“Single sensor, pressure and temperature mapping device for the prevention of diabetic foot re-ulceration.”

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Abstract

The aim of this study was to develop and validate a single-sensor, in-shoe pressure and temperature measuring device. This PhD study, sought to determine whether the specifically designed and innovative, device is effective in reducing re-ulceration in a high-risk diabetic population, when compared with the local current standard diabetic foot care management. To date diabetic foot care management consists of relying on visual observation and clinical experience to detect signs of ulceration and later design an appropriate treatment plan. This study sought to establish whether this innovative device could be used as a cost-effective alternative to the standard costly in-shoe measurement systems which can be used in a clinical setting to evaluate pressure areas of interest at risk of ulceration. Furthermore, it sought to determine whether the orthoses currently prescribed are indeed offering the intended reduction of plantar pressure to prevent re-ulceration.

The research comprised of 3 main phases. Phase one consisted of a detailed systematic review relating to the validity and reliability of in-shoe systems that are able to measure pressure and temperature simultaneously. It sought to identify studies that utilize in-shoe pressure and temperature systems as an identification technique for peak plantar pressures and raised skin temperatures in the diabetic high-risk foot at risk of ulceration. It also consisted of 2 local scoping studies which explored the local biomechanical and offloading management of the diabetic high-risk foot. In the second phase, an innovative, single sensor pressure and temperature mapping measurement device was developed and validated against a commercial, gold standard, in-shoe system. This device was used to validate effectiveness of pressure reduction in previously ulcerated sites in the high-risk foot. Once attained, this device was expected to offer a low-cost and easy to use system to be used in a clinical setting.

The third and final stage (Stage III) of this dissertation, comprised of recruiting participants living with type II diabetes mellitus with a history of ulceration and who had been prescribed standard hospital orthoses. These orthoses were assessed to determine whether they were reducing the peak plantar pressures by the recommended 30% reduction. Furthermore, this stage sought to develop a clinical protocol for the use of the innovative, single sensor temperature and pressure mapping device to

possibly replace the current expensive and time-consuming commercial in-shoe pressure and temperature measuring devices.

Findings of this PhD research highlighted that the biomechanical management of the high-risk diabetic foot consists of simple assessment of pedal range of motion and foot deformities. Furthermore, technology to assist the clinician in determining the effectiveness of prescribed offloading devices, through identification of in-shoe peak plantar pressures, in view of ulcer and re-ulceration prevention, is not available in local health care services. Results further showed that local clinicians deem the use of such technology as too expensive and time consuming to use in their busy clinical schedule and thus, clinicians tend to base their treatment plan on clinical experience and visual observation. Quality assessment of 17 studies relating to the validity and reliability of in-shoe pressure and in-shoe temperature devices being developed in view of diabetic foot ulcer prevention, demonstrated low quality of evidence. This highlighted the need for further improvement, reliability testing and clinical validations of in-shoe pressure and in-shoe temperature measuring devices.

An innovative, single sensor, in-shoe pressure and temperature measuring device, that is able to read pressure and temperature simultaneously, was developed and validated, on healthy participants, under both static and dynamic laboratory conditions. Results of both the static and dynamic validation studies showed high correlation results between the innovative device and the FScan® and Flir® thermal camera which served as reference standard for in-shoe pressure assessment and temperature assessment respectively. Lastly, clinical validation of the innovative, single sensor, in-shoe pressure and temperature measuring device, was confirmed in a clinical trial that involved the diabetic high-risk population. Results of the clinical trial demonstrated that participants who were monitored for peak plantar pressures and skin temperature with the innovative, single sensor, in-shoe pressure and temperature measuring device together with receiving the current standard diabetic foot care management, fared better in terms of presenting with less cases of re-ulceration, compared to the control group who only received the current standard diabetic foot care management.

These results highlight the need for change and improvement in the current diabetic foot care management plan if better outcomes in terms of ulceration and re-ulceration prevention are to be attained. The introduction of diagnostic technology in clinical care,

such as the innovative, single sensor, in-shoe pressure and temperature device, to monitor in-shoe plantar pressures and in-shoe temperature of the diabetic high-risk foot, is expected to bring about a change in the way that both patients and health care system could holistically benefit.

Key words: Diabetic foot; ulceration; foot plantar pressures; pressure mapping; biomechanics; offloading; orthoses.

To my mother,

You sacrificed a lot to give me an education.

I will use it to provide you a better future.

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Dissemination of Findings through Conferences and Publications

Conferences

Saliba Thorne, C., Bazena, A., Gatt, A., DeRaffaele, C., Formosa, C. (2021). Digital foot health technology and diabetic foot monitoring: A systematic review. This abstract was presented as an Oral Presentation at the International Foot and Ankle Biomechanics Community (i-FAB) in April 2021, Brazil.

Saliba Thorne, C., Gatt, A., Formosa, C. (2021). Digital Foot Technology in Ulcer Prevention and Re-ulceration: A Maltese Perspective. This abstract was presented as an Oral Presentation at the 19th Staffordshire Conference on Clinical Biomechanics (SCCB) conference in April 2021, Staffordshire, UK.

Saliba Thorne, C., Bazena, A., Gatt, A., DeRaffaele, C., Formosa, C. (2021). Foot health technology for the diabetic high-risk foot: A systematic Review. This abstract was presented as an oral presentation at the International Society of Biomechanics (ISB) Conference 2021, Stockholm.

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Saliba Thorne, C., Gatt, A., Formosa, C. (2022). Digital foot technology and the assessment of the diabetic foot. This abstract was presented as an oral presentation at the Association of Podiatrists of Malta Annual Conference 2022.

Saliba Thorne, C., Bazena, A., Gatt, A., DeRaffaele, C., Formosa, C. (2023). Dynamic validation of an innovative single sensor, in-shoe pressure and temperature measuring device. This abstract will be presented as an e-poster presentation at the Advanced Technologies and Treatments for the Diabetes 16th International Conference February 23rd 2023, Berlin.

Peer-reviewed Abstracts & Publications

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Saliba Thorne, C., Gatt, A., & C., Formosa, C. (2021). Digital foot technology in Ulcer Prevention and Re-ulceration. *Journal of American Podiatric Medicine*

Saliba Thorne, C., Gatt, A., DeRaffaele, C., Bazena, A. & Formosa, C. (2022). Innovative single-sensor, in-shoe pressure and temperature monitoring device: A dynamic laboratory validation study. *Gait & Posture*, ISSN 0966-6362, https://doi.org/10.1016/j.gaitpost.2022.11.013.

Papers under review

Saliba Thorne, C., Bazena, A., Gatt, A., DeRaffaele, C., Formosa, C. (2022) Static validation of an innovative, single-sensor, in-shoe pressure and temperature monitoring device. *Journal of Diabetes Science and Technology.*

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Chapter 1: Introduction

This chapter introduces the reader to this project which relates to plantar pressure and skin temperature in view of the prevention of diabetic foot ulceration. An overview of the international and local management of the diabetic foot is also presented, the literature gap which has led to the conception of this project is also highlighted within this chapter. Moreover, this chapter highlights the overarching research question, aims and objectives of this PhD project and provides an overview of the strategy of this dissertation.

1.1 Background

The conception of this project, which was to develop an innovative, low-cost, single-sensor pressure and temperature measuring device in view of diabetic foot ulcer prevention, originated from observing local prevalence of individuals living with diabetes mellitus who have experienced an amputation secondary to diabetic foot ulceration. In Malta, it is estimated that approximately 20% of individuals living with diabetes mellitus develop a foot ulcer and, that approximately 400 patients experience an amputation secondary to diabetic foot ulcer related complications (Mizzi & Falzon, 2018). This makes this country one with the highest prevalence of diabetes in the European Union (Cuschieri, 2020). Despite the efforts that the health care system is employing to prevent diabetic foot ulceration, we are still facing a disproportionate number of individuals who experience serious diabetic foot ulceration which often lead to lower limb amputation (Grima et al., 2018, Schembri et al., 2022).

Locally, the majority (90%) of lower limb amputations are secondary to diabetes mellitus (Grima et al., 2018). A local cohort study reported that the number of major lower limb amputations (above or below the knee joint) have reduced considerable since 2003 however, minor amputations (any part below the ankle joint) are still an increasing cause of concern (Schembri, 2022). This study further reported that between January 2018 and January 2019, 119 minor amputations were performed and mostly related to the amputation of the 1st, 2nd and 3rd digits (Schembri et al., 2022). This excessive amount of re-ulceration cases may be attributed to the possibility that causative factors for tissue breakdown, such as elevated foot plantar pressures, are still

present and/or not being properly dealt with (Bus, Waaijman, Arts, et al., 2013). This is clearly suggestive of anomalies within the management care of these high-risk patients.

The formation of diabetic foot ulceration amongst, patients with diabetes mellitus, is well recognised amongst health care professionals. The process of ulceration naturally initiates with continuous vertical strain (pressure) or lateral shear forces over the skin (Monteiro-Soares, M., Boyko, E.J., Ribeiro, J, et al., 2012; Bus, 2016) which in turn promotes an inflammatory process. This heats up the area of stress (Armstrong, Boulton & Bus, 2017; Mizzi & Falzon, 2018) which can last up to a week prior to tissue break down and ulcer formation (Sun et al., 2006; Gatt et al., 2018). Thus, plantar pressure monitoring and monitoring of skin temperature of the affected area is empirical as it can help in preventing skin damage, ulceration and re-ulceration (Mizzi & Falzon, 2018).

Investigating whether an innovative, low-cost, user-friendly, in-shoe device, which can measure plantar pressure and skin temperature simultaneously, is warranted to assist early and objective identification of those who are more likely to experience or re-experience diabetic foot complications. This device was developed to replace current commercial in-shoe pressure and temperature systems which are costly and time-consuming. This may be encouraging clinicians for using this device in their daily clinical practice.

1.2 Diabetes Mellitus

Diabetes Mellitus is a chronic metabolic disease that is caused by a defect in insulin secretion, insulin action or a combination of both which results in an increase in blood glucose level (hyperglycaemia) (WHO, 2022). Peripheral neuropathy and limited vascular perfusion to the lower limb, predisposes the diabetic foot to ulcerations, Charcot arthropathy and eventually amputations and are commonly associated with long term diabetes (Edmonds, Manu & Vas, 2021). Globally, the prevalence of the adult population diagnosed with diabetes mellitus has risen from 108 million (4.7%) people in 1980 to 422 million (8.5%) people in 2014 in the adult population (WHO, 2022) and is expected to rise to 592 million by 2035 (Saeedi et al., 2019; Iacobucci, 2021). The WHO has attributed nearly half of the all the deaths reported prior the age

of 70 years to diabetes mellitus and has named it to be the 7th leading cause of death by 2030 (WHO, 2022).

The consequences of diabetes on the public health are astounding considering the high morbidity and mortality rate associated with it. It is estimated that the life expectancy of a male diagnosed with diabetes is reduced by 12 years and that of a female by 19 years (Narayan et al., 2003) furthermore, people living with diabetes who undergo lower limb amputation are expected to live for only 5 years post-op (Armstrong et al., 2020). The major consequences of diabetes include blindness (2%), cardiovascular disease including increased risk of myocardial infarctions, strokes and peripheral vascular disease (50%) and foot ulceration. A study by Armstrong et al., (2020) reported that the mortality rate of patients living with diabetes mellitus is so high that is considered to be second in line to lung cancer (Figure 1).

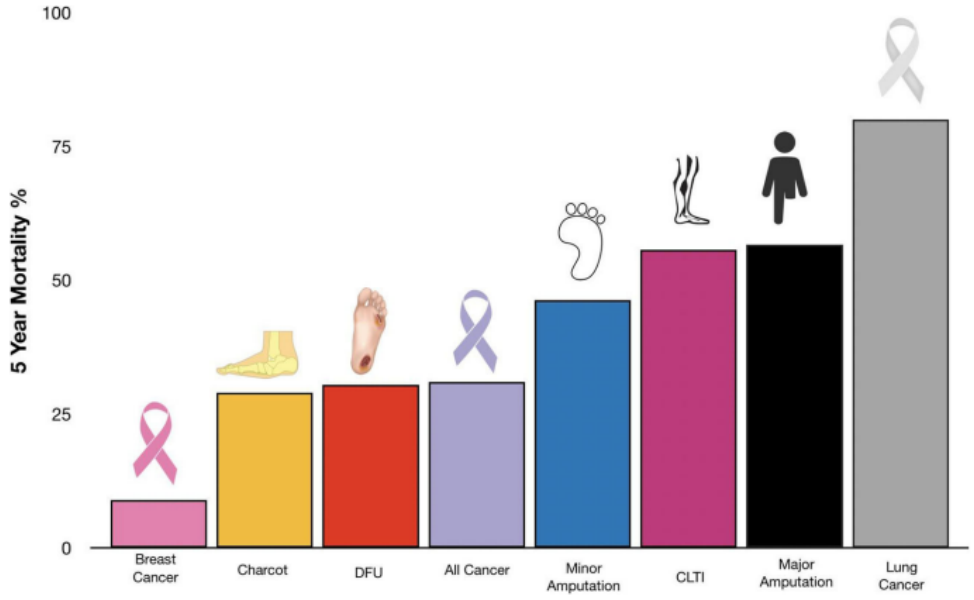


Figure 1: Major lower limb amputations being compared to lung cancer. Retrieved from Armstrong et al. (2020).

1.3 The role of temperature and pressure in ulcer pathogenesis

It is well known that foot biomechanics is strongly associated with ulcer development in the diabetic high-risk foot. Joint mobility and structural foot deformities lead to excessive plantar pressure and mechanical stress (Fernando, et al., 2016; Bus, 2016; Armstrong, Boulton & Bus, 2017) which when prolonged over the skin, the blood flow is hindered leading to localised damage to underlying soft tissue (Monteiro-Soares et al., 2012). Moreover, a correlation between excessive pressure and increase in skin

temperature has also been confirmed (Bus, 2016; Jones, Bibb, Davies, et al. 2020). When the skin is subjected to continuous plantar stresses in the diabetic high-risk foot, the skin temperature at the area of stress rises weakening the ability of the surrounding tissues to resist biomechanical abnormalities (Yavuz et al., 2019). This highlights the importance of encouraging clinicians to introduce plantar pressures assessment and skin temperature assessment as part of the routing diabetic foot management care. Measuring both skin temperature and plantar pressures simultaneously, may provide a more reliable tool in the early identification and management of the diabetic high-risk foot (Yavuz et al., 2019).

1.4 Management of patients with diabetic foot ulceration in Malta

1.4.1 The Local Context

This PhD study was conducted locally on the Maltese population. Malta is a small island in the Mediterranean Sea that makes part of 2 sister islands, Gozo and Comino. This archipelago is situated in the most southern part of Europe just 50 miles below Sicily and it has a population that counts up to 442,400 people (World Population Review, 2022).

Malta is known to have a high prevalence of diabetes mellitus. Despite it being a small island, the diabetes and obesity rate of its population is deemed amongst the highest when compared to neighbouring European countries (Cuschieri, 2020). In the past decade, the growing population of Malta has experienced a change in diet from a Mediterranean to a Westernised one. From a diet rich in fruit and vegetables, grains, seeds and oils to a diet high in carbohydrates and fats which (Formosa, Savona-Ventura & Mandy, 2012), together with environmental, genetic factors and a sedentary lifestyle, impact the role of insulin secretion brought the Maltese population to a higher predisposition to diabetes (Department of Health, Information and Research, 2010; Cuschieri & Mamo, 2014; Alkaf, Blakemore, Järvelin, et al., 2021).

In 2020, the International Diabetes Federation (IDF) reported that, 12% of the Maltese adult population (40,500 individuals) are living with diabetes mellitus (IDF, 2020). A recent cross-sectional local study reported that the prevalence of diabetes mellitus in Malta amounts to 10.31% of the population that is, 44,400 individuals and it is mostly common among adults over 40 years of age (Cuschieri, 2020). In fact, a rise of 12.2% in blood glucose level was noted amongst participants aged between 41 and 60 years

and that this percentage further increased to 21.6% as the group aged above 60 years (Directorate for Health Information and Research, 2010). The country health profile of the Maltese Islands reported that by 2020, the life expectancy in Malta was 2 years higher than the average life expectancy of neighbouring EU countries (European Observatory on Health Systems and Policies, 2021). The report further adds,

"Deaths from cardiovascular disease and cancer have declined substantially in recent decades, but deaths from diabetes remain high"

- European Observatory on Health Systems and Policies (2021).

Statistical data clearly illustrated a consistent death rate of 50.8 per 100 000 population amongst the Maltese population which was mainly attributed to diabetes mellitus and its complications (European Observatory on Health Systems and Policies, 2021). This high prevalence of diabetes was associated with premature deaths of individuals preceding the age of 65 making diabetes the third leading cause of death in Malta (European Observatory on Health Systems and Policies, 2021).

A study conducted by Cuschieri (2020) reported that geographical location may play a role in the prevalence of diabetes mellitus as its occurrence differed in all 6 districts across the Maltese Islands. For instance, the Western harbour exhibited the highest previously diagnosed prevalence of diabetes when compared to the rest of the districts. While the Southern harbour, Northern harbour and Gozo districts had the highest prevalence of newly diagnosed diabetes prevalence (Cuschieri, 2020).

The guidelines on diabetes screening, issued by the American Diabetes Association (2018), suggest that screening should start when the adults reach the age of 45 years. In Malta, due to the fact that diabetes has been frequently diagnosed at a fairly young age, and considering the high prevalence of diabetes in the Maltese adult population, it has been suggested that routine diabetes screening commences at an earlier age; perhaps at age 30 years or younger (Cuschieri, 2020).

The high rate of diabetes mellitus, brings about a great economic incumbrance on the healthcare of the Maltese Islands and this burden is thought to continue to grow especially with the current ever-aging population. The direct costs associated with diabetes are related to its chronic and severe complications which predisposes the patient to high risk of infections, wound care related treatments, medical tests,

medications, hospital admissions and amputations (Directorate for Health Information and Research, 2010). Considering the high rate of recurrence of foot ulcerations (>50%) the health care system is experiencing an increased yield in health care costs (Boulton et al, 2005; Rocchiccioli, O'Dounoghue, Buttigieg, 2005; Armstrong, Swerdlow, Armstrong et al., 2020). These costs not only include the current ulcer episode but also the provision of social services and home care. A Swedish study estimated that for the treatment of a single foot ulcer, the health care expenditure went up to €16,157.88 (with no amputation) and €30,521.12 (with amputation) (Ragnarson, Apelqvist & Magnus, 2000). Similarly, in the UK, it was estimated that a single foot ulcer costs the department of health an average of €3,347.72 to €8,370.70 and up to €72,546.09 if an amputation is required (NHS, 2018). Due to the frequent and prolonged in-patient care, the collective expenditure of treating diabetes in Maltese hospitals, primary care and special visits are estimated to be at least €9 million per year (EHIS, 2008). Local healthcare costs are expected to increase by €136,819,523 by year 2045 (IDF, 2020). In view of this, when dealing with patients living with diabetes mellitus it is empirical to prevent ulcer development and/or to prevent ulcer recurrence (Armstrong et al., 2017).

1.4.2 The health care system in Malta

In Malta, the healthcare system is provided free of charge for Maltese citizens and European Union (EU) residents who are in possession of a European Health Insurance Card (EHIC) (Directorate for Health Information and Research, 2010). The island, has one main public hospital, which forms part of the tertiary sector. The hospital is a general hospital which also offers teaching services to students interested in learning medicine. Patients who wish to receive medical care at the public hospital, are admitted via a doctor's referral through the emergency department or outpatients department. A network of 10 health centres, which form part of the primary sector, provide a wide variety of services such as General Practitioner, Podiatry, Physiotherapy and amongst others. Two private hospitals are also available allowing its residents to choose between the private and public sector (Directorate for Health Information and Research, 2010). Figure 2 provides an overview of the local sections of health services.

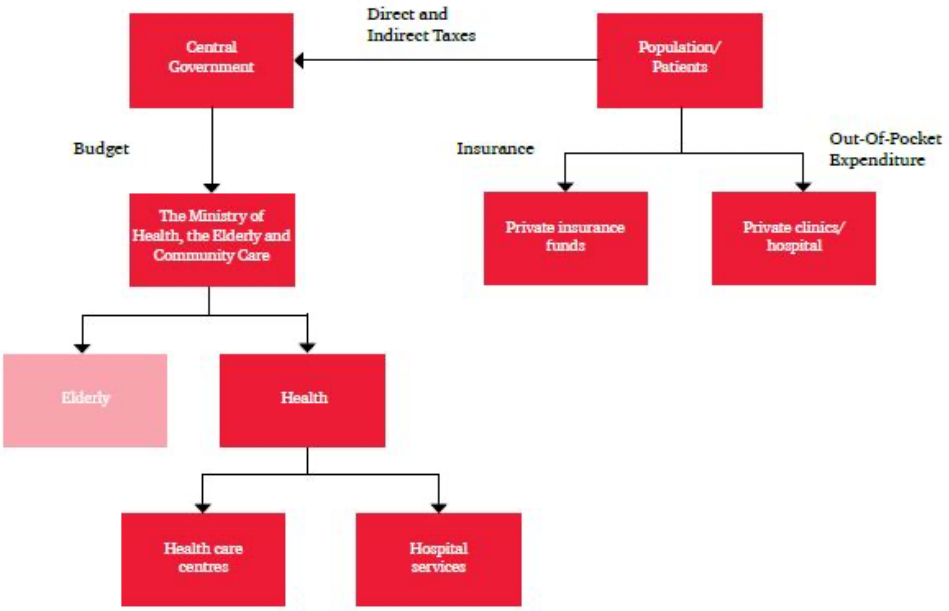


Figure 2: General overview of how the Maltese health care is organised. Retrieved from Spina (2013).

In view of the growing concern on the statistical data that illustrates an increase in diabetic cases (IDF, 2020), in 2014 the Maltese Parliamentary Working Group on Diabetes, published a draft strategy for the first national diabetes prevention program that aims to accentuate prevention through early diagnoses of diabetes and through the expansion of treatment modalities and integration in management care of the effected individuals (Directorate for Health Information and Research, 2010).

In the past decade, the Diabetes Clinic at the local hospital was established to offer clinicians and patients living with diabetes mellitus access to medical doctors, nurses and allied health professionals specialised in diabetes which provide these patients specialised care by following International Diabetic Federation Guidelines (IDF, 2018). Allied health professionals available include Ophthalmologists, Renal Physicians, Vascular Surgeons, Cardiologists, Physiotherapists, Occupational Therapists, Podiatrists, and Tissue Viability Nurses (Directorate for Health Information and Research, 2010).

Though there is no known, official national protocol on the referral of patients living with diabetes mellitus (Schembri et al., 2022), the Diabetes Clinic, as an outpatients department in the Tertiary Sector, has abridged its service to that of the local Primary HealthCare services and implemented a fast referral system in order to meet the great demand for this service. Patients living with diabetes mellitus categorised as low-risk

are managed by a practitioner at their respective health center in the Primary Sector. Concomitantly, these patients are also seen a number of times by specialists at the Diabetes Clinic.

The role of the Podiatrists in both Primary and Tertiary Sector comprises that of screening the diabetic foot (Diabetic Foot Screening) for any signs of risk factors that can lead to diabetic foot complications such as poor vascular perfusion and ulceration. All patients living with diabetes mellitus, especially new cases, are referred to the Podiatry department, for diabetic foot screening. Generally, the nurse in charge at the diabetes clinic in either the Primary or the Tertiary Sector ascertains that the patients are being referred and that the screening is being performed.

The patient care pathway concerning the diabetic foot screening is based on a hierarchal system of assessments referred to as Level 1, Level 2 and Level 3 screening. Level 1 screening relates to the initial assessment at which the patient is categorised as high- or low-risk of developing diabetic foot complications by his/her Podiatrist. The Podiatrist follows a form, the DH 140, (Appendix 1) to assess the patient for his/her neurological and vascular status by using tools such as the 10g monofilament and a doppler ultrasound. Once the patient is found to be of a low-risk category, he/she is given a yearly review. If a neurological and/or a vascular problem has been identified, the patient is categorised as high-risk. In such cases, the patient is referred for further assessment (Level 2 screening) where an in dept vascular assessment using the Dopplex ultrasound to perform Ankle Brachial Pressure Index (ABPI) and Toe Brachial Pressure Index (TBPI) is carried out. Should the patient be diagnosed with pathologically compromised lower limb/s, he/she is referred to a consultation with a Vascular Surgeon at the local hospital (Level 3 screening) otherwise, if the limb is identified as non-pathologically compromised, the patient is monitored regularly at Level 2 assessment. This process is summarised in Figure 3 below. It is important to observe that the DH 140 diabetic assessment (Appendix 1) form does not include a detailed biomechanical assessment of the diabetic foot.

With regards to biomechanics, the only form of biomechanical assessment performed in in the current diabetic foot care management plan is the observation of visible deformities of the diabetic foot being examined where the Podiatrist is guided to fill the dedicated screening form, DH140 form (Appendix 1). In cases of history of

ulceration, amputations or signs of ulceration/re-ulceration such as erythema, haematomas and hyperkeratotic lesions, especially in the presence of foot deformities such as prominent plantar metatarsal heads and fat pad atrophy, the patient is provided with offloading devices such as prescription orthoses, to offload the at-risk areas. The effectiveness of the prescribed offloading device, pre- and post- dispensing, is determined through visual observation and clinical experience of the clinician.

This local assessment pathway for patients living with diabetes mellitus is summarised in the flow chart below (Figure 3).

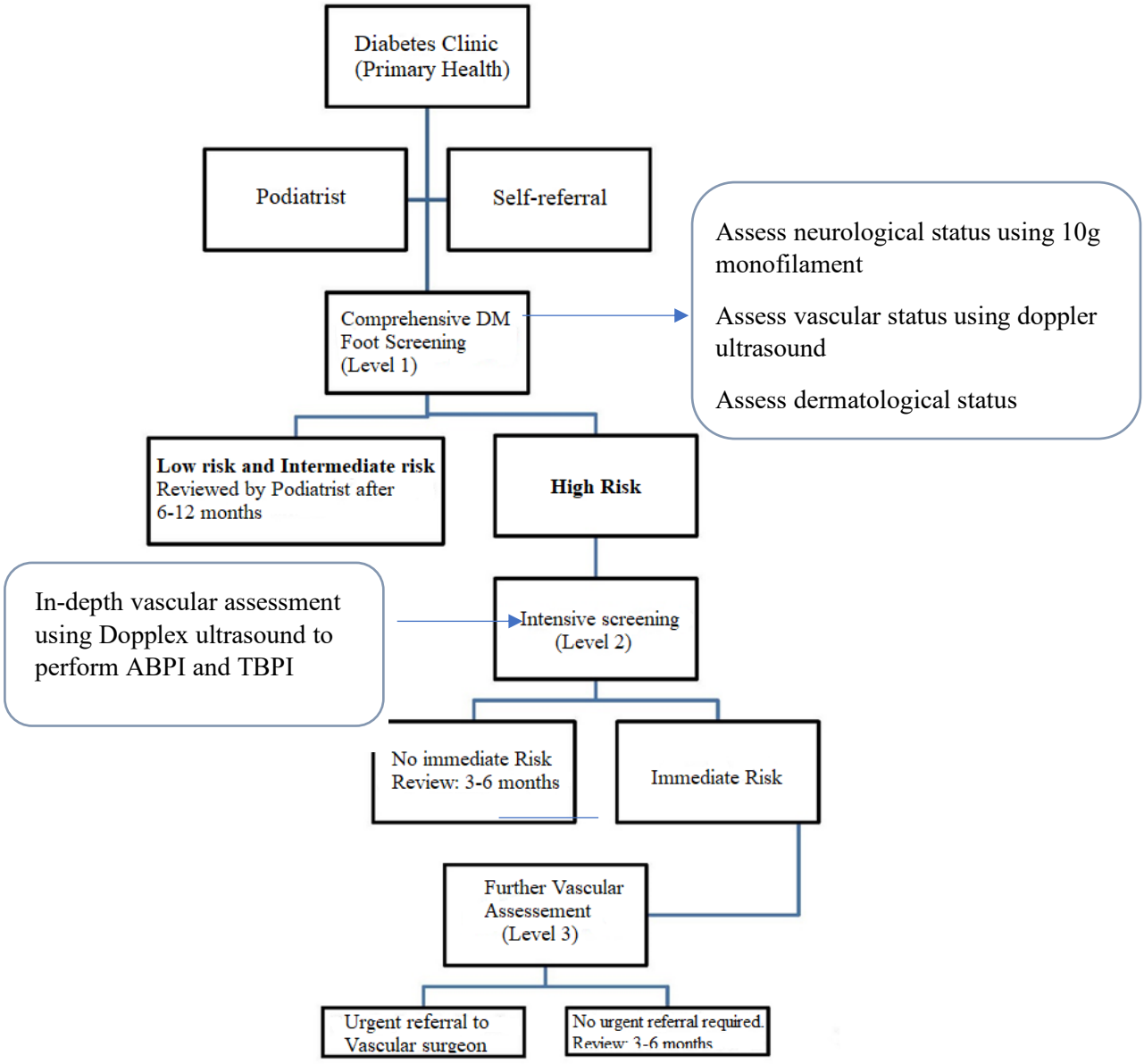


Figure 3: Flow diagram of the local assessment pathway for DM patients. Retrieved and adapted from Directorate for Health Information and Research (2010).

Locally, residents living with diabetes mellitus are free to choose to receive their care in either the private or the public sector, or even in both sectors. Like in the Public Sector, in the Private Sector patients are managed by a private Medical Doctor and/or Allied Health Care professional specialised in the field.

1.5 Guidelines on ulcer prevention

International guidelines on the prevention of diabetic foot complications, recommend the categorization of at-risk patients depending on active or history of ulceration, prior lower extremity amputation, peripheral neuropathy, long duration of diabetes and poor glycaemic control (NICE, 2015; IDF 2020; ADA 2022; Bus et al., 2020).

Local Public Health Authorities established a National Foot Screening Program which aimed to preserve functional limbs by avoiding and pre-empting the development of diabetic foot ulceration through a standardised approach (Directorate for Health Information and Research, 2010). This National Foot Screening Program is based on the IDF guidelines and thus categorises the patient at-risk of ulceration or low-risk, depending on the result of the neurological and vascular status and on the foot structure of the patient (Directorate for Health Information and Research, 2010).

Despite this standard approach, Malta is still experiencing an increase in diabetic foot complications with are leading to an increase in minor amputations (any part below the ankle) (Grima et al., 2018). The IDF guideline mostly focus on the importance of the vascular and neurological approach of the high-risk foot and fails to give any specific recommendations on the biomechanical aspect of the high-risk foot except for inspection for any bone deformities and reduced joint mobility (IDF, 2020). From a systematic review conducted by Formosa et al. (2017), a lack of evidence and recommendations with regards to effectiveness of footwear interventions and lower limb biomechanical assessment was reported.

Previous foot ulceration, callus formation, blistering and bruising of the skin are indeed strong predictors for foot ulceration and re-ulceration however, they can be aggravated by biomechanical factors such as foot structure, foot posture, joint range of motion, foot deformity and increased foot plantar pressures in weight bearing, non-weight bearing and most important of all, in dynamic situations (Peters et al., 2007; Monami et al., 2008; Dubský, Jirkovská, Bem, et al.., 2013; Waaijman, 2014; aan de Stegge, 2021). The podiatrist has a major role in the management of the diabetic foot, as

biomechanical risk factors are identifiable and correctable, and with proper treatment and patient compliance, recurrence of foot ulceration and amputation can be avoided (Hinchliffe et al., 2016; Bus et al., 2016; Mizzi & Falzon, 2018).

In cases of active or history of diabetic foot ulceration, the IWGDF guidelines recommend offloading of the ulcer site through offloading devices such as non-removable knee-high offloading devices, removable knee-high offloading devices, ankle-high offloading device as suggested in the study by Bus et al. (2015); orthoses or felted foam in combination with adequate footwear as later added by Bus et al. (2020). Choice of offloading device generally depends on the presenting case, type of ulcer and availability of the device (Schaper et al., 2020). The IWGDF guidelines also state that, to prevent ulcer development, previously ulcerated sites or pre-ulcerative sites (IWGDF risk 3) are to be offloaded using therapeutic footwear and/or orthoses that have demonstrated effective in relieving plantar pressure during walking. Despite these instructions, the IWGDF guidelines do not specify on how to measure pressures or temperature prior to the prescription of orthoses or how to ascertain the effectiveness of therapeutic footwear and the prescribed offloading devices in reducing peak plantar pressures to avoid further diabetic complication.

1.6 The literature gap

In Malta, foot orthoses are being prescribed with the intention of reducing plantar pressures however, according to the results of the scoping study conducted as part of this research project and which will be discussed later in Chapter 5, the evaluation of the effectiveness of offloading devices relies only on the clinical judgement and on the observational skills of the clinician. Several studies advocate that, clinical assessments for the prescription of orthoses done with the help of technology, not only permit the practitioner to obtain objective, precise and reliable measurements, but also helps the practitioner to understand how he/she can adapt or change orthoses to best achieve foot plantar pressure reduction and avoid re-ulceration (Mueller et al., 2006, Paton et al., 2012, Ibrahim et al., 2013). Furthermore, inadequate design of such devices that result from non-objective assessments, may not only be impractical but they may be hazardous enough to augment the targeted plantar pressures (Armstrong, Boulton, & Bus et al., 2017). Thus, quantifying the efficacy of prescription orthoses, especially where the diabetic high-risk foot is concerned, is deemed very important for the prevention of diabetic foot ulceration and/or re-ulceration.

Locally, though not an ongoing practice, a small number of clinicians refer for foot pressure analysis when pressure measurements are needed to identify the risk of ulceration however, this technology is only ideal for analysing the relationship of the barefoot to the ground (Gefen, 2007) as they consist of a flat, mat like device with an array of pressure sensors embedded within it (Shu, Hua, Wang, et al., 2010). Suitable technology to assess in-shoe plantar pressures, such as the in-shoe pressure system, does exist but is not being used within local hospitals or health centres as part of diabetic foot care management as it is currently not available as the current commercial in-shoe pressure systems are deemed costly and time-consuming to use in a busy clinical setting.

