1: Offloading Devices
Casts:

- **Total Contact Casts (TCC)** is a close fitting cast applied over minimal padding. Its advantages are redistribution of pressure, enforcing compliance, reducing oedema, and allowing for faster healing times. Some of its disadvantages are: it cannot be removed preventing a daily ulcer check, it reduces mobility, iatrogenic lesions are difficult to detect, it may lead to muscle wasting and weakness due to prolonged immobilisation.

- **Scotchcast Boot** can be used for neuroischaemic ulcers and is effective in reducing pressure on the plantar surface and margins of the foot.

- **Removable Cast Walkers (RCW)** like the Aircast is a device with two halves that are joined together with strapping, and it has air chambers that can be inflated to allow a comfortable fit. This cast allows for foot inspection, it is an immediate offloading device and can be reused. In terms of disadvantages they cannot accommodate severe deformity and it is easy to remove making compliance a challenge.


Therapeutic Shoes:

- **Dressing Shoes**: can accommodate feet that need large dressings

- **Weight Relief Shoes**:
  - **Orthowedge**: is a shoe that allows offloading from metatarsal heads and toes, with a rocker-bottom wedge;
  - **Forefoot-Relief**: is a shoe that redistributes weight from the forefoot to the hindfoot and has a semi-rigid heel to provide stability;
- **Heel Relief Shoe**: is a shoe that offloads the posterior end of the foot, and transfers weight from the heel to the midfoot and forefoot;

- **Half Shoe**: is a shoe were its front is cut to allow pressure relief on the forefoot and the posterior area of the sole is also cut for pressure relief of the hindfoot.


**Orthoses:**

- **Special made Insoles**: are used in therapeutic shoes or in conventional footwear that besides cushioning also redistribute pressure and can be made of cork and other materials;

- **Patellar tendon weight-relieving Orthoses**: is a patellar tibial brace where total offloading is possible while maintaining a moderate degree of mobility;

- **Ankle-Foot Orthoses**: is a device that stabilises the foot and ankle.


**Felt Padding or Felted Foam**: are used to relief pressure from ulcers and can be lifted for ulcer examination however, they do not substitute therapeutic footwear and should not cover a large area that could prevent complications from being noticed (Edmonds *et al* 2008: 85-95, Spencer 2008).
Appendix 2: Search Strategy in CINAHL database
CINAHL SEARCH

MeSH Diabetic Foot AND (MeSH Orthoses+ OR MeSH Foot Orthoses)

171

Limits: Research Article and Language – English/Portuguese

MeSH Diabetic Foot AND MeSH Casts

147

MeSH Diabetic Foot AND MeSH Shoes+

337

Titles of all articles were read

46

44

89

From a total of 55 articles 43 will be considered

15

24

16

From the 43 articles, 24 were also found in the other searched data bases
Appendix 3: Search Strategy in MEDLINE database
MEDLINE SEARCH

MeSH Diabetic Foot
AND
(MeSH Orthotic Devices+ OR MeSH Foot Orthoses)

Limits: Language – English/Portuguese

116

MeSH Diabetic Foot
AND
MeSH Casts, Surgical

110

MeSH Diabetic Foot
AND
MeSH Shoes+

351

Limits: Language – English/Portuguese

293

Limits: CCT, Meta-Analysis, RCT,
Language – English/Portuguese

35

Titles of all articles were read

28

26

15

From a total of 69 articles 57 will be considered

From the 57 articles, 33 were also found in the other searched data bases
Appendix 4: Search Strategy in EMBASE database
EMBASE SEARCH

MeSH Diabetic Foot+ AND (MeSH Orthosis+ OR MeSH Foot Orthosis+)

164

MeSH Diabetic Foot+ AND MeSH Plaster Cast+

111

MeSH Diabetic Foot+ AND MeSH Shoes+

509

Limits: Research Article

84

62

48

Limits: CCT, RCT, Prospective Study and Retrospective Study

Titles of all articles were read

8

10

8

From a total of 26 articles 23 will be considered

From the 23 articles, 20 were also found in the other searched data bases
Appendix 5: Search Strategy in COCHRANE LIBRARY database
COCHRANE LIBRARY SEARCH

MeSH Diabetic Foot+ AND *MeSH Orthotic Devices+
13

MeSH Diabetic Foot+ AND MeSH Casts, Surgical+
17

MeSH Diabetic Foot+ AND MeSH Shoes+
42

Titles of all articles were read

7
12
14

From a total of 33 articles 19 will be considered

From the 19 articles, 18 were also found in the other searched data bases
Appendix 6: Search Strategy in WEB OF KNOWLEDGE database
WEB OF KNOWLEDGE SEARCH

MeSH Diabetic Foot AND (MeSH Orthoses OR MeSH Foot Orthoses)

50

MeSH Diabetic Foot AND MeSH Casts

64

MeSH Diabetic Foot AND MeSH Shoes

312

Limits: Research Article and Language – English/Portuguese

42

54

242

Titles of all articles were read

2

16

16

From a total of 34 articles 31 will be considered

From the 31 articles, 21 were also found in the other searched data bases
Appendix 7: Data Extraction Table
# Data Extraction Table

<table>
<thead>
<tr>
<th>Author and Date of Study</th>
<th>Title</th>
<th>Source</th>
<th>Study Geographical Location</th>
<th>Research Question/Aim/Objective</th>
<th>Care Setting</th>
<th>Type and Characteristics of Wound</th>
<th>Inclusion/Exclusion Criteria</th>
<th>Sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Characteristics</td>
<td>Design Details</td>
<td>Study Type</td>
<td>Allocation</td>
<td>Intervention Details</td>
<td>Outcome Measures</td>
<td>Analysis</td>
<td>Results</td>
<td>Conclusions/Recommendations</td>
</tr>
</tbody>
</table>

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157
Appendix 8: Data Extraction Table for Included Systematic Reviews
## Data Extraction Table for Included Systematic Reviews

<table>
<thead>
<tr>
<th>Review Author</th>
<th>Data Assessed as up to date</th>
<th>Title</th>
<th>Source</th>
<th>Geographical Location</th>
<th>Population</th>
<th>Intervention and Comparison Interventions</th>
<th>Outcomes for which Data was Reported</th>
</tr>
</thead>
<tbody>
<tr>
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</tbody>
</table>
Appendix 9: EBL Critical Appraisal Checklist
<table>
<thead>
<tr>
<th>EBL Critical Appraisal Checklist</th>
<th>Yes (Y)</th>
<th>No (N)</th>
<th>Unclear (U)</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Section A: Population</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Is the study population representative of all users, actual and eligible, who might be included in the study?</td>
<td></td>
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</tr>
<tr>
<td>Are inclusion and exclusion criteria definitively outlined?</td>
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<tr>
<td>Is the sample size large enough for sufficiently precise estimates?</td>
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<tr>
<td>Is the response rate large enough for sufficiently precise estimates?</td>
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<tr>
<td>Is the choice of population bias-free?</td>
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<tr>
<td>If a comparative study:</td>
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<tr>
<td>Were participants randomized into groups?</td>
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<tr>
<td>Were the groups comparable at baseline?</td>
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<tr>
<td>If groups were not comparable at baseline, was incompatibility addressed by the authors in the analysis?</td>
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<tr>
<td>Was informed consent obtained?</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Section B: Data Collection</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Are data collection methods clearly described?</td>
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<tr>
<td>If a face-to-face survey, were inter-observer and intra-observer variances discussed?</td>
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<tr>
<td>Is the data collection instrument validated?</td>
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<tr>
<td>If based on regularly collected statistics, are the statistics free from subjectivity?</td>
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<tr>
<td>Does the study measure the outcome at the time appropriate for capturing the intervention's effect?</td>
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<tr>
<td>Is the instrument included in the publication?</td>
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<tr>
<td>Are questions posed clearly enough to be able to elicit precise answers?</td>
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<tr>
<td>Were those involved in data collection not involved in delivering a service to the target population?</td>
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<tr>
<td><strong>Section C: Study Design</strong></td>
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<tr>
<td>Is the study type/methodology utilized appropriate?</td>
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<tr>
<td>Is there face validity?</td>
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<tr>
<td>Is the research methodology clearly stated at a level of detail that would allow its replication?</td>
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<tr>
<td>Was ethics approval obtained?</td>
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<tr>
<td>Are the outcomes clearly stated and discussed in relation to the data collection?</td>
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<tr>
<td><strong>Section D: Results</strong></td>
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<tr>
<td>Are all the results clearly outlined?</td>
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<tr>
<td>Are confounding variables accounted for?</td>
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<tr>
<td>Do the conclusions accurately reflect the analysis?</td>
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<tr>
<td>Is subset analysis a minor, rather than a major, focus of the article?</td>
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<tr>
<td>Are suggestions provided for further areas to research?</td>
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<td></td>
</tr>
<tr>
<td>Is there external validity?</td>
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</tr>
</tbody>
</table>

**Calculation for section validity:** \((Y+N+U=T)\)

- If \(Y/T < 75\%) or if \(N4+U/T > 25\%\) then you can safely conclude that the section identifies significant omissions and that the study’s validity is questionable. It is important to look at the overall validity as well as section validity.

- **Section A validity calculation:**
- **Section B validity calculation:**
- **Section C validity calculation:**
- **Section D validity calculation:**

**Calculation for overall validity:** \((Y+N+U+T)\)

- If \(Y/T ≥ 75\%) or if \(N4+U/T ≤ 25\%\) then you can safely conclude that the study is valid.

**Overall validity calculation:**

---

EBLIP Critical Appraisal Checklist
Lindsay Giynn, MLIS
Memorial University of Newfoundland
lgiynn@mun.ca

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Appendix 10: Quality Appraisal of Systematic Reviews
<table>
<thead>
<tr>
<th>Steps for Conducting Systematic Reviews</th>
<th>Systematic Review</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (Y)</td>
</tr>
<tr>
<td>Background</td>
<td></td>
</tr>
<tr>
<td>Research Question</td>
<td></td>
</tr>
<tr>
<td>Aim</td>
<td></td>
</tr>
<tr>
<td>Objectives</td>
<td></td>
</tr>
<tr>
<td>Criteria for selecting studies for review:</td>
<td></td>
</tr>
<tr>
<td>Types of studies</td>
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<tr>
<td>Types of participants</td>
<td></td>
</tr>
<tr>
<td>Types of interventions</td>
<td></td>
</tr>
<tr>
<td>Types of outcome measures</td>
<td></td>
</tr>
<tr>
<td>Search methods for identification of studies</td>
<td></td>
</tr>
<tr>
<td>Data collection</td>
<td></td>
</tr>
<tr>
<td>Data analysis</td>
<td></td>
</tr>
<tr>
<td>Results:</td>
<td></td>
</tr>
<tr>
<td>Description of studies</td>
<td></td>
</tr>
<tr>
<td>Risk of bias in included studies</td>
<td></td>
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<tr>
<td>Effects of interventions</td>
<td></td>
</tr>
<tr>
<td>Discussion</td>
<td></td>
</tr>
</tbody>
</table>
Appendix 11: Table of Included Studies
<table>
<thead>
<tr>
<th>Study</th>
<th>Title</th>
</tr>
</thead>
</table>
Appendix 12: Table of Excluded Studies with reasons
<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Holstein et al (1976)</td>
<td>No clearly stated objectives, outcome measures and statistical analysis.</td>
</tr>
<tr>
<td>Laing et al (1991)</td>
<td>From a sample of 46 patients, 10 had other disorders than diabetes.</td>
</tr>
<tr>
<td>Myerson et al (1992)</td>
<td>Neuropathic ulcers due to other causes (alcoholism, hereditary motor and sensory neuropathy and pathological conditions involving the spinal cord.</td>
</tr>
</tbody>
</table>
Appendix 13: Data Extraction Table Armstrong et al. 2001
<table>
<thead>
<tr>
<th>Author and Date of Study</th>
<th>Title</th>
<th>Source</th>
<th>Study Geographical Location</th>
<th>Research Question/Aim/Objective</th>
<th>Care Setting</th>
<th>Type and Characteristics of Wound</th>
<th>Inclusion/Exclusion Criteria</th>
<th>Sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Armstrong <em>et al.</em> 2001</td>
<td>Off-loading the diabetic foot wound: a randomized clinical trial</td>
<td>Diabetes Care USA</td>
<td></td>
<td>Compare the effectiveness of TCC, RCW and half-shoes to heal neuropathic foot ulcers</td>
<td>Health Care Setting not clearly mentioned</td>
<td>Neuropathic foot ulcers</td>
<td><strong>Inclusion:</strong> Loss of protective sensation (&gt;25V), at least one palpable foot pulse, TcPO2 &gt;40mmHg, neuropathic DFU grade 1A (UTDFWCS), when there was more than one plantar ulcer present only the largest was used for inclusion</td>
<td>63 diabetic patients</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>All patients: Mean ulcer size (cm²) 1.3; mean ulcer duration (months) 5.2;</td>
<td></td>
<td></td>
<td><strong>Exclusion:</strong> Active infection, unable to walk without wheelchair assistance, wounds on the heel, rear foot, or other area than the plantar aspect of the foot, severe</td>
<td></td>
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<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>TCC: 19</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>RWC: 20</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Half-shoe: 24</td>
<td></td>
</tr>
</tbody>
</table>
### Patient Characteristics

**All patients:**
- Male 82.5%;
- Duration of diabetes (years) 16.9;
- TcPO$_2$ 60.4; vibration perception threshold (Volts) 44.6

### Design Details

- Three-arm prospective RCT

**Randomisation Sequence:** subjects were randomised through a computerised randomisation schedule, and this was performed after initial screening.

### Study Type

Quantitative

### Allocation

Blinding and concealment of allocation not mentioned

19 subjects used TCC
20 subjects used RCW
24 subjects used half-shoes

Subjects followed on a weekly basis for device inspection, wound care and debridement

Ulcers were measured using computerized planimetric video wound system

Subjects wore a pedometer that was calibrated at beginning of study and number

### Intervention Details

Primary outcome measures were proportion of complete wound healing at 12 weeks and activity.