Another aspect that is overlooked and under investigated, is skin temperature. In the IDF guidelines, the assessment of skin temperature is only recommended when diagnosing the Charcot foot (Lavery & Armstrong, 2007; Gatt et al., 2018). Monitoring of the skin temperature of the diabetic foot is highly recommended (Schaper et al., 2020). It strongly suspected that a rise in skin temperature, secondary to increased and prolonged plantar pressure, lead to inflammation and ultimately ulceration. Repetitive pressure elicits an inflammatory process which heats up the area under stress (Armstrong et al., 2017; Mizzi & Falzon, 2018). It has been recognized that the inflammatory process lasts up to a week prior tissue break down and ulcer formation (Sun et al., 2006; Gatt et al., 2018). Monitoring of skin temperature of the affected area is thus empirical as it can help in preventing skin damage and re-ulceration (Mizzi & Falzon, 2018).

Furthermore, further research is warranted on the relationship between in-shoe pressure and temperature in view of ulcer development. Where temperature assessment is concerned, it is common clinical practice to manually palpate the skin for any changes in temperature. This technique however, is not sensitive enough to capture subtle and multiple temperature changes on the skin and thus is not a reliable and repeatable technique. An alternative to manual palpation is skin monitoring using, a simple infrared thermometer however, local hospitals and clinics are not equipped with such technology yet, possibly because the equipment is quite expensive (Gatt et al., 2015; Mizzi & Falzon, 2018).

1.7 Justification of Study

In diabetes, individuals who have had a previous diabetic foot ulcer have double mortality risk compared to an individual who have never experienced a diabetic foot ulcer (Walsh, Hoffstad, Sullivan et al., 2016; Saluja, Anderson, Hambleton et al., 2020). Moreover, lower limb amputation secondary to diabetic foot ulcer infection increases the risk of death of the individual by 70% (Armstrong at el., 2017). Several studies have reported that 40% of diabetic foot ulcers recur within the same year of their healing (Gershater et al., 2011; Dubský et al., 2013; Bus, Waaijman, Arts et al. 2013; Armstrong, Boulton, Bus, 2017). Due to this high rate of ulcer recurrence, patients living with diabetes mellitus, who have had a previous foot ulcer, are referred to as being in remission (Khan & Armstrong (2018); Armstrong et al., 2020). The health care economy thus faces a hefty burden by dealing with diabetic foot ulcer infection, hospital admissions and other consequences of unhealed diabetic foot ulcers including lower limb amputations.

A correlation between skin temperature and increased plantar pressures in view of ulcer development has been found however this concept is still very new and it has only been investigated in a limited number of studies (Bus, 2016; Gatt et al., 2018; Jones, Bibb, Davies et al., 2020) It has been demonstrated that in general, the diabetic foot has warmer skin temperatures compared to a healthy individual (Gatt et al., 2018; Yavuz et al., 2019), and that this discrepancy in skin temperature is further exacerbated with the presence of neuropathy (Sun et al., 2006) and/or following short walks (Yavuz et al., 2015). In view of these statements, it can thus be hypothesised that when the skin is subjected to continuous plantar stresses in the diabetic high-risk foot, the skin temperature at the area of stress rises weakening the ability of the surrounding tissues to resist biomechanical abnormalities (Yavuz et al., 2019).

With proper treatment and patient compliance, recurrence of foot ulceration and amputation can be everted (Hinchliffe et al., 2016; Bus et al., 2016; Mizzi & Falzon, 2018). However, this high recurrence rate of ulceration seen in patients living with diabetes mellitus, may suggest that, causative factors for tissue breakdown and ulcer development such as elevated foot plantar pressures and skin temperatures, are still present and are not yet (or not) being properly addressed (Bus, 2013).

Ulcer prevention and prevention of ulcer recurrence is considered of utmost importance in diabetic patient care (Armstrong, Boulton, Bus, 2017). It has been demonstrated that the primary key to prevent ulceration and ulcer recurrence is through offloading and pressure re-distribution (Armstrong, Boulton, Bus, 2017). Inappropriate designs of offloading devices increase the risk of ulceration thus considering the huge impact of foot orthoses on foot offloading, and the wide variety of manufacturing choices, it is crucial to have an objective insight on the appropriate manufacturing of orthoses for the high-risk diabetic foot. This is where diagnostic technologies play a major role. Off-loading and pressure re-distribution has been found to have better outcomes when assisted by proper techniques and technologies such as in-shoe pressure mapping devices (Bus, 2016).

The literature has shown that clinical assessments of prescription orthoses done with the help of technology, not only permits the practitioner to obtain objective, precise and reliable measurements, but also helps the practitioner to understand how he/she can adapt or change orthoses to best achieve foot plantar pressure reduction and avoid re-ulceration (Mueller et al., 2006, Paton et al., 2012, Ibrahim et al., 2013). The quality and effectiveness of foot orthoses prescribed for the diabetic high-risk foot is highly influential for the prevention of diabetic foot re-ulceration. Furthermore, monitoring of skin temperature as encouraged by the IWGDF guidelines, may provide better insight on the at-risk of ulceration status of the patient's foot when used as an add-on assessment to in-shoe pressure measurement and standard care (Yavuz et al., 2019; Bus et al., 2020).

Though the Podiatrist has a major role in the management of the diabetic foot, locally, the concept of foot pressure mapping prior and following prescription of foot orthoses is yet to be integrated. Foot orthoses are being prescribed with the intention of reducing plantar pressures but the evaluation of their effectiveness relies only on the clinical judgement and observational skills of the clinician. Suitable technology for in-shoe pressure and barefoot temperature assessment, such as the in-shoe pressure system and thermographic cameras, do exist and are available in the local market but are not being used or incorporated in daily clinical practise mostly because such technology is deemed costly and time-consuming.

Because the right technology for assessing in-shoe skin temperature and in-shoe pressure measurements is costly and time-consuming, the local health care system has not yet invested in such systems and thus thousands of Euros are being spent yearly for the care of diabetic foot ulceration and amputations which could otherwise be possibly prevented. The researcher here questions whether the integration of an innovative and low cost, in-shoe pressure system, which also reads skin temperature simultaneously, could change clinical practice and patient outcomes. Furthermore, the question as to whether it can also change the notion from just relying on clinical experience to relying on more reliable sources such as advanced technologies, to ensure plantar pressure reduction and temperature monitoring.

1.8 Overarching Research

1.8.1 Overarching Research Question

The overarching research question of this PhD investigates whether an innovative, specifically-developed single-sensor in-shoe foot pressure and temperature mapping system, be effective in detecting in-shoe plantar pressure and skin temperature and thus help in the reduction of ulceration/re-ulceration in the high-risk diabetic foot?

1.8.2 Overarching Aim and Objectives

The overarching aim of this PhD is to determine whether the application of a specifically designed single-sensor, in-shoe pressure and temperature measuring device can be used as an objective and low-cost clinical tool, in the prevention of diabetic foot ulceration and re-ulceration.

For this aim to be reached, several objectives need to be met. The objectives are:

1. To identify all current evidence with regards to the application and importance of foot pressure and temperature mapping in the management of foot ulcerations in the diabetic high-risk foot (**Chapter 2 - Literature Review**). To identify the current local diabetic foot care management and referral pathway of the high-risk diabetic foot and to give a numerical perspective on the number of high-risk diabetic patients being referred for a comprehensive biomechanical assessment (**Chapter 5 – Scoping studies**). To identify studies that utilize validated in-shoe pressure and temperature measuring systems to identify areas of increased plantar pressure and increased skin temperature,

which could place the high-risk diabetic foot at risk of ulceration (**Chapter 6 – Systematic Review**).

2. To devise and validate an innovative, single sensor in-shoe pressure and temperature measuring device that can be used to evaluate pressure areas of interest that may be at risk of ulceration; and which can also be used to evaluate the effectiveness of foot orthoses for pressure reduction particularly where patients living with diabetes mellitus are concerned (**Chapter 7 - Development and Laboratory Validation of the Device**).
3. To compare the outcome of the application of a newly developed, single sensor, in-shoe pressure and temperature measuring device, to the standard care practise being followed in the prevention of diabetic foot ulceration and re-ulceration. Locally, the standard care practise consists of the identifying the need for offloading in cases of diabetic foot ulceration. Patients are then prescribed and given an offloading device, such as orthosis, of which the design is based on visual observation and clinical experience (**Chapter 8 – Clinical Trial**).
4. To create a compendium on the application of a low-cost, single sensor device to measure temperature and pressure and to encourage/recommend the introduction of this innovative device into clinical practice (**Chapter 9 – Concluding Discussion**).

1.8.3 Overarching Hypotheses

H_1: The innovative, single-sensor, pressure and temperature in-shoe device can be used for the prevention of diabetic foot re-ulceration.

H_0: The innovative, single-sensor, pressure and temperature in-shoe device cannot be used for the prevention of diabetic foot re-ulceration.

1.9 The Structure of the Thesis

This PhD investigation is divided into 3 phases (Figure 4), where each phase has its specific aims and objectives. The reader can also refer to the GANTT chart below, created to represent the time plan for this PhD project (Table 1).

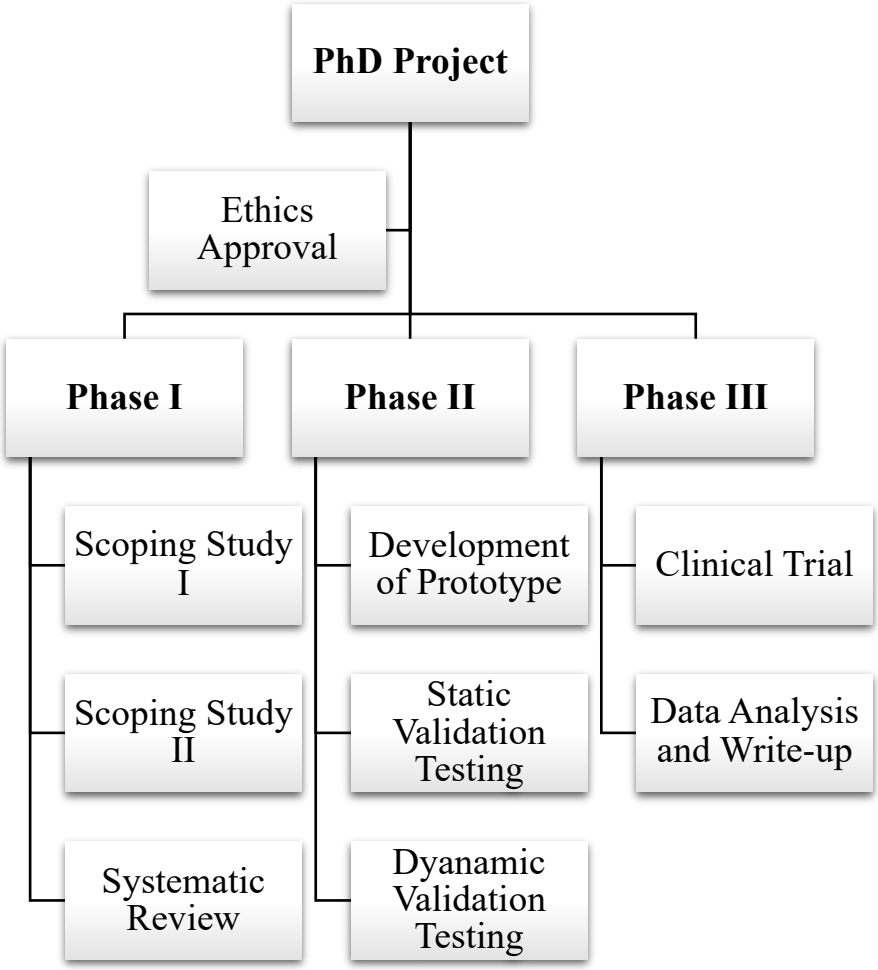


Figure 4: Flow chart summarizing the stages of this PhD project

Table 1: Gantt Chart showing the planned timeframe of this PhD project.

	Year 1	Year 2	Year 3
January			
February	Phase I: Scoping Studies + Systematic Review	Phase II: Static + Dynamic Validation of Prototype	Phase III: Data Analysis & write-up
March			
April			
May			
June	Phase II: Ethics Application + Development of Prototype		
July			
August		Phase III: Clinical Trial	
September			
October			
November			
December			

Phase I – This phase is divided into 2 parts. In **Part 1** of Phase I (**Scoping Studies**), a scoping study was conducted to investigate the referral and management pathways of patients living with diabetes mellitus within the local health care system. This study has been published in the Journal of American Podiatric Medicine Association (Appendix 2). **Part II** of Phase I (**Systematic Review**) presented a detailed systematic review which provides a more rigorous analysis of the existing literature related to the various technologies used to read and measure both in-shoe plantar pressures, and in-shoe skin temperatures. This systematic review proved very essential for this research as it provided insight on the existing gaps in research and points of improvement of the current available technology that can be used for the purpose of this investigation. A detailed description of this phase can be found in Chapter 5 and 6 of this dissertation. The systematic review has been registered under PROSPERO, registration number CRD42020183322 (Appendix 3), and it has been published in Diabetes Research and Clinical Practice https://doi.org/10.1016/j.diabres.2021.108783 0168-8227/ (Appendix 4).

Phase II - This stage takes the reader on a journey from the first assembly of the device to the justification of choice of equipment and static and dynamic validation process of the device and was divided into 3 parts. **Part I**, the **Development of the Device**, gives a detailed description of how the clinical tool was constructed. It describes the thoughts and brainstorming process of the researcher, with the help of qualified and experienced Engineers, that led to the development of the presented in-shoe single-sensor pressure and temperature measuring device. **Part II** (**Static Validation of the Prototype**) **and Part III** (**Dynamic Validation of the Prototype**), give an in-depth description of how the innovative, single-sensor, in-shoe pressure and temperature sensing devices was statically and dynamically validated. A detailed description of this phase can be found in Chapter 7 of this dissertation. The dynamic validation study has been published in Gait & Posture doi: 10.1016/j.gaitpost.2022.11.013 (Appendix 5).

Phase III – Inspired by a Post-Positivist philosophical perspective, this phase describes a matched parallel (non-crossover), prospective experimental clinical trial which sought to evaluate whether the information gathered from using this innovative, single-sensor, pressure and temperature measuring device can significantly improve the design of offloading devices thereby reduce peak plantar pressures at areas of interest. In this phase, the correlation between pressure and temperature was also

analysed. Furthermore, a compendium on the application of this innovative, single-sensor pressure and temperature measuring device was provided. A detailed description of this phase can be found in Chapter 8 of this dissertation.

1.10 Presentation of the Thesis

This dissertation is set out on 10 Chapters.

Chapter 1 (The Introduction) is an introductory chapter which provides a background which relates to plantar pressure and skin temperature in view of diabetic foot ulceration. An overview of the international and local management of the diabetic foot is also presented, the literature gap which has led to the conception of this project is also highlighted within this chapter. This chapter also introduces the research question, main aims, main objectives and hypothesis of this PhD study.

Chapter 2 (The Literature Review) presents a detailed literature search of topics that informs the reader about the pathogenesis of diabetic foot ulcers, and their relation to plantar foot pressures and skin temperature. This chapter also presents the reader with literature that discusses the biomechanical influences on diabetic foot ulceration and the various assessments techniques and related offloading techniques currently available for the management of the diabetic high-risk foot. furthermore, this chapter discusses the relationship between pressure and temperature as predictors of ulceration in the high-risk foot and highlights the gaps in research.

Chapter 3 (Position Statement of the Researcher) presents a narration from the researcher where the his/her world views, and the position adapted to approach the research problem, are discussed. In this chapter, the researcher shares some of his/her personal thoughts and emotions that were experienced during the conduction of this research.

Chapter 4 (Identifying the Philosophical Approach) this chapter presents the overall philosophical approach adopted in this study and how this informed and inspired the research conducted.

Chapter 5 (The Scoping Studies) portrays 2 small scoping studies that were conducted as part of the initial phase of this research project. Through an observational retrospective study design (**Study I**) and through a phenomenological qualitative study (**Study II**), these scoping studies also gave a numerical perspective on the number of

high-risk patients living with diabetes mellitus that are being referred for an in-depth biomechanical examination in view of ulcer prevention, and obtained a local perspective on the management and referral pathway of the high-risk diabetic foot respectively. This study has been published in the Journal of American Podiatric Medicine Association.

Chapter 6 (The Systematic Review) presents a detailed systematic review which provides a more rigorous analysis of existing literature related to the various technologies used to read and measure both in-shoe plantar pressures and in-shoe skin temperatures. This systematic review proved very essential for this research as it provided insight on the existing gaps in research and points of improvements of the current available technology that can be used for the purpose of this investigation. This systemic review has been published in the Diabetes Research and Clinical Practice Journal https://doi.org/10.1016/j.diabres.2021.108783 0168-8227/ (Appendix 4) and has been registered in PROSPERO, registration number CRD42020183322 (Appendix 3).

Chapter 7 Part I of this chapter **(Development of the Prototype)** gives a detailed description of how the innovative, single-sensor, temperature and pressure in-shoe device was developed. The thoughts and brainstorming process that led to the development of the prototype are discussed and presented. Part II and Part III of this chapter **(Static and Dynamic Laboratory Validation Process)** gives an in-depth description of the final development of the innovative, single-sensor, in-shoe pressure and temperature sensing device that was developed as a research tool for this PhD study. This chapter takes the reader on a journey from the first assembly of the device to the justification of choice of equipment and to the static and dynamic validation process of the device. The dynamic validation study has been published in Gait & Posture doi: 10.1016/j.gaitpost.2022.11.013 (Appendix 5).

Chapter 8 (Clinical Trial) relates to a matched parallel (non-crossover), prospective experimental clinical trial, which investigated whether or not the innovative, low-cost, single sensor, in-shoe pressure and temperature device can be used in the clinical prevention of diabetic foot ulceration. This study also served as a second validation study of the innovative, single-sensor, in-shoe pressure and temperature measuring device that was conducted on a larger population and on the targeted population

(people living with Type II Diabetes Mellitus). Furthermore, this study also investigated the suspected correlation between increased plantar pressure and raise in skin temperature in view of diabetic foot ulceration.

Chapter 9 (Concluding Discussion) This chapter presents an overall discussion drawn from this PhD dissertation. This chapter also highlights and presents the limitations met throughout this research project and the recommendations for future research.

Chapter 10 (Conclusion of the PhD Dissertation) This chapter presents the overall conclusions drawn throughout the entire PhD research dissertation.

Chapter 2: Literature Review

2.1 Introduction

This chapter provides an overview of previous literature on diabetes, its complications and on the use of technology to identify biomechanical influences that play a major role on the development of diabetic foot ulceration. This chapter also discusses the relationship between pressure and temperature and how we can use these parameters to prevent diabetic foot ulceration and/or re-ulceration. Reviewing previous literature helped to provide direction and perspective to this thesis. Through critical analysis of previous work, the literature review provided the opportunity to identify gaps in the research topic and previous research conducted, which ultimately informed the entire research study.

2.2 Research Strategy

A comprehensive literature search was conducted using electronic searches, textbooks and journal articles.

Electronic Search:

The main search engines used were PubMed; SAGE Publications; EBSCO; Science Direct; Hy-Di; Google Scholar, Google books and Medline.

Journal Search:

The following is a list of main journals used to search articles related to the subject that were published up till the year 2022.

Gait & Posture; Journal of American Medical Association; Journal of General Internal Medicine; Archives of Physical Medicine and Rehabilitation; Journal of Biomechanics; Journal of Physical Therapy Science; British Journal of Diabetes and Vascular Disease; Acta of Bioengineering and Biomechanics; Clinics in Developmental Medicine; Clinical Biomechanics; Journal of Bone and Joint Surgery; Journal of American Podiatric Medicine Association; Journal of Anatomy; Human Movement Science; Journal of Applied Physics; Journal of Surgical Research; Annals of Biomedical Engineering; International Journal of Molecular Medicine; Journal of Diabetes and Its Complications; Physical Therapy Journal; Diabetic Medicine;

Diabetes Care; Journal of Diabetes Science and Technology; Annals of Internal Medicine; BMC Musculoskeletal Disorders; Endocrine; International Journal of Molecular Science; Diabetes International Journal of Lower Extremity Wounds; Diabetologica.

Textbooks and Dissertations:

The University of Malta, Faculty of Health Science Library provided access to textbooks and dissertations related to diabetes, biomechanics of the lower limb and diabetic foot ulceration. Textbooks related to statistical and research methods were also consulted.

Keywords:

"Diabetes Mellitus Type 2", "Prevalence", "Epidemiology", "Gait", "Biomechanics", "foot", "Lower limb", "Diabetic foot", "risk factors", "mobility limitation", "peripheral neuropathy", "hyperglycemia", "in-shoe temperature", "in-shoe pressure mapping", "senors", "pressure sensors" "temperature sensors", "wearable sensors", "ulceration", "re-ulceration".

The literature was selected carefully to provide a comprehensive literature critique. Research articles in the English language were preferred and publications older than 10 years were only referred to when needed to reference historical contexts or where no recent evidence was available.

2.3 Diabetes Mellitus

For countless centuries, the researchers have been investigating a challenging metabolic disorder to better comprehend its management and prevention (Saliba Thorne, 2017). Diabetes, as a chronic metabolic health condition comprises of a defect in insulin secretion, insulin inaction or a combination of both which ultimately results in hyperglycaemia that is, a persistence raise in blood glucose level (WHO, 2022). Long term diabetes, especially in the presence of co-morbidities such as peripheral neuropathy, ischaemia and neuro-ischaemia, is known to predispose the individual to severe complications foot ulcerations, or even worse amputations (IDF, 2020).

Globally, the prevalence of the adult population diagnosed with diabetes mellitus has risen from 108 million (4.7%) people in 1980 to 422 million (8.5%) people in 2014 in the adult population and is expected to rise to 592 million by 2035 (Saeedi et al., 2019;

Iacobucci, 2021). The WHO has attributed nearly half of the all the deaths reported prior the age of 70 years to diabetes mellitus and has named it to be the 7th leading cause of death by 2030 (WHO, 2020).

The consequences of diabetes on the public health are astounding considering the high morbidity and mortality rate associated with it. It is estimated that the life expectance of a male diagnosed with diabetes is reduced by 12 years and that of a female by 19 years (Narayan et al., 2003). The major consequences of diabetes include blindness (2%), cardiovascular disease including increased risk of myocardial infarctions, strokes and peripheral vascular disease (50%) and foot ulceration. Evidence based research has shown that the majority of cases of hospitalization are mainly attributed to a diabetic foot complication particularly foot ulcerations (O'Loughlin, McIntosh, Dinneen & O'Brien, 2010). Chances of developing a foot ulceration is twice as common in patients living with diabetes mellitus compared to non-diabetics. Foot ulceration is regarded as the leading cause for non-traumatic amputations of the lower limbs and hospitalization. In effect, 8 to 10 non-traumatic amputations are attributed to diabetic foot ulceration where, 80% will develop a foot ulcer (Boulton et al., 2005; Hinchliffe et al., 2015; Jeffcoate, Vileikyte, Boyko et al., 2018). The annual prevalence for nontraumatic lower limb amputations in persons living with diabetes mellitus is between 2.1 and 13.7 per 1000 individuals (Armstrong, Boulton, & Bus, 2017). Furthermore, a recent study by Armstrong, Boulton, & Bus, 2020 estimated a 5-year mortality rate following diabetic lower limb amputation. This means that people living with diabetes mellitus who undergo a lower limb amputation are more likely to die within 5 years following the amputation, putting the mortality rate of diabetes second to that of lung cancer (Armstrong, Boulton, & Bus, 2020).

2.3.1 Financial Burden of Diabetes

The consequences of diabetes on the public health are astounding considering the high morbidity and mortality rate associated with it. It is estimated that the life expectance of a male diagnosed with diabetes is reduced by 12 years and that of a female by 19 years (Narayan et al., 2003). The major consequences of diabetes include blindness (2%), cardiovascular disease including increased risk of myocardial infarctions, strokes and peripheral vascular disease (50%) and foot ulceration. Diabetic foot ulcerations pose a great burden on health care economy due to the high risk of infection, hospital admissions and amputations. Considering the high rate of recurrence of foot

ulcerations (>50%) the health care system is experiencing an increased yield in health care costs (Boulton et al, 2005; Rocchiccioli et al., 2005). These costs not only include the current ulcer episode but also the provision of social services and home care. A Swedish study estimated that for the treatment of a single foot ulcer, the health care expenditure went up to €16,157.88 (with no amputation) and €30,521.12 (with amputation) (Ragnarson, Apelqvist & Magnus, 2000). Similarly, in the UK, it was estimated that a single foot ulcer costs the department of health an average of €3,347.72 to €8,370.70 and up to €72,546.09 if an amputation is required (NHS, 2018). Due to the frequent and prolonged in-patient care, the collective expenditure of treating diabetes in Maltese hospitals, primary care and special visits produced a total of €107,316,517.82 in 2017. This sum is estimated to increase up to €136,819,523 from 2017 to 2045 (Cushcieri, 2020). In view of this, ulcer prevention and prevention of ulcer recurrence is deemed of utmost importance in diabetic patient care (Armstrong, Boulton, & Bus, 2017).

2.3.2 The general foot care referral system for the diabetic high-risk foot in Malta

In Malta, patients living with diabetes mellitus have the opportunity to choose between receiving diabetic care from either the public sector, the private sector or a combination of both. In the private sector, patients are managed by their private General Practitioner, generally against payment, when need arises.

Any person diagnosed with diabetes mellitus in Malta has access to specialist care that is provided as a free service at local hospitals and/or health centres – the Public Sector. A specialized center for diabetes care, the Diabetic Outpatients Clinic, has been inaugurated several decades ago at the local hospital and is used as a reference point by all Allied Health Care Professionals and patients as the service follows the guidelines provided by the International Diabetes Federation (IDF) Clinical Practice Recommendations on the Diabetic Foot (IDF, 2020). In the Diabetic Outpatients Clinic, patients have access to medical practitioners, nurses and allied health care professionals such as physiotherapist, dieticians and Podiatrist, all specialized or have a particular interest in Diabetes. The service of this center is not limited to the outpatients only, but also extended to in-patient care.

Adults diagnosed with Type I or Type II Diabetes Mellitus (T1DM/T2DM), gestational diabetes, maturity onset diabetes of the young (MODY) and other rare types of diabetes, and persons living with the complications of diabetes mellitus are initially referred to the Diabetic Outpatients Clinic. Depending on the nature of the complications developed, the patient is referred to a specific professional within the Clinic this can include ophthalmologists, renal physicians, vascular surgeons, cardiologists, physiotherapists, occupational therapists, podiatrists, and tissue viability nurses.

Over the years, due to a noted increase of diabetic cases, this service has been also extended to local Health Centres in order to achieve better management of the service (Directorate for Health Information and Research, 2010). This shared program between the Diabetic Outpatients Clinic at the local hospital and the Health Centres in Primary HealthCare consists of referring patients living with uncomplicated diabetes mellitus to Health care providers, also specialist in diabetes, at local health centres. Patients here are seen at prescribed time intervals and a fast referral scheme is also available to allow in-between scheduled appointment in case of emergencies (Directorate for Health Information and Research, 2010).

2.3.3 National management of diabetic foot complications

Evidence based research has shown that the majority of cases of hospitalization are mainly attributed to diabetic foot complications particularly foot ulcerations (O'Loughlin, McIntosh, Dinneen & O'Brien, 2010). The chance of developing a foot ulcer is twice as common in patients living with diabetes mellitus compared to non-diabetic patients.

Foot ulceration is regarded as the leading cause for non-traumatic amputations of the lower limbs. In effect, 8 to 10 non-traumatic amputations are attributed to diabetic foot ulceration where, 80% will re-ulcerate (Boulton et al., 2005; Hinchliffe et al., 2015; Jeffcoate et al., 2018). The annual prevalence for nontraumatic lower limb amputations in persons living with diabetes mellitus is between 2.1 and 13.7 per 1000 individuals (Armstrong, Boulton, & Bus, 2017). Furthermore, it is estimated that the mortality rate associated with diabetic lower limb amputation ranges from 13% to 40% at 1 year, 35% to 65% at 3 years, and 39% to 80% at 5 years (Armstrong, Boulton, & Bus, 2017).

In view of this, local Public Health Authorities sought to establish a National Foot Screening Program which aimed to preserve functional limbs by avoiding and pre-empting the development of diabetic foot ulceration (Directorate for Health Information and Research, 2010). In this National Foot Screening Program, all patients living with diabetes mellitus are offered a series of appointments for Podiatric risk assessment of the foot at a local health center. This screening program entails a detailed vascular, neurological and biomechanical assessment of the lower limbs (Directorate for Health Information and Research, 2010).

The podiatrist has a major role here in the management of the diabetic foot, as biomechanical risk factors are correctable and with proper treatment and patient compliance, recurrence of foot ulceration and amputation can be everted (Hinchliffe et al., 2016; Bus et al., 2016; Mizzi & Falzon, 2018). Previous foot ulceration, callus formation, blistering and bruising of the skin are strong predictors for foot re-ulceration, which can be aggravated by biomechanical factors such as foot deformity and increased foot plantar pressures (Peters et al., 2007; Dubský et al., 2013; Waaijman, 2014). Foot orthoses are generally indicated to off-load excessive pressure areas to avoid the recurrence of diabetic foot ulceration (Bus et al., 2020).

According to the IWGDF guidelines, to demonstrate that a prescribed offloading device and/or therapeutic footwear the clinician would require a barefoot or in-shoe pressure measurement which to date is considered costly (Schaper et al., 2019). In Malta the concept of in-shoe foot pressure mapping prior and following prescription of foot orthoses is yet to be integrated. Foot orthoses are being prescribed with the intention of reducing plantar pressures but the evaluation of their effectiveness relies only on the clinical judgement and observational skills of the clinician. Though not an ongoing practice, some clinicians refer for plantar pressure measurement to identify the risk of ulceration however, such technology is only ideal for analysing the relationship of the barefoot to the ground forces (Gefen, 2007) as they consist of a flat, mat like device with an array of pressure sensors embedded within it (Shu et al., 2010). Suitable technology such as the in-shoe pressure system, does exist but is not being used within local hospitals or health centres as part of diabetic foot care management as it is deemed costly and time-consuming.

Moreover, the IWGDF Guidelines recommend skin temperature monitoring of the diabetic foot since a rise in skin temperature is known to indicate inflammation which can lead to ulceration (Bus et al., 2020). Locally, it is common clinical practice to manually palpate the skin for any changes in temperature. This technique however, is not sensitive enough to capture subtle and multiple temperature changes on the skin and thus is not a reliable and repeatable technique. Simple infrared cameras or thermographic cameras can be used as an alternative and more objective technique of measuring of barefoot skin temperature (Gatt et al., 2018; Mizzi & Falzon, 2018).

2.4 Ulceration: A Treacherous Complication of Diabetes Mellitus

The largest organ of the human body is by far the skin and its purpose is to act as a barrier against infections, to aid in thermoregulation, insulation and vitamin D synthesis (Kanitakis, 2002). This organ can be described as an external protective cover that is made up of seven layers of tissue, held together by connective tissue to form a unique structure (Liu et al., 2018).

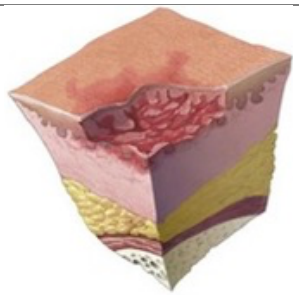
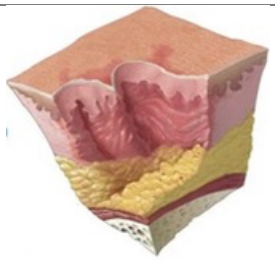
When the skin is exposed to loading, shear or torque, blistering or ulcer formation can occur. Blistering is known to occur secondary to overwhelming acute forces that impact the skin. The uppermost layer of the skin is forced to separate from the layers beneath it as it inflates with body fluid or blood. In the presence of repetitive trauma, skin compression and thickening of the epidermal layer occur. Depending on the amount and duration of force imposed on the skin, visible dermatological changes occur ranging from a protective callus formation to serious ulceration. (Duhon et al. 2016).

An ulcer is thus described as localised damage to soft tissue that is secondary to continuous and excessive loading on the skin, generally on a weight-bearing surface area (Syafril, 2018). In view of this, a pressure ulcer can be viewed as a biomechanical issue. Diabetic ulcers often result secondary to trauma from tight fitting shoes or from invasion of foreign objects. Another causative factor for ulcer formation is excessive pressure resulting from abnormal foot structure (Piaggesi & Apelqvist, 2018). Prolonged and excessive pressure over the skin hinders the blood flow damaging the skin tissues in the area (Syafril, 2018).

An ulcer can be either superficial, mostly engage the superficial tissues, or deep where tissue damage can be as deep as close to the surface of the bone (Shavelson, 2011) It

is common for ulcers to develop in four stages (Table 2). Though these four stages are deemed as the expected stages of development of an ulcer, it is possible that an ulcer is already at stage four but appears to be still in stage one or two. These types of ulcers are referred to as unstageable ulcers and are very difficult to diagnose.

Table 2: Table showing the 4 stages of ulcer development. Adapted from Sardina (2017)

Stage I	Erythema, bruising and discolouration of the superficial layer of the skin occurs. The sore might be very tender and deep enough to reach dermis. Mild burning sensation and pruritis may be reported. A localized rise in skin temperature due to the inflammation occurs.	
Stage II	Pain and soreness of the affected area as the skin now has an open and shallow wound. Erythema, swelling and bruising of the parameter area increase, giving the ulcer a yellowish appearance of similar to that of a blister indicating further tissue damage and possible death.	
Stage III	The skin breaks to a full demarked cavity deep enough to reach the fatty layer underneath the dermis. Apart from erythema, swelling and pain, foul odour with drainage of exudate and pus may be experienced.	
Stage IV	The cavity may deepen enough to reach muscles and tendons or even more seriously bones. The skin is now predisposed to high risk of infection. Symptoms at this stage include the formation of eschar, extreme pain, infection and necrosis.	

In diabetes, foot ulcers all follow the previously described stages but are generally aggravated by high levels of blood glucose otherwise referred to as glycosylation (Clayton & Elasy, 2009; Piaggesi & Apelqvist, 2018). Glycosylation effects both muscles and nerves leading to neuropathy and reduced peripheral blood flow. Neuropathy hinders the perception of pain or discomfort masking any signs of high

pressures or trauma to the skin. Further damage influences the balance between the muscles disrupting the normal structure of the foot creating deformities. Furthermore, the function of glands within the skin reduces their normal function reducing the natural moisture of the skin. All these factors contribute to the development of chronic diabetic foot wounds that, though treatable, can have serious complications which determine a patient's quality of life (Aumiller & Dollahite, 2015).