### Outcome Measures

- An analysis of variance with Tamhane’s post-hoc test for multiple comparisons was used to evaluate all continuous variables between off-loading groups. The effect of continuous variables on healing in general was evaluated using a Mann-Whitney U test. Dichotomous variables were evaluated with a $X^2$-test with odds ratio and 95% CI.

### Analysis

- To evaluate the
- Proportion of healing was 89.5% with TCC, 65% with RCW and 58.3% with half-shoes
- At 12 weeks the proportion of healing was significantly higher in the TCC group
- The mean time for healing within the 12 weeks period was significantly shorter in the TCC group compared with the half-shoes group, but not with the RCW group
- Subjects in the TCC group were significantly less active than those in the half-shoes group
- There was no

### Results

- Conclusion
  The study concludes that TCC heal a higher proportion of wounds in a shorter amount of time based on the results obtained. Moreover, the results show that patients are less active when using TCC than with the other devices.

### Conclusions/Recommendations

- Recommendation
  More work in this area is needed to assess various treatments and to provide clinicians with evidence to make informed treatment decisions.
of steps was recorded at each visit

healing characteristics of each device as a function of weeks of therapy and mean time to closure among patients healing within the 12-week study period, a Kaplan-Meier life-table analysis (log-rank test) was used.

Using the above analyses, a difference of 40% between any two arms could be detected with a sample size of 60 yielding a power exceeding 80%. For all analyses a $\alpha$ of 0.05 was used.

significant difference in activity levels between the RCW and TCC group or between the RCW and the half-shoe group

- No falls or cast/device related ulceration was reported during the study
Appendix 14: Data Extraction Table Armstrong et al 2005
<table>
<thead>
<tr>
<th>Author and Date of Study</th>
<th>Title</th>
<th>Source</th>
<th>Study Geographical Location</th>
<th>Research Question/Aim/Objective</th>
<th>Care Setting</th>
<th>Type and Characteristics of Wound</th>
<th>Inclusion/Exclusion Criteria</th>
<th>Sample size</th>
</tr>
</thead>
</table>
| Armstrong et al 2005     | Evaluation of removable and irremovable cast walkers in the healing of diabetic foot wounds: a randomized controlled trial | Diabetes Care | USA | Evaluate efficacy of a traditional RCW and iTCC to heal neuropathic foot ulcers | Health Care Setting not clearly mentioned | Neuropathic foot ulceration | **Inclusion:** loss of protective sensation, at least one palpable foot pulse, neuropathic plantar foot ulcer University Texas stage IA, when there was more than one plantar ulcer present only the largest was used for inclusion | **Exclusion:** Active infection, unable to walk without a wheelchair, with wound in locations on the heel, rearfoot, or other than the plantar aspect of the foot, with severe peripheral vascular disease | 50 diabetic patients | iTCC: 23  
RCW: 27 |
<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Design Details</th>
<th>Study Type</th>
<th>Allocation</th>
<th>Intervention Details</th>
<th>Outcome Measures</th>
<th>Analysis</th>
<th>Results</th>
<th>Conclusions/Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients: mean age (years) 65.6; male 88%; BMI 33.4; vibration perception threshold (volts) 37.1; HbA1c 8.2%.</td>
<td>Two-arm RCT</td>
<td>Quantitative</td>
<td>Blinding and concealment of allocation not mentioned.</td>
<td>23 subjects were assigned the iTCC</td>
<td>No clear mention of primary or secondary outcomes.</td>
<td>The influence of the effect of continuous variables on healing in general, were evaluated with a Mann-Whitney U test. Dichotomous variables were evaluated with an $X^2$ test with odds ratio (OR) and 95% CI. To evaluate the healing characteristics of each device as a function of weeks of therapy and mean time to closure among patients healing within the 12-week study period, we used a Kaplan-Meier life table analysis (log-rank test). With the above analyses, a difference of 40% between groups could be seen.</td>
<td>• From the 50 subjects, 4 did not complete the course of study and were considered treatment failures in the intention-to-treat analysis • Higher proportion of subjects healed at 12 weeks in the iTCC group 82.6%/19 compared with 51.9%/14 in the RCW group • The subjects whose ulcers healed during the study period, those in the iTCC group healed sooner 41.6 ±18.7 days compared with the RCW, 58.0±15.2 days • No falls and no re-ulcerations related to the casts • More subjects in the iTCC group presented with at least one episode of peri-wound maceration than</td>
<td>Conclusion: The application of a wrap around a traditional RCW, improves both the proportion and rate of wound healing by preventing patients from removing the device.</td>
</tr>
</tbody>
</table>
detected with a sample size of 18 per group, yielding a power exceeding 80%. For all analyses, we used an α value of 0.05. those of the RCW group
Appendix 15: Data Extraction Table Birke et al 2002
<table>
<thead>
<tr>
<th>Author and Date of Study</th>
<th>Title</th>
<th>Source</th>
<th>Study Geographical Location</th>
<th>Research Question/Aim/Objective</th>
<th>Care Setting</th>
<th>Type and Characteristics of Wound</th>
<th>Inclusion/Exclusion Criteria</th>
<th>Sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birke et al 2002</td>
<td>Comparison of forefoot ulcer healing using alternative off-loading methods in patients with diabetes mellitus</td>
<td>Advances in Skin and Wound Care</td>
<td>USA</td>
<td>Compare the healing rate of forefoot ulcers in patients with diabetes treated using a total contact cast with those treated using alternative offloading methods.</td>
<td>Louisiana State University Health Sciences Centre Diabetes Foot Program</td>
<td>Diabetic forefoot ulcers</td>
<td>Exclusion: Patients with postoperative wounds, recurrent ulceration, non-plantar, midfoot, or rear foot ulcers, wound abscess, osteomyelitis with radiologic evidence of bone destruction and ischemic wounds.</td>
<td>120 patients</td>
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<td></td>
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<td></td>
<td></td>
<td>Accommodative dressing: 26</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Healing shoe: 57</td>
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<td>Walking splint: 18</td>
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<td>TCC: 13</td>
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<td></td>
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<td>Other: 6</td>
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<tr>
<td>Patient Characteristics</td>
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<td>Wagner Grade 1.8; mean length/width/depth (cm) 1.6/1.1/0.5.</td>
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<tr>
<td><strong>TCC</strong>: mean ulcer duration (days) 183.9; mean Wagner Grade 2.2; mean length/width/depth (cm) 1.4/0.9/0.6.</td>
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<tr>
<td><strong>Other</strong>: mean ulcer duration (days) 150.7; mean Wagner Grade 1.8; mean length/width/depth (cm) 1.6/1.0/0.6.</td>
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</tbody>
</table>
Accommodative dressing: female 65%; mean age (years) 57.5.

Healing shoe: female 54%; mean age (years) 58.2.

Walking splint: female 22%; mean age (years) 56.5.

TCC: female 43%; mean age (years) 47.3.

Other: female 67%; mean age (years) 56.8.

Retrospective study. Medical records of 120 patients were retrospectively reviewed.

Patients with diabetic foot ulcers were offloaded with one of the following: accommodative dressing, healing shoe, walking splint, a total contact cast (TCC), or a combination of these methods (other).

Study outcome was ulcer healing time.

Analysis was done using a lognormal regression model where log₁₀(healing time) was used as the dependent variable.

- One hundred and thirteen of 120 (94%) patients with forefoot ulcers healed in an average time of 45.5 ± 43.4 days.
- Seven of 120 (5.8%) patients with ulcers either did not heal or were lost to follow-up.
- Healing time was lower in the accommodative dressing compared with the healing shoe or the walking splint.
- Forefoot ulcers were closed within 12 weeks in at least 81% of the cases, irrespective of offloading.

Conclusion: The healing rate of forefoot ulcerations using alternative off-loading methods or a TCC appeared to be comparable when the method was selected based on location of ulcer, patient age and duration of ulceration.

Recommendation: Further investigation to determine the effect of the accommodative dressing and the surgical shoe in ulcer healing.
Healing shoe: surgical shoe modified with a quarter-inch non-polyethylene foam inlay, a relief cut under the ulcer area, and a half-inch wedged sole.

Moisture retentive dressings, including a hydrogel, saline-moistened gauze, alginate, or hydrocolloid, were applied to all wounds except those receiving the total contact cast and the accommodating dressing.

Dry dressings were used with the total contact cast and the method.
accommodative dressing. Accommodative dressings were changed weekly; total contact casts were changed at 1- to 2-week intervals, depending on the amount of drainage.

Patients who were not treated with the total contact cast were instructed in daily dressing changes and were followed at weekly intervals for re-evaluation and wound debridement.

The specific dressings or topical agents used were not controlled.
Appendix 16: Data Extraction Table Caravaggi et al 2000
# Data Extraction Table

<table>
<thead>
<tr>
<th>Author and Date of Study</th>
<th>Title</th>
<th>Source</th>
<th>Study Geographical Location</th>
<th>Research Question/Aim/Objective</th>
<th>Care Setting</th>
<th>Type and Characteristics of Wound</th>
<th>Inclusion/Exclusion Criteria</th>
<th>Sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caravaggi et al 2000</td>
<td>Effectiveness and safety of a non-removable fiberglass off-bearing cast versus a therapeutic shoe in the treatment of neuropathic foot ulcers: a randomized study</td>
<td>Diabetes Care</td>
<td>Italy</td>
<td>Compare effectiveness of using the non-removable total off-loading cast made with fibreglass bandages or therapeutic shoes with rigid rocker-bottom sole with unloading insole in the treatment of neuropathic plantar ulcers</td>
<td>Health Care Setting not clearly mentioned</td>
<td>Neuropathic plantar ulcers</td>
<td><strong>Inclusion:</strong> Neuropathic plantar ulcers, insensitivity to Semmes-Weinstein 5.07 monofilament and vibration perception threshold of 25V (measured on the malleolus with biothesiometer.</td>
<td><strong>Exclusion:</strong> Deep or superficial tissue infection, osteomyelitis, TcPO₂ 30mmHg, equilibrium problems, severe visual deficit, other skin lesions of the foot or leg, amputation of a 50 diabetic patients</td>
</tr>
</tbody>
</table>

**Therapeutic shoe:** 24

**Fiberglass cast:** 26
**Patient Characteristics** | **Design Details** | **Study Type** | **Allocation** | **Intervention Details** | **Outcome Measures** | **Analysis** | **Results** | **Conclusions/Recommendations**  
--- | --- | --- | --- | --- | --- | --- | --- | ---  
**Shoe group:** Mean age(years) 59.2; male 16, female 8; insulin requirement 12; diabetes duration(years) 16.2; prior ulcers 9; BMI 27.3; smoking 10; hypertension 11; retinopathy 13; ABI 1.03; transcutaneous oxygen tension on dorsum of the foot 52.6.  
**Cast group:** Mean age(years) 60.5; male 18, female 8;  
**Randomisation Sequence:** subjects were assigned by phone to one of two pre-randomized treatment groups. The randomisation required that a patient was assigned to one of the groups by calling the Biometrics Institute, University of Milan, where a table of random numbers was consulted.  
Quantitative  
Blinding and concealment of allocation not mentioned  
24 patients received therapeutic shoe (cloth therapeutic shoe with rocker-bottom sole and a rolling point situated under the metatarsal arch) 26 patients received fibreglass off-bearing cast (fiberglass bandages of two types: one was composed of fiberglass impregnated with a polyurethane resin with characteristics of flexibility and resistance; the second was composed of fiberglass impregnated with a polyurethane resin of two different concentrations that confers high resistance to loading)  
Primary outcome measure was to evaluate and compare the rate of reduction of the surface area of neuropathic plantar ulcers in diabetic patients treated with non-removable rigidity-differentiated fibreglass off-bearing casts or a cloth shoe with a rigid sole with unloading alkaform insoles.  
Secondary outcome measure  
Mean values and standard deviations were calculated for all variables measured. Pearson $X^2$-test was used to compare the rates of events in the two groups and the Student’s $t$-test was used to compare the averages of continuous variables to follow the Gaussian distribution. Response rate was subdivided  
- Two patients in the group that used the therapeutic shoe presented an increase in ulcer size  
- No patient in the fibreglass off-bearing cast group has an increase in ulcer size  
- 5 subjects of the therapeutic shoe group reached ulcer healing  
- 13 subjects of the fibreglass off-bearing cast group reached ulcer healing  
- There was a significantly faster reduction in ulcer size in the fibreglass off-bearing cast group  
**Conclusion:** Therapeutic shoe was effective in the treatment of neuropathic plantar ulcers. However non-removable fibreglass bandages with variable flexibility and rigidity represent the elective treatment of neuropathic plantar ulcers.
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin requirement</td>
<td>13</td>
</tr>
<tr>
<td>Diabetes duration (years)</td>
<td>17.3</td>
</tr>
<tr>
<td>Prior ulcers</td>
<td>10</td>
</tr>
<tr>
<td>BMI</td>
<td>27.0</td>
</tr>
<tr>
<td>Smoking</td>
<td>5</td>
</tr>
<tr>
<td>Hypertension</td>
<td>13</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>14</td>
</tr>
<tr>
<td>ABI</td>
<td>1.00</td>
</tr>
<tr>
<td>Transcutaneous oxygen tension</td>
<td>53.5</td>
</tr>
</tbody>
</table>

Insulin requirement 13; diabetes duration (years) 17.3; prior ulcers 10; BMI 27.0; smoking 5; hypertension 13; retinopathy 14; ABI 1.00; transcutaneous oxygen tension on dorsum of the foot 53.5.

- Ulcer area was calculated at beginning of study and at the end of 30 days.
- Ulcers were debrided and medicated with paraffin gauze dressing throughout the study period and dressings were changed every 2 days.
- At the end of study patients were asked to evaluate acceptance of device by using a visual analogic scale ranging from 1 to 100.

- To evaluate the side effects and degree of patient acceptance of treatment.
- In quintiles of the percentages of healing of the ulcer surface, starting from complete healing (100%) and ranging to <20% of healed surface. The test for trend in the quintiles of response in the two treatment arms was done by the Mann-Whitney two-sample test for independent samples.