A classification and scoring system are generally used with the intention to provide better communication between healthcare professionals, to aid and guide the clinician in providing the best treatment and for statistical and research purposes. Where diabetic foot ulcers are concerned, classification and scoring systems are used to group diabetic foot ulcers into specific categories. A numerical scale or score is attributed, depending on the clinical features of an ulcer, to highlight the stage of ulcer development. Ideally, classification and scoring systems should be detailed enough to give accurate prediction but at the same time, easy enough to facilitate use. A classification system should also be validated for both intra- and inter-observer reliability (Bus et al., 2020).

A review conducted by Monteiro-Soares et al. (2019) identified a good number of classification systems for diabetic foot ulcerations namely the Meggitt-Wagner, the Site, Ischaemia, Neuropathy, Bacterial Infection and Depth (SINBAD), the IWGDF classification, University of Texas and the Wound, Infection and Foot Infection (Wi-Fi) classification systems.

2.4.1 Types of ulceration

In diabetic foot studies, one often encounters the term "Diabetic Foot Triad" (Pendsey, 2010). This concept describes the 3 main pathologies, neuropathy, peripheral vascular disease and immunopathy, that predispose a patient living with diabetes mellitus to diabetic foot complications such as ulceration. From one patient to another, the degree of influence of one or more of these pathologies varies. One of the 3 aforementioned pathologies may predominate in one patient or the patient might have a mixture of 2 or even have all 3 at the same time (Nather, Cao, Chen et al., 2018). Diabetic foot complications often arise secondary to neuropathy or secondary to a vascular disease and thus, neuropathic ulceration, ischaemic ulceration and neuro-ischaemic ulceration

are often regarded as the 3 main types of diabetic foot ulceration (Figure 5) (Pendsey, 2010).

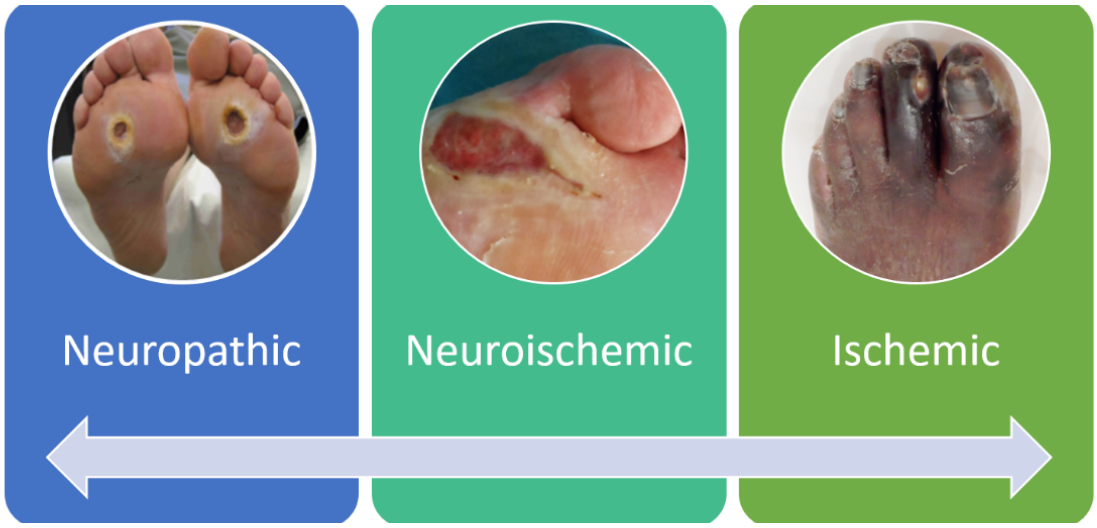


Figure 5: The 3 main types of diabetic foot ulceration. Retrieved from Cumming, n.d

Long standing diabetes and/or prolonged high blood glucose levels damage the patient's neurological capabilities and immunological responses (Nather, Cao, Chen et al., 2018). In fact, the majority of ulceration cases in patients living with diabetes are affected with diabetic peripheral neuropathy (Edmonds, Manu & Vas, 2021). Diabetic peripheral neuropathy compromises the sensation of the lower limb leaving the patient unable to feel heat, cold or pain. Furthermore, expectant complications such as muscle weakness and reduced reflexes lead to altered biomechanical and gait patterns which together with loss of sensation, increased plantar pressures and skin damage is highly unavoidable (Singer, Tassiopoulos & Kirsner, 2017).

Foot ulceration that develops within the presence of diabetic peripheral neuropathy are generally referred to as neuropathic ulcers. Neuropathic ulcers most commonly occur at the plantar surface of the foot especially at areas that bear the highest peak plantar pressures, friction or torsion weight baring or during gait (Pendsey, 2010).

Prolonged diabetes impairs the overall natural blood supply of the body especially to the periphery. Diabetic foot ulcers which form in the presence of ischaemia are referred to ischaemic ulcers and these, as neuropathic ulcers, tend to form at areas of peak pressures including the toes. Ischaemia can be a complication of atherosclerosis which

is very common in diabetes (La Sala, Prattichizzo & Ceriello, 2019). The narrowing of the arteries prevents wound healing by inhibiting the vascular system to provide the wound with the necessary oxygen and nutrients to regenerate tissue and close the wound (Li, Carter, Mashiach et al., 2017). Delayed wound healing leave the wound highly susceptible to infection and tissue death (Zhao et al., 2016).

It is very common for ischaemia to be a co-morbidity of another pathology such as peripheral neuropathy (Nukada, 2014). Ischaemic ulcers rarely present themselves as purely ischaemic ulcers. In fact, another form of diabetic foot ulcers is the neuro-ischaemic ulcer which, as the name implies, is an ulcer that develops in the presence of both neuropathy and ischaemia. Here, the symptoms of ischaemia are generally muted due to the presence of neuropathy making the disease even more treacherous. Neuroischaemic ulcers often present themselves at the peripheral margins of the foot such as the 1st and 5th Metatarsophalangeal joint (Edmonds & Foster, 2006; Boulton, 2022). The general characteristics and presentation of neuropathic, ischaemic and neuroischaemic ulcer are summarized in table 3 below.

Table 3: Summarized characteristics of the 3 main types of diabetic foot ulceration. Retrieved from Bhanushree, Chethan, Vinutha et al. (2017)

Feature	**Neuropathic**	**Ischaemic**	**Neuroischaemic**
Sensation	Reduced or absent sensation to touch, vibration, pain, and pressure	Sensation may be present but decreased if there is associated neuropathy	Degree of sensory loss
Foot temperature	Warm	Cold or decreased temperature	Cool
Ulcer location	On the plantar aspects (forefoot 80%) of the foot/toes	Distal/tips of the toes, heel, or margins of the foot	Margins of the foot and toes
Foot pulses	Present and often bounding. Dilated, prominent veins	Absent or markedly reduced	Cool with absent pulses
Callus present	Commonly seen on the weight-bearing areas and is generally thick	Not usually. If present, distal eschar or necrosis	Minimal callus Prone to necrosis
Other	Dry skin and fissuring	Delayed healing	High risk of Infection

2.5 Biomechanical influences on diabetic foot ulceration

It is well known that biomechanics has a strong association with ulcer development in the high-risk foot. Despite this fact, the link between biomechanics and ulcer prevention remains unclear. A person living with diabetes mellitus experiences changes in the temporal and spatial parameters, kinematics, kinetics and plantar pressures (Fernando et al., 2015). Prior to understanding these changes, the biomechanical characteristics of a healthy person should be understood.

The motion of the foot is said to be triplanar as it moves in the frontal, sagittal and in the transverse plane. An upward (dorsiflexion) and downward (plantarflexion) movement of the foot occurs within the sagittal plane, while adductory (inversion) and abductory (eversion) movements of the foot occur in the frontal plane. Internal and external rotation of the foot occurs only in the transverse plane however in this plane, adduction and abduction can also occur (Wilder, 2010). During locomotion, these triplanar movements repeat and adapt to the ground in a specific pattern referred to as the gait cycle. The gait cycle is categorized into two main phases of ambulation namely the swing phase and the stance phase (Figure 6).

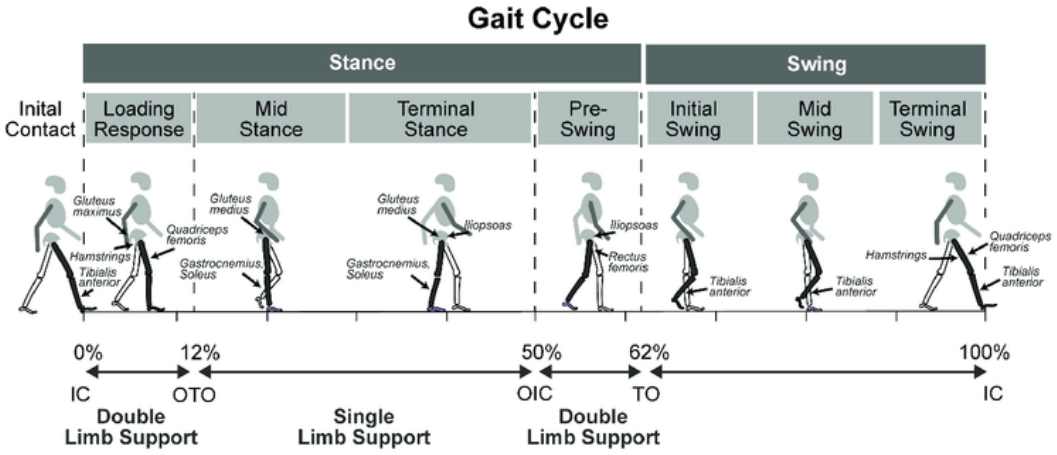


Figure 6: The human gait cycle. Retrieved from Zhou et al. (2017)

The swing phase of the gait cycle is characterized by its non-weightbearing period which starts at toe-off and ends at heel strike of the same limb (van Schie & Boulton, 2006). Throughout this phase, the ankle joint is maintained in dorsiflexion to provide clearance of the foot off the ground. The muscles of the lower limb stabilize the joints

of the foot, and permit deceleration of the foot in preparation for heel strike (Lavine et al., 2012).

The stance phase refers to the phase at which one foot touches the ground and is supporting the weight of the body. This phase starts when the foot makes contact with the ground, generally referred to as foot contact or heel strike. Once the foot is steady on the ground, the heel everts as the foot plantarflexes and pronates, causing the lower limb to internally rotate. The foot is maintained in plantarflexion until it enters midstance where the foot flattens to the ground and the weight of the body is transferred from heel to toes. The heel then everts as the foot moves into supination to externally rotate and extend the lower limb creating a progressive stability of the medial longitudinal arch till the end of the stance phase (Lavine et al., 2012). At this stage, the muscles of the calf area and the intrinsic muscles of the foot contract, aiding the heel to progressively lift off the ground to enter the final stage of the stance phase. In the toe-off stage, the lower limb rotates internally, the foot dorsiflexes, and the body weight is transferred over the metatarsals and toes. As the forefoot area is loaded, the talus firmly rests in the concavity of the navicular and the plantar fascia below the medial longitudinal arch is activated. The body propels forward and toes off into swing phase (Kim, 2013). Here, a high load of pressure is expected as the area at which the force is acting has decreased (Pham et al., 2000; Abouaesha et al., 2001; van Schie & Boulton, 2006). Once toe-off is complete and the movement progresses into swing phase, the lower limb externally rotates in preparation for heel strike back into the stance phase. Foot stability is encouraged by this external rotation through muscle and ligament contraction of the medial aspect of the hip, knee and ankle joint (Kim, 2013).

In the diabetic foot, the proprioceptive and sensory abilities diminish and become absent as the disease progresses (Kim, 2013). The initial contact of the stance phase may not always be marked with heel strike but can initiate at midstance due to midfoot deformities instead (van Schie & Boulton, 2006). This contributes to joint subluxation and encourages maladaptation to ground reactive forces. Adaptations to ground reactive forces are quite minor but are of empirical importance as they help to avoid excessive pressures and injury while standing and during ambulation and this is mostly influenced on joint mobility (Kim, 2013). A study conducted by Kim (2013) reported that hypermobility of the joints leads to an imbalance in the transfer of plantar ground reaction forces elevating them over the norm. In addition to this statement, Rao,

Saltzman, & Yack, (2010) outlined that opposed to hypermobility, limited mobility of the joints leads to higher peaks of plantar pressures. A review paper by Shavelson (2011) reported that there is enough evidence to confirm that limited joint mobility may be caused secondary to biomechanical pathologies of the lower limb and is known to be the cause of stress on ligaments and tendons.

Studies have shown that in patients living with diabetes mellitus, tendons, joint capsules and ligaments characteristics change from a smooth parallel texture to a dishevelled one reducing their elasticity and tensile strength (Pham, 2000; Armstrong, 2001; Armstrong, Lavery, Wunderlich, et al., 2003; Zimny et al., 2004). The first to be affected are the intrinsic muscles of the foot which are mostly engaged during the late midstance phase to the toe-off phase. The loss of these muscles brings about an imbalance between the flexor and extensor muscles of the lesser digits, clawing them to a deformed state. Secondary to clawing of the lesser digits, a proximal displacement of the plantar fat pad at the metatarsal area of the foot occurs. Being an area that is accustomed to withstand high loads of pressure, the displacement of the plantar fat pad and the joint subluxation has caused the foot to lose its protection against excessive pressures and is now prone to ulceration (Mueller et al., 2003). As the disease progresses, the damage proceeds to major muscles such as the quadratus plantae and flexor digitorum brevis, disrupting the function of the windlass mechanism (Sooriakumaran & Sivananthan, 2005). This change though innocuous on its own, can bring about joint instability or stiffness which in turn lead to excessive pressures and ulcerations (Shavelson, 2011).

A study by Formosa, Gatt & Chockalingam (2013) reported that compared to healthy non diabetics, participants living with diabetes mellitus exhibit higher plantar foot pressures (Ahsan, Shanab & Nuhmani, 2021). This is particularly evident among participants who have already experienced a foot ulcer (Wrobel et al., 2010; Waaijman et al., 2011: Fernando et al., 2014). In congruence to this statement, a study by Mueller et al. (2003) outlined that among 669 patients living with diabetes mellitus, participants who had had already a history of diabetic foot ulcer were more sensitive and withstood fewer stresses to their feet before re-ulcerating (Mueller et al., 2003). Thus, when managing patients who are living with diabetes mellitus, pressure measurement plays a very significant role (Razak et al, 2012; Falzon, Formosa, Camilleri & Gatt, 2018).

2.6 Offloading management of the diabetic high-risk foot

Being an incurable disease, the aim of the health care system has always been to reduce the number of morbidity and mortality cases. For this to be carried out effectively, the risk factors for diabetic foot ulceration need to be identified, and addressed, as promptly and as efficiently as possible. Early identification and intervention of such risk factors are important as they may prevent up to 85% of amputations in patients living with diabetes mellitus (Abbas, 2013). The most common complications of diabetes can be caused secondary to repetitive trauma, loss of sensation (neuropathy) or morphological foot deformities such as clawing of lesser digits, prominent metatarsal heads (Healy, Naemi & Chockalingam, 2013). Though the majority of diabetic foot ulcerations are a result of trauma, neuropathy or foot deformity, or a combination of all, it has been reported that 42% of cases are secondary to ill-fitting footwear (Healy, Naemi & Chockalingam, 2013) or inappropriately designed offloading devices (Armstrong et al., 2017).

Diabetic screening prevention programs were developed across the globe with the aim to reduce the prevalence of diabetes, delay or prevent the development of risk-associated complications of diabetes. Screening programs provide a systematic and reliable approach to risk identification and provide a framework for care. They have been deemed effective, both economically and strategically, compared to no screening at all (Gilmer & O'Connor, 2010).

There exist various diabetic screening prevention programs across the globe, all of which share the same aim and understanding (Formosa et al., 2015). All programs, emphasise on the importance of a thorough physical examination of the foot and include guidelines for screening for loss of protective sensation, screening for vascular status and proper history taking.

A study by Formosa, Gatt & Chockalingam (2016) reviewed 10 international guideline documents. The following is a list of aspects addressed in these 10 guidelines for diabetic screening by Formosa, Gatt & Chockalingam (2016):

- Peripheral neuropathy
- Peripheral Vascular Disease (PVD)
- Inspection and provision of footwear
- Foot deformation

- Patient foot care education
- Frequency of assessment and screening

Examination of the foot structure is also mentioned in various screening programs but no guidelines are available so far. The programs briefly encourage the clinicians to observe and look out for any structural abnormalities such as hammer toes, bone prominences and reduced joint mobility neglecting other important biomechanical aspects. Though visual observation of foot deformities helps in identifying potential areas at risk of ulceration, it is not enough to identify pressure changes resulting from structural compensations during foot functions. Unfortunately, screening guidelines only advice on tools related to the assessment of neuropathy and peripheral arterial disease, namely the Semmes-Weinstein 10g monofilament and the Doppler Ultrasound respectively (Leese et al., 2006). No tools are mentioned that relate to the biomechanical assessment of the diabetic foot.

A study by Sinwar (2015) describes the three principles of diabetic foot care management. The author believes that adequate and timely debridement of any foot callosities, infection control and reduction of high peak plantar pressures can help in controlling and avoiding the development of diabetic foot ulcers (Sinwar, 2015). Foot compensations brought about by biomechanical pathologies should be given greater attention and should not be underestimated as they make an integral component in the preventive care of the diabetic high-risk foot (Shavelson, 2011).

As previously mentioned, plantar pressures, joint mobility being reduced or hypermobile, foot type and the overall kinetics and kinematics of the diabetic foot all play a role in the development or prevention of ulcerations. In some referral pathways as instructed by these guidelines, indicate that when an abnormal foot structure is identified, the patient should be referred for foot pressure mapping with the aim to offload the area of peak pressure. A study by Singh et al. (2005) recommends plantar pressure platforms and in-shoe pressure systems as ideal for the true measurement of peak plantar pressures of the diabetic foot but it is not enough. The numerical values of the data gathered through such devices is not comparable as it is device-dependent. Thus, a generalized peak plantar pressure level which indicates a risk of ulceration is difficult to obtain. A specific pressure threshold has proven very difficult to be identified because the absolute pressure magnitude differs from one system to another. The quantity of pressure is influenced by the duration, repetition and direction of

pressure (Hunt & McPoil, 1995). This makes the information gathered device dependable which will be true only to that specific patient being studied (Armstrong, Boulton & Bus, 2017). For this reason, it is of the utmost importance to know whether the orthoses designed are indeed reducing the forces and/or increasing the area as intended there by the achieving the ideal percentage reduction to avoid ulceration.

Pathological forces can be controlled and offloaded from the plantar surface of the foot through the use of straps, pads, foot orthotics, muscle strengthening and training programs (Shavelson et al., 2011). Foot orthotics such as prescription orthoses act as a means to balance and support the overall body posture and control both muscles and tendons (Sinwar, 2015). Considering that pressure is directly proportional to force, pressure and tissue stress can be reduced by diminishing the force (Bus et al., 2020). Another method to reduce pressure is to increase the area underneath it (pressure is inversely proportional to area) (Bus et al., 2020). This allows better biomechanical performance thereby reducing peak plantar pressures and are known to have helped in reducing the number of diabetic foot ulcer cases (Shavelson, 2011). In support to this statement, a systematic review by Collings and his colleagues (2021) identified that prescription orthoses as an offloading technique in the management of the high-risk foot may indeed prevent diabetic foot ulceration if prescribed and manufactured correctly. However, clinical observations of the diabetic high-risk foot, if done without instrumentation, may impose subjectivity (Armstrong, Boulton & Bus, 2017) and thus may result in overlooking important information. This may also imply that risk factors not being identified in time, thus putting the patient at risk of ulceration or amputation. Furthermore, it is well known that high pressures from inadequate footwear or ill designed orthoses may increase plantar pressures which contributes to tissue breakdown (Armstrong, Boulton & Bus, 2017). Prolonged diabetes makes individuals unable to respond to excessive pressure stimuli this leads to pain and tissue injury which also contributes to tissue breakdown (Zhao et al., 2016).

2.7 Plantar Pressures: A Causative Factor for Diabetic Foot Ulceration

An important causal component is excessive plantar pressure and mechanical stress which relate to both joint mobility and structural foot deformities (Fernando, et al., 2014; Bus, 2016; Armstrong, Boulton & Bus, 2017). Pressure is defined as a type of

mechanical stress that is equivalent to the degree of force applied vertical to it. Pressure is directly proportional to the force but inversely proportional to the area. If a force acts on a large surface area, the resultant pressure will be relatively small conversely, if a force acts on a small surface area, the resultant pressure is expected to be high. Thus, by dividing the force over a known area, the magnitude of pressure can be calculated (Figure 7).

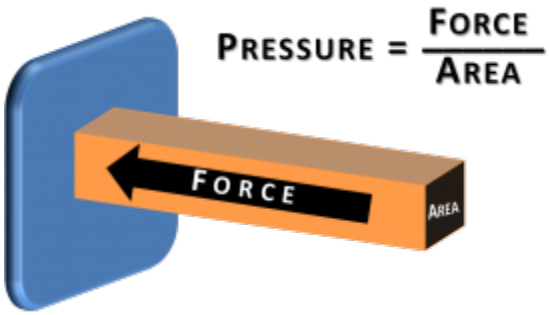


Figure 7: Image showing the force of area formula. Retrieved from Swanson (2011)

The amount of pressure is dependent on variables such as body posture, direction of external force and type of surface on which the force is applied (Swanson, 2011). When applied to the human foot, plantar pressure refers to the vertical force that acts between the foot and the ground during gait, and is strongly linked to tissue breakdown in patients living with diabetes mellitus (Razak et al, 2012). Excessive pressures on the foot are generally brought about by direct or repetitive trauma which bring about inflammation, atrophy, hypertrophy and formation of hyperkeratotic lesions, ulcer formation and necrosis (Kirtley, 2006).

Current technology allows the measurement of vertical forces that act on the foot during walking (Guldemond et al., 2007) nevertheless, due to the great variability between one technology to another, plantar pressures are standardised by measuring the normalised peak pressures in percentage (%) instead measuring the absolute pressure value. Measurement of the Peak Pressure Gradients (PPG) is another common approach of obtaining a quantifiable value of plantar pressure. PPG is deemed as the best method of identifying skin trauma as it identifies the special change in plantar pressure around the peak plantar pressure area (Mani et al., 2012).

The measurement of plantar pressures in clinical environments have proved to be a vital contribution to demonstrate the pathomechanics of the abnormal foot and track treatment progression (Hessert et al., 2005). However, due to the high variability in

plantar soft tissue, vascular perfusion, calibration of pressure measuring equipment, additional forces such as shear and duration of the subjected pressure, a general consensus on the absolute plantar pressure threshold that classifies risk of ulceration has not yet been identified (Mani et al., 2012). Studies by Armstrong et al. (1998) and Fernando et al. (2016) attempted to identify a plantar pressure threshold. In their study, the authors found that patients living with diabetes, especially those with peripheral neuropathy, exhibited high plantar foot pressures compared to healthy patients. Furthermore, patients with previous history of ulceration have even higher pressures at the site of ulceration (Fernando et al., 2016). However, a clear cut off pressure measurement between those with a history of ulceration and those without, could not identified (Armstrong et al., 1998; Fernando et al., 2016). Foot plantar pressures can be exacerbated depending on the type of footwear used, physical activities and presence of callosities. In a study by Spink et al. (2009) it was estimated that a hyperkeratotic lesion raises the average plantar pressure by up to 30%.

A study by Bus et al. (2020) that in patients living with diabetes mellitus at least 30% of maximum plantar pressure reduction should be achieved in order to reduce the risk of ulceration. A study by Zequera and Solomondis (2010) concluded that it is essential to provide the high-risk patient with individual assessment and thus with the help in-shoe pressure systems, footwear and prescription orthoses should be designed and then tested to confirm that they indeed are reducing the identified pressure points at a safe level. This statement was later supported by 2 systematic reviews by authors Paton et al. (2011) and Lewis & Lipp (2013).

2.7.1 Pressure Mapping Systems

With the help of today's technology, clinicians are able to identify pressure areas easily through various pressure mapping devices. Though plantar pressure measurements can be taken while the patient is standing (static), only dynamic measurements can be used to determine gait parameters and pressure load during gait. Systems to measure plantar pressures generally consists of a computer to receive, interpret and store the data, software packages that allow the clinician analyse and correlate the data to a pathology and the sensor measuring device itself (Orlin & McPoil, 2000). There are two types of pressure sensing devices these include the pressure distribution platforms (Figure 8) and the in-shoe systems (Figure 9). Though both types of devices read pressures, the devices may vary in sensor sensitivity and configuration (Razak et al, 2012).

Figure 8: Pressure distribution platform. Retrieved from Pedcad foot technology (n.d.)

Figure 9: In-shoe pressure measuring system. Retrieved from Tekscan (n.d)

Locally, it is common clinical practice to refer to pressure distribution platforms when pressure measurements are needed to identify the risk of ulceration. Pressure distribution platforms are ideal for analysing the relationship of the barefoot to the ground (Gefen, 2007) and consist of a flat, mat like device that is built from an array of pressure sensors, embedded within the floor particularly not to interfere with the patient's normal gait (Shu et al., 2010). This type of system is the most popular within the clinical setting as it is cheaper and is very easy to use compared to in-shoe systems

(Simon, 2004; Howell et al., 2013). Though less expensive and user friendly, this system is not free of shortcomings. The disadvantage of using a pressure platform is that the patient might need to familiarise with the device prior the actual measurement to ensure the measurement of natural gait (Simon, 2004; Howell et al., 2013). Though natural walk is ideal, the patient still has to aim to step at the center of the device for more accurate readings. Furthermore, pressure platforms can only be used indoors (MacWilliams & Armstrong, 2000).

In general, in-shoe systems have their sensors implanted within a very slim and flexible insole which allows it to be placed within the patient's footwear. This set-up makes the device adequate for the assessment of the interactions between the foot and shoe, and orthoses if any (MacWilliams & Armstrong, 2000; Gefen, 2007). However, compared to pressure platforms, in-shoe pressure systems can be quite costly, user dependent and tend to have lower spatial resolution attributed to a lower number of sensors and their arrangement (Howell et al., 2013). Furthermore, one major disadvantage is that currently available commercial in-shoe systems use electrical wires to connect the sensors to the acquisition system which can influence gait (Shu et al., 2010).

Currently available commercial in-shoe pressure devices have large number of pressure sensors within them allowing better resolution and identification of pressure points throughout the entire plantar surface of the foot (DeBerardinis et al., 2018). Early studies have investigated the variation in output measurements, hysteresis and creep of the FScan® system by Tekscan (Woodburn and Helliwell, 1996; Luo et al., 1998). The FScan® system is a full length, flexible insole which has 99 Force Sensing Resistor (FSR) type of pressure sensors embedded within it. Both studies by Woodburn and Helliwell (1996) and Luo et al. (1998), and more recently by Price, Parker & Nester (2016), confirmed that the FScan® system tends to exhibit high variability between its sensors and significant hysteresis and creep. In their study Nicolopoulos et al. (2000) investigated different calibration methods with the aim to reduce measurement errors of the FScan® system. It was concluded that by controlling calibration, hysteresis and limiting bending, the FScan® system is more likely to provide accurate readings.

The Pedar X®, similar to the FScan® system, is a full length, highly elastic and flexible insole like device that has 99 pressure sensors embedded within it. The system is designed by Novel and is able to measure pressures that range between 1 mmHg to 112 mmHg. Pedar X® can be connected to a computer via a cable or utilizes Bluetooth® technology for outdoor use (Giacomozzi et al., 2012). Both FScan® and Pedar X® have been tested and compared in loading experiments that showed that both systems tend to exhibit higher errors when performing beyond their specific range of pressure threshold (Hsiao et al., 2002) with the Pedar X® system showing the least error in the study by Giacomozzi et al. (2010) and later in the study by Price et al. (2016). What we can learn from these studies is that despite of the proven validity and reliability of these commercial pressure sensing devices, these devices can still exhibit errors, hysteresis and drift especially with repetitive use or exceedingly high pressures (DeBerardinis et al., 2018).

Current literature provides good rational and evidence in favour of using pressure assessment in clinical decisions for the prevention of diabetic foot ulceration and it is strongly preferred to clinical management without pressure mapping, (Bus et al., 2011; Waaijman et al., 2012; Chatwin et al., 2020). In view of this, researcher have sought multiple wireless, cost-effective techniques, as an alternative to commercial in-shoe systems, to identify plantar pressures as a risk factor for ulceration (Shu et al., 2010; Guo, 2012; Ostadabbas et al., 2012; Ferber et al., 2013; Price et al., 2016; Lee et al., 2019). An example of such a device was presented by Shu et al. (2010). The device was described as a thin polyimide film circuit board that acted as the insole; within it an array of soft pressure sensors was embedded. These soft pressure sensors were developed by the authors themselves and were described to be made out of conductive textile fabric sensing elements (Shu et al., 2010). Position of sensors was determined secondary to the areas noted to withstand the most pressures namely the heel and metatarsal area (Hessert et al., 2005). Though results of this study have shown that this affordable device is accurate in determining discrete pressures and any related changes, the authors suggested an addition of an extra sensor at the hallux area to help in reducing the minor differences between the output of their device and the reference standard (Shu et al., 2010). As opposed to Shu et al., (2010), Guo (2012) resorted to use commercially available pressure sensors that are made of piezoelectric material. Their device was also wireless and consisted of an array of piezoelectric sensors

positioned 3 different directions with the intention to read plantar pressures from 24 points. The device was also reported to measure 10mm by 20mm by 8mm. Results of this study also showed satisfactory and positive results without any reported technical failures (Guo, 2012).

SurroSense Rx^{TM} by Orpyx Medical Technologies Inc. was introduced as a wireless in-shoe pressure mapping device, with an array of 8 pressure sensors, designed to provide real-time feedback of plantar pressure points during dynamic activities (Ferber et al., 2013). Unfortunately, the authors did not specify on the type of sensors used within this system however, the system was reported to be consistent when compared to commercial devices and is able to provide the patient and clinician with feedback when a specific pressure threshold is exceeded while monitoring pressure over time (Ferber et al., 2013). The study further suggested that future studies should focus on the longitudinal validity and reliability of the device (Ferber et al., 2013). A recent passive cohort study by Najafi et al. (2017) also investigated the effectiveness of SurroSense Rx^{TM} in reducing the recurrence of diabetic foot ulceration. A total number of 17 participants with a history of diabetic foot ulceration were asked to wear the device for a period of 3 months. Results of this study suggested that the device is effective in determining elevated pressure areas and its ability to provide feedback to the wearer could increase adherence to treatment (Najafi et al., 2017).

2.7.2 Pressure Sensor Selection

The most vital component of a pressure measurement device is the pressure sensors embedded within it (DeHennis et al., 2016). Pressure sensors exist in various forms and sizes however, despite of this, their role remains the same. A pressure sensor changes a physical pressure force into an electrical signal that can be quantified (Bao, 2000).

'Pressure sensors' is generally used as a collective term to refer to pressure sensors, pressure transducers and pressure transmitters, the difference lying in terms of electrical output (Das & Das, 2018). Pressure transmitters covert pressure measurements into a distinct analogue and/ or digital signal. Pressure transducers have two types of connections, process and electrical connection but unlike transmitters, they do not convert the measurement into an electrical signal. Both pressure transducers and transmitters are ideal to use in power battery operated devices as

utilize low currents to function but are powerful enough to reach a voltage of 10V with a frequency that ranges between 1 to 6kHz due to an amplifier built within them (Avenet Abacus, 2023). Conversely, in pressure sensors, the electronics that transmits the signal amplification is not embedded within them but are connected with wiring systems that effect resistance. The shorter the wiring, the lower resistance is lost. Furthermore, the output signal produced is low compared to that of pressure transducers and transmitters but is also directly proportional to the voltage that supplies the device with power (Das & Das, 2018).

Prior describing the different types of pressure sensors, it is important to explore the important language that relate to the measurement of pressure (Table 4; Figure 10) and the key specifications that make a sensor efficient (Morris & Langari, 2012; National Instruments, 2020).

Table 4: Key terminology related to pressure measurement

Term	**Definition**
Gauge Pressure	Measurement that indicates the value of the pressure being measured relative to the environment pressure
Absolute Pressure	Measurement that indicates the value of the pressure being measured relative to the zero pressure of the vacuumed space within the sensor itself
Differential Pressure	Measurement that indicates the resultant value of difference between two pressure values
Vacuum Pressure	Measurement that indicates the resultant value of difference between the absolute pressure and environmental pressure.

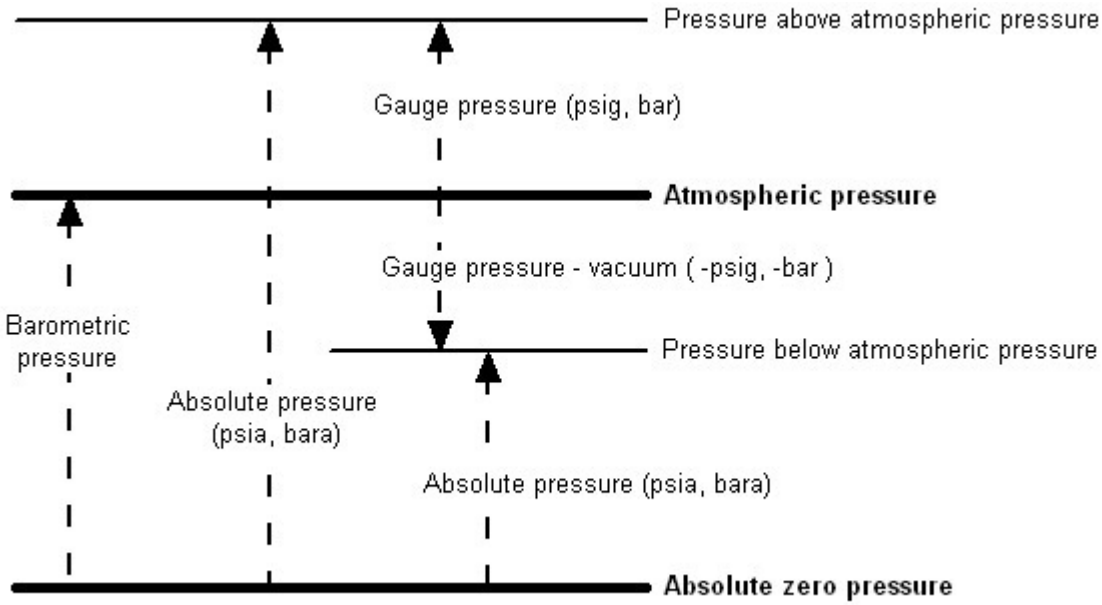


Figure 10: Relationships of the different pressure measurements. Retrieved from Engineering ToolBox (2004).