- No side effects were observed in both groups.
- There was no difference in patient acceptance of the two treatments.

- Bearing cast group (P=0.0004)
Appendix 17: Data Extraction Table Dumont et al 2009
<table>
<thead>
<tr>
<th>Author and Date of Study</th>
<th>Title</th>
<th>Source</th>
<th>Study Geographical Location</th>
<th>Research Question/Aim/Objective</th>
<th>Care Setting</th>
<th>Type and Characteristics of Wound</th>
<th>Inclusion/ Exclusion Criteria</th>
<th>Sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dumont et al 2009</td>
<td>A proof-of-concept study of the effectiveness of a removable device for offloading in patients with neuropathic ulceration of the foot: the Ransart boot</td>
<td>Diabetic Medicine</td>
<td>Belgium and France</td>
<td>To undertake a formal observational study of the effectiveness of the Ransart boot and to compare outcomes with published reports of the use of non-removable cast devices</td>
<td>Seven specialist units where non-removable fiberglass cast was or not available or not common practice</td>
<td>Diabetic foot ulcer on the plantar or lateral aspect of the foot</td>
<td><strong>Inclusion:</strong> aged 18-85; type 1 or 2 diabetes mellitus complicated with distal symmetrical neuropathy; presence of ulcer on the plantar or lateral aspect of the foot for more than 7 days. <strong>Exclusion:</strong> active Charcot disease or if patients were receiving any therapy including negative pressure therapy, larvae, bone resection or revascularization.</td>
<td>155 patients were included</td>
</tr>
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<td></td>
<td></td>
<td>20 were excluded from analysis: 14 recruited in error, 6 underwent surgery except amputation during course of follow-up 135 were part of the study</td>
</tr>
</tbody>
</table>

**Patient Characteristics**

- **Design Details**
- **Study Type**
- **Allocation**
- **Intervention Details**
- **Outcome Measures**
- **Analysis**
- **Results**
- **Conclusions/Recommendations**
Mean age 60.3 (23-85 years old); diabetes duration 15.2 (0-42 years); 118 patients were diabetes mellitus type 2; 96 were male; mean HbA1c 7.7%, median creatinine concentration 79µmol/l; mean ulcer duration before presentation was 90 days; 97 ulcers were on the forefoot, 20 in the mid foot and 18 on the heel.

Seven of the 135 patients were lost to follow-up, seven developed serious co-

| Mean age 60.3 (23-85 years old); diabetes duration 15.2 (0-42 years); 118 patients were diabetes mellitus type 2; 96 were male; mean HbA1c 7.7%, median creatinine concentration 79µmol/l; mean ulcer duration before presentation was 90 days; 97 ulcers were on the forefoot, 20 in the mid foot and 18 on the heel. | Uncontrolled observational study | Quantitative | Not applicable. | All patients wore the Ransart boot and ulcer dressings were managed according to the principles of the International Consensus on the Diabetic Foot, these dressings were not standardized and were chosen by the supervising clinician and changed as often as judged necessary. Each patient was reviewed weekly and the wound debrided as necessary and the boot changed as necessary. Patients were managed as outpatients, were instructed to wear the device every | No clear distinction between primary and secondary outcome measures. | Spearman’s rank correlation was used for continuous variables and $X^2$-test for dichotomous variables. Study mentions rate of healing, healing time and looks at incidence of amputation, and at correlation between: baseline ulcer classification and both time to healing and incidence of amputation; ulcer duration at presentation and time to healing, University of Texas (UT) classification, HbA1c and incidence of amputation. Adverse effects/ complications of Ransart boot. | $\bullet$ Ulcers in 82 of the remaining 117 patients healed in 60 days. 
$\bullet$ In 22 cases ulcer did not heal until amputation. 
$\bullet$ There were 21 minor amputations and one major amputation. 
$\bullet$ There was a significant correlation between baseline ulcer classification and both time to healing (p<0.001) and the incidence of amputation (p<0.001). 
$\bullet$ There was a positive correlation between ulcer duration at presentation and time to healing (p<0.02), UT classification (p<0.01), HbA1c (p<0.02), and incidence of amputation (p<0.04). 
$\bullet$ No correlation between time to healing and age, gender, type of diabetes mellitus, | Conclusions: 82 ulcers of the 135 patients healed with a median time to healing of 60 days. Rate of healing was 97.8%. The rate of healing using the Ransart boot may be comparable with those achieved using a non-removable device and may be cheaper and very much more acceptable to the patient. Recommendations: There is a need for a prospective comparison of the effectiveness, acceptability and costs of irremovable and removable casts in routine management. |
morbidity, and four died, thirteen patients were judged non-compliant.

time they were on their feet and were encouraged to undertake normal activities.

duration of diabetes, HbA1c, serum creatinine concentration and previous amputation.

- No correlation between the incidence of amputation and age, gender, type of diabetes mellitus, duration of diabetes, HbA1c, serum creatinine concentration.
- There were 11 minor complications while wearing the Ransart boot: 8 skin abrasions on the instep, 2 areas of redness in the 5th metatarsal head and 1 blister on the heel. All complications healed quickly after slight changes in the boot.
Appendix 18: Data Extraction Table Faglia et al 2010
<table>
<thead>
<tr>
<th>Author and Date of Study</th>
<th>Title</th>
<th>Source</th>
<th>Study Geographical Location</th>
<th>Research Question/Aim/Objective</th>
<th>Care Setting</th>
<th>Type and Characteristics of Wound</th>
<th>Inclusion/Exclusion Criteria</th>
<th>Sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Faglia et al 2010</td>
<td>Effectiveness of removable walker cast versus non-removable fiberglass off-bearing cast in the healing of diabetic plantar foot ulcer: a randomized controlled study</td>
<td>Diabetes Care</td>
<td>Italy</td>
<td>Evaluate healing outcomes in diabetic patients managed with TCC and new removable off-loading device (Stabil-D) specifically designed for the management of neuropathic plantar foot ulcers.</td>
<td>Two centres specialised in DFU management</td>
<td>Neuropathic plantar ulcers</td>
<td>Inclusion: Neuropathic plantar forefoot ulcer with University Texas stage IA. Exclusion: Presence of ankle-brachial pressure index &lt;0.9 and/or TcPO$_2$ &lt;50mmHg, signs of infection, osteomyelitis, use of steroids or antibiotics, visual impairment, active foot on contra lateral foot, previous major amputation of contra lateral limb, previous or</td>
<td>45 diabetic patients 3 patients did not complete study and were considered dropouts</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Design Details</th>
<th>Study Type</th>
<th>Allocation</th>
<th>Intervention Details</th>
<th>Outcome Measures</th>
<th>Analysis</th>
<th>Results</th>
<th>Conclusions/Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TCC group:</strong> Mean age (years) 59.0; female 8, male 15; diet 4, insulin 16, oral therapy 3; duration of diabetes (years) 17.7; BMI 32.3; HbA1c 9.1%; previous foot ulcer 15; previous minor amputation 11; mean area of lesion (cm²) 1.4.</td>
<td>Two-arm RCT</td>
<td>Quantitative</td>
<td>Blinding and concealment of allocation not mentioned</td>
<td>23 subjects were assigned the TCC</td>
<td>Primary outcome measure was decrease in ulcer size.</td>
<td>Homogeneity of the initial distribution of baseline primary variables between groups was tested using a Fisher exact test for dichotomous variables and Student’s t-test for continuous variables. The differences in ulcer size reduction between the two groups were compared using the Mann-Whitney test. The Wilcoxon test was used for analysis of ulcer size.</td>
<td>In the TCC group one subject presented partial rupture of the stirrup and another presented hitching that resolved after removal of German cotton. In the Stabil-D group one of subjects complained of odour and presented peri-ulcer skin maceration which resolved.</td>
<td><strong>Conclusion:</strong> This study concludes that off-loading using the Stabil-D or using TCC are equally effective in the treatment of neuropathic forefoot plantar ulcers.</td>
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<td><strong>Stabil-D group:</strong> Mean age (years) 61.7;</td>
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<td>22 subjects were assigned the Stabil-D</td>
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<td><strong>Randomisation Sequence:</strong> subjects were randomised by opening randomisation code break envelopes containing one of the two options, then separate randomisation was performed for each centre, and a copy of all randomisation envelopes was kept at the statistical department of the</td>
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<td>Ulcers were debrided, measured with Vistrak system, photographed and dressed with paraffin gauze and covered with single sterile gauze. Patients were followed-up weekly for 90 days and devices were removed and dressings changed at each visit.</td>
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</table>

- In the TCC group ulcer size decreased from
- In the Stabil-D group ulcer size decreased from
| Multimedica centre | reduction over time within groups. Healing rate over time was analysed by the Kaplan-Meier test and the log-rank test were used to detect differences between the two groups. | 1.41 to 0.21cm²  
- In the Stabil-D group ulcer size decreased from 2.18 to 0.45cm²  
- 73.9% of subjects in the TCC group achieved complete healing and the same happened in 72.7% of subjects in Stabil-D group  
- The mean healing time was 35.3±3.1 days in the TCC group and 39.7±4.2 days in the Stabil-D group  
- The total cost of treatment with Stabil-D was €3,300 and for the TCC the total cost was €6,688.50 |
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</thead>
<tbody>
<tr>
<td>female 7, male 15; diet 5, insulin 10, oral therapy 7; duration of diabetes (years) 17.2; BMI 30.3; HbA1c 7.5%; previous foot ulcer 15; previous minor amputation 12; mean area of lesion (cm²) 2.2.</td>
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</tbody>
</table>
Appendix 19: Data Extraction Table Katz et al. 2005

<table>
<thead>
<tr>
<th>Table Title</th>
<th>Katz et al. 2005</th>
<th>Data Source</th>
</tr>
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<tbody>
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</tr>
<tr>
<td>Author and Date of Study</td>
<td>Title</td>
<td>Source</td>
</tr>
<tr>
<td>--------------------------</td>
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</tbody>
</table>
| Katz et al 2005          | A randomized trial of two irremovable off-loading devices in the management of plantar neuropathic diabetic foot ulcers | Diabetes Care | USA | Compare the efficacy of a RCW rendered irremovable (iTCC) with the TCC in the treatment of neuropathic plantar FU  
**Hypothesised** that iTCC if worn continuously should not differ in healing times and complications from the TCC | Diabetic Foot Clinic | Neuropathic diabetic foot ulcers  
Ulcer surface area 3cm²  
Ulcer duration 216 days  
Ulcer location 29 forefoot, 11 midfoot, 1 heel | **Inclusion:** Chronic, non-ischemic, non-infected University Texas stage IA or IIA ulcers, when there was more than one plantar ulcer present only the largest was used for inclusion  
**Exclusion:** Active infection at ulcer site, Charcot neuro-arthropathy, significant peripheral arterial disease, inability to walk. | 41 diabetic patients  
Lost to follow up total of 7, 4 in the iTCC group and 3 in the TCC group.  
**TCC:** 20  
**iTCC:** 21 |

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Design Details</th>
<th>Study Type</th>
<th>Allocation</th>
<th>Intervention Details</th>
<th>Outcome Measures</th>
<th>Analysis</th>
<th>Results</th>
<th>Conclusions/Recommendations</th>
</tr>
</thead>
</table>

195
| **Mean age 50.9 (23-65 years); 28 subjects were male, 5 were white, 14 black and 25 hispanic; 38 had type 2 DM; the mean duration of diabetes was 14.1 (2-33 years); insulin dependents 19; current smokers 5; ever smoked 18; Neuropathy Disability Score was around 9.2 and the vibration threshold in volts was 46.** | **Two-arm prospective RCT** | **Randomisation Sequence:** subjects were randomised using a pre-prepared random number table | **Quantitative Blinding and concealment of allocation not mentioned.** | **21 subjects were assigned iTCC. 20 subjects were assigned TCC. Initially ulcers were evaluated, debrided and dressed after which casts were applied. Subjects were followed on a weekly basis. At each visit devices were inspected, ulcers evaluated, debrided, measured on acetate sheet and photographed** | **Outcome measures were assessed at the earlier of either complete wound healing or 12 weeks.** **Primary end point was the proportion of patients with healed ulcers in ≤ 12 weeks in each group.**  **Secondary were complication rates, median healing times, time to place and remove the devices and** **A two sample t-test was used to analyse normally distributed dichotomous variables. A Wilcoxon rank-sum test was used for non-normally distributed variables. A log-rank test was used for survival data.**  **Study power was of 95% to detect a 5% difference in the proportion of patients with healed ulcers at or before 12 weeks and a 355 power to detect a 25% difference in complication rates between the two groups.**  **All parameters were analysed as intention to treat were two tailed.**  | **- From the 20 subjects in the TCC group four were lost to follow-up**  **- From the 21 subjects in the iTCC group two were lost to follow-up**  **- One subject was found to have osteomyelitis before entry in study**  **- The proportion of subjects whose ulcers healed in ≤12 weeks was 74±45% for the TCC group and 80±41% for the iTCC group**  **- For subjects whose ulcers healed in the 12 week period the mean healing time was 5 weeks for the TCC group and 4 weeks for the iTCC**  **- In the TCC group 65% of subjects had a form of complication, and of these 54% was local skin maceration**  **- In the iTCC group there were 38% of complications, of which 75% were local skin maceration**  **- When patients with maceration were removed from analysis, complication rates dropped to 46% and 13%** | **Conclusion:** This study suggests that iTCC may be as effective as TCC in healing DFU, no more or less associated complications, takes less time to place/remove and costs less.**  | **Recommendations None made** |
and used an $\alpha$ value of 0.05. in the TCC and iTCC groups respectively, corresponding to a 71% relative risk reduction and an absolute risk reduction of 33% at week 12.