When applied to foot biomechanics, hardware-related requirements for an in-shoe pressure sensor necessitates that the sensor should be thin and flexible to fit in footwear and to conform to the shape of the foot. The device should also be small in size and lightweight (max. 300g) (Razak et al., 2012). Furthermore, in order to avoid loss of resistance and influence on gait the device should be wireless (Bamberg et al., 2008). Number of sensors is also an important factor. In pressure mat systems, the higher the number of sensors, the more accurate the measurement of pressure is however, when it comes to in-shoe systems, there is a risk that due to the proximity between each sensor, the chance of cross talk between sensors increases, limiting performance of the device (Price et al., 2016).

Ideal sensors should test low in creep performance where creep is defined as the permanent deformation of a material due to increased temperature and stress over time (Madou, 2001). A study by Lee et al. (2001) determined that a low temperature sensitivity, generally between 20^{o}C – 37^{o}, is desired when using pressure sensors. Temperature influences and alters the sensor output, giving a varied pressure reading (Bolton, 2018). Furthermore, sensors should also test low in hysteresis and high in linearity (Xia, 2021). Hysteresis is a measure of repeatability following repetitive use (Razak et al., 2012). It is defined as the maximum difference in input pressure measurement first with increasing the load followed by decreasing the load (Beeby,

2004). In other words, hysteresis occurs secondary to a lag in pressure readings when the device is loaded and offloaded. Linearity is defined as the proportional measure between the authentic values of a measurement to the output measurement of an instrument. Bamberg et al. (2008) in their study on wireless sensor systems, argued that because pressure sensors measure stress over a slightly non-uniform area, they are naturally non-linear, giving a slightly curved output measurement which must be linearized to improve usability and accuracy.

A systematic review conducted by Razak et al. (2012) identified that, in addition to the previously mentioned characteristics, other factors such as sensor type, maximum pressure that the sensor can withstand prior deformation, and the operating pressure range of a pressure sensor should be considered. The operating pressure range of a pressure sensor is generally recommended to be up to 1,900kPa for the assessment of foot plantar pressures (Razak et al., 2012). Additionally, it is important to consider the resolution (size and number of sensors used) and the sensing area of the pressure sensor generally recommended not exceed 5mm x 5mm x 5mm as one of a larger area may underestimate peak plantar pressures. Last but not least is the sampling frequency, generally recommended be at least 200Hz as it is deemed sufficient for the evaluation of everyday gait activities (Razak et al., 2012).

All sensors within the pressure sensing device, being a platform or an in-shoe type of system, provide an electrical yield that is equivalent to the amount of pressure detected (Wang, Song, Fekete, & Gu, 2019). However, sensors from one device to another can vary in type. The selection includes the capacitive, the resistive, the piezoelectric and the piezoresistive type of sensors (Wilson, 2005). Capacitive sensors are made up of a dielectric elastic polymer layer tightly packed between two electrically charged plates (Figure 11). When a force is exerted on the plates, the dielectric elastic layer expands, changing the electrical voltage within it which then can be calibrated to provide a pressure reading. The electrical change is directly proportional to the force applied to it (Loverich, 2006). Examples of plantar pressure sensing devices that utilize capacitive sensors include the emed® platform system and the Pedar® in-shoe system by Novel (Razak et al., 2012).

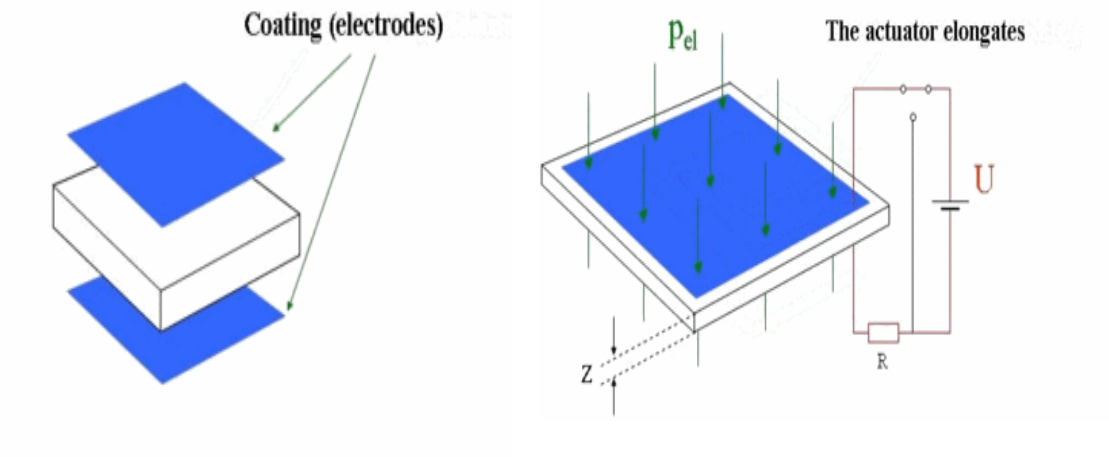


Figure 11: Image showing the construction of a capacitive type of sensor. Retrieved from Wikipedia (2020).

Force Sensing Resistors (FSR) are thin and flexible sensors made up of a semiconductor layer, a spacer and a layer with active element electrodes (Figure 12). Upon pressure, the electrodes touch the semiconductor changing the resistance of the electrical impulse through it. The amount of force applied to sensor is inversely proportional to the resistance it produces that is, the larger the force applied, the lower the resistance produced. Examples of pressure sensing devices that utilize FSRs include the MatScan® platform system and the F-Scan® in-shoe system by Tekscan.

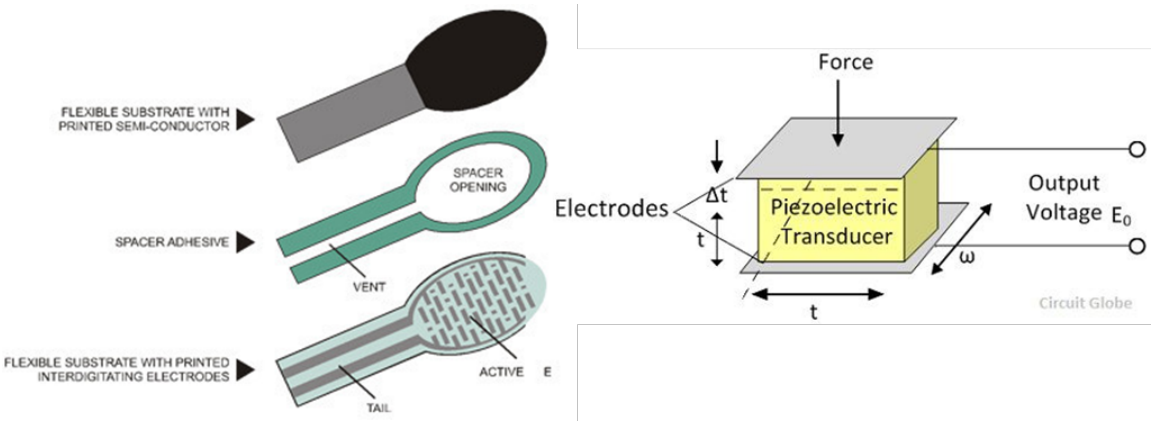


Figure 12: Image showing the composition of a Force Sensing Resistor (left) and the composition of a piezoelectric sensor (right). Retrieved from Circuit Globe (n.d) & Adafruit Learning Systems (2017)

Finally, piezoresistive sensors consist of piezoelectric semi conductive element, generally quartz crystals in type, where its resistance is inversely proportional to the magnitude of the force applied (Figure 13). As a high force is applied to the device, the resistance decreases and vice-versa (Gefen, 2007). Examples of pressure sensing devices that utilize piezoresistive sensors include FlexiForce® by Tekscan and ParoTec by Paromed (Razak et al., 2012).

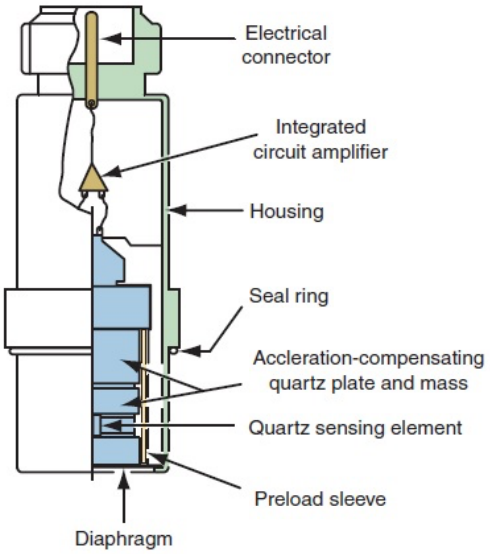


Figure 13: Image showing the construction of piezoelectric sensors. Retrieved from Automationforum (2018)

Of all types of sensors, piezoelectric sensors can be deemed as the most accurate however, piezoelectric sensors are generally bulky and thus are more likely to be found in pressure mats rather than in-shoe systems as they require a good amount of thickness when embedded within a device (Kirtley, 2006).

2.8 Temperature: An identification factor for diabetic foot ulceration

As a natural protective response, the body elicits a series of complex processes upon contact with an irritation to eliminate harmful pathogens and clear out unwanted damaged cells and tissues (Ferrero-Miliani, 2007). This process involves both blood vessels and immunity cells and is referred to as inflammation. There are five classical signs that characterise inflammation namely heat, pain, redness, swelling and loss of

function (Houghton et al., 2013). The process of inflammation is initiated with the acute phase where a stimulus such as an excessive pressure on the skin, causes a localized irritation over the area. This generates a movement of plasma cells, leukocytes and hormones such as cytokines and chemokines, from blood vessels which then bind to the receptors of the injured cells. If the stimulus is prolonged, the inflammation progresses, eliciting the presence of other cells which cause more vasodilation of the blood vessels, activate nerve cells and release immunity cells in preparation of eliminating unwanted waste and healing the injured tissues. Although the role of inflammation is to protect the body against infection, amplification of this process may cause significant damage to the skin primarily ulceration (Hall, 2011).

Repetitive traumatic stress and inflammation are commonly accepted as the primary factors that lead to the formation of diabetic foot ulcers (Seixas et al., 2018). In the presence of neuropathy, swelling, erythema and pain may not always be gradable due to the loss of innervation of the sensory nerves (Gershater et al., 2011; Dubský et al., 2013; Bus, Waaijman, Arts et al. 2013; Ulbrecht et al., 2014; Armstrong et al., 2017). Thus, temperature is the remaining factor that can be used to detect the presence of inflammation (Bergtholdt, 1979; Ulbrecht et al., 2014; Sturgeon Delia, 2018, Gatt, Mercieca, Borg et al., 2020). Skin temperature has been proven to be detected from up to a week prior to tissue breakdown and ulcer formation (Sun et al., 2006; Gatt et al., 2018).

Skin temperature increase in the diabetic high-risk foot can be classified as acute or chronic, where acute changes are noted to occur secondary to friction following weight bearing activities. Conversely, chronic changes are noted to occur secondary to prolonged exposure to repetitive stress and are highly characterised by inflammation (Yavuz et al., 2019). Being either acute or chronic, a localised increase in skin temperature may exacerbate the tissue metabolic rate of the high-risk foot by 6% to 13% per 1-degree Celsius (Ruch, 1965; Shrestha, Acharya, & Gurung, 2020). In patients living with diabetes mellitus and peripheral arterial disease, this increase in metabolic rate may not be achieved due to the lack of tissue perfusion, leading to quickened cell autolysis at the area of stress (Yavuz et al., 2015). Under non-weight bearing situations, an increase in skin temperature is observed to cause vasodilation of blood vessels so that tissue perfusion is promoted however, when the foot is in a weight bearing position, the sustained pressure hinders vasodilation of blood vessels leading

to localised occlusion of blood circulation and eventually tissue breakdown (Lachenbruch, Tzen, Brienza et al., 2013).

Compared to healthy patients, the resting skin temperatures of the diabetic foot are higher than that of the healthy foot (Yavuz et al., 2019). Plantar foot temperatures of the diabetic foot are further increased by 5.3°C when walking barefooted for a short period of time. Furthermore, a damage threshold of up to 35°C can be reached while wearing insulated custom footwear (Yavuz et al., 2019). In view of this, patients living with diabetic neuropathy who are instructed to wear insulated protective footwear, might be predisposed at a high risk of ulceration due to the in-shoe microclimate (Mizzi, 2016). Continuous monitoring of skin temperatures of the diabetic high-risk foot as a preventive measure of diabetic foot ulceration is highly encouraged (Armstrong, Lavery, Wunderlich et al., 2003; Yavuz et al., 2019).

In the review by Bennett (2017) favourable evidence concerning the effectiveness of monitoring of foot temperatures was found. The comparative review suggested that if measured objectively, once daily foot temperature monitoring can be used to identify inflammation prior diabetic foot ulcer formation and infection (Bennett, 2017). In view of this evidence, daily monitoring of foot temperature to effectively identify local increases in skin temperature as pre-sign of foot ulceration (Mizzi & Falzon, 2018; Boulton et al., 2020) has been introduced in multiple clinical guidelines (Bus et al., 2016; Lavery et al., 2016; Frykberg et al., 2000) and is supported by evidence from randomized controlled trials (Frykberg et al., 2000; Lavery et al., 2004; Lavery et al., 2007; Armstrong et al., 2007; Bus et al., 2016; Lavery et al., 2016).

A study conducted by Armstrong et al. (2007) observed that their participants experienced a 4.8 times local rise in skin temperature one week prior to tissue breakdown. Lavery et al. (2007) in their randomized control trial have confirmed that observing changes of localised skin temperature can help in ulcer prevention as opposed to the standard guidelines. In this study, clinical guidelines were described as a combination of diabetes education, foot self-monitoring, customized padded insoles and footwear and routine clinical follow-ups. The researchers enrolled 173 participants which were divided into 3 groups – a group that followed standard guidelines, a group that used a mirror to easily inspect the plantar aspect of the foot for signs of inflammation, and a third group that used a digital infrared thermometer to monitor

any changes in plantar foot temperature. Results of this study concluded that standard guidelines and visual observation for signs of inflammation are not sufficient to prevent the development of foot ulcerations. Furthermore, there was a four-fold significant decrease in ulcer occurrence in the group that used temperature monitoring (Lavery et al., 2007) showing that temperature monitoring alone can dramatically reduce the risk of ulceration by 50% (Lavery et al., 2007; Houghton et al., 2013; Reyzelman & Dionisopoulos, 2018).

When evaluating the risk of ulceration, temperature asymmetry is highly recommended (Rutkove, 2001; Kang, Hoffman, Krimitsos et al., 2003; Nagase, Sanada, Takehara, et al., 2011; Hasselberg, McMahon & Parker, 2013). Temperature asymmetry is a clinical technique carried out by comparing the temperature of the limb being investigated to the contralateral limb. The contralateral limb serves a control as it rules out variables such as ambient temperature, physiological fluctuations, systemic inflammatory responses and transient temperature changes secondary to physical activity and footwear (Lavery et al., 2019). In their study Lavery et al. (2019), identified key point locations which should be matched to the contralateral limb when measuring skin temperatures namely the hallux, first, third, and fifth metatarsal heads, midfoot, and heel. Once a temperature difference exceeding 2.2°C is observed between the corresponding contralateral site, that is prolonged for at least two consecutive days, preventive care can be initiated (Lavery et al., 2019). Frykberg et al. (2017) evaluated the predictive accuracy of measuring foot temperatures in using temperature asymmetry to indicate the risk for ulceration. Results of this study have shown that by measuring plantar foot temperatures and using the 2.2 asymmetry approach, 97% of ulcer cases can be predicted 35 days prior to clinical presentation (Frykberg et al., 2017). A more recent study by Gatt et al. (2018) reported that in comparison to healthy individuals, patients living with diabetes mellitus exhibited higher levels of localised skin temperatures, irrelevant to the presence or absence of neuro-ischaemic diabetic foot ulceration. The study further showed that the assessed ulcerated and non-ulcerated digits showed no significant difference in localised skin temperatures (still high compared to healthy participants), this implied that both the ulcerated and non-ulcerated digits were at risk of developing diabetic foot complications (Gatt et al., 2018).

The problem with the temperature asymmetry technique is that patients with an at-risk foot might be on treatment for active ulceration and/or may have experienced an amputation of the contralateral limb thus comparison would not be possible in such cases (Glaser, Bensley, Hurks et al. 2013; Font-Jiménez, Llaurado-Serra, Roig-Garcia et al., 2016). In view of this issue, a study by Lavery et al., (2019) aimed to validate an approach for identifying foot inflammation using the measurements of a single foot. the study relied on the approach of comparing ipsilateral temperature measurements to ambient temperature measurements using a telemedicine mat. Results of this study concluded that repetitive temperature measurements from a single foot available can be used to predict the development of foot ulceration but with less accurate results when compared to temperature asymmetry techniques.

The subtle markers of inflammation are difficult to assess and thus they are often overlooked. Locally, it is common clinical practice to manually palpate the skin for any changes in temperature. This technique however, is not sensitive enough to capture subtle and multiple temperature changes on the skin and thus is not a reliable and repeatable technique. With the help of today's technology, as an alternative to manual palpation, a change in skin temperature can be detected and quantified using various types of temperature-measuring technologies (Welles et al., 2018). Two main types of temperature-measuring technologies have been identified namely infrared thermographic cameras (Figure 14) and liquid crystal thermography (Figure 15) (Roback, 2010).

Figure 14: Image of an infrared thermographic camera. Retrieved from I&E Technologies (n.d).

Figure 15: Liquid thermographic plate being used during a scientific experiment. Retrieved from Stess, Sisney, Moss, et al. (1986).

Infrared thermometers help in providing accurate and real-time temperature measurement of the skin by producing a coloured image of the skin temperatures being measured (Armstrong et al., 2017) and provide an accurate, real-time, non-contact method of measuring skin temperature changes of a specific surface on the skin (Mizzi & Falzon, 2018). One major limitation of this technique however, is that monitoring has to be carried out within a clinical setting, the equipment is quite expensive and that the readings have to been taken while the individual is stationary without shoes and socks (Gatt et al., 2014; Mizzi & Falzon, 2018).

Liquid crystal thermography shares the same disadvantage as thermographic cameras but differ as they do not quantify the temperature change but it gives information about the distribution of the plantar skin surface. The device is made up of two plates that enclose a thin sack-like layer filled with thermochromic liquid crystals that change colour depending on the amount of heat transmitted from skin to plate (Stasiek, Jewartowski & Kowalewski, 2014).

Various studies have been exploring and have proven the relationship between temperature and tissue breakdown (Armstrong, Holtz-Neiderer, Wendel et al, 2007; Lavery et al., 2007), some of which date back to 1971 (Goller, Lewis & McLaughlin, 1971; Sandrow et al., 1972). Researcher have sought multiple cost-effective techniques, in form of insoles or smart textiles, to identify inflammation through change in temperature (Sandoval-Palomares et al., 2016; Coates et al., 2016; Lugoda et al., 2018; Reyzelman, Koelewyn, Murphy et al., 2018; Ming, Walter, Alhajjar et al.,

2019). For instance, Coates et al. (2016) developed a wearable multimodal skin sensing device for the diabetic foot. The device consisted sensors that were able to detect temperature, humidity, applied force, acceleration, rotation rate and galvanic skin response of the foot. Furthermore, capacitive couple bioimpedance was used as means of measuring inflammation. The force sensors were placed at the center of the plantar aspect of the calcaneus so to receive the load during heel strike. Four temperature sensors were placed at the calcaneus adjacent to the force sensor, 1st metatarsal, 5th metatarsal and the apex of the hallux. All sensors were mounted on the foot with zinc oxide tape and connected through Bluetooth wireless technology to permit mobility while the data is being read and recorded. This innovative device has introduced an alternative way to monitor in-shoe environment of the high-risk foot at any setting being laboratory, clinic or home. The authors argue that this system has provided multifactorial measurements of which can be later adapted to measure sensors required by the investigator. Furthermore, the authors reported that the system can be further improved to be accessible through mobile phones for ease of use and access.

Sandoval-Palomares et al. (2016) has presented us with a continuous monitoring portable device that consists of an array of 10 temperature and humidity sensors. Their system consisted of two modules allowed the data acquisition (module one) and connected the sensors to the computer being used (module two) via Universal Serial Bus (USB) interface. The sensors were placed as following: 2 sensors at the forefoot, 2 sensors at the midfoot, and one sensor at the hindfoot. The sensors consisted of SHT15 type of sensors that are able to read humidity that ranges 100% RH ±2% and temperature readings that range between -40°C to 123.8 ± 0.3°C. The authors reported that the device demonstrated positive viability their device as means to monitor in-shoe microclimates of the high-risk foot.

2.8.1 Temperature sensors

Prior to developing a temperature sensing device, one must be mindful of the vast variety of types of temperature sensors that are commercially available. A temperature sensor is a device that has the ability to convert heat from its environment to an electrical signal, that quantifies that same amount of heat (Jost, 2019). Temperature sensors are generally embedded within electrical devices and are used to monitor and measure temperature changes. These sensors exist in various types and size and might

require direct (contact temperature sensors) or in-direct contact (non-contact temperature sensors) with the source that is being measured (Jost, 2019). Temperature sensors can be found in various forms and are categorised into 3 groups, depending on the sensor's characteristics and performance when subjected to a variety of conditions (Table 5) (Areny, 2004; Quintela & Melchor, 2005; Scherz, 2006). Though they vary in type and category, the overarching role of temperature sensors is that of transmuting a physical measure into an electric voltage (Anliker et al., 2004).

Table 5: Table showing sensors categorised according to type, adapted from Martín-Vaquero, Hernández Encinas, Queiruga-Dios et al., (2019).

Electrical	**Mechanical**	**Thermal Radiation**	**Other**
Thermocouples	Dilation systems	Infrared radiation	Colour indicators
Thermoresistance	Glass Thermometers	Thermography	(paints and pencils)
Thermistors	with liquids		Pneumatic probes
Diodes	Bimetallic		Ultrasonic sensors
Programmable	thermometers		Pyrometric indicators
electronic devices			Acoustic thermometers

Despite of the ample variety of type of temperature sensors, the electrical type remains the most popular where temperature measurement is concerned. As summarised in the previous table (Table 5), examples of electrical temperature sensors include thermocouples, thermoresistors, thermistors, diodes and programmable devices (Martín-Vaquero, Hernández Encinas, Queiruga-Dios et al., 2019). A thermocouple is constructed of two metals of different of sort, such as copper and constantan, which are fused together to form two junctions. One of the junctions is kept at a constant temperature and is referred to as the cold junction, while the other is exposed to heat and is referred to as the hot junction (Figure 16). With the help of these junctions, a thermocouple is able to generate an electrical voltage that equivalent to the amount of heat sensed a phenomenon referred to as the thermoelectric effect (National Instruments, 2019). Thermocouples are generally preferred for industrial use (Martín-Vaquero, Hernández Encinas, Queiruga-Dios et al., 2019).

Figure 16: Image showing an example of a thermocouple. Retrieved from Encardio rite. (2019)

Thermistors are temperature sensors that instead of reading temperature by creating a voltage, the temperature is read by changing the resistance of the sensor itself. Thermistors are composed from a combination of metal oxides and change their physical appearance when subjected to a change in temperature (Figure 17). Thermistors are subcategorized as Negative Temperature Coefficient (NTC) and Positive Temperature Coefficient (PTC) thermistors. NTC thermistors are generally composed of a combination of magnesium, nickel, cobalt, copper and iron oxides that are shaped into a ceramic form of various sizes (Lugoda, 2018). With NTC thermistors, temperature is inversely proportional to resistance that is, as the temperature increases, the resistance of the sensor decreases. Their resistance typically varies between 50 Ω and 1 mΩ at 25 ◦C, with a sensibility of 4% at 25 ◦C (Martín-Vaquero, Hernández Encinas, Queiruga-Dios et al., 2019). As opposed to NTCs, with PTC thermistors, temperature is directly proportional to resistance that is, as the temperature increases, the resistance increases (Jha, 2015) and are typically composed of barium and of a combination strontium and titanium (Martín-Vaquero, Hernández Encinas, Queiruga-Dios et al., 2019).

Figure 17: Image showing an example of a thermistor. Retrieved from Encardio rite. (2019)

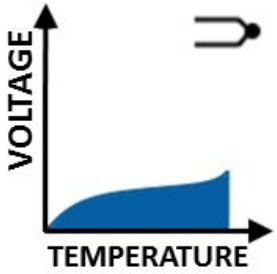
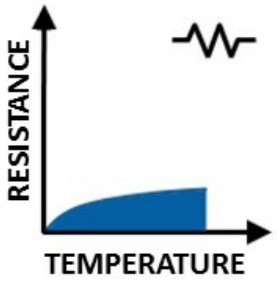
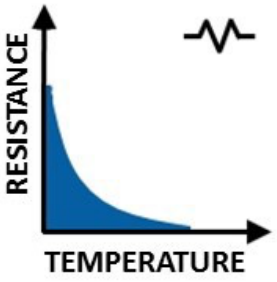
Similar to thermistors are Resistance Temperature Detectors (RTD) which are also known as thermoresistors (Figure 18). The difference between the two lies within their composition. While thermistors are made of ceramics such as oxides, nickel, manganese or cobalt, RTDs are made of high-purity conducting metals such as platinum, or copper that are wound into a coil (Kalsoom et al., 2020). Overall, RTDs are considered the most accurate as the temperature resistance ratio of the platinum wire used is very reproducible however, to achieve measurement precision, temperature measurement with this type of sensor should be carried out under specific conditions (Martín-Vaquero, Hernández Encinas, Queiruga-Dios et al., 2019). RTDs are also considered to be the most expensive type of direct contact sensors, followed by thermistors that compared to thermocouples, are able to read low temperatures that ranges between 0.05 ºC to 1.5 ºC (Jha, 2015).

Figure 18: Image showing an example of a Resistance Temperature Detector. Retrieved from Encardio rite. (2019)

A recent addition to the temperature sensing technology are programmable electronic devices. Like diodes, these types of sensors are already integrated within a circuit that is connected to a microprocessor. Programmable electronic devices work by altering the voltage and current at the point that connects the two types of semiconductor materials within it, otherwise referred to as the p-n junction (Kitai, 2011).

The accuracy of a sensor is determined by characteristics such as temperature range, linearity, sensitivity, response time, stability, and durability (Table 6). Temperature range is defined as the ability of the sensor to read temperature change within a specific temperature range. Compared to thermocouple sensors, thermistors and RTDs have lower temperature ranges but then are much better in terms of sensitivity and linearity respectively (Morris & Langari, 2016).

Table 6: Advantages and Disadvantages of Temperature Sensor Types. Retrieved from National Instruments (2019)

	Advantages	Disadvantages
THERMOCOUPLES 	✓ Simple ✓ Rugged ✓ Inexpensive ✓ No external power ✓ Wide temperature range ✓ Variety of styles	× Nonlinear response × Small sensitivity × Small output voltage × Requires CJC × Least stable
RTD 	✓ Most stable ✓ Good Linearity ✓ Most accurate	× Low sensitivity × Externally powered × Costly × Small output resistance × Self-heating error
THERMISTOR 	✓ Fast ✓ High output ✓ Minimal lead resistance error	× Limited temperature range × Externally powered × Nonlinear × More fragile × Self-heating error

A linear response is also desired in a temperature sensor however, no sensor can achieve perfect linearity. Linearity is defined as a directly proportional change in voltage and temperature which can be plotted as a straight line and it determines how sensitive a temperature sensor is to detect temperature change. The more linear a sensor is, the more sensitive it is and thus the better it is to sense and measure minute changes of temperature as opposed to a less sensitive sensor. Referring to table 7 below, where measurement of low temperatures is required, thermistors and RTDs are suggested. Another important characteristic of a sensor is response time which in turn affects durability. As the name implies, response time is defined as the time taken for

a sensor to respond to a change in temperature (Lugoda, 2018). Response time is influenced by various factors and the desired period is dependent on what one wants to achieve. For instance, large sized thermistors exhibit longer response time but have a less chances of over-heating during use (Hughes-Riley et al., 2017).

Table 7: Table showing the characteristics of different types of temperature sensors. Retrieved from Engineering ToolBox (2004)

Attribute	**Thermocouple**	**RTD**	**Thermistor**
Cost	Low	High	Low
Temperature Range	Very wide -350°F +3200°F	Wide -400°F +1200°F	Short to medium -100°F +500°F
Interchange ability	Good	Excellent	Poor to fair
Long-term Stability	Poor to fair	Good	Poor
Accuracy	Medium	High	Medium
Repeatability	Poor to fair	Excellent	Fair to good
Sensitivity (output)	Low	Medium	Very high
Response	Medium to fast	Medium	Medium to fast
Linearity	Fair	Good	Poor
Self-Heating	No	Very low to low	High
Point (end) Sensitive	Excellent	Fair	Good
Lead Effect	High	Medium	Low
Size/Packaging	Small to large	Medium to small	Small to medium

Having high linearity, high sensitivity and a balanced response time is not sufficient. A sensor must also have high output stability that is, a sensor should be able to perform consistently over time. The type of material is a determining factor for stability as some materials tend to react when exposed to heat. For example, RTDs are well known for their low reactivity due to the platinum material they are made of however, there is a greater chance that the material that holds the platinum together, deforms after prolonged exposure to heat (Hughes-Riley et al., 2017).

Skin temperature assessment can provide the clinician with a non-invasive, objective and reliable way of assessing temperature change (Bus, 2016). Various studies have reported positive outcome when monitoring the high-risk foot for temperature change (Ring & Ammer, 2000; Otsuka et al., 2002; Hildebrandt, 2010; Gatt et al., 2014; Bus et al., 2016) however, to date, temperature measurement as a diagnostic tool has not yet been introduced as part of the routine diabetic foot care prevention (Gatt et al., 2014; Bus et al., 2016). In the literature, techniques for monitoring in-shoe foot temperatures are sparse and is probably attributed to the fact that temperature sensors should to be very minute in size, sturdy and comfortable to fit between the shoe and the foot. Moreover, the sensor should effective enough to give precise readings even after prolonged use (Martín-Vaquero, Hernández Encinas, Queiruga-Dios. et al., 2019).

2.9 The relationship between pressure and temperature in relation to the high-risk foot

The correlation between skin temperature and plantar pressures, and their role in the causation of diabetic foot ulcers, is a relatively new concept and investigations on this concept are becoming more popular (Bus, 2016; Jones, Bibb, Davies et al., 2020).

In 1995, an animal study has proven that swine skin showed signs of deep tissue damage and necrosis following the application of a constant pressure of 13.3kPa maintained at a temperature of 35°C or higher (Kokate, Leland, Held et al.1995). A more recent study has evaluated this concept in 17 human participants where results have confirmed a correlation between increased tissue temperature and pressure ulcer development. The authors stated that participants who developed pressure ulcers were recorded to have an increase in skin temperature of 1.2°C prior ulceration compared to participants who did not ulcerate (Sae-Sia et al., 2004).

In view of these statements, it can thus be hypothesised that when the skin is subjected to continuous plantar stresses in the diabetic high-risk foot, the skin temperature at the area of stress rises weakening the ability of the surrounding tissues to resist biomechanical abnormalities (Yavuz et al., 2019). Furthermore, as previously discussed, the plantar skin temperature of the diabetic foot is noted to be warmer compared to healthy individuals. This discrepancy is further exacerbated with the presence of neuropathy (Sun et al., 2006) and/or following short walks (Yavuz et al.,

2015). Thus, measuring skin temperature as an add-on assessment technique to plantar pressure mapping, may provide a more reliable tool in the management of the diabetic high-risk foot (Yavuz et al., 2019).

2.9.1 In-shoe pressure and temperature measurement technology

Currently, to put this theory to practice, the clinician is to obtain temperature and pressure data separately using a thermographic camera and an in-shoe pressure device a technique which can result as both expensive and time consuming (Gatt et al., 2014). In the literature, in-shoe technologies are generally developed to monitor only one of these parameters (Rascio et al., 2018). As of yet, researchers are still developing and validating technology that is able to measure both in-shoe plantar skin temperature and pressure simultaneously (Maluf et al., 2001) to provide a more effective way to pre-empt the development of diabetic foot (Bus, 2016).
The systematic review, conducted as part of this research project as presented in Chapter 6 of this dissertation, has identified that to date, only 4 studies investigated and described an in-shoe device that was built to measure both temperature and pressure at the same time (Saliba Thorne, Gatt, DeRaffaele et al., 2021).

Maluf et al. (2001) achieved laboratory validation and presented their device as a Plastazote insert that incorporated 4 resistive types of hydrocell sensors by Paromed. With each sensor measuring 2.55cm by 2.05cm in dimension. Results from this study concluded that data measurements obtained from both pressure and temperature sensors are valid and thus can be used in future studies to identify the mechanism of tissue breakdown with the diabetic population however, the authors also pointed out that temperature measurements resulted to be slightly lower than that of their reference standard, a regular thermometer. This difference was mainly attributed to Plastazote, which can act as an insulator, as their choice of material for the insert. Within the same year, Morley et al. (2001) developed a 16.8cm by 8.5cm by 3.5cm laminated sensor pod which, as in the study by Maluf et al. (2001), held an amalgamation 4 Paromed pressure and temperature sensors, and a Honeywell HIH series humidity sensor within it (Morley et al., 2001). The sensor pod was described as connected to a wiring harness which joins to a battery-operated micro-processor. The micro-processor is then tied to the participant's calf during use. The device was designed to measure, record and analyse temperature, pressure and humidity within the environment of the shoe. The

sensors within the laminated pod were placed to match the location of the plantar aspect of the heel and of the medial, central and lateral metatarsal heads of the subject's foot. the authors were able to obtain data that visualized activity levels, humidity, temperature and pressure changes over a period of 4.5hrs. Congruent to Maluf et al. (2001) results, Morely et al. (2001) also concluded that such device can be used to obtain valid and reliable measures of the in-shoe environment however, the relationship between temperature and pressure in relation to the diabetic foot has yet to be investigated (Morley et al., 2006).

SmartSox, designed by Novinoor LLC were developed using 5 highly flexible fibre optic sensors based on Fibre Bragg Gratings woven with a sock. Similar to the previously mentioned studies, the sensors were embedded to measure temperature and pressure under the hallux, metatarsals and calcaneus. Najafi et al. (2017) used this device to test its accuracy of measuring temperature and pressure within a clinical setting. In their study, 33 participants living with type 2 diabetes mellitus and peripheral neuropathy were recruited. During the trial, patients were asked wear SmartSox and their sandals were also fitted with computerized pressure insoles, the FScan by Tekscan as a reference standard for pressure. Plantar skin temperature of the subject's foot, using an infrared thermal camera, were taken prior to, and following the walk. This served as a reference standard for temperature measurements. Results of this study concluded that SmartSox is accurate in measuring both temperature and pressure with minimal cross-talk.

Another example of an in-shoe device that is able to measure temperature and pressure simultaneously is that of Rascio and colleagues (2018). The authors presented a wireless smart insole that can be used to prevent diabetic foot ulceration. The system is made up of 8 force resistive sensors and a thermistor embedded within a thin and flexible film. Preliminary laboratory testing indicated valid and accurate outcomes when measuring both temperature and pressure (Rascio et al., 2018).

A great proportion of the studies present their device as an insert or insole which can be fitted within the subject's footwear (Morely et al., 2001; Shu et al., 2009; Ostadabbas et al., 2012; Guo et al 2012; Ferber et al., 2013; Wang et al., 2015; Price et al., 2016; Najafi et al., 2017; Rascio et al., 2018). The position and placement of sensors on specific anatomical landmarks was mostly determined by locating

previously ulcerated sites or sites showing as withstanding the highest peak plantar pressure. These areas of high peak plantar pressures included the lateral medial aspect of the heel, 1st to 5th Metatarsal head, midfoot and hallux (Shu et al., 2009; Ostadabbas et al., 2012; Guo, 2012; Wang, Song, Fekete, & Gu et al., 2015; Najafi et al., 2017; Lee et al., 2019). Researcher are also creating temperature (Lugoda et al., 2020) and/or pressure sensitive socks or yarns which might be used as a wearable textile in future research (Gaeul et al., 2020; Drăgulinescu et al., 2020).

The design and development of the innovative, single-sensor, in-shoe pressure and temperature measuring device will be discussed in Chapter 7.

2.9.2 Shortcomings of in-shoe pressure and temperature devices under research

As previously discussed, from the systematic review conducted as part of this research project, 4 studies were identified to have investigated an in-shoe device said to measure in-shoe temperature and pressure concurrently (Saliba Thorne, Gatt, DeRaffaele et al., 2021).

Though these 4 devices were built with the aim to measure in-shoe pressure and temperature simultaneously, shortcomings of these devices were identified through the QUADAS-2 assessment tool which determined their quality of evidence. Though all 4 studies reported to have achieved laboratory validation of their device (Morley et al., 2001; Maluf et al., 2001; Najafi et al., 2017; Rescio et al., 2018; Rescio et al., 2020), only 2 studies reported to have conducted reliability testing (Morley et al., 2001; Najafi et al., 2017). Reliability is the ability to give the consistent results over time, across subjects and across different users. Thus, a device can be deemed as reliable once it is confirmed to provide consistence measurements over a time, across subjects, and across different users. Reliability testing is important in research as it ensures that the measurements obtained are representative and stable over time (Heale & Twycross, 2015).

Moreover, the overall data quality of evidence (QUADAS-2) of these 4 studies, with regards to validity and reliability, resulted to be low (Saliba Thorne, Gatt, DeRaffaele et al., 2021). The number of participants on which these devices were tested for validation was less than 4 participants per study of which their patient population was

either not specified (Morley et al., 2001; Rescio et al., 2018; Rescio et al., 2020), or conducted on healthy participants (Najafi et al., 2017). The magnitude of a sample is important in research as it impacts the accuracy of a measurement and the power of the study to draw conclusions (Nayak, 2010). In a study by Moher, Dulberg & Wells (1994) it was highlighted that in literature, only a small percentage of trials (out of 102 trials) had enough statistical power to detect any discrepancy between the investigated groups. The larger the sample size is, the more precise the measurements are and, the more likely to have a statistically significant result (statistical power). Moreover, larger samples tend exhibit a smaller margin of error compared to small samples of recruited participants (Nayak, 2010).

A reference standard to confirm the validity of the temperature aspect of the device was not used in 2 studies (Morley et al., 2001; Maluf et al., 2001) however, it is important to point out that to date, a gold standard for an in-shoe temperature measuring device is not yet available. Other studies, such the ones listed in the systematic review, used thermal cameras or a regular thermometer as reference standards (Najafi et al., 2017; Rescio et al., 2018; Rescio et al., 2020; Reyzelman et al., 2018; Lugoda et al., 2018). Reference standards play an important role in research as they are tools or investigations that can be used to confirm the validity of another investigation or tool. By comparing outcomes to the outcomes of a reference standard, one can ascertain that the tool under investigation is actually measuring what it is intended to measure and that the measurement corresponds well to the actual measurements (Groot, Reitsma & Moons, 2014).

2.9.3 Proposed innovative in-shoe pressure and temperature measuring device

On the market, the only commercially in-shoe devices available are exclusively designed to measure in-shoe plantar pressure. A rigorous analysis of existing literature on the currently available in-shoe technology that can measure pressure and temperature simultaneously, identified that there is a lack in reliability testing and clinical validation on such devices (Saliba Thorne, Gatt, DeRaffaele et al., 2021).

Given the lack of commercially available technology for the identification of in-shoe plantar pressure and in-shoe skin temperature, and that the low quality of evidence of the current devices identified in the systematic review (Saliba Thorne, Gatt,

DeRaffaele et al., 2021), highlighted the potential for the creation of an innovative pressure and temperature measuring device which could simultaneously read skin temperature and that could be integrated as a low-cost alternative to the currently expensive, commercially available in-shoe pressure systems (circa EUR 60,000) and temperature devices (price ranges from EUR 1,000 to EUR 42,170.27) became evident.

This innovative pressure and temperature measuring device was designed, not only to aid the clinician to detect changes in skin temperature and plantar pressures as parameters for tissue breakdown, but also to be used in a clinical setting to determine whether the offloading treatment prescribed to patients is actually achieving its intended goal especially when the diabetic high-risk foot is concerned.

This newly proposed, in-shoe device consists of a single pressure sensor superimposed on a single temperature sensor that together can read plantar pressures and skin temperature changes at one single point on the plantar aspect of the foot. A mobile application was also built so that it could be used to provide an interface to control and manage the device via the Bluetooth protocol and store the collected data in the database hosted on cloud servers. In addition to both hardware and mobile application, a multi-function web-based dashboard was developed. The idea of this web-based dashboard was to provide the user with a space where the data collected is displayed in the form of graphs and visualizations, and to allow users to manage the system and perform operations such as, adding devices and users, searching/filtering of data based on user, date, device, and so on.

This innovative in-shoe pressure and temperature device could change clinical practice as its design allows pressure and temperature assessment within a clinical setting and eventually, it will allow for in-shoe home monitoring which would capture a more realistic prediction of tissue breakdown in the high-risk diabetic foot. Using this device as an adjunct to the standard health care management of the high-risk foot can help preserve functional limbs as it will change the notion of just relying on clinical evaluation to ensure plantar pressure reduction.

2.10 Gap in Research and Need for Study

Cases of diabetic foot ulcerations are increasing at an astounding rate globally and they are leaving a marked impact on the individuals, putting a great burden on the healthcare system (NHS, 2018; Cuschieri & Mamo, 2014). Furthermore, the diabetic foot ulcerations that lead to lower limb amputations are known to increase the morbidity and mortality rate in diabetes (Grima et al., 2018; Cuschieri, 2020) estimated to be the 7th leading cause of death by 2030 (Mathers & Loncar, 2006; WHO, 2022).

This literature review highlighted the role of temperature and pressure during ambulation in individuals living with diabetes mellitus. Excessive plantar pressures especially if chronic, damage soft tissues initiating a process of inflammation characterised as erythema, warmth and swelling (Houghton et al., 2013). If area remains under pressure and not offloaded, the development of foot ulceration or a re-current ulceration is likely to occur. Skin temperature can be used as a predictor for foot ulcer development is it plays a role in inflammation (Hall, 2011).

The literature search has also highlighted that there is a limited number of studies that investigate on the correlation between in-shoe skin temperature and in-shoe plantar pressures in relation to the diabetic high-risk foot and that were investigated on a population living with diabetes mellitus. Furthermore, a deficiency of prediction models of the relationship between skin temperature, plantar pressure and diabetic foot ulceration was also deficient. Further investigation on the role of in-shoe plantar pressure, skin temperature and the development of diabetic foot ulceration is required as previous studies only addressed the relationship of plantar soft tissue characteristics, mobility and foot deformities to plantar pressure in diabetes (Spink et al., 2009; Mani et al., 2012; Paton et al., 2011; Lewis & Lipp, 2013; Fernando et al., 2016). Very few studies were found to relate skin temperature to plantar pressure and ulceration (Bus, 2016; Seixas et al., 2018; Gatt et al., 2018; Jones, Bibb, Davies et al., 2020).

2.11 Development of the research question

The focus of this PhD study emerged following the completion of a comprehensive literature search. Important aspects such as knowledge on the local situation of the diabetic foot ulceration, diagnostic techniques pertaining to the in-shoe pressure and temperature identification, current in-shoe technology, and the current management of

diabetic foot ulceration were highlighted (Figure 19). This information contributed in the development of the theoretical framework of this PhD.

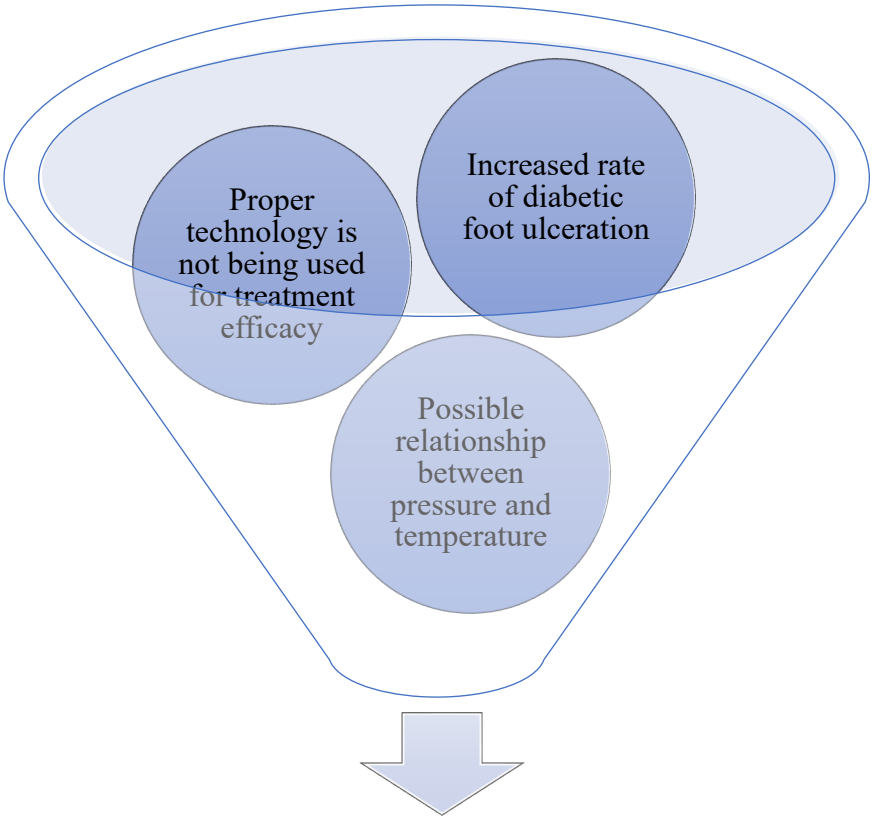


Figure 19: Key concepts that shaped the research question

The literature search showed that prevention of ulceration and its recurrence is deemed of utmost importance in diabetic patient care (Armstrong et al., 2017). Previous foot ulceration, callus formation, blistering and bruising of the skin are strong predictors for foot re-ulceration, aggravated by biomechanical factors such as foot deformity and increased foot plantar pressures (Peters et al., 2007; Monami et al., 2008; Dubský et al., 2013; Waaijman, 2014).

Though the podiatrist has a major role in the management of the diabetic foot, the concept of foot pressure mapping prior and following prescription of foot orthoses is yet to be integrated. Foot orthoses are being prescribed with the intention of reducing plantar pressures but the evaluation of their effectiveness relies only on the clinical judgement and observational skills of the clinician. Suitable technology, such as the in-shoe pressure system, does exist but is not being used in daily local clinical practice as it is deemed costly and time-consuming.

While health care systems might be hesitant to invest in costly and time consuming in-shoe pressure mapping system that could identify the effectiveness of an offloading device, millions are being spent yearly for the care of diabetic foot ulceration and amputations (Cushcieri, 2020). The researcher here questions whether the integration of an innovative and low cost, in-shoe pressure system, which also reads skin temperature, for orthoses assessment could change clinical practice and change the notion of just relying on clinical evaluation to ensure plantar pressure reduction.

The overarching aim of this PhD is to determine whether the application of a specifically designed single-sensor, in-shoe pressure and temperature measuring device can be used as an objective and low-cost clinical tool, in the prevention of diabetic foot ulceration and re-ulceration.

The integration of a low-cost in-shoe pressure mapping systems, which also read skin temperature, might provide insight on whether standard hospital prescription orthoses are indeed reducing excessive plantar pressure areas which are known to be responsible for foot ulceration in the diabetic foot. As it will be described in more detail in chapter 7, a cost-effective, portable and wireless single sensor pressure mapping device was designed and developed. This device can be used both during normal daily activities as well as in a clinical setting. The device also incorporates a micro-thermographic sensor which will help determine whether orthoses have any effect on the thermodynamic behaviour of the skin at previously ulcerated areas, making this a novel investigation for the high-risk foot. To date, no such system has yet been validated to measure temperature and pressure simultaneously.

2.12 Conclusion

This chapter underlined key concepts that circle the current increasing prevalence of diabetic foot ulceration. Foot ulceration and its recurrence can be identified through

predictors such as callus formation, increased skin temperature, blistering and bruising of the skin which are strongly influenced by increased plantar pressures (Peters et al., 2007; Monami et al., 2008; Dubský et al., 2013; Waaijman, 2014). Through the use of technology such as in-shoe pressure systems and temperature sensors, plantar pressures and in-shoe skin temperature can be used as predictors of ulceration (Singh, Armstrong & Lipsky, 2005). Though the podiatrist has a major role in the management of the diabetic foot, the concept of foot pressure mapping prior and following prescription of foot orthoses is yet to be integrated. Hence, suitable technology to measure both pressure and temperature does exist but is not being used locally as it is deemed time-consuming and costly.

Considering the huge impact of foot orthoses on foot offloading, and the wide variety of manufacturing choices, a better insight on the appropriate fit of orthoses in high-risk patients is empirical. Inappropriate fit could increase the risk of ulceration. Off-loading and pressure re-distribution has been found to have better outcomes when assisted by proper techniques and technologies such as pressure mat systems and in-shoe pressure mapping devices (Bus, 2016).

Clinical assessments for prescription orthoses done with the help of technology, not only permits the practitioner to obtain objective, precise and reliable measurements, but also helps the practitioner to understand how he/she can adapt or change orthoses to best achieve foot plantar pressure reduction and avoid ulceration and re-ulceration (Bus et al., 2004, Mueller et al., 2006, Koenraadt et al., 2012, Paton et al., 2012, Ibrahim et al., 2013). Where the diabetic high-risk foot is concerned, it is very important to assess the quality and efficacy of the prescribed offloading device if prevention of diabetic foot ulceration and prevention of re-ulceration is to be achieved.

In view of this, the idea of a cost-effective, portable and wireless single sensor in-shoe pressure and temperature measuring device which reads these parameters in one particular area in the plantar aspect of the foot, both during normal daily activities as well as during clinical practice as an alternative to current costly in-shoe pressure and temperature technology was conceived.

The following chapter consists of two local scoping studies that helped the researcher gain insight on the local management and local referral pathway of the high-risk diabetic foot and also gave a numerical perspective on the number of high-risk patients

living with diabetes mellitus that are being referred for an in-depth biomechanical examination in view of ulcer prevention.

Chapter 3: The Position Statement of the Researcher

3.1 Introduction

My role as a researcher was to explore and understand the current local situation in terms of the current foot care services and clinical management of the individuals living with type II diabetes mellitus categorised as high-risk of ulceration and/or re-ulceration. My interest was especially focused on the use of diagnostic technology within the Podiatric clinical environment in relation to the biomechanical assessment of the diabetic high-risk foot. This research presented itself as a cascade of studies has led to the development and validation of an innovative, low-cost, single sensor, in-shoe pressure and temperature measuring device that proved to be beneficial in reducing the number of re-ulceration and/or amputation cases when in combination to the current standard diabetic foot care.

3.2 Introducing the Researcher

I am a State Registered Podiatrist working as a lead clinician at the Biomechanics and Gait Analysis Clinic at the Podiatry Centre of Excellence in a local health centre. I enrolled in a four-year undergraduate course of Podiatry BSc (Hons) offered by the University of Malta in 2008. I graduated in 2012 as a Podiatrist and was employed by the Ministry of HealthCare that same year. The first two years of my career as an employee of the Podiatry department were spent in core clinics and I also acted as a reliever both for core clinics in other health centres and at the Biomechanics and Gait Analysis Clinic at the Podiatry Center of Excellence. In 2014, I was appointed as the lead of the Biomechanics and Gait Analysis Clinic and have been doing so for the past 8 years.

As a student I have always had a particular interest in human biology and having been introduced to the complexity of the lower limb, especially where the diabetic foot was concerned, I became more intrigued to want to know more about it. Perhaps this particular interest evolved within me since my mother was diagnosed with type II diabetes mellitus.

Having worked as a Podiatrist with the Ministry for HealthCare, I have had the opportunity to work with patients living with diabetes mellitus in both core clinics and specialised clinics. My first study on diabetes was an amalgamation of biomechanics and diabetes when I fulfilled a Master's Degrees in Clinical Biomechanics in 2017. The research of my Master's Degree investigated the influence of peripheral arterial disease on the kinetics and kinematics of the lower limb in the type II diabetic population. This work is published in the Journal of the Review of Diabetic Studies.

As I got more exposed and experienced in the use of technology such as of Pressure Measuring Systems (both in-shoe and platforms), Force plates, Surface Electromyography (EMG) and 3D motion capture analysis, I began to appreciate the value of objective measurement when treating the diabetic foot. I thus began to question certain aspects of the current health care services being offered to these patients and this has led me to the commencement of this PhD study.

3.3 The research Project

The desire to understand the current local situation with regards to biomechanical management of the high-risk individuals living with type II diabetes mellitus, made me venture in a new research journey. Before I commenced this research project, I first wanted to reflect on my research position that is, from which perspective I wanted to address this investigation.

From my experience as a Podiatrist, I wanted to include the introduction of diagnostic technology such as in-shoe pressure mapping to permit objective assessment of the prescription orthoses. I also wanted to form a special liaison with both the Orthotics and Prosthetics Unit and the Diabetes Foot Clinic so that together we could use this technology and set up a dedicated service for the high-risk foot. It is then that I realised that I wanted to bring about a change or an improvement of the current service and that my way of thinking resonated best with the Post-positive perspective that was ultimately applied to this research.

To bring about a change, I first needed to clearly understand what the real local situation was and to do so, I decided to conduct a scoping study which employed a quantitative methodological approach. Although results from the scoping study answered a few of my initial questions, it unexpectedly raised more questions which, I could not answer from a quantitative approach. I felt that a qualitative study was best

suited to gain the clinicians' perspective on the use of diagnostic technology in the podiatric clinical setting and thus, the second scoping study was conducted. The second scoping study did not come easy to me since my earlier research experiences involved quantitative research and so, this type of methodology was all new to me. Nonetheless, I must confess that I did enjoy the experience and I am very pleased to have tried a new way of approaching research but I also believe that I still have a lot to learn with regards to this approach.

The results obtained from the 2 scoping studies, together with a comprehensive literature review about the application and importance of foot pressure and temperature monitoring in the management of foot ulceration in diabetes, and a systematic review on the currently available in-shoe pressure and temperature technologies, informed my PhD research on what was needed in order to introduce objective assessment in the management of the diabetic high-risk foot. Discussions with my project supervisor and co-supervisor, both Podiatrists with special interest in diabetes and clinical biomechanics, and advisor on this project who is a Systems and Control Engineer by profession, led to the development of a prototype device. We wanted to create a device which could provide the clinician with a low-cost alternative to the current expensive technology. We wanted this device to be easy-to-use because as clinicians we know that during a busy clinical schedule, one might not have time to include time-consuming assessments utilizing technology. We wanted to develop a device that allowed for specific assessment in such a way that the clinician can specifically choose which area of the foot to assess rather than having to assess the whole foot just to focus on one anatomical landmark of intent. We also wanted the device to be compact so not to interfere with the natural gait of the patient and also for aesthetic reasons.

Following the construction of this device, my role was to validate this device in both the laboratory and clinical setting. The laboratory validation gave very promising results. The experience of working as a team from different professionals was new to me, as I always worked with Podiatry colleagues or colleagues with similar medical background. This experience made me realise how important it is to share different knowledge and expertise to develop something innovative which could help improve patients' quality of life.

I feel that the biggest challenge that I faced in conducting this research, was during the clinical trial. I remember that I was very concerned about the recruiting process in particular as this coincided with the second national, mandatory lock-down and social isolation associated with the COVID-19 pandemic. Many of the potential participants, being high-risk, were socially isolating themselves to the extreme that were not attending for their regular diabetic foot care appointments or other appointments for that matter. In fact, a study by Grima, Dimech, Pisani et al. (2022) stated that

"*During this time, it was noted that few patients were presenting to hospital with signs and symptoms of chronic limb threatening ischaemia (CLTI). Furthermore, it was felt that patients with CLTI were presenting to hospital late, requiring either palliation or major amputation, and more patients required major amputation than in previous years*."

The article continues…

"*During the first wave of the pandemic, significantly more major amputations were carried out than in the previous year*."

Due to this unfortunate social crisis, from which we all have suffered, and because I was employing a matching design where I matched participants according to certain criteria, I was limited with the number of participants which I could enrol in the clinical trial. To complicate matters further, some participants withdrew from the study, which further reduced the sample size, this made me very concerned. Though I did not reach the targeted population sample size, I still had a good number of participants and managed to achieve remarkable results in the clinical trial. Working with these participants, during data collection, was easy for me, since all participants were very co-operative and interested in participating in this study to improve their health. Furthermore, as a clinician, I am used to working with patients and I was very familiar with the technology I was using.

This research journey has helped me grow from the start of this journey up till now both as a researcher and also as a clinician. I have always had the interests and needs of patients at heart and I always strived to offer the best advice and professional service. This PhD journey has truly been an inspiring one and hopefully will bring about a change in how the diabetic foot and high-risk patients are managed with regards to the

introduction of innovative diagnostic technology to assess and monitor the high-risk foot.

Chapter 4: Identifying the Philosophical Approach of the Research

4.1 Introduction

The approach of the method of investigation to answer the overarching research question was determined. As the terms methodology and methods are often confused, the distinction between the two was highlighted. In this thesis, "methodology" refers to a philosophical framework which acts as a foundation for a systematic and scientific approach that is conducted to solve the research problem (Brown, 2006). By way of explanation, methodology refers to the rationale and philosophical assumptions concerning human societies which inform research (McGregor & Murname, 2010). Conversely, "methods" refers to the approaches used to collect the data that will be used to solve a research problem that concerns a specific population and topic. Such approaches include observational studies, experiments, and interviews to name a few (Howell, 2013).

In line with these definitions, this chapter presents a detailed description of the research methodology employed in this PhD study. The philosophy that supports the approach taken with this research study is discussed, highlighting the postpositivist viewpoint of the researcher towards the research and the eventual adoption of a quantitative approach. Furthermore, this chapter discussed the rationale that led to the research design.

4.2 Philosophy

Research philosophy can be defined as the belief or school of thought on how data in research should be collected, analysed and interpreted (Žukauskas, Vveinhardt, & Andriukaitienė, 2018). Research philosophy is thus based on the idea of finding the truth about a phenomenon being studied. Saunders et al. (2015) defined research philosophy as an umbrella term that deals with the gain of knowledge and its nature. For centuries, and through a variety of philosophical perspectives, the human kind have been trying to study and provide an understanding of what is real, what is the significance of our existence and how can we gain this knowledge? (Chandra & Sharma, 2006).

Knowledge, truth and reality as interpreted in this PhD study

When researchers talk about knowledge, they refer to the concept of having the proficiency to comprehend the world as it is, a skill which would help society move forward and evolve (Burgess & Burgess, 2011). Thus, the importance of gaining of knowledge through research lies within the fact that it can be useful to society to predict events and ultimately use the gained information to avoid negative occurrences (Vallejo-Lopez et al., 2020). Knowledge can be obtained through empirical means (the gaining of information through experience) or logical means (the gaining of information through reasoning and scientific calculations) or a combination of both (Kivunja & Kuyini, 2017). According to Nasimi et al. (2013) knowledge can be described as the identification and awareness of what is real and through investigation and dissemination of finding, it can grow and enhance human intellect. Mohajan (2017) further added that we gain knowledge through the analyses of raw data and information, and by comparing the results to already established information.

In research, knowledge is often associated with truth where truth is then associated with reality. This triangulation necessitates a clear distinction between the 3 concepts. According to Nakkeeran (2010) when the gaining of information is based on an observation or scientific measurement, it has to be true. However, Howell (2013) argues that knowledge differs from truth as its role is to try explain and understand the nature of reality and the truth and theories that reflects it.

The concept of truth can be explained as a being conceived on the interpretation of an idea that corresponds to an evidence-based fact (Burgess & Burgess, 2011). Truth has a valuable role in research as it gives the research integrity and value (Emanuel, 2008). In research philosophy, truth is regarded to stem from reality. This is because, reality is defined as an agreed opinion of an evidence-based idea which is independent from the influence of the mind (Howell, 2013). Being a collective ideology, reality is still highly influenced by societal beliefs and values relevant to a specific society which change over time (Burgess & Burgess, 2011). Thus, reality is regarded as time-specific, and since it is discovered and interpreted it is liable to falsification (Popper, 1963). Thus, truth can be viewed as a reflection of reality over a specific time and it is bound to change as the nature of reality also changes (Howell, 2013).

In this PhD research project, philosophy played a very important role as it provided the researcher with basic principles on how to build a theory, how to perceive and approach a theory (methods) and how to interpret any findings related to the theory. Although philosophical studies are very complex, for the purpose of this dissertation philosophical studies were categorised into 5 main philosophical domains; metaphysics, axiology, epistemology, ontology and logic (Moon & Blackman, 2014) each domain proposing its own assumptions about the nature of reality, knowledge and values.

4.2.1 Reflection on philosophical domains

Philosophy is comprised of multiple subfields and areas of study to which we refer to as domains. The flow chart below (Figure 20) was created by the researcher to give an overview of the main domains of philosophy and their branches. Though each domain appears to focus on a particular area of study, the domains may interrelate and may be integrated within a single study (Hallebone & Priest, 2009).

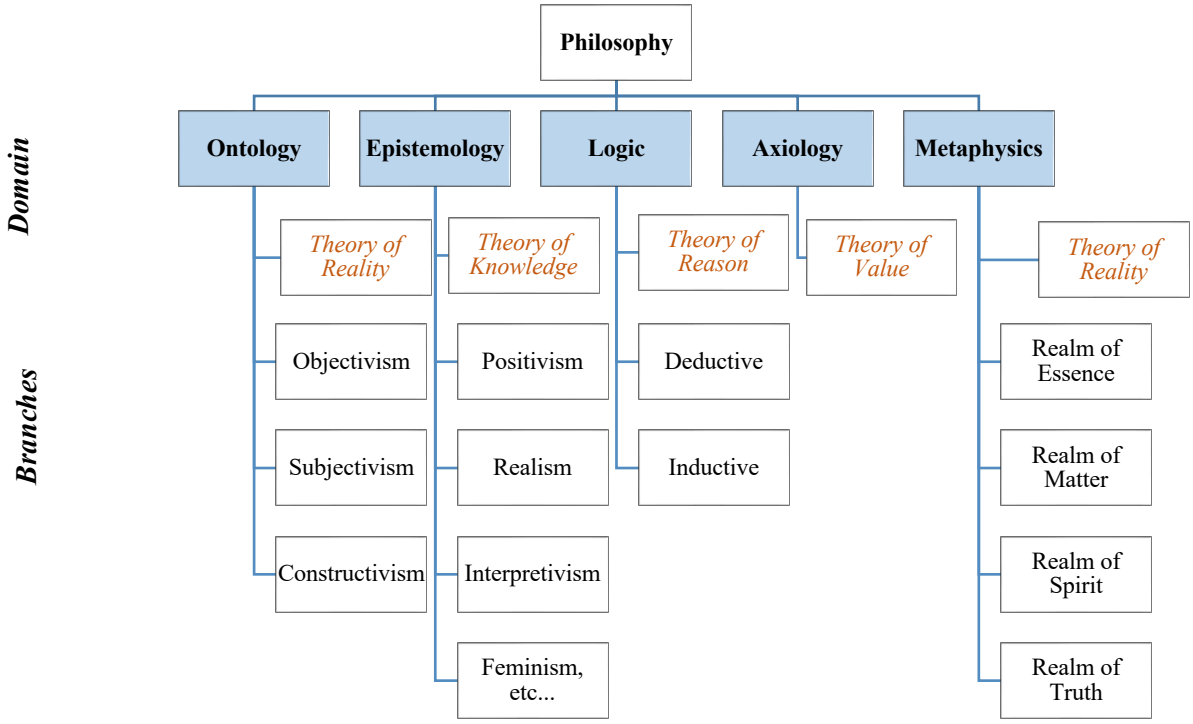


Figure 20: Flow chart showing the divisions of philosophy

Evidence based research has shown that the majority of cases of hospitalization are mainly attributed to a diabetic foot complication particularly foot ulcerations (O'Loughlin et al., 2010). Chances of developing a foot ulceration is twice as common

in patients living with diabetes mellitus compared to non-diabetics. Foot ulceration is regarded as the leading cause for non-traumatic amputations of the lower limbs and hospitalization (Jeffcoate et al., 2018).

Foot orthoses are generally indicated to off-load excessive pressure areas to avoid the development and recurrence of diabetic foot ulceration (Bus et al., 2016). Despite being recommended by the international diabetic foot guidelines (van Netten et al., 2018; Schaper, van Netten, Apelqvist. et al., 2020; Bus et al., 2020), in Malta the concept of in-shoe foot pressure mapping prior and following prescription of foot orthoses is not yet integrated in the service. Foot orthoses are being prescribed with the intention of reducing plantar pressures but the evaluation of their effectiveness, to date, relies only on the clinical judgement and observational skills of the experienced clinician. The ideal technology, such as the in-shoe pressure system, does exist but is not being used within local hospitals or health centres as part of diabetic foot care management as it is deemed costly and time-consuming. A change in assessment and management for the prevention of ulceration and ulcer recurrence in diabetes should be considered in order to try to obtain a significant reduction of foot re-ulcerations and amputations. It is empirical to improve and expand our knowledge on the relationship between foot plantar pressures and skin temperature from both a scientific and a clinical perspective if better outcomes are to be achieved.

Based on this key concept, the researcher embarked on a research investigation to develop and validate a unique and innovative, low-cost, in-shoe device which not only measuring pressure, but also measures temperature, a feature which current in-shoe devices lack. Prior to identifying a theoretical perspective that was used to guide the researcher during the investigation, the researcher had to identify what constitutes as knowledge and what not pertaining to this research project.

The metaphysical aspect of philosophy questions *"how the reality and the universe were created?"*. This branch of philosophy questions the origin and existence of human kind and its relationship to the physical universe (Lynch, 2016). The Metaphysical domain is associated with the theory of reality, and it was highly influential to a period of time that corresponded to the time where people believed in higher power of the divine but, to an extent, also had a scientific mindset (Comte, 1858). People in this stage believed that behind every understanding there is the

intervention of a higher power. To mention a few, people like Aristotle, Sir Isaac Newton, Voltaire and Thomas Jefferson argued that an abstract power guides events in the world according to certain fixed principles (Giddens, 1974). Thus, the metaphysical domain focuses on the ideology that the scientific and religious worldviews co-exist in order to make sense of the world. Every occurrence can be explained through some kind of structure provided by a high being such as God (Cohen, 2020). In view of this PhD study, the researcher feels that the metaphysical domain does not reflect his/her ideology. The domain of Axiology focuses on principles and values which include the ethical values and the aesthetical values (Lynch, 2016).

Ontology is a philosophical branch that studies reality or truth, and it focuses on the study of human nature and its existence in society and in the universe (Lynch, 2016). In simple terms, ontology questions *"how can we obtain knowledge/reality?"* (Scotland, 2012). The domain ontology further branches into 3 positions: objectivism where theories emerging from this position are based on the idea that social phenomena are not influenced by individuals; subjectivism where theories emerging from this position are based on the idea that social phenomena are influenced by the individual and finally, constructivism where theories emerging from this position base their ideology on the idea that knowledge and the truth are what the individual makes them (a construction of society) (Bunge, 2001). To answer the question "what is reality?" the Positivist ideology believe that reality is existent and tangible and it can be obtained by observing occurrences through the scientific method that is, through observation and experimentation (Cohen et al., 2007). From an ontological perspective, positivists view society and the physical world to follow general laws and that independent of the researcher's influence (Macionis & Plummer, 2012). Post-positivists do agree with this concept but differ from positivists where bias is concerned. Ontologically, post-positivists believe that though reality is tangible and singular, it is not free from the influence of human error and thus we as humans can only gain an approximation to the truth which eventually it can be disproven (Mertens, 2009; Ponterotto, 2005).