- Other complications were: broken cast, second ulcer, abrasions, oedema, kissing ulcer and fall.
- There was a single toe amputation in each group
- Most of the patient wore a medium-sized iTCC which weighed 1.1kg compared to 1.5kg for the TCC and the large sized iTCC weighed 1.4kg.
- The mean time for application of TCC was 12.4±1.9min and for removal 3.6±0.8min
- The mean time for application of iTCC was 7.6±1.6min and for removal 2.3±0.6min
- The direct cost of treatment course was for the TCC $210.67 and for the iTCC $158.47.
Appendix 20: Data Extraction Table Mueller et al 1989
<table>
<thead>
<tr>
<th>Author and Date of Study</th>
<th>Title</th>
<th>Source</th>
<th>Study Geographical Location</th>
<th>Research Question/Aim/Objective</th>
<th>Care Setting</th>
<th>Type and Characteristics of Wound</th>
<th>Inclusion/Exclusion Criteria</th>
<th>Sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mueller et al 1989</td>
<td>Total contact casting in treatment of diabetic plantar ulcers: controlled clinical trial</td>
<td>Diabetes Care</td>
<td>USA</td>
<td>Compare the effectiveness of TCC and traditional dressing treatment (TDT) for the management of neuropathic plantar ulcers in patients with diabetes mellitus.</td>
<td>Diabetic foot centre and physical therapy department at Washington University School of Medicine</td>
<td>Neuropathic plantar ulcers</td>
<td>Inclusion: patient that had been diagnosed with diabetes mellitus and currently had a plantar ulcer but no evidence of gross infection (no significant oedema or drainage), osteomyelitis or gangrene.</td>
<td>40 patients TCC: 21 TDT: 19</td>
</tr>
</tbody>
</table>

**Patient Characteristics**

**Design Details** | **Study Type** | **Allocation** | **Intervention Details** | **Outcome Measures** | **Analysis** | **Results** | **Conclusions/Recommendations**
| TCC group: Mean age (years) 54; male 13, female 8; insulin dependent 5, non-insulin dependent 16; mean duration of diabetes (years) 17; mean ulcer duration (days) 155. | TDT group: Mean age (years) 55; male 14, female 5; insulin dependent 6, non-insulin dependent 13; mean duration of diabetes (years) 17; mean ulcer duration (days) 175. | Two-arm prospective CCT | Randomisation Sequence: Independent random sampling. | Quantitative Blinding and concealment of allocation not mentioned | In the TCC group the ulcer was covered with one thin layer of gauze, cotton was placed between toes; stockinet was applied to the lower leg with felt pads placed in the malleoli and anterior tibia, with foam pads placed around toes. A total contact plaster shell was then moulded around the lower leg. The shell was reinforced with plaster splints, and a walking heel was attached to the plantar surface. A fiberglass roll was applied around the plaster for extra durability and to allow bearing weight sooner than would be allowed with plaster alone. Casts were removed after 5-7 days, and the ulcer and skin inspected. If there were no complications the cast was reapplied and changed every 2-3 weeks until the ulcer was completely healed. Other devices like crutches or no clear stated outcome measures but main objective is looking at ulcer healing. | A two-way $\chi^2$ - test test for two independent variables with two levels was used to determine whether there was a significant difference in the distribution of healed compared with not healed ulcers in the two groups. The $\alpha$-level was 0.05. | Conclusion: The use of TCC was more effective in the number of ulcers healed than conventional treatment with. |
walkers were provided to patient who needed them.

In the TDT group the wound was covered with a wet-to-dry dressing (sterile saline), and patients were instructed to change the dressing two to three times daily. All patients were prescribed appropriate accommodative footwear (healing sandal and extra depth shoe with plastazote insert)

Patients who refused to receive treatment from their assigned treatment group before complete wound closure were considered not healed. Ulcers that became grossly infected, increased in size, or showed no improvement after 6 weeks were considered not healed.
Appendix 21: Data Extraction Table Nabuurs-Franssen et al 2005
<table>
<thead>
<tr>
<th>Author and Date of Study</th>
<th>Title</th>
<th>Source</th>
<th>Study Geographical Location</th>
<th>Research Question/Aim/Objective</th>
<th>Care Setting</th>
<th>Type and Characteristics of Wound</th>
<th>Inclusion/ Exclusion Criteria</th>
<th>Sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nabuurs-Franssen et al 2005</td>
<td>Total contact casting of the diabetic foot in daily practice: a prospective follow up study</td>
<td>Diabetes Care</td>
<td>The Netherlands</td>
<td>This study was undertaken to determine the outcome and complication rate of TCC in a wide range of diabetic foot ulcers in daily practice.</td>
<td>Not mentioned</td>
<td>Neuropathic diabetic foot ulcers Off all ulcers: Mean ulcer size (cm²) 1.3; mean duration (days) 31; infection 29%; location: digit 1 plantar 22, metatarsal 1 plantar 15, ray 2,3,4 plantar 30, ray 5 plantar 14, dorsum/ midfoot 9, heel 9</td>
<td>Inclusion: diabetic patients with polyneuropathy and a foot ulcer were offloading was indicated but not possible with simple measures. Exclusion: critical limb ischaemia and major illness affecting wound healing, infection higher than grade 2 of the PEDIS system.</td>
<td>98 patients TCC group: 50 RCC group: 22 SMC group: 26</td>
</tr>
</tbody>
</table>

**Data Extraction Table**
<table>
<thead>
<tr>
<th>Off all patients: mean age (years) 67; male 65%; mean duration of diabetes (years) 18; PAD 44%; Type 2 diabetes 70%.</th>
<th>Prospective data collection</th>
<th>Quantitative</th>
<th>Not applicable</th>
</tr>
</thead>
<tbody>
<tr>
<td>At every visit, patient characteristics, cast details, and complications were registered electronically. Three total contact casting modalities were used: a non-removable TCC, a removable TCC (RCC) and a shoe-model cast (SMC) that could not be removed by the patient. Choice of cast was based on both patient and cast characteristics. At every visit, necrotic tissue and callus were surgically debrided. TCCs were renewed every 1–2 weeks,</td>
<td>Primary outcomes percentage of ulcers healed with a cast, time to heal, and number of complications.</td>
<td>Data are expressed as median and interquartile ranges. Comparisons were performed using Fisher’s exact, Mann-Whitney U and Kruskal-Wallis tests. In all analyses, correction was made for ulcer duration. Multivariate analyses were performed to further delineate the effect of PAD and infection on the percentage healed and cast failure (logistic regression). In this analysis we included PAD, infection at baseline, type and duration of diabetes, age and sex, size and duration of the ulcer at baseline,</td>
<td>PAD was present in 44% and infection at baseline in 29% of the patients. Overall, healing was achieved in 74 (76%) of the patients, with a median healing time of 33 days (interquartile range 14–63). In 22 patients, the ulcer did not heal during cast treatment (cast failure). Nine of these patients developed progressive infection, six were hospitalized for intravenous antibiotics, and three underwent amputation. Due to impaired healing, a revascularization procedure was performed in two patients and free-flap transplantation in three patients. Seven patients, casting was stopped due to discomfort with the cast and noncompliance in one patient. In all the above mentioned patients, alternative offloading techniques were used, which resulted in</td>
</tr>
<tr>
<td>Conclusion: Best results were obtained in patients with non-infected pure neuropathic ulcers. Due to poor outcome, alternative strategies should be used in patients with the combination of PAD and (superficial) infection and in patients with heel ulcers.</td>
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</table>
and RCC and SMC devices were modified if necessary.

Felt was applied around the ulcer to reduce peak pressure.

Patients with a removable cast were instructed to remove the device only during wound care.

Cast treatment was terminated when there was no reduction in wound size or depth during 4 consecutive weeks.

and type of cast. The SPSS statistical package, version 11.0 (Chicago, IL), was used.

healing of 20 of the 22 ulcers at the end of the study period.

Two patients were lost to follow-up before healing had occurred and were included in the analyses as cast failures (n= 24 in total).

In patients without infection and without PAD, healing occurred in 90%, and in patients without PAD but with infection, healing was observed in 87%.

In patients without infection but with moderate PAD, healing occurred in 69%.

In patients with infection and PAD, healing was markedly impaired; only 36% of the ulcers healed during cast treatment.

Time to heal was 18 days in the patients without infection and without PAD (range 10–41 days) and 29 days in patients without PAD but with infection (range 27–68...
In patients without infection but with moderate PAD, the time to heal was 42 days (range 14–65 days).

Only a minority of patients with infection and PAD healed during cast treatment, so the numbers were too small to calculate the time to heal.

No differences were observed between the healing rates of the three types of cast.

Patients with cast failure had, in comparison with patients in whom the ulcer healed, more frequent moderate PAD (75 vs. 34%), longer duration of the ulcer (61 vs. 21 days), and more frequent infection at baseline (46 vs. 24%).

Anatomical location was clearly related to outcome, all ulcers (n =15) in the metatarsal head 1 region healed, irrespective of the presence of PAD and/or
Infection. In contrast, the minority of heel ulcers healed. Logistic regression analysis showed that infection at baseline (OR 3.6), PAD (OR 7.4), and the location at the heel (OR 11.4) were associated with a lower percentage of healing in the cast.

**Complications:** New superficial ulcers were observed in 9% of the patients and were not related to ischemia, infection, or the anatomical location of the primary ulcer. These ulcers healed within a maximum of 13 days in a revised cast. Pre-ulcerative lesions developed in 28% of the patients but resolved within a few days after minor adaptations of the cast. Abrasions were found in 8% of the patients, and temporary joint problems were reported in 7% of the patients.
Appendix 22: Data Extraction Table Piaggesi *et al.* 2007
<table>
<thead>
<tr>
<th>Author and Date of Study</th>
<th>Title</th>
<th>Source</th>
<th>Study Geographical Location</th>
<th>Research Question/Aim/ Objective</th>
<th>Care Setting</th>
<th>Type and Characteristics of Wound</th>
<th>Inclusion/ Exclusion Criteria</th>
<th>Sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Piaggesi et al 2007</td>
<td>An off-the-shelf instant contact casting device for the management of diabetic foot ulcers: a randomized prospective trial versus traditional fiberglass cast</td>
<td>Diabetes Care</td>
<td>Italy</td>
<td>Test the safety, efficacy and cost between TCC and Optima Diab Walker in the management DFU</td>
<td>Diabetic foot clinic of the University of Pisa between April and October 2005</td>
<td>Diabetic foot ulcers</td>
<td><strong>Inclusion:</strong> type 1 or 2 DM for at least 5 years, peripheral neuropathy, forefoot plantar ulcer for a period of at least 3 weeks with an area wider than 1 cm², University Texas stage IA or IIA <strong>Exclusion:</strong> peripheral vascular disease, signs of infection, previous ulcer in the same site in the past 6 months, probing to bone or osteomyelitis, Charcot neuroarthropaty, bilateral ulcers, serum creatinine</td>
<td>43 patients were screened but three did not enter the study one refused to release informed consent and two were unable to attend follow-up visits due to distance to travel.</td>
</tr>
<tr>
<td>Patient Characteristics</td>
<td>Design Details</td>
<td>Study Type</td>
<td>Allocation</td>
<td>Intervention Details</td>
<td>Outcome Measures</td>
<td>Analysis</td>
<td>Results</td>
<td>Conclusions/Recommendations</td>
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</tr>
<tr>
<td>TCC: Mean age (years) 59.8; duration of diabetes (years) 14.7; A1C 7.9%; Vibration perception threshold (volts) 36.8; area of lesion (cm²) 3.7.</td>
<td>Two-arm prospective RCT</td>
<td>Quantitative</td>
<td>Blinding and concealment of allocation not mentioned</td>
<td>20 subjects were assigned the TCC (group A). 20 subjects were assigned the Optima Diab device (group B). Subjects received instructions on how to manage the off-loading devices. Ulcers were debrided and measured with Visitrak and photographed Ulcers were dressed with paraffin gauze and covered with</td>
<td>Primary outcome measure was the rate of healing at 12 weeks. Secondary outcome measures were number and severity of adverse events, mean healing time, time of application and removal of the devices, cost of treatment, and level of</td>
<td>Data was analysed according to the intention to treat model, with Student’s t-test for normally distributed variables. Kaplan-Meier analysis of survival data, and the X² tests for dichotomous variables using commercially available software Stat</td>
<td>• Five subjects of the TCC group reported minor adverse events, in one the TCC was partially ruptured and in other four skin maceration was present • Subjects of the Optima Diab device reported, one an episode of paraesthesia, two showed skin maceration and one superficial haematoma due to trauma • No new ulcers were observed in both groups</td>
<td>Conclusions: This study confirms the effectiveness and the safety of non-removable off-loading devices in the management of DFU at an equal level as TCC and is superior to the previous in terms of practicability, cost and patient satisfaction.</td>
</tr>
<tr>
<td>Optima Diab Walker: Mean age (years) 61.1; duration of diabetes (years) 13.4; A1C 7.6%; Vibration perception</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
| threshold (volts) 39.1; area of lesion (cm²) 3.9. | single sterile gauze before off-loading application  
Time to apply and remove off-loading devices was calculated  
Level of subjects satisfaction was recorded using a visual analogic scale were 0 is no satisfaction at all and 10 maximum satisfaction | satisfaction expressed by patients. | View.  
- One subject in each group develop infection which was treated with antibiotic and resolved in one week  
- 95% of ulcers healed in TCC group and 85% in Optima Diab group within the 12 week study period  
- The mean duration of healing time was 6.5±4.4 weeks in TCC group and 6.7±3.4 weeks in optima Diab group  
- Time for application of devices differed significantly, in the TCC group 15.1±2.3 min and in the Optima Diab group 2.1±0.7 min  
- Time devices for removal also differed significantly, in the TCC group 2.1±0.9 min and in the Optima Diab group 0.9±0.4 min  
- The cost of |
treatment was higher in the TCC group compared to the Optima Diab group.