Epistemology stems from the Greek word *episteme* which literally translates to the word knowledge (Steup & Ram, 2020). Epistemology is a form of study that tries to conceptualise the origin, nature and scope of reality. In other words, epistemology is the theory of knowledge that deals with how can knowledge that is real and relevant

to society be obtained (Cooksey & McDonald, 2011). Epistemology thus questions *"how can knowledge be attained?"*. Knowledge can be obtained through empirical means (the gaining of information through experience), by logical means (the gaining of information through reasoning and scientific calculations), or through a combination of both. The choice of which means is used to obtain knowledge is solely dependent on the researcher him/herself but mostly on the assumptions on which the theory of the study is based (Kivunja & Kuyini, 2017). Epistemology had a major role in this PhD research as it helped the researcher narrow down what was relevant and what contributed to the body of knowledge in context to this dissertation. Research paradigms/approaches that are generally associated with epistemology include Positivism and Anti-positivism (constructivism and pragmatism). For example, positivists would argue that the physical world to follow general laws which can only be identified through methodological experimentation and observation (Macionis & Plummer, 2012). Positivist philosophy argues that through the right systematic, empirical and objective research, the understanding and prediction of an outcome will guide the researcher to identify evidence-based "truth" which once found, cannot be disproven (Park, Konge & Artino, 2020). Post-positivism believes that no matter how systematic and independent of bias research is, it can never be purely objective as the researcher's influence is unavoidable (Bisel & Adame, 2017). In considering the epistemology of this research project, the researcher reflected and questioned the nature of the knowledge to be discovered; whether it could be directly acquired or gained through experience; and what is the relationship between the researcher and the knowledge to be discovered. This helped the researcher determine his/her position within the research context.

The fourth branch of philosophy is logic. This branch helps the researcher organize reasoning through structured thinking and is further subdivided into 2 branches: deductive and inductive logic (Lynch, 2016). Inductive and deductive reasoning differ in their purpose of use. Deductive reasoning approaches the research by first developing one or more hypothesis and then, through testing develop new theories (Wilson, 2010). This approach emphasizes on causality and is generally associated with quantitative research (Dudovskiy, 2016). Conversely, inductive reasoning is an approach that develops new theories from data collected and uses the research question to focus on the scope of the study. Both positivist and post-positivist ideologies refer

to the deductive method to prove a priori hypotheses that is, hypotheses based on assumptions and conclusions of previous research on the topic (Nestor & Schutt, 2014). The logical domain, associated with the theory of reason, helped the researcher distinguish what inferences are valid in context to this research and which are not. Through logic, the researcher was able to categorize arguments relevant to the research topic that were especially independent of psychological influence. Arguments relevant to this dissertation had to be consistent, thorough and complete. In this PhD research project, hypotheses were formulated to test for statistical significance concerning the possibility to predict better lower limb prognosis when assessing for effectiveness of the dispensed offloading device in the high-risk diabetic foot. Thus, deductive reasoning was adopted throughout the study as the hypothesis was formulated prior to data collection and analysis (Nestor & Schutt, 2014).

Thus, based on the above-mentioned assumptions and based on the above-mentioned reflections, this PhD project considered a Post-positive epistemological point of view as the knowledge to be obtained from this research is something which can be acquired rather than experienced. The nature of the knowledge to be discovered, as reflected in the research question of this PhD study, can be obtained through logical, deductive means and the relationship between the researcher and the knowledge to be obtained is independent from one another but with the acknowledgement that knowledge gained through this research is not ultimate and absolute and that it may in future be refuted. Thus, in summary, the assumptions of knowledge of this research proceeds as follows (Figure 21):

Metaphysics	Axiology	Ontology	Epistemology	Logic
• Disregarded in this study	• study should be free from bias as much as possible	• objective assessment is important • acknowledging results may not be absolute	• Post-positivism as reality obtained by humans objective but it is approximate to the truth	• Deductive reasoning

Figure 21: Assumptions of knowledge relevant to this PhD project

4.3 Delineating the philosophical paradigm of the PhD research

"*A paradigm is a universally recognized scientific achievement that, for a time, provide model problems and solutions for a community of practitioners*"

- Thomas Kuhn, 1996, *The Structure of Scientific Revolution*

In Sociology, a theoretical perspective is referred to as a collection of conjectures on the definition of 'reality' (Crossman, 2020). Crossman (2020) defined theoretical perspective as a lens through which one perceives and distorts reality. Simply put, theoretical perspectives can be defined as paradigms which indicate how we perceive society to function.

Theoretical perspectives are important in research as they reflect the rationale of the study and reveal the assumptions that the researcher is making about the research. Through a theoretical perspective, the thoughts of the researcher are better organised and presented more clearly to the reader. A theoretical perspective hence, influences the overall research process of a study and is used as a guide to obtain knowledge systematically on a particular area of study (Hassan et al., 2019). The term 'paradigm' was first introduced by Thomas Kuhn in 1962 where he defined it as a manner of contemplation. Paradigm was later defined by Saunders et al, (2009) as the way in which knowledge can be gained and explained through the assessment of an occurrence. Kivunja & Kuyini (2017) wrote that research paradigm is a perspective, or school of thought, that serves as foundation on which the discovery and interpretation of knowledge is built. The authors further added that a research paradigm ultimately reflects the ideas and beliefs of the researcher and the way he or she interprets the world (Kivunja & Kuyini, 2017).

In research, paradigms or theoretical perspectives, play an important role as through them the researcher, not only is he/she provided with a set of beliefs, but also with a set of guidelines on how the research should be conducted; this includes the methodology, analysis and interpretation of data (Moon & Blackman, 2014). A research paradigm is constructed on assumptions, norms, beliefs and values and since it indicates the means with which we knowledge can be gained, it can also guide the researcher to in grasping what is reality (Saunders et al., 2009). Paradigms are considered to define the way we see and interpret the world (Schwandt, 2001).

A research paradigm is said to stand on two main elements, 'ontology' (what is reality?) and 'epistemology' (how can I know reality?), that serve as foundation to the entire research study (Cooksey & McDonald, 2011). Figure 22 below represents the amalgamation of ontological and epistemological domains of philosophy from which theoretical perspectives/paradigms are generated (Moon & Blackman, 2014) and from which the 3 major research of Philosophy are considered to emerge (Saunders, 2009).

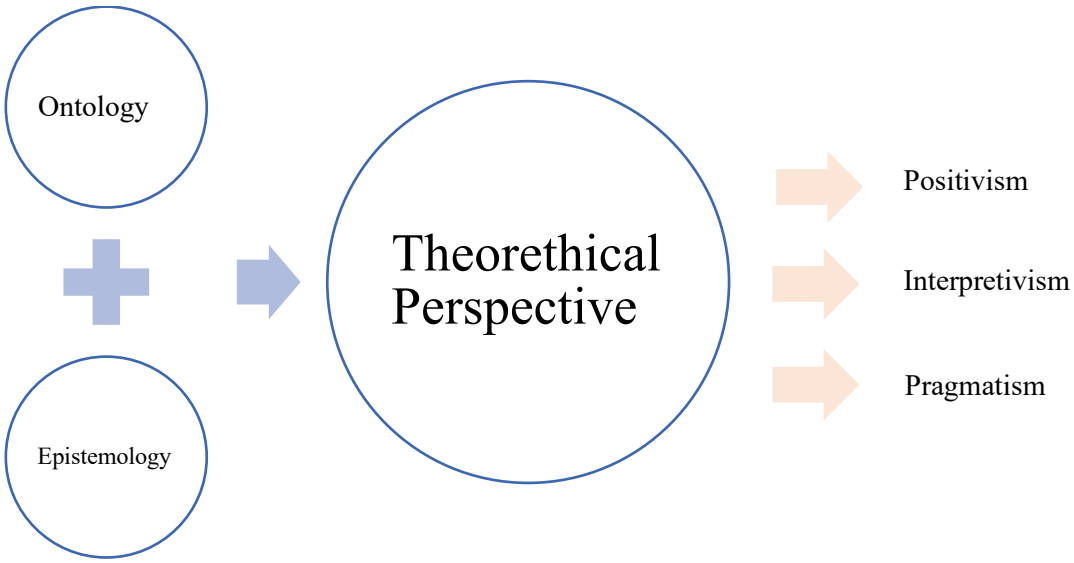


Figure 22: Diagram depicting the relationship between epistemology, ontology and theoretical perspective

The methodology of a research investigation is thought to revolve around the thoughts and believes of the researcher investigating it. The most popular paradigms that underpin the Philosophy of Science include Pragmatism, Realism, Interpretivism, Positivism, Post positivism and Critical Realism (Zukauskas, Vveinhardt & Andriukaitienė, 2018). As a general rule, though not always the case, each paradigm is used to meet a specific purpose. For instance, interpretivist theories are generally applied to research that wants to understand a behaviour or the cause of a problem because interpretivism believes that knowledge can only be obtained through history and culture (Travers, 2001). Pragmatist theories deals with facts and see words and thoughts as a means to predict and solve problems. They argue that a researcher is free to use all approaches to understand a research problem and thus this theory can be applied to any type of research (Saunders, Lewis, and Thornhill, 2012; Alghamdi & Li, 2013). Finally, Positivist theories are generally applied to research that aim to

predict an outcome or a solution to a problem because positivism argues that knowledge can be obtain trough objective methodology (Travers, 2001). Stemming from and as a critique to Positivism, post-positivism emerged a new paradigm. Post-positivists concur with Positivists that objective and systematic research is essential to finding the truth and attain knowledge however it is not the only way. This ideology also argues that once knowledge is obtain it can still be disproven as technology and research advances (Young & Ryan, 2020).

Identification of the philosophical paradigm of this PhD research study was only possible through reflexion on the nature of the research problem. Questions were raised to identify whether the nature of research was quantitative or qualitative in nature and how can it be acquired. Thus, the research question, aims and objectives of the topic being investigated in this PhD study were formulated and used to identify the appropriate research paradigm.

Following an extensive research investigation on the vast variety of philosophical approaches and paradigms, the researcher concluded that the Philosophy of Science resonated best with the researcher's ideology. The Philosophy of Science focuses on what constitutes research as science. This is determined based on the choice of methodological approach and on the outcomes of the investigation. The emphasis here is on the reliability, validity and purpose of the research (Okasha, 2016).

One might recollect that the overarching aim of this PhD was to determine whether the application of a specifically designed single-sensor, pressure and temperature measuring device can be integrated to the standard clinical practice, as an objective and low-cost clinical tool, in the prevention of diabetic foot ulceration and re-ulceration. To achieve this, the innovative in-shoe pressure and temperature measuring device had to be designed and built and tested for its validity and reliability. Once proven reliable and valid, the device was then tested on the targeted population to prove its purpose.

As previously mentioned, various research paradigms nested under the Philosophy of Science. Initially a Positivist theoretical perspective inspired this PhD research project as, based on the literature search and scoping studies, the researcher felt the need to consider a new, cost effective, easy to use, in-shoe pressure and temperature measuring device that could be used as an alternative to the expensive in-shoe pressure

technology that is not being used in the clinical setting. In the 19th century, French philosopher and sociologist Augusté Comte introduced Positivism as a philosophy that believes in the concept that the only valid knowledge, is knowledge obtained through the scientific method. This ideology exclusively focuses on the observation of occurrences through the scientific method that is, through observation and experimentation (Macionis & Plummer, 2012). For this reason, Positivism initially inspired this PhD study as it is a philosophical paradigm that focuses on obtaining certainty which facilitates the understanding and prediction of an outcome when observing relationships between the causal and explanatory factors (Ponterotto, 2005). This philosophical perspective uses the deductive method to prove a priori hypotheses that is, hypotheses based on assumptions and conclusions of previous research on the topic (Nestor & Schutt, 2014). Positivist philosophy argues that through a systematic, empirical and objective research, the understanding and prediction of an outcome will guide the researcher to identify evidence-based "truth" (Park, Konge & Artino, 2020).

However, though Positivism laid the foundation of modernist philosophy of science that inspired renowned scientists such as Darwin, Freud and Niche, this philosophy has been criticised for its reductionism that is, to assume that all social process can be reduced to aspects that can be understood through scientific experiment only (Phillips & Burbules, 2000). Stemming from, and as a critique of Positivism, the movement recognised as Postpositivism challenged Positive thinkers on their strong believe that knowledge obtained through the scientific method is the only truth and thus cannot be disproven. Postpositivists argue that just like any other research, scientific theories can be disproven (Popper, 1963). Karl Popper raised an argument against positivism that states that no scientific theory, no matter how often it was experimented upon or observed, can be fully confirmed. Once one single counterexample is presented, the conclusions derived from that theory may no longer be 'true'. To support this statement, a notorious example is given as follows:

"*If enough swans are observed, we conclude that all swans are white. However, a single black swan would falsify the conclusion, therefore falsifying the generalization that all swans are white*" - Young and Ryan, 2020

Popper strongly supported the idea of Falsification that is, a theory can only be considered scientific if it can be disproven (Thornton, 2018). A falsifiable theory

implies that such a theory can be proven wrong, changed and improved through current technology, different experimentation and different observation that ultimately contradict the original theory.

In a nutshell, Popper argues that in order to achieve growth in knowledge, one can only falsify a theory and not prove it (Popper, 1994). For a single problem, a number of hypotheses may be drawn and each hypothesis may be subjected to different experimentation in attempt to falsify each and every one of them until the truth is found, by elimination. Popper argued that just like Darwin's theory of natural selection (Popper 1994), theories are closer to the truth when throughout the years they are not rejected.

The hypothesis of this dissertation questions whether the innovative, single-sensor, pressure and temperature in-shoe device can be used for the prevention of diabetic foot re-ulceration. Furthermore, this PhD study aimed to understand the relationship between pressure and temperature in view of ulcer development. Through a postpositivist perspective, the researcher here can only disprove the alternative hypothesis that is, confirm the null hypothesis with the technology available to us at this point in time. Assuming a Post-positive ideology, absolute confirmation of the alternative hypothesis cannot be achieved (Ladyman, 2002; Ryan, 2006). In other words, as seen through the eyes of a Post-positivist, this study confirmed whether this device is able to read and measure pressure and temperature parameters well enough to provide improved design of the offloading device which ultimately, if used as part of diabetic foot management, may lead to reduce cases of diabetic foot ulceration, hospitalisation and amputations. It is through this continuous contradiction of hypothesis that true theories can be identified and ultimately lead to advancements of scientific knowledge (Popper, 1963).

It is at this point that Positivist and the Post positivist point of view differ. If we look at this study from a Positivist point of view, once the newly developed, in-shoe, single-sensor, pressure and temperature measuring device is confirmed able to read and measure pressure and temperature parameters well enough to lead to a reduction of diabetic foot ulceration, the theory of this dissertation is proved true. This means that once proven to be true, it cannot be disproven as the one true knowledge has been achieved. The researcher of this dissertation does not agree with this statement as in

view of the advancing technology, the researcher is cognisant that the device developed may further be improved. Since this device is innovative and is the first laboratory and clinically validated in-shoe pressure and temperature measuring device, it is expected to be a tool that will bring about a change in practice but it is also expected to be a stepping stone for future, more improved and sophisticated in-shoe pressure and temperature measuring devices. Thus, as the literature search progressed, the researcher felt more resonant with Post-positivism rather than to the Positivist philosophy.

4.4 The influence of Post positivism on the Theoretical Framework of this PhD study

Through a thorough literature review (Chapter 2), the researcher identified a key concept concerning the diabetic foot ulceration and re-ulceration that has informed the theoretical framework of this dissertation. Theoretical framework is defined as the foundation that holds and supports a theory of the research (Grant & Osanloo, 2014).

Being influenced by a Post-positive perspective theory, the deductive approach was employed in this dissertation. This means that theories and hypothesis concerning the topic in question were formulated prior to the data was collected, and these remained relatively unchanged throughout the dissertation. Inspired by the theory of Thomas Kuhn in his work *'The Structure of Scientific Revolution*' this study aimed to provide an innovative, cost-alternative, in-shoe pressure and temperature device which could be used to inform the clinician with an objective treatment plan in view of diabetic foot ulcer prevention. The table below gives an overview of the brainstorming of the researcher during the planning of the theoretical framework for this PhD research project (Table 8).

Table 8: Brainstorming on the Theoretical framework of the PhD study

Theory	What is the relationship between peak pressure and skin temperature in view of diabetic foot ulceration? What is the currently available technology that can be used to predict in-shoe plantar pressure and in-shoe skin temperature?
Hypothesis	What can be improved in the current standard care management plan of the diabetic high-risk foot? Can a new method be proposed as an alternative or as an adjunct to the current standard care of the diabetic high-risk foot? What can be used to measure in-shoe peak plantar pressures and in-shoe skin temperatures at the same time to assess the relationship amongst them?
Observation	Study 1 – scoping study to observe the local management and referral pathway of the high-risk diabetic foot, and gain a numerical perspective on the number of high-risk patients living with diabetes mellitus that are being referred for an in-depth biomechanical examination in view of ulcer prevention Study 2 – systematic review on the currently available technology that can read and measure in-shoe pressure and temperature simultaneously Study 3 – Design and validate a new method/device of diabetic in view foot care Study 4 – obtain clinical validation of a new method/device in view of diabetic foot care
Results	What do the validation results suggest on the introduction of the new method of diabetic foot care? Can it be introduced as an adjunct to the standard diabetic foot care to prevent diabetic foot complications? Is there a correlation between a rise in peak plantar pressure and increase in skin temperature in view of ulcer development? Can pressure and temperature change be used as predictors of ulcer formation?

4.5 The influence of Post positivism on the Conceptual Framework of this PhD study

Post positivism emerged as a critique for the Positivist movement in the mid-19th century. As previously discussed, Post-positivists highly criticized positivists for arguing that if the research is well planned, systematic and objective, results are then free from bias (theory of verification) (Bergman, 2016). Post-Positivists, like the Positivists, do encourage objectivity in research but also acknowledge that the theories and hypothesis of the researcher may still influence what is being observed and thus, an element of bias is unavoidable (Robson, 2002).

Karl Popper was first to introduce the term '*Falsification*' to exemplify and explain why the ideology of Post-positivism can be improved. Through this term he explained that when conducting a research investigation, instead of confirming a research hypothesis (*Verification*), one should aim at disproving the hypothesis (*Falsification*). According to Popper, due to the element of bias in research, and to the advancing technology, a theory can never be confirmed but only refuted. Applying the theory of Falsification to this PhD research, the researcher aimed to confirm the null hypothesis that stated that: the innovative, single-sensor, pressure and temperature in-shoe device cannot be used for the prevention of diabetic foot care re-ulceration. The methodology and results of this investigation will be later introduced in Chapter 8.

Building on the theory of Falsification, Thomas Kuhn introduced a concept that had a significant impact on how this PhD research was shaped and conducted. In '*The Structure of Scientific Revolutions'* (1962), written by Kuhn himself, the term '*Paradigm shift*' was described (Kuhn & Hacking, 2012). In his book, Kuhn described the progress of scientific research as linear and that it can only be accepted as scientific if it advances through 4 specific phases of science.

When a new scientific concept is introduced, it does not simply advance through stages as a Positivist would argue, but it remains within the same state of advancement for a period of time until it no longer serves its purpose or it is challenged. This first stage of science is referred to as the *Pre-paradigmatic* stage, a stage in which consensus on the fundamentals of a concept has not yet been reached. This stage is described as chaotic and disorganised with multiple conflicting theories. Once a common framework of assumptions on the topic are identified and established, that is a

Paradigm is created, the scientific concept enters into the second stage of science, referred to as the *Normal Science*. Here, the concepts of the topic are more established and start to be more coherent and effective when put to practice. After a significant period of time, a *Paradigm shift* occurs. This phenomenon describes the 3rd stage of scientific advancement, which is also referred to as the *Crisis* stage, in which anomalies of the now established concept are identified, questioned and even challenged, bring a crisis within the established concept. In this stage, resistance to change the established concepts is expected and various innovative theories are proposed in order to improve or completely change a perspective. If the identified anomalies are disproven, the original scientific concept resumes the *Normal Science* stage (reverts to stage 2) however, if the innovative theory disproves the original scientific concept, then the original scientific concept falls introducing, what Kuhn refers to as, a *Scientific Revolution* (stage 4).

Applying this theory to the conceptual framework of this PhD the Pre-paradigmatic stage (stage 1) would have corresponded to the time where diabetic foot care and diabetic foot ulceration management was still a new concept and thus, society was overwhelmed with diabetic foot disease and cases of lower limb amputations.

Following extensive research and experimentations, a consensus over what causes diabetic foot ulceration and how to prevent them was established. As a result, multiple, evidence-based guidelines, and expert consensus documents, on how to identify the predictors of ulceration and how to manage the diabetic foot and cases of ulceration were published (Formosa et al., 2016). These guidelines, were adopted in various clinics and hospitals across the globe and are now perceived as the standard medical care for the diabetic high-risk foot. The researcher of this PhD project associates this occurrence to Kuhn's *Normal Science stage* (stage 2).

Over the last decade, these evidence-based guidelines proved coherent and effective in reducing the number of major diabetic foot ulceration however, despite their introduction, cases of re-ulceration and the number of minor lower limb amputations are still increasing at an alarming rate (Grima et al., 2018). This fact led to the 3rd stage of science (*Crisis*) in which questions were raised in view of what could the anomaly be with regards to this persistent increase in diabetic foot ulceration, ultimately encouraging the start of this PhD project. From the literature review, the systematic

review and 2 scoping studies, this research concluded that the following anomalies pertaining to the increased cases of diabetic foot ulceration and minor foot amputations are as follows:

- Though various clinical guidelines have been set on how to assess the diabetic high-risk foot for predictors of ulceration and what offloading techniques of previously ulcerated sites or sites of high peak pressure areas are beneficial, the guidelines do not specify on which instrumentation is best used to identify peak plantar pressures and hence the use of such instrumentation is not recommended within these guidelines (NICE, 2015; IDF 2020; Bus et al., 2020; ADA 2022). Several studies advocate those clinical assessments of prescription orthoses done with the help of technology, not only permit the practitioner to obtain objective, precise and reliable measurements, but also helps the practitioner to understand how he/she can adapt or change orthoses to best achieve foot plantar pressure reduction and avoid re-ulceration (Bus et al., 2004, Hsi et al., 2005, Mueller et al., 2006, Koenraadt et al., 2012, Paton et al., 2012, Ibrahim et al., 2013). Furthermore, inadequate design of such devices that result from non-objective assessments, may not only be impractical but they may be hazardous enough to augment the targeted plantar pressures (Armstrong et al., 2017).
- The scoping studies conducted as part of this PhD project have confirmed that locally, the effectiveness of these offloading devices in reducing peak pressure areas off previously ulcerated sites or sites at risk of ulceration, is being purely based on clinical experience and visual observation. Objective assessment of the effectiveness of an offloading device is not being determined as the appropriate technology is not yet available within the state hospitals and health centres as it is deemed expensive and extremely time-consuming (Williams et al., 2016; Saliba Thorne, Gatt, DeRaffaele et al., 2022).
- Skin temperature as a predictor of diabetic foot ulceration is still overlooked and its relationship to in-shoe plantar pressure in view of ulcer development is still under investigated. Diabetic foot guidelines in the prevention of diabetic foot ulceration state that monitoring of the skin temperature of the diabetic foot is recommended (Schaper et al., 2020) as a correlation between temperature, plantar pressure and ulcer development is strongly suspected (Armstrong et al., 2017; Mizzi & Falzon, 2018; Gatt et al., 2018). Current temperature assessment

techniques involve barefoot manual palpation as concrete evidence on the correlation between in-shoe temperature and pressure measurement, as a predictor of diabetic foot ulcer development, has not yet been established. Furthermore, the technology to measure both in-temperature and in-shoe pressure is not yet available.

This brings us to the 4th stage of science as described by Kuhn. This stage is referred to as the stage of *Revolution*. It is at this stage in which a new paradigm that better explains what is true is established. Assimilating this stage to the concept of this PhD study, a change in practice is highly recommended as the increasing rate of diabetic foot ulceration exemplifies the need of a new, improved clinical practise in the prevention of high-risk foot complications. It is essential that orthoses and other offloading devices prescribed with the aim to protect the high-risk foot, should be evaluated on their level of effectiveness prior and following dispensing to the patient. For this to happen, innovative technology such as in-shoe pressure and in-temperature measuring devices should be introduced and made available for the clinician to use swiftly and objectively.

Thus, from a Post-positive perspective, should the concept of the current standard management care of the diabetic high-risk foot be refuted through this PhD investigation, the information obtained through the innovative specifically designed, single-sensor, pressure and temperature in-shoe device may be used to significantly improve the design of an offloading device resulting in pressure reduction at the targeted area. This revolutionary concept may bring about a change clinical practice and patient outcomes. It may also change the notion from just relying on clinical experience to relying on more reliable sources to ensure plantar pressure reduction.

The figure below (Figure 23) gives an overview of the key concepts of the research problem that constructed the conceptual framework of this PhD dissertation. Conceptual framework, also goes by the name analytical framework, helped in providing an argument about the importance of the study and why the methods proposed are appropriate and rigorous. Though a literature review that embodies a thorough review of the key concepts of the area of study, may in itself serve as conceptual framework (Ocholla & LeRoux, 2008; Maxwell, 2012), in this PhD project, the literature review served as a means to highlight the key concepts of the research

problem thus enabling the researcher to design the conceptual framework of this study (Figure 29).

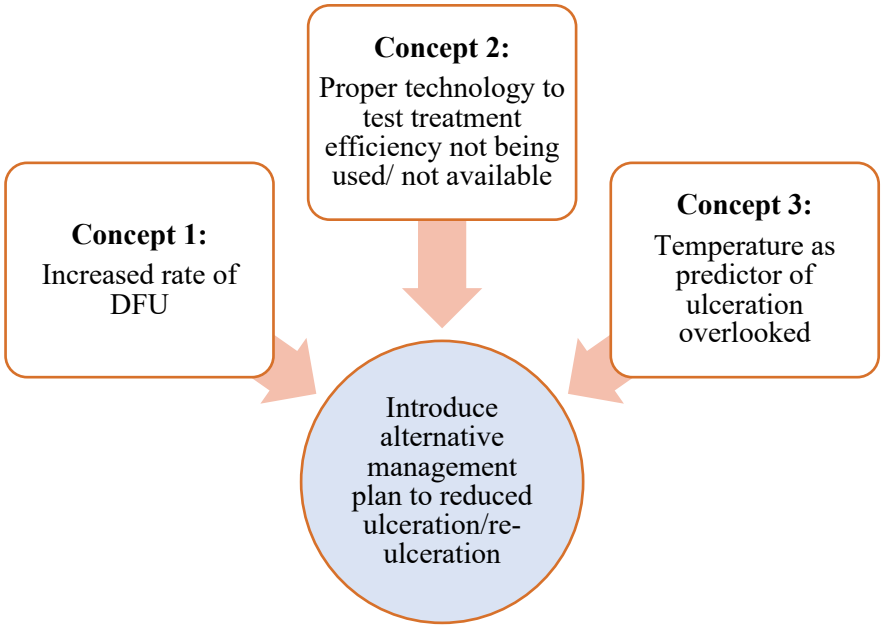


Figure 23: Conceptual framework of this PhD

4.6 Conclusion

Following a thorough literature search on the topic (Chapter 2), the research problem was identified which formed the basis which constructed the theoretical framework of this study. Key variables of the research and how other authors approached this, or if it is new concept, similar research problems were identified. Various literature pertinent to the topic including material on theories and analytic models relevant to the investigation were identified. A theory that best suited the research project was identified as the theory of *Structure of Scientific Revolution* by Thomas Kuhn (Kuhn, 1996). The assumptions of the selected theory were discussed, and its relevance to this research highlighted in the previous section (Section 4.5).

The knowledge obtained on the topic through personal clinical experience and following a thorough literature search, helped in the planning of the theoretical framework of this PhD project. Since this research project followed a Post-Positivist, deductive approach, the theoretical framework was planned prior the commencement

of the investigation. The selection of the theory was not only based on the suitability to this research but also on the ease of application and explanatory power.

Prior to the commencement of the main study, exploratory studies were conducted which served as a foundation which supported the whole concept of the main study. This dissertation revolved around 4 studies each having their own method and objectives as detailed in separate chapters of this dissertation.

The first and second study consisted of 2 small scoping studies that were conducted as part of the initial phase of this research project (Chapter 5). Study I consisted of an observational retrospective study which gave a numerical perspective on the number of high-risk patients living with diabetes mellitus that are being referred for an in-depth biomechanical examination in view of ulcer prevention. Study II consisted of a phenomenological qualitative study which gave a local perspective on the management and referral pathway of the high-risk diabetic foot.

The third study consisted of a detailed systematic review (Chapter 6) which provided a more thorough analysis of literature relating to the different technologies that were developed to measure in-shoe plantar pressures and in-shoe skin temperatures, or a combination of both. This systematic review proved very essential for this research as it provided insight on the existing gaps in research and points of improvements of the current available technology that were used for the purpose of this investigation.

The fourth study, which also served as the pilot study to the main study (Chapter 7, part III), related to the development and validation of the innovative, single-sensor, in-shoe pressure and temperature sensing device that was developed as a research tool for this PhD study. The final and 5th study is the main study (Chapter 8) in which the innovative in-shoe pressure and temperature measuring device has been clinically validated on the targeted patient population.

Chapter 5: Local Scoping Studies in Relation to Local Services

5.1 Introduction

This chapter introduces the reader with the first 2 studies conducted as part of Phase I of this research. These studies were conducted to gain a clearer perspective on the current local situation in terms of local management and referral pathway of the high-risk diabetic foot.

This research was published in the Journal of the American Podiatric Medical Association (JAMPA). Cited as Saliba Thorne, C., Gatt, A. & Formosa, C. (2021). Journal of the American Podiatric Medical Association (Appendix 2).

5.1.2 Rational

Malta, compared to other countries across the globe, has a high prevalence rate of diabetes (>10%, circa 40,000 patients) (Cuschieri, 2020; IDF, 2020) and a high prevalence rate of lower limb amputations (Mizzi & Falzon, 2018; Grima et al., 2018). The National Health System Strategy for Malta (Parliamentary Secretary for Health, 2022), a project implemented since 2014, builds on the solid foundation strategy that health care systems should be sustainable and should provide the best access to health for our population through prevention, efficiency and better use of available resources in order to deliver best patient care in the health sector. Strengthening prevention is believed to be the key and is implemented within the health care system to maintain a healthy population and achieve early identification of foot disease (Parliamentary Secretary for Health, 2022). To help prevent foot morbidity such as amputations and mortality following severe lower limb complications (Armstrong et al., 2017).

To date, following the International Diabetic Federation Guidelines (IDF, 2020) guidelines, in view of the prevention of diabetic foot ulcers, clinicians in local health care services determine patients' risk-assessment on tactile examinations and observation of the foot structure and skin, for any signs of tissue damage. The IDF guidelines recommend monitoring of the vascular and neurological status of the diabetic lower limb however it fails to give recommendations on detailed biomechanical assessment of the diabetic foot. Locally, monitoring of skin

temperature in view of ulcer formation is currently being observed through manual palpation of the skin and previously ulcerated areas or areas at risk of ulceration are being offloaded through the use of off-loading devices such as plantar paddings or foot orthoses. If available, offloading of peak plantar pressures are determined through the use of pressure sensing platforms prior to the prescription of foot orthoses or bespoke footwear (Bus et al., 2020).

Pressure sensing platforms can only be used to predict pressures generated between the bare foot and the ground however, it gives no information on the relationship between the foot and the shoe and the orthoses if available. Furthermore, an important concern relates to how the orthoses or any other offloading devices are tested for their efficiency in reducing the excessive pressure? It is well known that high pressures from inadequate footwear or poorly designed foot orthoses may increase plantar pressures thereby exacerbating tissue damage (Armstrong et al., 2017).

In Malta, the only recorded source of plantar pressure identification is a pressure platform/mat that is only available in the Biomechanics and Gait Analysis Clinic is situated at the Podiatry department, at a local health center a public clinic that falls under the local Primary Healthcare. This clinic offers Maltese and foreign citizens, irrelevant to their medical background, the service of an in-depth biomechanical examination of the lower limb that includes assessment of kinetics and kinematics of the knee joint, ankle joint and individual pedal joints of the foot; and barefoot plantar pressure analysis to identify barefoot peak pressure areas, utilizing a pressure platform/mat system. Locally, the Primary Health Care, is the place in which patients living with diabetes mellitus receive their first line of care and are flagged for further assessment and treatment if found to be a high-risk of ulceration; the Orthotics and Prosthetics Unit is where patients obtain their hospital prescribed footwear and/or orthosis in order to offload the high-risk foot and/or prevent further complications from happening.

Thus, prior to commencing the main research investigation of this PhD, and following a thorough systematic review on the current available in-shoe temperature and pressure technologies, two scoping studies with regards to the referral for an in-depth biomechanical assessment of the diabetic foot and the management pathways of patients living with diabetes mellitus were conducted.

This aim of these scoping studies was to provide a numerical perspective on the approximate number of referrals of patients living with diabetes mellitus that are referred for a diagnostic biomechanical examination within the Primary HealthCare sector; and to gain an understanding of how the high-risk foot is being managed within the Maltese healthcare with regards to the identification of ulcer development from the perspective of local clinicians.

5.2 Scoping Study I – Biomechanical assessment of the diabetic foot: the Maltese context

5.2.1 Aims and Objectives

The aim of this scoping study was to identify the number of current referrals for a detailed lower limb biomechanical assessment and pressure mapping of patients living with diabetes mellitus by retrospectively reviewing all available patient records, over a period of 1 year, at the only Biomechanics Clinic, situated at a local health center in Malta.

In order to meet the aim of this study, the following objectives were set:

- To determine the approximate number of referrals of patients living with diabetes mellitus who were referred for a diagnostic biomechanical examination within the Primary HealthCare sector within a timeframe of 1 year. (This included who refers these patients for a comprehensive biomechanical assessment and the reason for such referrals to the biomechanics clinic).
- To determine the approximate number of referrals of patients living with diabetes mellitus that are categorized as at-risk of ulceration mellitus who are referred for a diagnostic biomechanical examination within the Primary HealthCare sector within a timeframe of 1 year.

5.2.2 Methodology

This study followed an observational retrospective study design that utilized a service evaluation approach. A service evaluation approach was used to gather information on how patients living with diabetes mellitus are being managed within the Primary Care Services. A service evaluation approach can be defined as a systematic method that can be used to define current care and identify the standards that it is able to achieve (Moule, Armoogum, Dodd et al., 2016).

Like a service audit, service evaluation is utilized to increase the knowledge through the systematic collection of pre-existing data. However, a service evaluation approach differs from an audit in terms of using that information based on specific areas of interest to identify strengths and points of improvements of current practices rather than using an evidence based clinical standards (NHS, 2018). Since a service evaluation is based on interest and does not utilize a reference standard to define or judge current care, it cannot be generalized to other services (Moule, Armoogum, Dodd et al., 2016). Ethical approval was sought and granted to conduct this study.

5.2.2.1 Inclusion and Exclusion Criteria

Inclusion Criteria

The inclusion criteria comprised of new cases records that give information related to patients living with type II diabetes mellitus who were referred for a detailed biomechanical consultation over a 1-year period.

Exclusion Criteria

The exclusion criteria comprised all records that were not related to patients living with type II diabetes mellitus such as healthy participants or participants living with conditions other than diabetes and required a biomechanical evaluation.

5.2.2.2 Methods

A retrospective analysis of clinical records of new cases of patients living with type II diabetes mellitus attending the Biomechanics Clinic at a local health center was conducted. Clinical records accessed, dated between January 2019 and January 2020 as more recent data was not available due to temporary disruption of the service, due to restrictions related to COVID-19. Data such as age and gender of the patients, source of referral (who and from where were the patients referred from), clinical diagnosis and management plan given to the patients were of key interest and thus were recorded anonymously on an excel sheet.

5.2.2.3 Data Analysis

Data analysis was conducted using simple mathematical calculations on Microsoft Excel to calculate the number and percentage of patients attending to the clinic, evaluate the most common source of referral, calculate age and gender distribution of

patients, estimate the most common clinical diagnosis and management plan given to the patients.

5.2.3 Results

5.2.3.1 Patients per annum

A total of 965 recorded cases were retrieved from the database of the Biomechanics Clinic, of which, 97 cases were related to patient living with Type II diabetes mellitus, 6 cases related to type I diabetes mellitus and 862 cases related to healthy patients or patients who presented with other medical conditions other than diabetes. Thus, a total of 97 case records were included in this service evaluation. These 97 records included a more or less equal distribution of male (49.4%) versus female (50.5%) patients. Their age distribution ranged between 30 to 89 years of age with a mean age of 66 for females and 62 for males as shown in Figure 24.

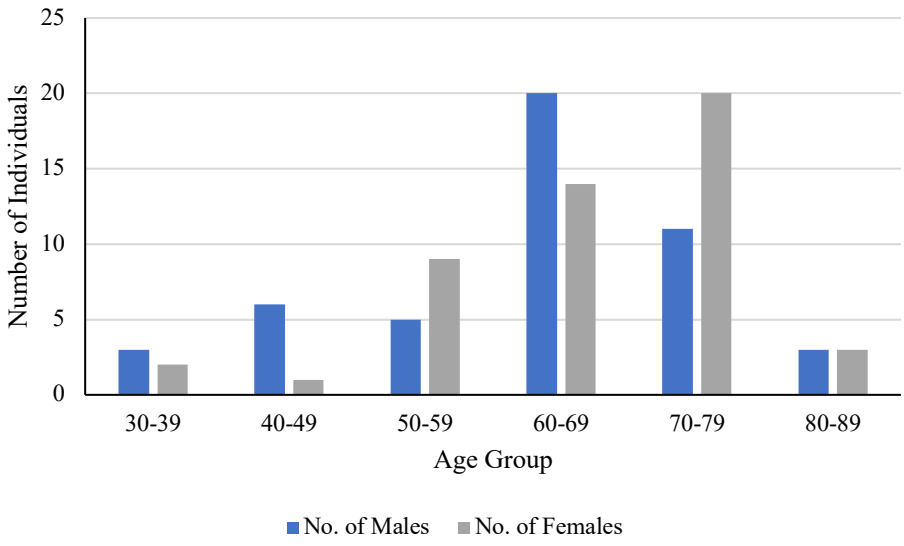


Figure 24: A multiple bar graph showing the age distribution according to gender

5.2.3.2 Sources of referral and clinical diagnosis

During this study, it was identified that in the primary sector, patients living with diabetes mellitus are generally referred to the biomechanics clinic for an in-depth biomechanics examination in view of prescription orthoses by their Podiatrist generally from other local health centres located across the island.

Within this specified period, January 2019 to January 2020, participants were mostly referred for a biomechanical examination in view of orthotic prescription by

Podiatrists (65.6%), Medical Doctors (26.6%), and Physiotherapists (3.3%). It was identified that 5.5% of the referrals were not signed and that only one referral was received from the tertiary sector (from an Orthopaedic Surgeon) (Figure 25).

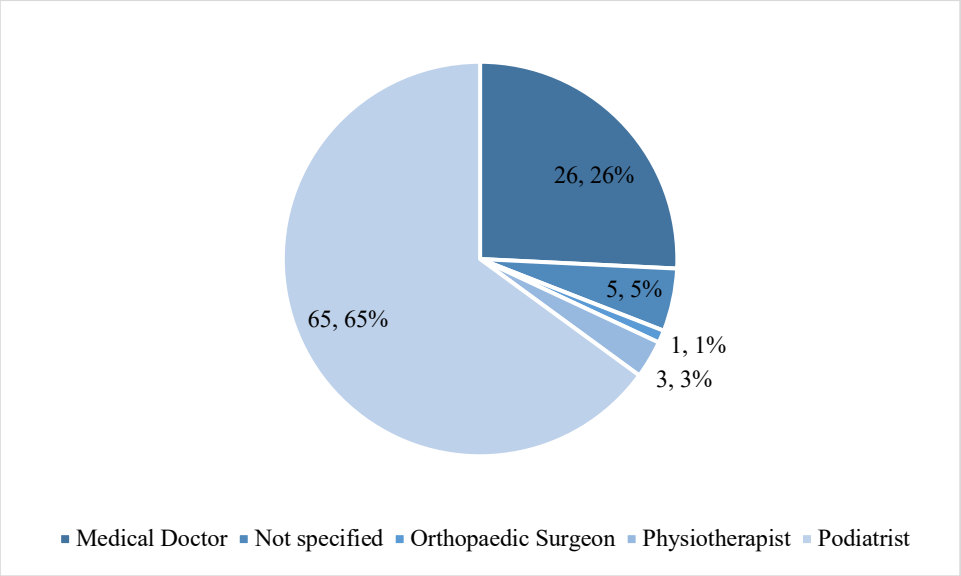


Figure 25: Pie chart showing the distribution of sources of referral for an in-depth biomechanical evaluation using pressure mat.

The chief complaint of the majority of referred patients was attributed to overpronation (18.6%), followed by Limb Length Discrepancy (LLD) (14.4%) and plantar fasciitis (9.3%) (Figure 26). It was observed that 11% of referred cases listed as "other", were given a diagnosis secondary to non-biomechanical cause. These include asymptomatic cases referred for check-ups; purely vascular, neurological and dermatological cases, a case which required prosthesis re-alignment; and localized arthritic changes.

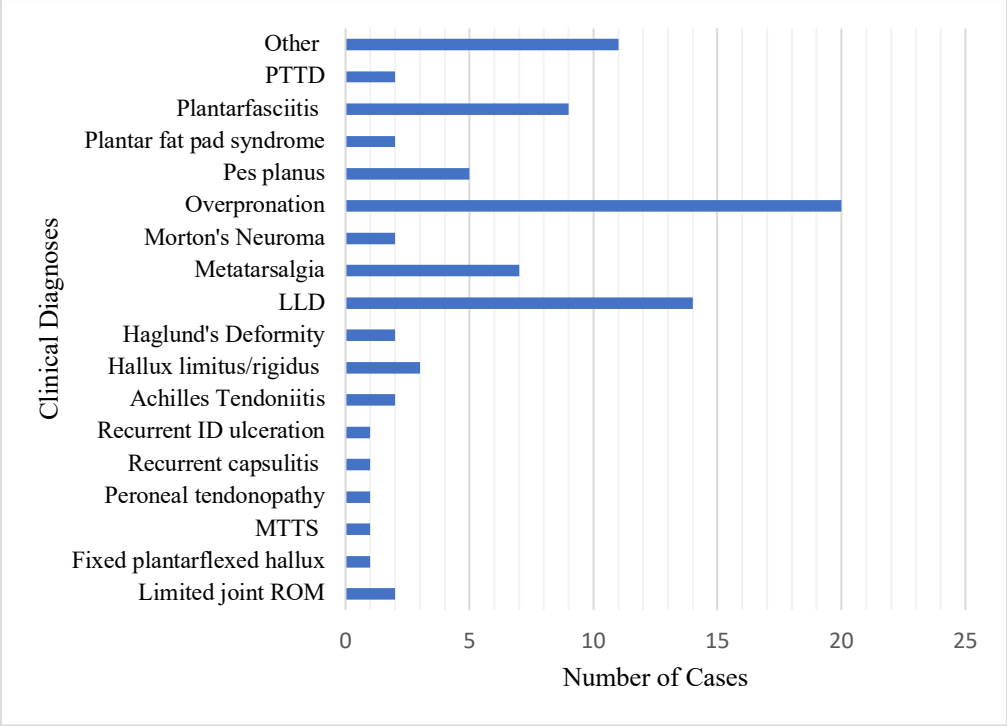


Figure 26: Rotated bar graph showing the distribution of clinical diagnosis of the referred patients following an in-depth biomechanical assessment within a period of 1 year.

5.2.3.3 Clinical Management

Following a thorough examination, the majority of cases were observed to be referred to the Orthotics and Prosthetics Unit (OPU) as new cases for prescription of orthoses (58%) and as f/up cases for change of orthoses (10.3%). A small percentage of cases were noted not to require prescription orthoses due to the nature of their problem. These included cases that only required yearly check-ups (9%), physiotherapy (4.1%), vascular and orthopaedic consultations (3.1%), or had had already an appointment at OPU (2.1%) (Figure 27). It was also observed that 6% of the cases did not attend for their review after being sent for further investigations such as blood test or x-rays to the GP.

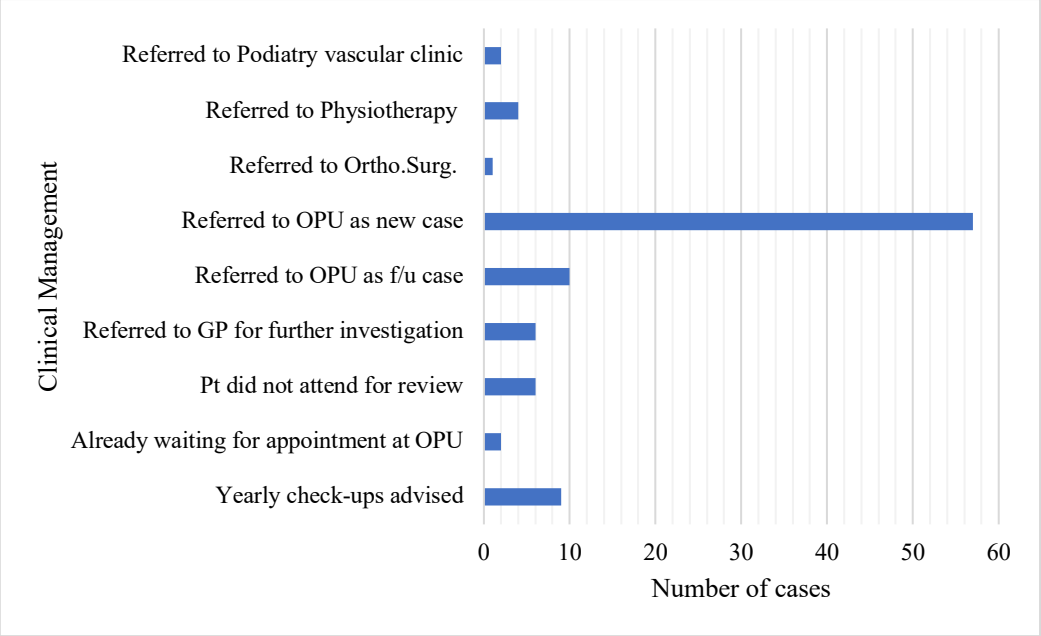


Figure 27: Rotated bar graph showing the distribution of clinical management and referral pathway of the cases referred.

5.2.4 Discussion

This scoping study was first to provide a local numerical perspective on the number of patients living with diabetes mellitus who were referred for an in-depth biomechanical assessment, in view of pressure offloading and ulcer prevention, within the local Biomechanics Clinic which is the only clinic to offer this service within the local Primary Sector in Malta.

In Malta, local government hospitals and health centres only have access to one pressure sensing platform across the nation which is situated at the Podiatry department at a local health center. The service in this clinic is offered to both Maltese and foreigner citizens and it involves an in-depth biomechanical examination of the lower limb that includes assessment of the knee joint, ankle joint and individual pedal joints of the foot; and barefoot plantar pressure analysis to identify barefoot peak pressure areas, utilizing a pressure platform/mat system. Data from this scoping study have shown that, considering the local prevalence for diabetes mellitus (40,000 patients), over a period of a year, only 97 cases were reported to have been referred for an in-depth biomechanical examination and foot pressure mapping at the only local clinic within the governmental sector that provides this service.

It is of a great concern to note that the majority of the identified 97 cases were referred by Podiatrists and only a small percentage of Medical Doctors referred their patients for an in-depth biomechanical assessment. It is even of a greater concern to note that among these cases, there were no patients living with diabetes mellitus categorised as at high-risk of developing diabetic foot complications; all cases registered were considered low-risk. Reason behind this lack of referrals needs to be explored and addressed accordingly since a number of questions arose from this study findings with regards to the referral pathway and biomechanical management of these high-risk patients.

Monitoring and inspection of the diabetic high-risk foot is consequential as the lower limb is regarded as the primary site for diabetic foot complications (Shavelson, 2011; Arad et al., 2011). It is well known that diabetes, with or without the presence of comorbidities such as peripheral arterial disease and peripheral neuropathy, amplifies pre-existing biomechanical anomalies that are often overlooked thus, over time, clinical signs tend to present themselves as persistent plantar wounds (Shavelson et al., 2011). The total range of motion of the joints of the foot, together with the relationship between the position of rearfoot to the forefoot, can be used to guide the clinician to describe the foot posture and related compensatory mechanisms (Shavelson et al., 2011).

A study by Shavelson et al. (2011) reported that when a thorough biomechanical examination is not taken as seriously as a well performed history taking, the orthoses and treatment plan may prove inadequate for the patient (Shavelson et al., 2011). Thus, since the etiological forces that influence the biomechanics of the foot differ from one patient to another, employing the 'functional foot typing system' without a complete, in-depth biomechanical examination is not recommended.

A study by Armstrong et al., (2017) demonstrated that off-loading and pressure re-distribution off the ulcerated area help in preventing recurrence of plantar ulceration. The study further reported that there are several designs and techniques in manufacturing foot orthoses and all are dependent on the clinical experience and choice of the Podiatrist or Orthotist prescribing them (Armstrong et al., 2017). In addition to this, studies by Bus et al. (2013) and later by Ulbrecht et al. (2014) reported that, considering the huge impact of foot orthoses on foot offloading, and the wide

variety of manufacturing choices, a better insight on the appropriate manufacturing of orthoses in high-risk patients is empirical as inappropriate designs increase the risk of ulceration. Off-loading and pressure re-distribution has been found to have better outcomes when assisted by proper techniques and technologies such as in-shoe pressure mapping devices (Bus, 2016).

Studies by Owings et al. (2008) and Ulbrecht et al. (2014) revealed that prescription orthoses designed based on the results of barefoot plantar pressures are superior to foot orthoses designed on visual observation and clinical experience. This means that though in-shoe pressure mapping is the ideal tool to be used to ascertain effectiveness of an offloading device, when unavailable, barefoot pressure mapping is the next best option towards an objective treatment plan and thus clinicians are encouraged to refer their high-risk patients for plantar pressure evaluations prior to planning their offloading treatment plan.

Further investigation is required to evaluate how locally, objective evaluation on the effectiveness and function of prescription of orthoses is currently being tested prior and following dispensing.

5.2.5 Conclusion

This study provided detail on how many patients living with diabetes mellitus are being referred for in-depth biomechanical assessment at the only local public biomechanics clinic over a 1-year period. The results of this study, led to raise questions concerning the local management of diabetic high-risk foot with regards to biomechanical assessment and screening for the early identification of risk factors leading to ulceration.

This study advocates for better awareness of local healthcare professionals with regards to the existence of a biomechanical clinic which offers the service of in-depth biomechanical assessment of the lower limb and the identification of barefoot plantar pressure measurement utilizing a pressure mat. This study also advocates for the education of these professionals to refer more patients living with diabetes mellitus so to provide the high-risk foot the necessary in-depth biomechanical assessment and pressure mapping to early identify peak pressure areas responsible for ulceration and to offload these areas by referring them to the Orthotics and Prosthetics Unit where

clinicians can provide offloading strategies as they deem necessary prior the development of ulceration/re-ulceration.

5.3 Scoping Study II – HealthCare perspective on the management of the DM foot – A Qualitative Analysis (Phase I)

Results from the first scoping study raised certain questions which led the researcher to conduct a second scoping study where clinicians working within the Primary Sector and the Tertiary Sector, and also a clinician working in the Education Sector with a biomechanical background, were interviewed to evaluate their perspectives with regards to the current local clinical biomechanical management of patients living with diabetes mellitus in different health care settings.

The primary questions which were raised from the results of the first scoping study included:

- How are high-risk patients with diabetes mellitus managed when an in-depth biomechanical examination and identification of peak pressure areas are warranted to predict diabetic foot ulceration and the associated complications?
- Which technique is being used to objectively assess plantar pressures and inform the need of offloading devices?
- How are offloading devices deemed effective in reducing the peak pressure areas identified in view of ulcer management and re-ulceration?

5.3.1 Aims and Objectives

The aim of this scoping study was to provide an understanding of the current local clinical biomechanical management of the diabetic high-risk foot were offloading of peak pressure areas in view of ulcer development is concerned.

In order to meet the aim of this project, the following objectives were set.

- To interview clinicians from different sectors to obtain their perspective on how the diabetic high-risk foot is currently being assessed for biomechanical pathologies.
- To obtain the perspective with regards to the use of diagnostic technology such as in-shoe pressure mapping as part of their routine clinical biomechanical management of the high-risk foot.

5.3.2 Outcome measures

Outcomes of interest included:

- The referral pathway employed by the Primary and Tertiary Sector as perceived by the interviewees
- The current local clinical biomechanical management of the high-risk foot in terms of ulcer management and ulcer prevention
- The methods/techniques employed by the interviewed clinicians to ensure that their treatment is indeed effective in offloading peak pressure areas
- The equipment used, if any, by the interviewed clinicians to maintain an objective treatment plan
- Concerns and recommendations the interviewed clinicians have for improvement of service.

5.3.3 Methodology

A qualitative study, based on the phenomenological discipline and inspired by the works of phenomenological theorist such as Edmund Husserl, was chosen to describe and understand the experiences of these clinicians (Moran, 2013).

Phenomenology, is the study of how the awareness of the human mind is structured from the person's own experience and point of view (Creswell & Creswell, 2018). Phenomenology can be literally described as the study of the perception of "phenomena" that is, the appearance of objects or situations as seen through the eyes of a person. The phenomenology discipline deals with the meaning of objects, tool, events or situations from a person's own experience particularly from the person's insight, thought, recollection, imagination, feelings and needs. According to the Husserlian phenomenology, what constitutes an experience is "intentional" that is, an experience is a representation of the same thoughts, insights, recollections, imaginations, feelings and needs that has formed it and thus each experience may carry a different meaning to each and every one of us (Tassone, 2017; Woodruff Smith, 2013).

Experiences can be broken down into two main types; experiences that are only seen or heard (passive experiences) and experiences in which the person is actively performing a task (active/conscious experiences). Conscious experiences are considered stronger than passive experiences as living through a situation gives a first-

person perspective which then builds a sounder structure of the conscious experience. Conscious experiences are also considered to have both a phenomenological and an ontological feature as they represent what the person has actively experienced (phenomenological) and the person him/herself as part of that experience (ontological) (Woodruff Smith, 2013).

5.3.3.1 Method

A purposive sampling technique was used in this study as this type of sampling technique allows the researcher to target specific people that fit the category of expertise (Andrade, 2021), the diabetic foot and its management, required to achieve the aim of this qualitative study. Participants who were interviewed were selected on the bases of having experience in managing the diabetic foot within the Public HealthCare System. A participant was specifically selected as he/she had also experience in training future clinicians and Podiatrists in clinical biomechanics and its application to managing the diabetic foot (Education Sector).

Four key clinicians experienced in the management of the diabetic foot were recruited and interviewed. The sample consisted of the following clinicians:

1. A clinician working at the Orthotics and Prosthetics Unit (Tertiary Sector)
2. A clinician working at the Diabetic Foot Clinic (Tertiary Sector)
3. A clinician working at the Biomechanics and Gait Analysis Clinic (Primary Sector)
4. A clinician working at the local University with special interest in clinical biomechanics (Educational Sector)

Description of Interviews:

Interviewee 1

Interviewee 1 was an experienced clinician who works at the Orthotics and Prosthetics Unit (OPU) at a local hospital under the Tertiary Sector. The OPU is the only department that is responsible for fabricating and dispensing custom-made orthotics and prosthesis, free of charge, to local or foreign patients holding a Maltese residency permit. Patients in need of offloading devices such as orthoses or customized footwear, are generally referred to the OPU department as long as they are in position of the

Schedule V (Pink) form and/or suffer from bone deformities or are at risk of developing foot ulceration.

Interviewee 1 was contacted and asked whether he/she would be interested in answering a few questions pertaining to this scoping study. As preferred by the interviewee and due to the current COVID-19 pandemic restrictions, the interview was conducted via telephone call, in the English language, which lasted 30 minutes.

Interviewee 2

Interviewee 2 was an experienced clinician who works at the Diabetic Foot Clinic, situated at the Outpatients Department, at a local hospital under the Tertiary Sector. The Diabetic Foot Clinic offer clinicians and patients living with diabetes mellitus access to medical doctors, nurses and allied health professionals specialised in diabetes which provide these patients specialised care by following international diabetic guidelines (Bus et al., 2020). Allied health professionals available include Ophthalmologists, Renal Physicians, Vascular Surgeons, Cardiologists, Physiotherapists, Occupational Therapists, Podiatrists, and Tissue Viability Nurses.

The Diabetes Clinic as an outpatients department in the Tertiary Sector, has abridged its service to that of the local Primary HealthCare services and implemented a fast referral system in order to meet the great demand for this service. Patients living with diabetes mellitus categorised as low-risk are managed by a practitioner at their respective health center in the Primary Sector. Concomitantly, these patients are also seen a number of times by specialists at the Diabetes Clinic.

Interviewee 2 was contacted and asked whether he/she would be interested in sharing his/her experience with regards to the current local clinical biomechanical management of patients living with diabetes mellitus. As preferred by the interviewee and due to the current COVID-19 pandemic restrictions, the interview was conducted via telephone call, in the English language, which lasted approximately 35 minutes.

Interviewee 3

The third interviewee was an experienced clinician who works in the Biomechanics and Gait Analysis Clinic at a local health center, under the Primary Sector. The Biomechanics and Gait Analysis Clinic is the only public clinic in Malta and Gozo

that offers in-depth biomechanical assessments and pressure mapping analysis (using a pressure mat) of the lower limb.

Interviewee 3 was contacted and asked whether he/she would be interested in answering a few questions pertaining to the current local clinical biomechanical management of patients living with diabetes mellitus. As preferred by the interviewee and due to the current COVID-19 pandemic restrictions, the interview was conducted via telephone call, in the English language, which lasted 20 minutes.

Interviewee 4

Interviewee 4 was an experienced clinician who works in the Educational Sector at the local University. He/she had a particular interest in the biomechanics of the lower limb and also works part-time as a clinician in the Private Sector. He/she was contacted to participant in this scoping study and be asked a few questions relating to the local clinical biomechanical management of patients living with diabetes mellitus. Like the rest of the interviewees, the interview was conducted via telephone call, in the English language, which lasted around 40 minutes.

5.3.3.2 Structure of the interviews

A semi-structured interview was conducted. The interview utilized open-ended question, with the addition of a content question (sub-question) that served as a leading question. As detailed below in Table 9. The open-ended question served to gain the perspective of the consenting participants with regards to the current local clinical biomechanical management of patients living with diabetes mellitus in different health care settings.

Table 9: Table showing the interview questions posed to the participants

Interview questions	
The open-ended question **(Leading Question)**	As an experienced Podiatrist who works in the [Educational Sector/Primary Health Care/Tertiary], what are your views on the management of the biomechanics of the high-risk diabetic foot? Do you have any concerns and/or recommendation to improve or commend the service?
Content Question (Sub-question)	What are the advantages/disadvantages of using diagnostic equipment as part of your clinical management routine?
Probing questions	"could you kindly explain what you mean by…" "could you kindly elaborate on this aspect?"

Though a face-to-face interview would have been preferred, so that the researcher/interviewer could have noticed mannerisms and behaviour of the interviewees, due to the current COVID-19 pandemic restrictions, the researcher had no choice but to carry out the interviews via telephone calls, as was preferred by the interviewed clinicians.

The data collection of the interviews was conducted by the researcher herself and following consent from the participants, all interviews were recorded using a digital voice recorder. To maintain anonymity of the interviewees, the recordings did not include the identity of the interviewee and the word "clinician" was used instead of using the title of profession of the interviewees to ensure that the participant is not recognised through his/her profession. All recordings were then transcribed in the English language, with the help of a professional linguist, in preparation for the Thematic Analysis.

5.3.4 Data Analysis

The recording of each interview was listened to and transcribed, word by word, as it was recorded on the digital audio recorder, to ensure that no important aspect of the interview was overlooked. The raw version of each interview was then analysed using the Thematic Analysis approach.

Congruent to the Thematic Analysis approach, the data was organized into codes and themes to identify, analyse and report existing patterns among the different sectors available locally as simplified in Figure 28 (Vaismoradi, Turunen & Bondas, 2013). Coding of data involved a process that involves categorising the data into segments which are then labelled with a specific term. Codes that share the same concept are then grouped into one theme (Rossman & Rallis, 2012).

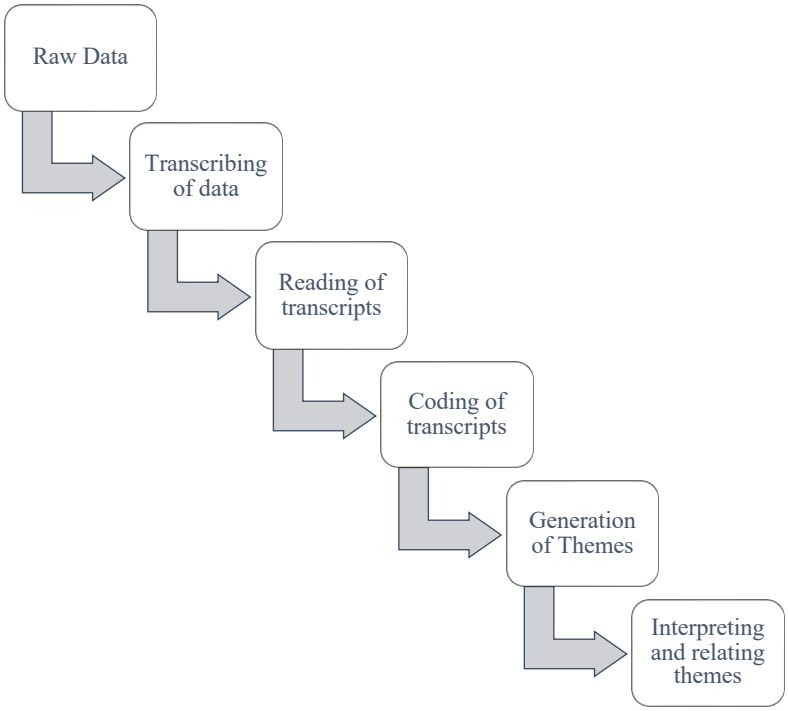


Figure 28: Process of data analysis used in this study

During the analysis of the data collected in this study, both an inductive and deducted approach were used while analysing the data. First, an inductive approach was utilized to allow the research to objectively build themes, categories and patterns from the transcripts until a comprehensive set of themes have been established. The deductive approach was then utilized for each theme to determine whether existing evidence-based literature can be used to support such information. In this study, a total of 8 themes have been identified following the coding of each transcript which are discussed in Section 5.3.5

5.3.5 Results and Discussion

An apprehensive account of the experience and perspective of the interviewed clinicians, on the local management of the diabetic high-risk foot was presented in this section.

5.3.5.1 Types of referrals received to each interviewed department

This theme related to the type of patients referred to each department, how often high-risk patients are reviewed and on what basis does the clinician base the frequency of review. It was identified that the OPU, the Primary Health Care and the Educational Sector attend to various patients with diverse medical histories including healthy (no diagnosed medical conditions), patients living with diabetes mellitus, patients living with other medical pathologies. Conversely, the Diabetic Foot Clinic, as the name implies, reported to only attend to patients living with diabetes mellitus and that a substantial number of patients get referred for a diabetic foot screening assessment – a type of assessment which is reported to include a neurological and vascular assessment of the diabetic foot and which categorizes the patient as at-high or at-low-risk depending on the results of the assessment. The OPU reported that in general, when they receive referrals of patients living with diabetes mellitus, they are referred in view of prescription orthoses and/or footwear. The interviewed clinician working within the Educational Sector reported that generally,

"I get referred patients who refuse to… not refuse, who has delayed healing and the Podiatrist suspects that there is a biomechanical aspect to it". – Interviewee 4

Interviewees reported that all health care professionals, medical practitioners, house officers and surgeons can refer their patients to either of the interviewed departments. This also includes the professionals who work in private hospitals and private clinics. The diabetic foot clinic also reported that a very small percentage of patients visited the clinics are self-referred.

"They would have heard of the service on the media and that they would like to start attending the clinic here." – Interviewee 2

All patients living with diabetes mellitus are reported to be entitled to be referred to the OPU and the Diabetic Foot Clinic and the service of prescription orthoses and/or footwear is free for this patient population.

The OPU use the referral system to help them categorize their patient appointments due to the high influx of cases received from across Malta and Gozo. It was reported that the referrals are categorized according to the urgency of the presented case for example, cases of active ulceration and/or severe foot deformities take priority over patients with minor biomechanical issues.

Another important aspect that has been reported is that most of the referrals sent to the OPU do not present the patient in detail. The interviewed clinician reported that the majority of referrals lack some important information, such as neurological and vascular status of the patient, that influences on how urgent the referral is stratified.

"Diabetics are all entitled so no matter what they are entitled, they don't need the pink card, of course, if this person has had a history of ulceration or active ulceration or an amputation, he is obviously prioritised. This is all if it is written in the referral so usually podiatrists forget to put down that info erm so that doesn't really help us with stratifying."

– Interviewee 1

5.3.5.2 Foot Biomechanics Assessment

This theme related to whether or not a lower limb biomechanics assessment is performed to assess the biomechanical status of the diabetic high-risk foot. The majority of the interviewed clinicians, reported that they do perform an in-depth biomechanical assessment of the diabetic lower limb. Differing from the rest of one interviewee reported that as part of the diabetic foot screening, only the foot structure and the ranges of motion of the pedal joints are assessed.

"…as such, we do not do thorough biomechanical examination… because a lot of people they have reduced range of motion and such, the joint movement and such doesn't remain that good, and a good percentage of them also have neuropathy and neuropathic deformities"

-- Interviewee 2

It was further reported, that in cases where the foot is noted to be at risk of ulceration, the patient is referred to OPU for prescription orthoses.

"...their foot shape and their condition warrant a referral to OPU for offloading or else to provide them with something to reduce the chances of a pressure site to become an ulcer site, we refer" – Interviewee 2

In cases that are identified to have pressure points that are compensating well, and are not directly affecting the patient, other interviewees reported to prefer giving advice on general foot care as opposed to advise on orthoses at that point in time.

"we see pressure points, we do not automatically tell the patient you need orthoses apart from the fact that I, personally, I don't see that if something is not causing trouble to the person and that he is compensating well to it, I am not of the frame of mind that you just have a pronated foot and you are compensating for that and you stay doing something about it personally" – Interviewee 2

5.3.5.3 Treatment Plan

This theme related to patient education and describes the brainstorming on how treatment is planned and executed in terms of offloading, patient education, history taking, designs and techniques. Interviewed clinicians reported that they advise their patient on general foot care and foot health, footwear and orthoses therapy.

"...sometimes with good patient education and some advice it is enough to help the quality of life overall" – Interviewee 1

When it comes to offloading a pressure area which is a cause of concern for ulcer development, the interviewed clinicians reported that orthotic therapy is their treatment of choice. The interviewed clinician generally refers to felt padding to temporary offload a peak pressure area until prescription orthoses are dispensed. However, in view of this remedy, other interviewees reported that the use of felt padding is an extremely temporary measurement if used as an offloading device and thus, it should be used to a minimum.

"...with felt you do not have that offloading property that a more durable material can give you. The offloading properties of felt padding are lost within one or two days of use and thus it becomes ineffective" – Interviewee 4

Apart from basing their design of orthoses on the biomechanical status of the lower limb of the diabetic high-risk patient, the interviewed clinicians reported that they also

base their design on a detailed history taking which includes ulcer history in terms of duration and cause, vascular and neurological status of the patient's lower limb.

In addition to the biomechanical profile and patient's history, the use of assistive diagnostic technology, was only reported by the on interviewee. This clinician reported that an in-shoe pressure mapping system is used to aid him/her in designing the offloading device based on the patient's peak pressure points and location of pressures. The clinician further reported that in cases of the diabetic high-risk foot, the in-shoe system is used to investigate the area of interest that is, the area at which the ulcer is developing or has previously developed. Following the investigation of peak plantar pressures, the clinician reported that he/she designs the orthoses from scratch by taking the impression of the patient's foot using an impression foam box, or if permissible, modify the orthoses the patient came with, depending on the case.

The interview with interviewee 1 identified that patients noted to require offloading devices are generally prescribed custom-moulded orthoses that fit within their own footwear and that it is very rare for a patient to be prescribed a simple insole. The impressions of the patient's feet are taken by using an impression foam box which then are sent abroad for the fabrication of the orthoses. In cases where both orthoses and footwear are required, the clinician reported that both the impressions of the feet and the details for the footwear are ordered together to avoid fitting errors.

"We don't do the insole order alone and the shoe abroad because 99% chance that they won't fit perfectly there will be not enough allowance for the foot, not enough allowance for the insole, they might be too narrow in the front, there might be a gap etc"

– Interviewee 1

5.3.5.4 Treatment Quality Check

This theme refers to how the clinician base his/her decision that the treatment is effective or not. The results of this study showed a unanimous concept of using prescription orthoses as the preferred offloading device when the diabetic high-risk foot is concerned. This theme was constructed based on codes that identified how the interviewed clinicians determine the effectiveness of the treatment planned for their high-risk patient. These codes include clinical experience and visual observation and the use of assistive technology.

Visual observation and clinical experience are what the interviewed clinicians, have reported to base their decision that their treatment is effective in reducing peak plantar pressures at previously ulcerated sites or at sites that are at risk of ulceration.