- Patient satisfaction was higher in the Optima Diab group compared to the TCC group.
Appendix 23: Data Extraction Table Van de Weg et al 2008
## Data Extraction Table

<table>
<thead>
<tr>
<th>Author and Date of Study</th>
<th>Title</th>
<th>Source</th>
<th>Study Geographical Location</th>
<th>Research Question/Aim/Objective</th>
<th>Care Setting</th>
<th>Type and Characteristics of Wound</th>
<th>Inclusion/Exclusion Criteria</th>
<th>Sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van De Weg et al 2008</td>
<td>Wound healing: total contact cast vs. custom-made temporary footwear for patients with diabetic foot ulceration</td>
<td>Prosthetics and Orthotics International</td>
<td>The Netherlands</td>
<td>Compare the effectiveness of irremovable total-contact casts (TCC) and custom-made temporary footwear (CTF) to heal neuropathic foot ulcerations in individuals with diabetes.</td>
<td>Rehabilitation departments of two hospitals.</td>
<td>Diabetic plantar ulcers. <strong>TCC group:</strong> Median duration of ulcer (weeks) 4; mean WSA ( \text{(cm}^2 \text{)} ) at baseline 4.2; ulcer grade 1; forefoot location 20. <strong>CTF group:</strong> Median duration of ulcer (weeks) 5; mean WSA ( \text{(cm}^2 \text{)} ) at baseline 3.0; ulcer grade 1; forefoot location 18.</td>
<td><strong>Inclusion:</strong> Confirmed diabetes, sensory neuropathy and a plantar ulcer Grade 1 or 2 using the Wagner scale <strong>Exclusion:</strong> Patients unable to walk indoors, with dementia or life-threatening co-morbidity, ABI &lt; 50.4 and/or osteomyelitis were excluded.</td>
<td>43 patients TCC: 23 Shoe (CTF): 20</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Design Details</th>
<th>Study Type</th>
<th>Allocation</th>
<th>Intervention Details</th>
<th>Outcome Measures</th>
<th>Analysis</th>
<th>Results</th>
<th>Conclusions/Recommendations</th>
</tr>
</thead>
</table>

214
| **TCC group:** | mean age (years) 64.8; gender 32% females; median duration of diabetes (years) 12; mean HbA1c 7.8; mean ABI 0.69; prescription of antibiotics 41%.  | **Two-arm prospective RCT** | **Randomisation Sequence:** An independent person prepared a randomization list in advance with an equal number of treatment assignments (5/5) per block of ten to ensure approximately equal numbers of patients in each treatment group. | **Quantitative Allocation was concealed using opaque, sealed envelopes.** | **Before the intervention ulcers were debrided of necrotic tissue and hypertrophic edges were removed. All patients received the same educational guidelines on foot care and general information on the importance of appropriate footwear. All patients attended the out-patient department regularly for device inspection. Wound care and wound debridement was carried out by a podiatrist blinded to treatment mode, and antibiotics dispensed if necessary. Patients having difficulty performing dressing changes were provided with assistance from a home care nurse.** | **Primary outcome measure was reduction of wound surface area (WSA) during the 16 weeks follow-up.** | **The analysis of effectiveness was done according to the intention-to-treat principle. WSA changes since baseline were calculated for each participant for each moment of follow-up. Subsequently differences in these changes between groups were analysed using linear regression analysis. All analyses were adjusted for potential confounding by difference in baseline WSA by entering the baseline WSA in the regression analysis.** | **Four patients were lost to follow-up: one died, one was amputated on the affected side and two withdrew from follow-up (all from the TCC group). At baseline the median WSA was 3.6 cm$^2$ in the TCC group and 1.9 cm$^2$ in the CTF group. At 16 weeks the median WSA was 0.4 cm$^2$ in both groups. After adjustment for differences in baseline values, the difference between groups in reduction of wound surface was 0.10 cm$^2$. Six patients wearing shoes and six patients using a cast had a completely healed ulcer. The mean time to healing was shorter for the patients using a cast: 59 (SD 39) days for TCC vs. 90 (SD 12) days for CTF.** | **Conclusions:** The authors found little difference in the effectiveness between the TCC and CTF and suggest further investigation regarding the benefits of the CTF. |
**Interventions:** TCC, a well-moulded and minimally padded non-removable below-knee cast that maintains contact with the entire plantar aspect of the foot and lower leg, which was changed on a weekly basis.

CTF was a custom-made of felt and supplied with a rigid leather socket stiffened with Rhenoflex, a composite of rubber and plastic with thermoplastic properties. This ensures that movement of the foot in the shoe is restricted to an absolute minimum.

Both crude and adjusted mean differences between groups in the reduction of WSA, including 95% CI, p values <0.05 were considered significant. Analyses were carried out using SPSS 12.01 software.

Ulcers that did not heal completely has a size of 0.8cm$^2$ (1.1±1.2) for the CTF group, and 0.9cm$^2$ (1.5±1.6) for the TCC group.
Appendix 24: Data Extraction Table Zimny et al 2003

<table>
<thead>
<tr>
<th>Table</th>
<th>Data</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
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<td></td>
</tr>
<tr>
<td>Author and Date of Study</td>
<td>Title</td>
<td>Source</td>
</tr>
<tr>
<td>--------------------------</td>
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</tr>
<tr>
<td>Zimny et al 2003</td>
<td>The effects of applied felted foam on wound healing and healing times in the therapy of neuropathic diabetic foot ulcers</td>
<td>Diabetic Medicine</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Design Details</th>
<th>Study Type</th>
<th>Allocation</th>
<th>Intervention Details</th>
<th>Outcome Measures</th>
<th>Analysis</th>
<th>Results</th>
<th>Conclusions/ Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Felted foam group: Mean age (years) 62.1; mean BMI 27.4; male 13, female</td>
<td>Two-arm prospective RCT Randomisation</td>
<td>Quantitative</td>
<td>Concealment of allocation not mentioned. When wounds</td>
<td>All patients received identical standard ulcer wound care that included debridement and daily care</td>
<td>Outcome measures not clearly mentioned, however main</td>
<td>The statistical analyses included descriptive statistics, the standard error of</td>
<td>• In the felted foam group, the initial average wound area was 102.3 ± 45.3mm² and 5.4 ± 3.1mm² after 2 weeks. Conclusion: The main finding indicates that the application of felted foam underneath</td>
<td></td>
</tr>
</tbody>
</table>
**Half-shoes group:** Mean age (years) 62.1; mean BMI 28.5; male 17, female 13; type 1 diabetes 13, type 2 diabetes 17; mean diabetes duration (years) 22.1; mean HbA1 7.5%; mean TcPO2 8.7; mean ABI 1.0.

**Sequence:** not mentioned

| were measured the observer was no blinded to the treatment group. | monitoring of the ulcer. In one group pressure relief in the ulcerated area was accomplished using felted foam dressings and the other group received half-shoes (Thanner, Hoechstaedt) | objective is evaluation of wound radius reduction and healing times. the mean and analyses of the variance using the t-test. Differences between the groups regarding the patients’ sex, type of diabetes and ulcer depth were calculated using Fisher’s exact test. The relationship between the mean wound radius reduction and healing times was then calculated by linear regression analysis, the 95% confidence intervals were also calculated. The proportion of healed ulcers over time was assessed by Kaplan–Meier curve. The statistical analyses were done using JMP V4.0 for 10 weeks. • In the conventional therapy group, the initial average wound area was 112.5±50.8 mm² and 10.6±4.2 mm² after 10 weeks. • Regarding the ulcer depths, there were more ulcers with a Wagner grade 2 than 1 in both groups, but the ulcer areas were not dependent on the ulcer depths (P=0.27, P=0.78, respectively). • The frequency of soft tissue infections did not differ between the treatment groups (25% felted foam group, 23% conventional group). • The average healing time in the felted foam group was 75.2 days [95% confidence interval (CI) 67–84] and 85.2 days (95% CI 79–92) in the conventional group (P= 0.03). • The statistical power to detect a difference of 5

11; type 1 diabetes 7, type 2 diabetes 17; mean diabetes duration (years) 18.2; mean HbA1 7.9%; mean TcPO2 8.9; mean ABI 1.0.

The foot reduced the wound area as effectively as the half-shoes. Thus, the felted foam technique seems to be as effective as the half-shoes for the treatment of diabetic plantar ulcers.
The mean wound radius reduction in both groups appears to have a near linear relationship with the healing time. It decreased by 0.48 mm (95% CI 0.42–0.56) per week in the felted foam group, and by 0.39 mm (95% CI 0.35–0.42) per week in the conventional group (P=0.005).
Appendix 25: Data Extraction Table for Included Systematic Reviews
<table>
<thead>
<tr>
<th>Review Author</th>
<th>Data Assessed as up to date</th>
<th>Title</th>
<th>Source</th>
<th>Geographical Location</th>
<th>Population</th>
<th>Intervention and Comparison Interventions</th>
<th>Outcomes for which Data was Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spencer</td>
<td>2008</td>
<td>Pressure Relieving Interventions for Preventing and Treating Diabetic foot Ulcers (Review)</td>
<td>Cochrane Library</td>
<td>UK</td>
<td>Patients with diagnosis of type / and/or type 2 diabetes and with foot ulcers or callus</td>
<td>Relief or redistribution of pressure in the neuropathic and/or neuro-ischaemic diabetic foot with or without the presence of ulceration. No comparison of interventions.</td>
<td>Healing rate, patient satisfaction and quality of life, complication and Morbidity, economic analysis</td>
</tr>
<tr>
<td>Mason et al</td>
<td>1999</td>
<td>A systematic review of foot ulcer in patients with Type 2 diabetes mellitus. II: treatment.</td>
<td>Diabetic Medicine</td>
<td>UK</td>
<td>No clear identification of characteristics that populations in articles to be reviewed should have. Only mentions that type1 and type 2 diabetes mellitus will be included.</td>
<td>Systematic review looking at studies that address an intervention for patients with diabetic foot ulcers. Not focused in any specific intervention, but assessing various treatments. No comparison of interventions present.</td>
<td>No primary or secondary outcomes reported. Aims to assess the value of treatment for foot ulcers in patients with type 2 diabetes mellitus.</td>
</tr>
</tbody>
</table>
Appendix 26: Description of devices characteristics from the study by Birke *et al* (2002)
**Accommodative Dressing**

The accommodative dressing consisted of a 6-inch-long piece of quarter-inch-thick adhesive felt attached to the forefoot with a cut out over the ulcer area. The foot was fit into a surgical shoe modified with a half inch wedged sole to promote heel weight bearing.

**Healing Shoe**

Patients in this group were instructed in daily dressing changes and were followed up weekly reassessment and ulcer debridement as needed. In this group 54% were females; the mean age was 58.2 years; the mean ulcer duration was 67.9 days; the mean ulcer grade was 1.7 (Wagner Grade): the mean ulcer length, width and depth was 1.2, 0.7 and 0.3 cm respectively (Birke *et al* 2002: 212-13).

**Walking Splint**

The walking splint was fabricated as follows: the leg was generously wrapped with cotton cast padding. Relief areas for the posterior heel and plantar lesion were provided with adhesive-backed foam-rubber padding. Bony prominences, such as the malleoli and the navicular, were padded with 0.32-cm (1/8 in) felt. The inner shell was made of two sets (five layers each) of plaster splints overlapped in the centre. The strength of the device was improved by extending the medial and lateral trim lines to the midline of the

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2 The information relating to the fabrication of the walking splint for the study by Birke *et al* (2002) was adapted from the study of Birke *et al* (1991: 117,119) ‘Methods of Treating Plantar Ulcers’.
malleoli and reinforcing the plastic layers with fiberglass casting tape. A rubber walking heel (positioned and levelled as described for the walking cast) was secured to the bottom of the splint with a second roll of fiberglass casting tape. The fiberglass taping that covers the dorsum of the foot was removed. The inner layer of cast padding was cut along the anterior leg and dorsum of the foot to allow removal of the device. An elastic wrap was used to secure the splint to the leg.

**TCC**

The fabrication of the TCC involves thin cotton stocking that is the innermost layer. Orthopaedic felt (0.32 cm [1/8 in] thick) was used to pad the malleoli, navicular, and tibial crest. Adhesive-backed foam-rubber padding encloses the toes and covers the ulcer area. The toes are covered to prevent direct trauma or entry of foreign objects. In recent years, we have added cotton cast padding to minimize the risk of secondary lesions from friction within the cast. The cast padding is layered over the less prominent bony areas, such as the posterior heel, base of the fifth metatarsal, and dorsum of the foot. To obtain an optimal total contact fit, the inner layers of plaster are applied without stretching and are carefully moulded over the contours of the foot. The combination of selective padding and moulding, results in pressure redistribution from the lesion area to the remaining foot and leg. Plaster splints reinforce the posteroplantar and mediolateral aspects of the cast. A 0.64-cm (1/4 in) section of plywood and a rubber walking heels are positioned such that the centre of the heel is at a location 40% of the distance from the heel to the toe. This heel placement creates a smooth rocking motion during walking the plywood board reinforces the bottom of the cast to prevent the heel from penetrating.

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3 The information relating to the fabrication of the TCC for the study by Birke et al (2002) was adapted from the study of Birke et al (1991: 117,119) 'Methods of Treating Plantar Ulcers'.
the plaster. Small pieces of plaster are used to fill the space between the plywood board and the plantar surface of the cast, so that the board appears level when viewed from the side and the front. Additional plaster bandages are used to strengthen the cast and secure the walking heel.
Appendix 27: Description of devices characteristics from the study by Caravaggi et al (2000)
**Therapeutic Shoe**

The therapeutic shoe consists of a cloth with a rocker-bottom sole and a rolling point situated beside the metatarsal arch during walking. The therapeutic shoe is predisposed (extra depth) for lodging an 8-mm–thick cushioned elastic insole made of plastazote (alkaform) on which an area of unloading is prepared in the area of the plantar ulcer. The unloading area must be 5–8 mm larger than the perimeter of the ulcer. The shoe is opened dorsally with Velcro straps that permit the dressing to stay in place (Caravaggi et al 2000: 1748)

**Fiberglass Cast**

The fiberglass cast was fabricated as follow, two types of fiberglass bandages were used for the construction of the pressure-relief apparatus. The first type of bandage was composed of fiberglass imbued with a polyurethane resin with characteristics of flexibility and resistance. The other bandage was composed of fiberglass imbued with a polyurethane resin of two different concentrations that confers high resistance to loading. Before using both types of bandages, a tubular stockinet was placed onto the lower limb, which was first covered with German cotton to protect the skin adequately, especially on bony protrusions. To further protect bony protrusions, such as the malleolus and tibial crista, some pieces of protective rubber foam were also applied. The plaster bandages were applied so that the boot conformed to the shape of the leg as much as possible. The first two layers were applied using the Softcast bandage. The structure was then reinforced with a stick made with a Scotchcast bandage placed in the middle of the two malleoli, extending beyond them for at least 20 cm, giving rigidity to the cast. The same material was used to build a rigid plantar sole. The number of layers
applied to construct the sole depended on the weight of the patient (range 3–8 layers). The final structure was reinforced with more Softcast bandages. An aluminium stirrup or rubber heel was anchored to the structure as a support to allow walking. The side supports were secured with an outer layer of Softcast. The choice of using the stirrup or the rubber heel as a support for walking depends on the position of the ulcer. The stirrup is used if the ulcer is localized in the midfoot region. This support leaves the entire plantar surface of the boot free from pressure and permits the construction of an opening precisely in the ulcerated region. Therefore, examination and changes of dressing to the ulcer can be performed as frequently as needed. A rubber heel is used when lesions are located on the forefoot, the plantar surface of the toes, or the heel because it allows an open window directly above the ulcer. The rubber heel is positioned in the centre of the plantar surface to allow comfortable walking. In all subjects, the sole of the unaffected foot’s shoe was elevated to ease walking. After very brief training, all patients were able to walk properly without crutches (Caravaggi et al 2000: 1748).
Appendix 28: Description of device characteristics from the study by Dumont *et al* (2009)
**Ransart boot**

For the use of the Ransart boot, the ulcer is protected with a simple protective dressing. The foot or lower leg is covered with stockinet and this is then encased in a roll of Soft Cast®. The sole of the device is reinforced with Scotch Cast® before the application of a second roll of Soft Cast®. The cast is moulded to the foot and no special protection is applied to bony prominences. The cast is left open just below the malleoli and an additional window is cut out over the ulcerated area. The cast is then shaped to make it more easily removable and secured with Velcro® (Dumont *et al* 2009: 779).
Appendix 29: Description of device characteristics from the study by Faglia et al (2010)
TCC

The TCC was casted according to the technique described previously by Caravaggi et al (2000). All casts were made by personnel with particular expertise in the use of this device. Two types of fiberglass bandages were used for construction of the pressure-relief apparatus. The first type of bandage was composed of fiberglass imbued with a polyurethane resin with characteristics of flexibility and resistance. The other bandage was composed of fiberglass imbued with a polyurethane resin of two different concentrations that confers high resistance to loading. A bandage with German cotton and tubular stockinet was placed on the limb. To further protect bony protrusions, such as the malleolus and tibial crista, pieces of protective rubber foam were also applied. The structure was then reinforced with a stick made of a Scotchcast bandage placed in the middle of the two malleoli, extending beyond them for at least 20cm to give rigidity to the cast. The same material was used to build a rigid plantar sole. The number of layers applied to construct the sole depended on the weight of the patient (range 3–8 layers). An aluminium stirrup was anchored to the structure as a support to allow walking. The side supports were secured with an outer layer of Softcast3M. After very brief training, all patients were able to walk properly without crutches (Faglia et al 2010:1420)

Stabil-D

The Stabil-D was composed of a specifically designed rigid, boat-shaped and fully rocker bottom sole: its rounded extremities (at the heel and tiptoe) facilitate gait, and its middle section improves the mid-stance phase. The insole height (24mm) avoids excessive lifting of the contralateral limb during walk, thus lowering the barycentre and favouring more stable walking. The cover is made of Elastam®, a yarn composed of
polyurethane segments and block copolymers that confer high transparency and stability to the system, mixed with polyethylene glycol segments with the characteristic of elasticity. At the ankle, the cast is provided with removable, lateral stabilizer inserts made of ABS, which ensure stability to the tibiotarsal joint and/or adequate support during gait. Moreover, a rigid brace made of a thermo formable polymer material properly supports the Achilles tendon and contributes to stability during rolling steps; such a brace can be adapted to the foot deformity using a hot air gun and malleolar forceps. The cast is closed dorsally with Velcro wrap placed over the forefoot to relieve skin pressure and Velcro straps with self-fitting rings placed against the instep to secure perfect fastening, provide foot stability, and ensure a perfect fit of the heel in the rigid brace. Finally, more Velcro® straps are placed or secured with rings against the tibia to provide a secure fit. The cast has a special foot arch support (Modus) with small adaptable inserts. This modular insole is made of multiple layers of different stiffness and is specifically designed to allow proper offloading by removing the small inserts from the ulcerated area, without the need for traditional milling procedures. The bottom layer is composed of chemically knitted closed cell polyphenylic foam. The middle layer is composed of knitted, expandable, and mouldable closed cell polystyrene foam (plastazole). The Diapod cover, specifically designed for feet at risk of ulcer formation, is composed of chemically knitted dermo compatible Eva Diflex Vibram (closed cell polyphenylic foam), which also has bactericidal and fungicidal properties. Patients in the Stabil-D group were carefully trained for proper cast wearing, in particular for accurate closure of Velcro straps, and were prescribed continuous cast wear of the Stabil-D, patients were allowed to remove the cast only during nocturnal rest (Faglia et al 2010:1420).
Appendix 30: Description of device characteristics from the study by Mueller et al (1989)
**TCC**

In the TCC group, the ulcer was covered with one thin layer of gauze, cotton was placed between the toes to prevent maceration, and a stockinette was applied to the lower leg with 1/8-inch felt pads applied to the malleoli and anterior tibia and a foam pad placed around the toes. A total contact plaster shell was then moulded around the lower leg and this was reinforced with plaster splints, and a walking heel was attached to the plantar surface. Then a fiberglass roll was applied around the plaster for extra durability and to allow bearing weight sooner than would be allowed with plaster alone. Patients were given a written list of precautions and instructed to limit ambulation to 33% of their usual activity. Assistive devices (walkers or crutches) were provided to patients who required them. TCCs were removed after 5-7 days, and the ulcer and skin inspected (Mueller et al 1989: 386).

**TDT**

For the TDT group the wound was covered with a wet-to-dry dressing (using sterile saline), and patients were instructed to change the dressing two to three times daily. If patients had difficulty performing dressing changes home-health nurse visits were provided to assist patients and monitor their treatment. All patients were prescribed appropriate accommodative footwear (healing sandal and extra-depth shoe with plastazote insert), were instructed to avoid bearing weight on the involved lower extremity (with walkers or crutches) (Mueller et al 1989: 386).
Appendix 31: Description of device characteristics from the study by Piaggesi et al (2007)
**TCC**

In the TCC group a layer of isolating foam was positioned in relation to the ulceration site, in this way the lesion was better isolated from contact with the cast, to avoid friction or trauma with bony prominences extra layers of cotton-wool were applied. The fiberglass material used for manufacturing each cast was produced by 3M® and consisted of two Scotchcast longuettes (10x90 or 7.5x70 cm, depending on the size of the foot) to create the plantar support and block the ankle, and three Sofcast rolls (10.1 or 7.6 cm) to make the boot. Each cast was provided with one or two rubber heels to allow the patients to stand and walk, and at each visit TCCs were removed with an oscillating saw (Piaggesi *et al* 2007: 587).

**Optima Diab Walker**

The Optima Diab Walker was adapted according to the patient’s foot condition and secured to the patient’s leg with a plastic non-removable lace, which was an integral part of the device. The patients’ foot and leg were protected by a layer of cotton-wool to avoid friction with the device, and the three-layer insoles were modelled to accommodate the position of the ulcer site and the Optima Diab Wallker was removed cutting the non-removable lace (Piaggesi *et al* 2007: 587).
Appendix 32: Description of device characteristics from the study by Van de Weg et al (2008)
**TCC**

The TCC group casts were well-moulded and minimally padded non-removable below-knee maintaining contact with the entire plantar aspect of the foot and lower leg. These were applied by a cast technician with at least five years’ experience using the Kominsky technique. Technique not explained. Prior to casting, ulcers were debrided and dressed with Aquacell®, a single layer of cast padding was applied and adhesive foam was used over bony prominences. Cast shoes with a polyphasic rocker were supplied and patients with poor postural stability were advised to use a crutch/cane to maintain balance. The casts were changed on a weekly basis for the duration of the trial (Van de Weg *et al* 2008: 5).

**CTF**

The CTF was composed of a custom-made felt and supplied with a rigid leather socket stiffened with Rhenoflex®, a composite of rubber and plastic with thermoplastic properties, which ensures that movement of the foot in the shoe is restricted to an absolute minimum. The height of the shoes was twice the distance from the foot base to the lateral malleolus. The custom full-length insoles were made from cork and a plastazote and polyethylene foam and polyurethane covering. Extra depth was provided in the inlay for the ulcer. To ensure maximal relief of pressure under the MTPs, the pivot point of the rocker bar was placed proximal to the MTPs and the outsole stiffened to facilitate the distribution of forces exerted on the foot. A plastic trial cast was always made for a test fitting to check the last measurements, innersole accommodation and balance before the shoe was completed. Patients were instructed to wear their footwear at all times whilst out of bed. Detailed instructions regarding routine care of the cast and
shoes were given to all patients. All patients were advised to decrease their activity levels considerably (Van de Weg et al. 2008: 6).
Appendix 33: Description of device characteristics from the study by Zimny et al (2003)
**Felted Foam**

In the Felted foam group, a combination of 0.635 cm thick rubber foam with a 0.158cm layer of felt adhered, rubber glue was used. The felted foam was measured exactly to fit the plantar aspect of the foot. Using a scalpel, an aperture was cut in the felted foam at the exact location of the ulcer, allowing clear visualization of the ulcer. A gauze Peha-haft® was then wrapped around the foot and the felted foam pad to secure the pad. The wound was covered with a saline-soaked sponge VacuSeal®, which was changed every day. A compress was placed over the wet sponge and fixed with Peha-haft®. The felted foam dressing was exclusively used for plantar ulcerations under the forefoot and was changed, every third day (Zimny et al 2003: 623).
Appendix 34: Selection Bias (Randomisation)
<table>
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<tr>
<th>Study</th>
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<th>Selection Bias (Randomisation)</th>
</tr>
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<tr>
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<tr>
<td>Caravaggi et al 2000</td>
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<tr>
<td>Faglia et al 2010</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Katz et al 2005</td>
<td>Low risk</td>
<td>All patients were reported to be have been randomised</td>
</tr>
<tr>
<td>Mueller et al 1989</td>
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<td></td>
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<tr>
<td>Piaggesi et al 2007</td>
<td></td>
<td></td>
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<tr>
<td>Van de Weg et al 2008</td>
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<tr>
<td>Zimny et al 2003</td>
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Appendix 35: Selection Bias (Allocation)
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<th>Selection Bias (Allocation)</th>
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<td></td>
<td>High Risk</td>
<td>No allocation concealment reported.</td>
</tr>
<tr>
<td>Armstrong et al 2005</td>
<td>Low risk</td>
<td>Allocation sequence through a computerised randomisation schedule.</td>
</tr>
<tr>
<td></td>
<td>High risk</td>
<td>Allocation provided to the treating clinician by a single study coordinator via telephone.</td>
</tr>
<tr>
<td>Caravaggi et al 2000</td>
<td>Low risk</td>
<td>Allocation sequence by phone to one of two pre-randomized treatment groups.</td>
</tr>
<tr>
<td></td>
<td>High Risk</td>
<td>No allocation concealment reported.</td>
</tr>
<tr>
<td>Faglia et al 2010</td>
<td>Low risk</td>
<td>Allocation sequence through code break envelopes containing one of the two options. Then separate allocation was performed for each centre, and a copy of all envelopes was kept.</td>
</tr>
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<td>No allocation concealment reported.</td>
</tr>
<tr>
<td>Katz et al 2005</td>
<td>High risk</td>
<td>Allocation sequence using a pre-prepared random number table. No allocation concealment reported.</td>
</tr>
<tr>
<td>Mueller et al 1989</td>
<td>High risk</td>
<td>Allocation sequence was done through independent random sampling. No allocation concealment reported.</td>
</tr>
<tr>
<td>Piaggesi et al 2007</td>
<td>Low risk</td>
<td>Allocation sequence through a computer generated randomisation list.</td>
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<td>High Risk</td>
<td>No allocation concealment reported.</td>
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<td>Van de Weg et al 2008</td>
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<td>Allocation sequence through an independent person who prepared a randomization list in advance with an equal number of treatment assignments (5/5) per block of ten to ensure approximately equal numbers of patients in each treatment group. Allocation was concealed using opaque, sealed envelopes.</td>
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<tr>
<td>Zimny et al 2003</td>
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Appendix 36: Performance Bias
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</tr>
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<td>Piaggesi et al 2007</td>
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<td>Zimny et al 2003</td>
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Appendix 37: Detection Bias
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</tr>
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<td>Armstrong et al 2005</td>
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<td>Piaggesi et al 2007</td>
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<td>Van de Weg et al 2008</td>
<td>Low Risk</td>
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<td>Zimny et al 2003</td>
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Appendix 38: Attrition Bias
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<td>12 participants did not complete study and were excluded from analysis.</td>
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<td>4 participants did not complete the course of study and were considered treatment failures in the intention-to-treat analysis.</td>
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<tr>
<td>Caravaggi et al 2000</td>
<td>Low Risk</td>
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<td>Faglia et al 2010</td>
<td>High Risk</td>
<td>3 patients did not complete study and were considered dropouts, data relating to these participants was not analysed.</td>
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<td>Katz et al 2005</td>
<td>High Risk</td>
<td>7 participants were lost to follow up however it is not clear if they were included in the intention-to-treat analysis as treatment failures.</td>
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<td>Mueller et al 1989</td>
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<td>Patients who refused to receive treatment from their assigned treatment group before complete wound closure were considered not healed however there is no mention in the study if any participants did refuse treatment and how these data would be interpreted.</td>
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<td>1 cross-over to the other group but data was analysed in original group; 2 discontinuations not included in analysis.</td>
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<td>Zimny et al 2003</td>
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Appendix 39: Reporting Bias
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<tr>
<td>Are inclusion and exclusion criteria definitively outlined?</td>
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<tr>
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<tr>
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<tr>
<td>Is there external validity?</td>
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**Calculation for section validity:** \((Y+N+U=T)\)

If \(Y/T < 75\%\) or if \(N+U/T > 25\%\) then you can safely conclude that the section identifies significant omissions and that the study’s validity is questionable. It is important to look at the overall validity as well as section validity.

**Calculation for overall validity:** \((12+6+2=T)\)

If \(Y/T \geq 75\%\) or if \(N+U/T \leq 25\%\) then you can safely conclude that the study is valid.

- **Section A validity calculation:** 43% or 57%
- **Section B validity calculation:** 100% or 0%
- **Section C validity calculation:** 25% or 75%
- **Section D validity calculation:** 83% or 17%
- **Overall validity calculation:** \(12/20= 60\%\) or \(8/20= 40\%\)
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</table>

**Calculation for section validity:** \((Y+N+U=T)\)
- If \(Y/T < 75\%\) or if \(N+U/T > 25\%\) then you can safely conclude that the section identifies significant omissions and that the study’s validity is questionable. It is important to look at the overall validity as well as section validity.

**Calculation for overall validity:** \((10+7+2=19)\)
- If \(Y/T \geq 75\%\) or if \(N+U/T \leq 25\%\) then you can safely conclude that the study is valid.

<p>| Section A validity calculation: 40% or 60% | Overall validity calculation: 10/19=53% |
| Section B validity calculation: 75% or 25% | 9/19=47% |
| Section C validity calculation: 40% or 60% | |
| Section D validity calculation: 80% or 20% | |</p>
<table>
<thead>
<tr>
<th>EBL Critical Appraisal Checklist Nabuurs-Franssen et al (2003)</th>
<th>Yes</th>
<th>No</th>
<th>Unclear</th>
<th>N/A</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Section A: Population</th>
<th>Is the study population representative of all users, actual and eligible, who might be included in the study?</th>
<th>✓</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Are inclusion and exclusion criteria definitively outlined?</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Is the sample size large enough for sufficiently precise estimates?</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Is the response rate large enough for sufficiently precise estimates?</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Is the choice of population bias-free?</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>If a comparative study: Were participants randomized into groups?</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Were the groups comparable at baseline?</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>If groups were not comparable at baseline, was incomparability addressed by the authors in the analysis?</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Was informed consent obtained?</td>
<td>✓</td>
</tr>
<tr>
<td>Section B: Data Collection</td>
<td>Are data collection methods clearly described?</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>If a face-to-face survey, were inter-observer and intra-observer bias reduced?</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Is the data collection instrument validated?</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>If based on regularly collected statistics, are the statistics free from subjectivity?</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Does the study measure the outcome at a time appropriate for capturing the intervention’s effect?</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Is the instrument included in the publication?</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Are questions posed clearly enough to be able to elicit precise answers?</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Were those involved in data collection not involved in delivering a service to the target population?</td>
<td>✓</td>
</tr>
<tr>
<td>Section C: Study Design</td>
<td>Is the study type / methodology utilized appropriate?</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Is there face validity?</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Is the research methodology clearly stated at a level of detail that would allow its replication?</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Was ethics approval obtained?</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Are the outcomes clearly stated and discussed in relation to the data collection?</td>
<td>✓</td>
</tr>
<tr>
<td>Section D: Results</td>
<td>Are all the results clearly outlined?</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Are confounding variables accounted for?</td>
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</tr>
<tr>
<td></td>
<td>Do the conclusions accurately reflect the analysis?</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Is subset analysis a minor, rather than a major, focus of the article?</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Are suggestions provided for further areas to research?</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Is there external validity?</td>
<td>✓</td>
</tr>
</tbody>
</table>

Calculation for section validity: 
\[(Y+N+U=T)\]

If \(Y/T < 75\%\) or if \(N+U/T > 25\%\) then you can safely conclude that the section identifies significant omissions and that the study’s validity is questionable. It is important to look at the overall validity as well as section validity.

Calculation for overall validity: 
\[(13+1+5=19)\]

If \(Y/T \geq 75\%\) or if \(N+U/T \leq 25\%\) then you can safely conclude that the study is valid.

| Section A validity calculation: 40\% or 60\% | Overall validity calculation: 13/19= 68.4\% |
| Section B validity calculation: 75\% or 25\% | 1+5/19= 32\% |
| Section C validity calculation: 100\% or 25\% | |
| Section D validity calculation: 80\% or 20\% | |

<table>
<thead>
<tr>
<th>Reviews</th>
<th>Yes (Y)</th>
<th>No (N)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Background</td>
<td>✓</td>
<td></td>
<td>Concise background mentions incidence of diabetes and DFU, potential complications and enumerates traditional treatments and new developments.</td>
</tr>
<tr>
<td>Research Question</td>
<td>✓</td>
<td></td>
<td>Not mentioned.</td>
</tr>
<tr>
<td>Aim</td>
<td>✓</td>
<td></td>
<td>Reported.</td>
</tr>
<tr>
<td>Objectives</td>
<td>✓</td>
<td></td>
<td>Not differentiated in the main text.</td>
</tr>
<tr>
<td>Criteria for selecting studies for review:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Types of studies</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Types of participants</td>
<td>✓</td>
<td></td>
<td>Characteristics of participants not clearly mentioned. Only mentioned type 1 and type 2 diabetes and patients with DFU.</td>
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<tr>
<td>Types of interventions</td>
<td>✓</td>
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<td>Looking at individual types of treatment.</td>
</tr>
<tr>
<td>Types of outcome measures</td>
<td>✓</td>
<td></td>
<td>Not mentioned.</td>
</tr>
<tr>
<td>Search methods for identification of studies</td>
<td>✓</td>
<td></td>
<td>Incomplete, only databases and other resources used for searching are mentioned. Did not report terms used or a flow chart with results of search.</td>
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<tr>
<td>Data collection</td>
<td>✓</td>
<td></td>
<td>Does not report how this will be done.</td>
</tr>
<tr>
<td>Data analysis</td>
<td>✓</td>
<td></td>
<td>Does not report how this will be done.</td>
</tr>
<tr>
<td>Results:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Description of studies</td>
<td>✓</td>
<td></td>
<td>Presented in tables on author, date of study, intervention, trial details and results.</td>
</tr>
<tr>
<td>Risk of bias in included studies</td>
<td>✓</td>
<td></td>
<td>Not reported.</td>
</tr>
<tr>
<td>Effects of interventions</td>
<td>✓</td>
<td></td>
<td>Summarises findings of studies individually, poor critical appraisal.</td>
</tr>
<tr>
<td>Discussion</td>
<td>✓</td>
<td></td>
<td>Critically appraises study quality, not too detailed.</td>
</tr>
</tbody>
</table>

Appendix 44: Quality Appraisal Spencer (2008)

Adapted from The Cochrane Handbook – Protocol for Cochrane Reviews (Higgins& Green 2011)
<table>
<thead>
<tr>
<th>Steps for Conducting Systematic Reviews</th>
<th>Spencer (2008)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Background</td>
<td>Yes (Y)</td>
</tr>
<tr>
<td>Research Question</td>
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<td>Aim</td>
<td>Yes (Y)</td>
</tr>
<tr>
<td>Objectives</td>
<td>Yes (Y)</td>
</tr>
<tr>
<td>Criteria for selecting studies for review:</td>
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</tr>
<tr>
<td>Types of studies</td>
<td>Yes (Y)</td>
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<tr>
<td>Types of participants</td>
<td>Yes (Y)</td>
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<tr>
<td>Types of interventions</td>
<td>Yes (Y)</td>
</tr>
<tr>
<td>Types of outcome measures</td>
<td>Yes (Y)</td>
</tr>
<tr>
<td>Search methods for identification of studies</td>
<td>Yes (Y)</td>
</tr>
<tr>
<td>Data collection</td>
<td>Yes (Y)</td>
</tr>
<tr>
<td>Data analysis</td>
<td>Yes (Y)</td>
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<tr>
<td>Results:</td>
<td></td>
</tr>
<tr>
<td>Description of studies</td>
<td>Yes (Y)</td>
</tr>
<tr>
<td>Risk of bias in included studies</td>
<td>Yes (Y)</td>
</tr>
<tr>
<td>Effects of interventions</td>
<td>Yes (Y)</td>
</tr>
<tr>
<td>Discussion</td>
<td>Yes (Y)</td>
</tr>
</tbody>
</table>

Adapted from The Cochrane Handbook – Protocol for Cochrane Reviews (Higgins & Green 2011)
Appendix 45: Outcome Measures Armstrong et al 2001
<table>
<thead>
<tr>
<th>Study</th>
<th>Sample</th>
<th>Healing Rates</th>
<th>Healing Times</th>
<th>Reduction in Ulcer Size</th>
<th>Activity Daily steps</th>
<th>Ulcer Size (cm²)</th>
<th>Adverse Effects</th>
<th>Cost</th>
<th>QoL</th>
<th>Compliance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Armstrong et al (2001) Prospective RCT</td>
<td>63 patients</td>
<td>89.5% (n=17)</td>
<td>33.5±5.9 days</td>
<td>Not reported</td>
<td>600.1±320.0</td>
<td>Healed ulcers were smaller at baseline than unhealed ulcers.</td>
<td>Not reported</td>
<td>None reported</td>
<td>None reported</td>
<td>None reported</td>
</tr>
<tr>
<td></td>
<td>TCC: 19</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>RWC: 20</td>
<td>65.0% (n=13)</td>
<td>50.4±7.2 days</td>
<td></td>
<td></td>
<td>767.6±563.3</td>
<td>HU 1.1±1.0 UHU 1.9±1.3</td>
<td>Not reported</td>
<td>None reported</td>
<td>None reported</td>
</tr>
<tr>
<td></td>
<td>Half-shoe: 24</td>
<td>58.3% (n=14)</td>
<td>61.0±6.5 days</td>
<td></td>
<td></td>
<td>1,461.8±1,452.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Appendix 46: Outcome Measures Armstrong et al 2005
<table>
<thead>
<tr>
<th>Study</th>
<th>Sample</th>
<th>Systematic Review Primary Outcome Measures</th>
<th>Other Relevant Aspects</th>
<th>Systematic Review Secondary Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Healing Rates</td>
<td>Healing Times</td>
<td>Ulcer Size (cm²) At Baseline</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12 weeks ITT</td>
<td>12 weeks (n=46)</td>
<td></td>
</tr>
<tr>
<td>Armstrong et al (2005)</td>
<td>50 patients</td>
<td>iTCC: 23</td>
<td>82.6%</td>
<td>86.4%</td>
</tr>
<tr>
<td>RCT</td>
<td></td>
<td>RCW: 27</td>
<td>51.9%</td>
<td>Not reported</td>
</tr>
<tr>
<td></td>
<td></td>
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<td>58.3%</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>58.0±15.2</td>
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</tr>
</tbody>
</table>

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Appendix 47: Outcome Measures Birke et al 2002
### Systematic Review Primary Outcome Measures

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample</th>
<th>Healing Rates at 12w</th>
<th>Healing Times (days)</th>
<th>Reduction in Ulcer Size</th>
<th>Other Relevant Aspects</th>
<th>Systematic Review Secondary Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birke et al (2002) Retrospective analysis</td>
<td>120 patients&lt;sup&gt;6&lt;/sup&gt;</td>
<td>n=113 (94%) 81% of forefoot ulcers closed</td>
<td>45.5±43.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TCC: 13</td>
<td>92%</td>
<td>47.7±41.4</td>
<td>Not reported</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Accommodative dressing: 26</td>
<td>93%</td>
<td>36.1±36.3</td>
<td>Not reported</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Healing shoe: 57</td>
<td>81%</td>
<td>41.4±41.9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Walking splint: 18</td>
<td>83%</td>
<td>50.5±29.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other: 6</td>
<td>Not reported</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

#### Other Relevant Aspects

<table>
<thead>
<tr>
<th>Ulcer Size (cm)</th>
<th>At baseline</th>
<th>Adverse Effects</th>
<th>Cost/QoL/Compliance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length</td>
<td>Width</td>
<td>Depth</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.4±0.9</td>
<td>0.9±0.5</td>
<td>0.6±0.5</td>
<td></td>
</tr>
<tr>
<td>1.3±1.2</td>
<td>0.9±0.7</td>
<td>0.4±0.4</td>
<td></td>
</tr>
<tr>
<td>1.2±0.9</td>
<td>0.7±0.5</td>
<td>0.3±0.6</td>
<td></td>
</tr>
<tr>
<td>1.6±1.3</td>
<td>1.1±0.9</td>
<td>0.5±0.6</td>
<td></td>
</tr>
<tr>
<td>1.6±0.7</td>
<td>1.0±0.5</td>
<td>0.6±0.8</td>
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</tr>
</tbody>
</table>

---

<sup>6</sup> Seven ulcers (5.8%) did not heal or were lost to follow-up.
Appendix 48: Outcomes Measures Caravaggi et al 2000
<table>
<thead>
<tr>
<th>Study</th>
<th>Sample</th>
<th>Systematic Review Primary Outcome Measures</th>
<th>Other Relevant Aspects</th>
<th>Systematic Review Secondary Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Healing Rates</td>
<td>Healing Times</td>
<td>Ulcer Size (mm$^2$) At Baseline</td>
</tr>
<tr>
<td>Caravaggi et al (2000)</td>
<td>50 patients</td>
<td>n= 5</td>
<td>Not reported</td>
<td>431.7 [391.7]</td>
</tr>
<tr>
<td>RCT</td>
<td>Therapeutic shoe: 24</td>
<td>n= 13</td>
<td>587.3 [587.7]</td>
<td>n= 0</td>
</tr>
<tr>
<td></td>
<td>Fiberglass cast: 26 After 30days</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix 49: Outcome Measures Dumont et al 2009
Seven patients were lost to follow-up, seven developed co-morbidities, four died.

22 (18.8%) patients ulcer unhealed until amputation of which 21 minor and one major amputation.

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample</th>
<th>Healing Rates</th>
<th>Healing Times Median (IQR)</th>
<th>Reduction in Ulcer Size</th>
<th>Ulcer Size</th>
<th>Adverse Effects</th>
<th>Compliance</th>
<th>Cost / QoL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dumont et al (2009)</td>
<td>135 patients&lt;sup&gt;7&lt;/sup&gt; n=117&lt;sup&gt;8&lt;/sup&gt;</td>
<td>n=82 (70.1%)</td>
<td>60 days (43-99)</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Abrasions in instep: n=8 Redness on 5&lt;sup&gt;th&lt;/sup&gt; metatarsal head: n=2 Bli</td>
<td>Judge non-compliant n=13 (9.6%)</td>
<td>Nothing reported</td>
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<tr>
<td>Observational study</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ster on the heel: n=1 Complications healed after modifications of the Ransart boot.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix 50: Outcome Measures Faglia et al 2010
For an obese patient extra bandage was required increasing the price to €89.5.

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample</th>
<th>Systematic Review Primary Outcome Measures</th>
<th>Other Relevant Aspects</th>
<th>Systematic Review Secondary Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Healing Rates (days)</td>
<td>Healing Times (days)</td>
<td>Reducing in Ulcer Size (cm²) At Baseline</td>
</tr>
<tr>
<td>Faglia et al (2010)</td>
<td>45 patients</td>
<td>TCC: 23 (%)</td>
<td>73.9% (n=17)</td>
<td>35.3±3.1</td>
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<tr>
<td>RCT</td>
<td>Stabil-D: 22 (%)</td>
<td>72.7% (n=16)</td>
<td>39.7±4.2</td>
<td>2.18 to 0.45 cm² 90% reduction</td>
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</table>
Appendix 51: Outcome Measure Katz et al 2005
<table>
<thead>
<tr>
<th>Study</th>
<th>Sample</th>
<th>Healing Rates ≤ 12 weeks</th>
<th>Healing Times (mean)</th>
<th>Reduction in Ulcer Size</th>
<th>Other Relevant Aspects</th>
<th>Systematic Review Secondary Outcome Measures</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>n=41</td>
<td>n=34</td>
<td></td>
<td></td>
<td>Adverse Effects</td>
</tr>
<tr>
<td>Katz et al (2005)</td>
<td>TCC: 20</td>
<td>74±45%</td>
<td>93±26%</td>
<td>5weeks</td>
<td>Not reported</td>
<td>Maceration n=7 (35%)</td>
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<tr>
<td></td>
<td>iTCC: 21</td>
<td>80±41%</td>
<td>94±24%</td>
<td>4weeks</td>
<td>3.1 (1.6, 0.9-3.5)</td>
<td>Maceration n=6(29%)</td>
</tr>
</tbody>
</table>

10 TCC group 4 lost to follow-up, iTCC group 2 lost to follow-up and 1 had osteomyelitis before study entry.
Appendix 52: Outcome Measure Mueller et al 1989
<table>
<thead>
<tr>
<th>Study</th>
<th>Sample</th>
<th>Healing Rate</th>
<th>Healing Time (days)</th>
<th>Reduction in Ulcer Size</th>
<th>Ulcer Size at Baseline</th>
<th>Adverse Effects</th>
<th>Cost</th>
<th>Compliance/QoL</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCT</td>
<td>40 patients</td>
<td>90% (n = 19)</td>
<td>42±29 (range 8-91)</td>
<td>Not reported</td>
<td>1.8±2.5</td>
<td>Foot Infection that required hospitalisation</td>
<td>n=0</td>
<td>Not reported</td>
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<tr>
<td>TCC: 21</td>
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<td></td>
<td></td>
<td></td>
<td>3.6±3.2</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>TDT: 19</td>
<td>32% (n = 6)</td>
<td></td>
<td>65±29 (range 12-92)</td>
<td>Not reported</td>
<td>2.8±3.4</td>
<td>n=5 (26%) of which 2 required forefoot amputation</td>
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<td>Not reported</td>
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</table>
Appendix 53: Outcome Measures Nabuurs-Franssen et al 2005
<table>
<thead>
<tr>
<th>Study</th>
<th>Sample</th>
<th>Healing Rates</th>
<th>Healing Times (median)</th>
<th>Reduction in Ulcer Size</th>
<th>Ulcer Size [median (IQR)]</th>
<th>Adverse Effects</th>
<th>Compliance</th>
<th>Cost/ QoL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nabuurs-Franssen et al (2005)</td>
<td>98 patients (n=74)</td>
<td>33 days (14-36)</td>
<td>1.3 cm² (0.6-7.1)</td>
<td>1.2 cm² (0.6-3.1)</td>
<td>Infection: n=9</td>
<td>Non-compliance n=1</td>
<td>Lost to follow-up n=2</td>
<td>Not reported</td>
</tr>
<tr>
<td>Prospective data collection</td>
<td>TCC: 50</td>
<td>RCC: 22</td>
<td>SMC: 26</td>
<td></td>
<td>Hospitalise for IV ant. n=6</td>
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<tr>
<td></td>
<td>n=74 (76%)</td>
<td></td>
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<td>Amputations n=3</td>
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<td></td>
<td></td>
<td></td>
<td>Revascularisation n=2</td>
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<td></td>
<td></td>
<td></td>
<td>Free-flap transplantation n=3</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>Cast stopped due to discomfort n=7</td>
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<td></td>
<td>New superficial ulcers: 9% which healed in 13 days with new revised cast</td>
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<td></td>
<td>Pre-ulcerative lesions: 28% resolved in few days after minor adaptations in cast</td>
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<td>Chafed skin: 8%</td>
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<td>Joint problems: 7%</td>
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</table>

### Healing Rate (Patient groups)
- No PAD + No infection = 90%
- No PAD + Infection = 87%
- PAD + No infection = 69%
- PAD + Infection = 36%

### Healing Times (Patient groups)
- No PAD + No infection = 18 days (10-41)
- No PAD + Infection = 29 days (27-68)
- PAD + No infection = 42 days (14-65)
- PAD + Infection = only a minority healed, being the numbers too small to calculate time to heal
Appendix 54: Outcome Measures Piaggesi et al 2007
<table>
<thead>
<tr>
<th>Study</th>
<th>Sample</th>
<th>Healing Rate At 12 weeks</th>
<th>Healing Time (weeks)</th>
<th>Reduction in Ulcer Size</th>
<th>Ulcer Size (cm²) At Baseline</th>
<th>Adverse Effects</th>
<th>Cost</th>
<th>Compliance</th>
<th>QoL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Piaggesi et al (2007)</td>
<td>40 patients</td>
<td>95%</td>
<td>6.5±4.4 (2-14)</td>
<td>Not reported</td>
<td>3.7±1.6</td>
<td>Maceration</td>
<td>110.5±4.38 (€) per cast</td>
<td>6.85±2.39</td>
<td>Not reported</td>
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<tr>
<td></td>
<td>TCC: 20</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>727.29±491.25 (€) per patient</td>
<td></td>
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<tr>
<td></td>
<td>Optima Diab walker: 20</td>
<td>85%</td>
<td>6.7±3.4 (2-17)</td>
<td></td>
<td>3.9±1.8</td>
<td>Paraesthesia n=1</td>
<td>€130 each</td>
<td>8.45±1.79</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Haematoma of calf n=1</td>
<td>162.5±57.75 (€) per patient</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample</th>
<th>Healing Rate At 12 weeks</th>
<th>Healing Time (weeks)</th>
<th>Reduction in Ulcer Size</th>
<th>Ulcer Size (cm²) At Baseline</th>
<th>Adverse Effects</th>
<th>Cost</th>
<th>Compliance</th>
<th>QoL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Piaggesi et al (2007)</td>
<td>40 patients</td>
<td>95%</td>
<td>6.5±4.4 (2-14)</td>
<td>Not reported</td>
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<td>Maceration</td>
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<td>6.85±2.39</td>
<td>Not reported</td>
</tr>
<tr>
<td></td>
<td>TCC: 20</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>727.29±491.25 (€) per patient</td>
<td></td>
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<tr>
<td></td>
<td>Optima Diab walker: 20</td>
<td>85%</td>
<td>6.7±3.4 (2-17)</td>
<td></td>
<td>3.9±1.8</td>
<td>Paraesthesia n=1</td>
<td>€130 each</td>
<td>8.45±1.79</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Haematoma of calf n=1</td>
<td>162.5±57.75 (€) per patient</td>
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</table>
Appendix 55: Outcome Measures Van de Weg et al 2008
Follow-up not achieved for 4 patients: one died, one was amputated and two withdrew from study.

Not described, but all identified as device related.

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample</th>
<th>Healing Rates</th>
<th>Healing Times</th>
<th>Reduction in Ulcer Size</th>
<th>Other Relevant Aspects</th>
<th>Systematic Review Secondary Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van de Weg et al (2008)</td>
<td>43 patients</td>
<td>TCC: 23</td>
<td>n=6</td>
<td>59±39 days</td>
<td>Ulcer Size (cm²)</td>
<td>Adverse Effects</td>
</tr>
<tr>
<td>Prospective RCT</td>
<td>32 patients</td>
<td>CTF: 20</td>
<td>n=6</td>
<td>90±12 days</td>
<td>At Baseline: 3.0±3.1 Median US: 0.4</td>
<td>Minor Abrasion: n=0 Complications: n=5 (2 had to d/c)</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>16 weeks: 3.0±3.1 Median US: 0.4</td>
<td>Minor Abrasion: n=0 Complications: n=5 (2 had to d/c)</td>
</tr>
</tbody>
</table>

11 Follow-up not achieved for 4 patients: one died, one was amputated and two withdrew from study.

12 Not described, but all identified as device related.
Appendix 56: Outcome Measures Zimny et al 2003
<table>
<thead>
<tr>
<th>Study</th>
<th>Sample</th>
<th>Healing Rate</th>
<th>Healing Time (days)</th>
<th>Reduction in Ulcer Size</th>
<th>Ulcer Size (mm²)</th>
<th>Adverse Effects</th>
<th>Cost</th>
<th>Compliance/ QoL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>At Baseline</td>
<td>After 10 weeks</td>
<td></td>
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</tr>
<tr>
<td>Zimny et al (2003)</td>
<td>54 patients</td>
<td>Not reported</td>
<td>75.2 (67-84)</td>
<td>0.48mm per week (0.42-0.56)</td>
<td>102.3±45.3</td>
<td>5.4±3.1</td>
<td>Soft tissue infection</td>
<td>25%</td>
</tr>
<tr>
<td>Prospective RCT</td>
<td>Felted Foam: 24</td>
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<tr>
<td></td>
<td>Half shoes: 30</td>
<td></td>
<td>85.2 (79-92)</td>
<td>0.39mm per week (0.35-0.42)</td>
<td>112.5±50.8</td>
<td>10.6±4.2</td>
<td>23%</td>
<td></td>
</tr>
</tbody>
</table>
Appendix 57: Systematic Review Checklist\textsuperscript{13}

<table>
<thead>
<tr>
<th>Section/topic</th>
<th>#</th>
<th>Checklist item</th>
<th>Reported on page #</th>
</tr>
</thead>
<tbody>
<tr>
<td>TITLE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Title</td>
<td>1</td>
<td>Identify the report as a systematic review, meta-analysis, or both.</td>
<td></td>
</tr>
<tr>
<td>ABSTRACT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Structured summary</td>
<td>2</td>
<td>Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.</td>
<td>13</td>
</tr>
<tr>
<td>INTRODUCTION</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rationale</td>
<td>3</td>
<td>Describe the rationale for the review in the context of what is already known.</td>
<td>14</td>
</tr>
<tr>
<td>Objectives</td>
<td>4</td>
<td>Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).</td>
<td>24-25</td>
</tr>
<tr>
<td>METHODS</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Protocol and registration</td>
<td>5</td>
<td>Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.</td>
<td>N/A</td>
</tr>
<tr>
<td>Eligibility criteria</td>
<td>6</td>
<td>Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.</td>
<td>49</td>
</tr>
<tr>
<td>Information sources</td>
<td>7</td>
<td>Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.</td>
<td>50</td>
</tr>
<tr>
<td>Search</td>
<td>8</td>
<td>Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.</td>
<td>148</td>
</tr>
<tr>
<td>Study selection</td>
<td>9</td>
<td>State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).</td>
<td>50-51</td>
</tr>
<tr>
<td>Data collection process</td>
<td>10</td>
<td>Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.</td>
<td>51-52</td>
</tr>
<tr>
<td>Data items</td>
<td>11</td>
<td>List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.</td>
<td>50</td>
</tr>
<tr>
<td>Risk of bias in individual studies</td>
<td>12</td>
<td>Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.</td>
<td>52</td>
</tr>
<tr>
<td>Summary measures</td>
<td>13</td>
<td>State the principal summary measures (e.g., risk ratio, difference in means).</td>
<td>52</td>
</tr>
<tr>
<td>Synthesis of results</td>
<td>14</td>
<td>Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.</td>
<td>51-52</td>
</tr>
<tr>
<td>Risk of bias across studies</td>
<td>15</td>
<td>Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).</td>
<td>51-52</td>
</tr>
<tr>
<td>Additional analyses</td>
<td>16</td>
<td>Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.</td>
<td>52</td>
</tr>
</tbody>
</table>

**RESULTS**

| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 56, 168 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 169-223 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | 64-66 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 70-98, 267-290 |
| Synthesis of results | 21 | Present in the main results of the review. If meta-analyses are done, include for each, confidence intervals and measures of consistency. | 70-98 |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | 64-66, 245-256 |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | 66-67 |

**DISCUSSION**

| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 101-115 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 116-117 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 118-120 |
| **FUNDING** | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 298 |
Appendix 58: Gantt chart
Proposed Timetable for conducting the Systematic Review, to be submitted May 9th of 2013

<table>
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Appendix 59: Resources
The writer had no sponsorship to conduct this systematic review.