The orthoses are checked against the patient's foot to determine their offloading capacity and fit. Once ascertained that the fit is adequate to the patient's size and biomechanical requirements, the patient monitored for signs of improvements this includes improvement of symptoms such as pain and seeing that the ulcer is improvement or not getting worse.

"We also see if he is doing well, that it is closing up, it is not getting worse, you're not getting the complications of an unhealing ulcer, so you know it is working well"

– Interviewee 1

"I pretend that with the offloading device the ulcer should be healing, always excluding the vascular element of it" – Interviewee 2

The interviewed clinician disclosed that, when possible, cases that have persistent ulceration despite having prescription orthoses, are sent to a colleague who can test the efficiency of the patient's orthoses through in-shoe pressure mapping.

"we had a patient recently, my only to go to place, when I have such a case… though I cannot do it often because the tools are not always available to us first hand, but I sometimes refer the case to Podiatrist [name omitted to maintain anonymity] and I tell him, listen I have this particular patient, I would like to know if this orthotic that he has is actually working properly" – Interviewee 2

One interviewee differed from the rest of the interviewees, as he/she reported to use an in-shoe pressure mapping system prior designing the offloading device and following dispensing the device in order to assess whether the device is actually reducing the peak pressures identified. This process is repeated until the desired pressure reduction is achieved.

"I design an offloading insole and then depending on the results, I would do an in-shoe pressure test…With each step I do the test again until I am satisfied that there is a 30% decrease in pressure" – Interviewee 4

5.3.5.5 Follow-up and reviews

This theme related to whether or not patients are given a follow-up/review appointment and how follow-up/review appointments are determined. Half of the interviewees reported that their patients are not discharged unless the patient opts to schedule their visits with another department or decides that he/she wants to stop the visits entirely. Follow-up appointments, also referred to as review appointments are always scheduled to monitor the patient and/or treat accordingly. The frequency of appointments is determined depending on the case and needs of the patient. Interviewee I reported that as a general rule, a patient is given a 3-month review after dispensing offloading devices however, this rule changes depending on the need of the patient especially if the patient has an active ulcer. Interviewee 2 reported that if the results of the diabetic foot screening results as low-risk that is, the patient is diagnosed with adequate vascular and neurological status, then the review is set within a year.

5.3.5.6 Experience in using in-shoe technology

This theme related to whether or not assistive diagnostic technology such as in-shoe pressure mapping system is available within their clinical practise. This theme also related any positive and/or negative experience of the interviewed clinicians with using such technology.

Availability of diagnostic technologies was reported in half of the interviewees. These clinicians reported that diagnostic tools related to biomechanics and in-shoe pressure and/or temperature testing are not available in either of the departments and it is something that is extremely missed in clinical practice. The in-shoe system is reported to give the clinician a great advantage as it provides the clinician with objective measurements. This advantage was reported in all four interviews.

"When it comes to using tools to assist in diagnoses it is mostly related to neuropathic or neuroischaemic problems" – Interview 2

Despite being available or not, the interviewed clinicians reported specific limitations related to the in-shoe pressure system that discourage them from integrating it in their clinical practise. To perform a single assessment with the in-shoe pressure mapping system is very time-consuming.

"It takes about 30 to 35 minutes just to do a single in-shoe assessment" – Interview 4

The insole which contains the sensors of the in-shoe system have to be cut and adjusted to fit within the patient's footwear and can only be used for a number of times as the sensors degrade with use. Furthermore, once the insole is cut, it can only be used to fit that particular size it was adjusted for. Another point that was brought up is that the in-shoe system can only be used in within a set environment with limited walking distance due to the wiring and connections.

"...you are limited with the space you can ask the patient to walk while testing. So, it can't give you a real picture of what is going on all the time" – Interview 2

All 3 interviews agree that the in-shoe system is also very expensive not only to buy but also to maintain. One interviewee remarked that the expenses required to invest in such technology could be a reason as to why such a system is not available within the government sector.

"A foot pressure system will cost about 15 thousand euros and I don't see any reason as a clinician to spend 15 thousand euros that you are going to use every now and then…the sensors are expensive…" – Interview 4

An interviewee disclosed that due to the related expenses involved with using the in-shoe pressure system, he/she does not use it very often and refers to it only when presented with cases of persistent ulceration. The system is very time-consuming for just one assessment let alone for analysing the report. Also, the system can take up most of the clinician's time with frequent technical errors such as problems of connection. The clinician further revealed that using it too often gives the clinician no choice but to increase his charges of service as it can become quite expensive in terms of material and time. Overcharging is something to avoid as these patients already have personal expenses and problems related to their high-risk foot.

"If I had to really stick to like how much time and how much you spend you increase the charge it would be very, very expensive to the patient…I did not want to give the patient the impression that I was overcharging" – Interview 4

5.3.5.7 Concerns Raised

This theme relates to the apprehensions of the interviewed clinicians on the complications, management and quality of treatment of the diabetic high-risk foot.

The first concern that was raised, by all interviewed clinicians, is that of not having an in-shoe pressure system to assist the clinician objectively diagnose peak plantar pressures before and after prescription orthoses or any other offloading device.

"I don't understand how within the Maltese health care system there does not exist one in-shoe pressure system… I cannot see why no one does this kind of technique"– Interview 4

The interviewed clinicians speculated that the reason for this lack could be attributed to the expenses related to using the in-shoe system and that it requires a lot of time to perform a single assessment.

"…it does take a long time to use in-shoe pressure to assess the patient in this manner. You have a specific amount of time…"– Interview 4

One interviewee remarked that in spite of the expenses related to using the in-shoe pressure system, the in-shoe system an essential asset in the clinician's routine practise as when treating the diabetic high-risk foot, one cannot afford to wait for clinical signs to prove whether or not the offloading device is effective.

"As they say, time is tissue and if I made an offloading insole and then waited 2 weeks, 3 weeks, 4 weeks, to see if the lesions are going to get better, to see if the insole is working or not, those 3 to 4 weeks that have passed put the patient at risk of getting complications most probably an infection. They get an infection because there is a wound, they can get osteomyelitis, cellulitis and so forth…we cannot afford to wait" – Interview 4

Moreover, the clinician reported that, when testing the orthoses that were designed without the assistance of the in-shoe pressure system, it is often for him/her to find that those orthoses were not offloading the area sufficiently but where actually increasing the pressure at the targeted area. Without diagnostic technology, the interviewed clinicians are concerned on how to ascertain that the offloading device is actually working.

"Sometimes we use felt padding and you wonder… am I positioning it correctly? Is it enough to reduce the excessive pressure?"– Interview 2

"I believe that due to this lack, there is a big mismanagement of patients"– Interview 4

5.3.5.8 Recommendations for service improvement by interviewees

This theme highlighted the recommendations of the interviewed clinicians on how the service can be improved codes related to this theme included 'Evidence-based research', 'Improvement of ulcer prevention modalities', 'Low-cost alternative tools', 'Integration of biomechanics in diabetic foot screening' and finally, 'home-monitoring devices'.

The interviewed clinicians show shared ideas on the lack of diagnostic tools that can be integrated in their clinical practise. It was reported that it would be of great help to have a tool, such as an in-shoe pressure system, that gives the clinician objective assessment, other than relying on experience and clinical judgement, on which to base their treatment plan.

"Having something that can determine whether the offloading capacity of a given orthotic is being effective it would be a great help" – Interview 2

"Without any doubt, any and all patients at risk of ulceration, should be screening with in-shoe pressure mapping and any offloading device should be tested" – Interview 4

It was also recommended that in-depth biomechanical evaluation, together with the use of diagnostic technology, is given more weight and thus should be integrated within the diabetic foot screening assessments.

"Equipment which evaluates the gait patterns and pressure distributions of the foot during gait would be highly beneficial when used in conjunction with a full physical biomechanical examination"– Interview 3

"Without any doubt, any and all patients at risk of ulceration, should be screening with in-shoe pressure mapping and any offloading device should be tested"– Interview 4

There also seems to be a unanimous consensus that, even if current in-shoe technology was available for them to use at their place of work, the interviewed clinicians are hesitant to integrate it in their busy daily practise as the system is too laborious and time-consuming. On this note, interviewed clinicians remarked that it is more likely for them to use and integrate a low-cost and easy-to-use device.

"By providing the opportunity of low-cost alternatives to these technologies would provide an incentive even in the private sector, to invest in such equipment"– Interview 3

"When an equipment is readily accessible, user-friendly and low-cost, it is natural that you get more people using it"– Interview 4

One of the interviewees remarked that he/she is more interest in a tool that is easy-to-use and that gives minimal technical errors. It would also be positive to have a tool that is time-efficient and that does not take up much time to perform a single assessment as with the currently available commercial in-shoe systems. It was further added that in spite of having a fancy system with 99 sensors that gives you details of pressures across the whole foot, the clinicians in reality only uses it to assess a specific area of interest such as previously ulcerated site.

"I just connect the system, insert the sensor at the area of interest, ask the patient to walk and you have the result in a few minutes. And you don't even need to analyse the data afterword"

– Interview 4

It was further added that it would be even more remarkable if such a tool would give the clinician the opportunity to home-monitor the patient and assess pressure patterns over a prolonged period of time while the patient performs his/her daily activities.

"Another advantage would be to lock patients over a whole day. Where the patients walk within his normal surroundings for a whole day something which cannot be done with the in-shoe system. Home monitoring of in-shoe plantar pressure over a period of 24 hrs would give enough data sample that is representative of the patient's pressures"– Interview 4

All in all, the main points of recommendations (Figure 29) related to the need of improvement in services with regards to ulcer prevention modalities that is based on the fact that assistive diagnostic technologies, such as the in-shoe pressure system is not available within the Government Sector and clinicians are not investing in such a system within the Private Sector. Interviewed clinicians reported that low-cost alternative tools which are not as time-consuming as the current in-shoe systems, could encourage to integrate in-shoe pressure mapping and in-depth biomechanics assessments in their routine clinical practice.

Figure 29: Image summarizing the highlighted recommendations.

The overall results, reflecting the common and different aspects in patient management and clinical practise investigated in this study, are summarised in Figure 30.

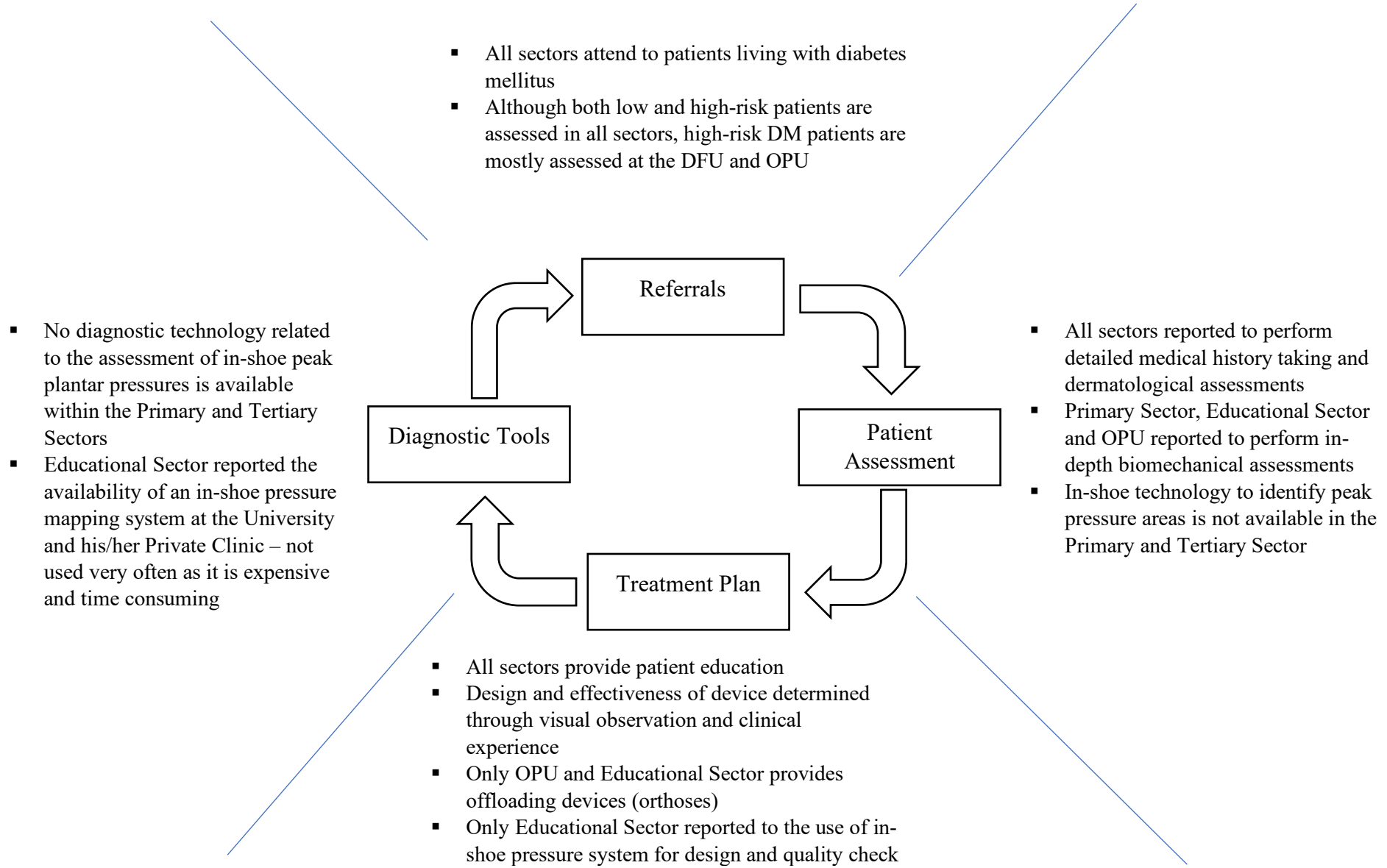


Figure 30: Figure summarising the results of the study. This figure highlights the common and different aspects in patient management and clinical practise related to clinical biomechanics evaluation

5.3.6 Conclusion

This scoping study has provided evidence on the management pathway and clinical practices within the Educational, Primary and Tertiary Sectors. It also highlighted the points of concerns the interviewed clinicians have in terms of patient management of the diabetic high-risk foot where offloading and ulceration is concerned. Change and improvement in the current clinical biomechanical related management of the diabetic foot was recommended in which the patient and in turn the health care system could holistically benefit.

It is of the utmost importance for clinicians to understand and give greater attention to the biomechanics of the diabetic high-risk foot. A full biomechanical assessment with the assistance of diagnostic technology such as the in-shoe pressure system could change clinical practice and change the notion of clinicians to just relying on their clinical evaluation such as tactile examinations and observation of the skin where tissue damage and foot deformities are concerned.

Chapter 6: Wearable in-shoe temperature and pressure systems to monitor the diabetic high-risk foot: A systematic review and planned meta-analysis.

6.1 Introduction

This chapter presents the reader with a comprehensive systematic review on the currently available in-shoe technology that can read and measure pressure and temperature parameters for the prevention of diabetic foot complications. This research is registered under PROSPERO, registration number CRD42020183322 (Appendix 3), and it has been published in Diabetes Research and Clinical Practice https://doi.org/10.1016/j.diabres.2021.108783 0168-8227/ (Appendix 4).

6.1.2 Rationale

A big percentage of individuals living with diabetes mellitus develop a foot ulcer this increases the morality risk of the affected individual two-fold and if it becomes infected, healing of the ulcer delays thereby increasing the risk of amputations by 70% (Walsh et al., 2016; Armstrong et al., 2017). In their study, Mizzi & Falzon (2018) reported that around 400 patients experience an amputation secondary to diabetic foot ulcer related complications (Mizzi & Falzon, 2018). Diabetic foot ulcers, also referred to as pressure ulcers, naturally develop by continuous vertical (pressure) strain or lateral shear forces over the skin (Monteiro-Soares et al., 2012; Bus et al., 2016). An inverse relationship was observed between the size and duration of the loading applied to the skin. In brief, the higher the load applied, the less time is taken to initiate tissue breakdown and vice versa.

When the superficial layer of the skin sustains excessive loading of pressure, it macerates and detaches from the deeper layer. If the loading persists, the skin sustains further damage, tissue breaks down and thus an ulcer is formed (Bhattacharya & Mishra, 2015). In cases where the pressure is sustained upon a bony prominence, the deep muscle layers underneath the skin are also involved (Cifu, 2016). These deep ulcers are the most delicate to treat. Unlike superficial ulcers, the extent of damage of deep ulcers progresses towards the surface of the skin hence, signs of damage may not

always be obvious on the skin. Furthermore, deep ulcers predispose a higher risk of ulcer complications such as necrotic lesions which eventually lead to amputations.

Besides pressure, previous foot ulceration, callus formation, blistering and bruising of the skin, and skin temperature, are strong predictors for foot re-ulceration. Monitoring of skin temperature is a relatively new concept especially where the management of the diabetic high-risk foot is concerned and due to this it is often overlooked as predictive measurement for foot ulceration (Peters et al., 2007; Monami et al., 2008; Dubský et al., 2013; Waaijman, 2014). It is very essential that foot temperature monitoring is introduced as part of the clinical assessment in view of diabetic foot ulcer prevention (Bus et all., 2020).

The literature has shown that an increase in 1ºC in skin temperature leads to an 13% rise in tissue metabolic requirements (Shrestha, Acharya, & Gurung, 2020). Correlation analysis has confirmed a positive correlation between pressure and skin temperature (Perren et al., 2020). With persistent pressure, the perfusion of blood to skin tissues is hindered causing localised ischaemia which in turn limits the supply of nutrients and oxygen to the surrounding tissue. Studies have observed a rise in local skin temperature secondary to induced pressure and the insulating effects of foams and other materials (Houghton et al. 2013). This knowledge further confirms that the importance of the role of skin temperature in the development of foot ulceration.

Prevention of diabetic foot ulceration and its recurrence is very significant to the health care economy (Armstrong et al., 2017). The health care economy faces an imposing incumbrance as a result of the high rate of ulcer recurrence and diabetic foot complications such as infections, hospital admissions and lower limb amputations secondary to unhealed diabetic foot ulceration (Gershater et al., 2011; Armstrong et al., 2012; Dubský et al., 2013; Bus et al., 2013; Ulbercht et al., 2014; Cushcieri, 2020). It is speculated that this high rate of ulcer recurrence might be because, despite clinicians are doing their utmost to prevent ulceration and re-ulceration, factors that lead to tissue breakdown are not being fully addressed (Bus, 2012).

Monitoring of predictive factors and off-loading and pressure re-distribution off the ulcerated area, help in preventing recurrence of plantar ulceration (Armstrong et al., 2017; Bus et al., 2013; Ulbrecht et al., 2014). The quality and effectiveness of foot orthoses prescribed for the diabetic high-risk foot is empirical for the prevention of

diabetic foot re-ulceration. Inappropriate designs of off-loading devices increase the risk of ulceration. Off-loading and pressure re-distribution has been found to have better outcomes when assisted by proper techniques and technologies such as pressure mat systems and in-shoe pressure mapping devices (Bus, 2016).

To date, standard clinical practices in view of the prevention of diabetic foot ulcers, focus on tactile examinations and observation of the skin for any signs of tissue damage. Offloading of peak plantar pressures are assessed, if available, through the use of pressure sensing platforms prior prescription of foot orthoses or bespoke footwear (Bus et al., 2019). Early identification of the initial pathological changes of deep ulcers are difficult to observe with the current available assessment techniques (Shrestha, Acharya, & Gurung, 2020). From the prevalence of ulcer recurrence (Gershater et al., 2011; Armstrong et al., 2012; Dubský et al., 2013; Bus et al., 2013; Ulbercht et al., 2014), it is safe to say that current attempts to prevent ulceration are only contributing to a minimum. A change in assessment and management method is required in order to obtain a significant reduction of the problem. It is empirical to improve and expand our knowledge on the relationship between foot plantar pressures and skin temperature from both a scientific and a clinical perspective.

The role of skin temperature and plantar pressures in relation to diabetic foot ulcer development has been of a growing interest amongst clinicians and researcher. Our understanding and knowledge on the topic however, is still limited (Bus, 2016; Jones, Bibb, Davies et al., 2020). Current literature has identified that early identification of excessive plantar pressures and monitoring of skin temperatures, play an important role in the prevention of ulceration and its recurrence (Bus, 2016). Special technology can be developed and used to identify plantar pressures and skin temperatures to identify the pre-ulcerative state (inflammation) thereby predict ulceration (Bus, 2016). The review by Jones, Bibb, Davies et al. (2020) investigated and confirmed a correlation between the microclimate (temperature and humidity) characteristics of the foot and the development of diabetic foot ulceration. following the results of this review, Jones and her colleagues (2020) argued that the prediction of diabetic foot ulcer development remains clinically challenging as temperature and pressures, as predictors of diabetic foot ulcerations, are not being monitored simultaneously and that the majority of studies tend to focus on pressure, shear and/ or comparing temperature from one limb to the other (Jones, Bibb, Davies et al., 2020).

Pre-existing systematic reviews on the related topic have given valuable insight on the need of further investigation on how we can use newly developing technologies in view of ulcer prevention however, their reviews included studies that may be considered out dated (Jones, Bibb, Davies et al., 2020) and the majority of studies included, utilized non-in-shoe temperature measuring equipment such as infrared cameras (Bus, 2016; Jones, Bibb, Davies et al., 2020).

This systematic review and meta-analysis aim to provide thorough analysis of current available literature that relates to the technology developed to asses in-shoe plantar pressures, and in-shoe skin temperatures. Their validity and reliability an identification technique for foot plantar ulceration and/or re-ulceration of the diabetic high-risk foot was compared.

6.2 Objectives

Research Question: What is the current evidence on the validity, reliability and effectiveness of in-shoe pressure and temperature systems and their role in the prevention of the diabetic high risk-foot ulceration/re-ulceration?

Aim: The aim of this systematic review was to identify and analyse current literature that address the validity, reliability and responsiveness of in-shoe pressure and temperature systems, for the prevention of the diabetic high risk-foot ulceration/re-ulceration.

Objectives:

1. To determine the validity of in-shoe temperature and pressure mapping devices utilized in studies preferably addressing the diabetic population.
2. To determine the reliability of in-shoe temperature and pressure mapping devices utilized in studies preferably addressing the diabetic population.
3. To determine the responsiveness of in-shoe temperature and pressure mapping devices utilized in studies preferably addressing the diabetic population.

The following questions were answered:

1. What current evidence exists on the validity, reliability and responsiveness of in-shoe pressure and temperature monitoring that address the diabetic population?

2. What statistical analysis have been used to report the integration of data and knowledge from different sources used, pertinent to the research topic?

6.3 Methods

6.3.1 Eligibility criteria

Studies were selected according to the following criteria outlined.

Study Designs

All study designs were considered in this review particularly, randomized controlled trials (RCT), controlled clinical trials (CCT).

Participants

Studies examining human adults, male or female of 18 years of age and older, and living with type II diabetes mellitus were included. Studies on the diabetic high-risk foot, which is at risk of ulceration or has previously ulcerated, were included. Similar studies who have included overweight or obese participants, participants living with musculoskeletal conditions or participants who walk aided, were excluded.

Interventions

Of interest were clinical assessment techniques that addressed peak plantar pressures causative of ulceration in the diabetic high-risk foot. In addition to that, studies which explored the correlation between peak plantar pressures and skin temperature were also be considered.

Comparators

Comparisons to clinical assessment procedures that do not utilize in-shoe pressure mapping or that utilize other assistive technologies were made.

Outcome measures and prioritisation

At least one of the following outcome measures were of primary interest and required to be investigated in the included studies:

Primary outcome measures:

1. Validity of devices used – studies reporting the validity results of either in-shoe plantar pressure devices and/or in-shoe temperature measuring devices in view of the diabetic population.
2. Reliability of devices used – studies reporting the reliability results of either in-shoe plantar pressure devices and/or in-shoe temperature measuring devices in view of the diabetic population.
3. Responsiveness of the device –studies reporting that in-shoe pressure mapping device and/or in-shoe pressure temperature sensing device is indeed accurate in determining pressure reduction and/or determining temperature changes within the shoe. Responsiveness is the ability of a device to detect change in the construct that is measured over time

Secondary outcome measures:

4. Type and size of pressure and/or temperature sensing devices – Studies reporting the type and size of sensors used to detect in-shoe plantar pressures and/or in-shoe skin temperature changes.
5. Number and placement of sensors – Studies reporting the number of sensors used and the specific anatomical landmarks at which the sensors were placed for investigation.
6. Statistical analysis that has been used to report the integration of data and knowledge from different sources pertinent to the research topic.

Timing

The literature search was limited to studies published between the 2000-2020.

Setting

There were no restrictions by type of setting.

Language

Only articles reported in the English were included.

6.3.2 Information Sources

Literature search strategies were developed using medical subject headings (MeSH) and text words related to the topic. The following sources were used for the literature search:

1. MEDLINE OVID
2. PubMed
3. Cochrane Library
4. CINAHL
5. PROSPERO
6. Elsevier

Reference lists from each publication were screened for additional studies that match the inclusion criteria.

The literature search was limited to studies published between the 2000-2020 and to studies published in the English language.

6.3.3 Search Strategy

Database sources such as Medline OVID, Cochrane Library, PubMed, CONAHL, PROSPERO, and Elsevier were searched. No restrictions were imposed on the search however, only literature written in the English language were selected.

A draft Medline OVID search strategy is included in Appendix 6. This search strategy was adapted to search in other databases.

6.3.4 Study Records

Selection Process

The primary and secondary authors screened against the inclusion and exclusion criteria all the abstracts and titles separately and blindly. A second screening of full reports of titles and abstracts that met the inclusion criteria was carried out and documented. Disagreement on the selected studies were resolved through discussion between the primary and secondary author.

Data Collection Process

Data was extracted independently by reviewers and it includes demographic information, methodology, intervention details, results and outcomes.

6.3.5 Data Items

The following data was extracted:

Demographic data of participants including age, gender, medical history, history of ulceration; type, size and number of pressure sensing device; manufacturer of sensor

or device, anatomical placement of sensor, design of device, reference standard, trial design, population size; limitations of study; results and outcomes of validation and reliability studies. The first category shows 5 studies that have included a device that is able to measure both in-shoe pressure and temperature. The second and third category include studies that have utilized a device that is able to measure in-shoe pressure and in-shoe temperature respectively.

6.3.7 Risk of Bias Individual Studies

The assessment risk of bias of each study that met the inclusion criteria was conducted with the help of the QUADAS-2 risk assessment tool (Appendix 7). The QUADAS-2 comprises of 4 main domains. These domains are the namely patient selection, index test, reference of standard, flow and timing. For each domain, procedures from every study were described and a score on the possible risk of bias was given, finally categorized as “low risk” or “high risk”. In cases where an item was unclear, the authors were contacted for clarification. If clarification was not obtained, the item was marked as “unclear”. All studies were assessed for possible risk of bias independently by two reviewers.

6.4 Data Extraction

A thorough literature search through databases as mentioned in Section 6.3.2, identified a count of 113 trials that matched the inclusion criteria of this systematic review. An additional 5 articles were also obtained from secondary resources. Studies were included if they investigated the validity and/or reliability and/or the effectiveness of a wearable, in-shoe device, that is able to concurrently measure plantar pressures and skin temperature of the diabetic foot (n=5).

Unfortunately, due to limited published research, the inclusion criteria had to be broadened to research studies that utilized the above-mentioned devices in a non-specified population (n=3), and/or non-diabetic, healthy participants (n=1). The inclusion criteria were also extended to studies that investigated the validity and/or reliability and/or the effectiveness of in-shoe devices that measure plantar pressures alone (n=8); or wearable, in-shoe devices that measure plantar skin temperatures alone (n=6). Such inclusions were only included in this systematic review if the studies were related to the diabetic foot and/or diabetic foot ulcer prevention. Table 10, 11 and 12 show the articles that best matched the inclusion criteria of this systematic review. As

presented in these tables, the studies were categorised into 3 groups depending on the ability of the device to assess pressure (Table 11) or temperature measurements (Table 12) or both at the same time (Table 10).

Studies were excluded on the basis of using measuring techniques irrelevant to this systematic review such as, barefoot pressure mapping and thermographic cameras (that requires the patient to be barefoot and non-weight bearing in order to take measurements). Studies that have reported unrelated outcome measures, inadequate exclusion or inclusion criteria or lacked specific outcome measures from their results were excluded from this study. A total number of 10 duplicates were removed.

The studies selected were categorized into 2 main groups:

Primary Studies – articles that investigated the investigated the validity and/or reliability and/or the effectiveness of a wearable, in-shoe device, that is able to concurrently measure plantar pressures and skin temperature of the foot.

Secondary Studies – articles that investigated either the validity and/or reliability and/or the effectiveness of a wearable, in-shoe device that measures plantar pressures of the foot; and of an in-shoe device that reads and measures the temperatures of the foot.

Table 10: Data extraction sheet of characteristics extracted from studies on devices able to read pressure and temperature simultaneously.

	Study	Participant Characteristics		Index Test							Reference Standard	
	Authur & Year	Final N	Disease Severity	Index Test	Manufacturer	Measurement	Type of sensor	No. of Sensors (per foot)	Sensor Placement	Sensor Size (cm)	Reference Standard	Manufacturer
Combined Pressure and Temperature	**Morley et al. (2001)**	1	NS	In-shoe Sensor Pod	Paromed	Temperature & pressure	Resisitve	4	MTH & heel	NS	FSCAN	Tekscan Boston
	Maluf et al. (2001)	4	Healthy	4 sensors in Plastozote insert	Paromed	Temperature & pressure	Resistive	4	MTH & heel	2.55x2.05	FSCAN	Tekscan Boston
	Najafi et al. (2017)	33	DM+neuropathy	SmartSox	Novinoor LLC	Temperature & pressure	Fibre optic/ fiber Bragg gratings	5	Hallux, MTH, midfoot, heel	<0.03	FSCAN / Fluke Ti25 (IR Thermal Camera)	Tekscan Boston / Fluke Corporation
	Rescio et al. (2018)	5	NS	Smart Insole	Self designed	Temperature & pressure	FSR & Maxim (MAX30205)	8	Hallux, MTH, midfoot, heel	NS	aluminum plate with accurate temperature gradient control/BTS Pwalk platform	NS
	Rescio et al. (2020)	n/a	n/a	Temperature & pressure sensors between polyurethane based layers	Self designed	Temperature and pressure	FSR & Maxim (MAX30205)	8	n/a	NS	Baropedometry Pwalk platform/FEA simulations using Comsol Multiphysics	NS

Table 11: Data extraction sheet of characteristics extracted from studies on devices able to read in-shoe pressure only

	Study	Participant Characteristics		Index Test							Reference Standard	
	Authur & Year	Final N	Disease Severity	Index Test	Manufacturer	Measurement	Type of sensor	No. of Sensors (per foot)	Sensor Placement	Sensor Size (cm)	Reference Standard	Manufacturer
In-shoe Pressure	**Ferber et al. (2013)**	10	n/a	SurroSense Rx™ Insole	Orpyx Medical Technologies Inc	Pressure	Resistive	8	Hallux, MTH, midfoot, heel	NS	Pedar X®	Novel
	Lee et al. (2019)	23	DM+neuropathy	Pedar® X	Novel	Pressure	NS	99	Hallux, MTH, midfoot, heel	NS	n/a	n/a
	Najafi et al. (2017)	17	DM	SurroSense Rx™ Insole	Orpyx Medical Technologies Inc	Pressure	NS	8	Hallux, MTH, midfoot, heel	NS	n/a	n/a
	Ostadabbas et al. (2012)	11	NS	FlexiForce force sensors between 2 shoe insoles	NS	Pressure	NS	5	Toes, MTH, Midfoot, heel	2.54	n/a	n/a
	Shu et al. (2010)	8	NS	Insole with embedded pressure sensors	NS	Pressure	Resistive	6	MTH & heel	NS	Pedar X®	Novel
	Price et al. (2016)	n/a	n/a	Medilogic/Pedar/Tekscan	NS		Resistive/capacitive/resistive	NS/99/NS	NS	NS	TruBlue Device	NS
	Guo et al. (2012)	3	NS	Insole with embedded piezoelectric sensors	NS	Pressure	piezoelectric	8	MTH & heel	1x2x0.8	n/a	n/a
	Wang et al. (2015)	NS	NS	FreeWalker: pressure+gyroscope+accelerometer	Self designed	Pressure	NS	8	MTH, Midfoot, Heel	0.5	n/a	n/a

Table 12: Data extraction sheet of characteristics extracted from studies on devices able to read in-shoe temperature only

	Study	Participant Characteristics		Index Test							Reference Standard	
	Authur & Year	**Final N**	**Disease Severity**	**Index Test**	**Manufacturer**	**Measurement**	**Type of sensor**	**No. of Sensors (per foot)**	**Sensor Placement**	**Sensor Size (cm)**	**Reference Standard**	**Manufacturer**
In-shoe Temperature	**Reyzelman et al. (2018)**	35	DM+neuropathy	Siren Diabetic Socks	Siren Care Inc	Temperature	NS	6	Hallux, MTH, midfoot, heel	NS	High precision, thermostatic water bath + mercury thermometer	Zhejiang Jinbo Electronic Co. Ltd.
	Lugoda et al. (2018)	n/a	n/a	Temperature-sensing yarns	Murata	Temperature	Murata 10kΩ 100mW 0402 SMD NTC thermistor	16	n/a	0.087 by 0.153	NTC thermistor in an Ecotherm™ Chilling/Heating Dry Bath	Murata
	Sandoval-Palomares et al. (2016)	2	Healthy	Temperature & humidity sensors embedded in insole	Sensirion	Temperature	SHT15	5	MTH, Midfoot, Heel	5x7x3	n/a	n/a
	Coates et al. (2016)	16	Healthy	HYT271 sensors	Ardunino Nano	Temperature	capacitive	4	Hallux, MTH, midfoot, heel	NS	PT104 Pico Technology	NS
	Ming et al. (2019)	300	DM+neuropathy	Medixfeet Insole®	Thoris Technologies GmbH	Temperature	NS	6	Hallux, MTH, midfoot, heel	NS	Standard routine care	n/a
	Shoureshi & Albert (2006)	60	DM+neuropathy	Smart insole for diabetics	Self designed	Temperature	MC65F103B thermitor and Fenwal thermistor	7	Hallux, MTH, midfoot, heel	0.165cm and 0.241cm	n/a	n/a

6.5 Results

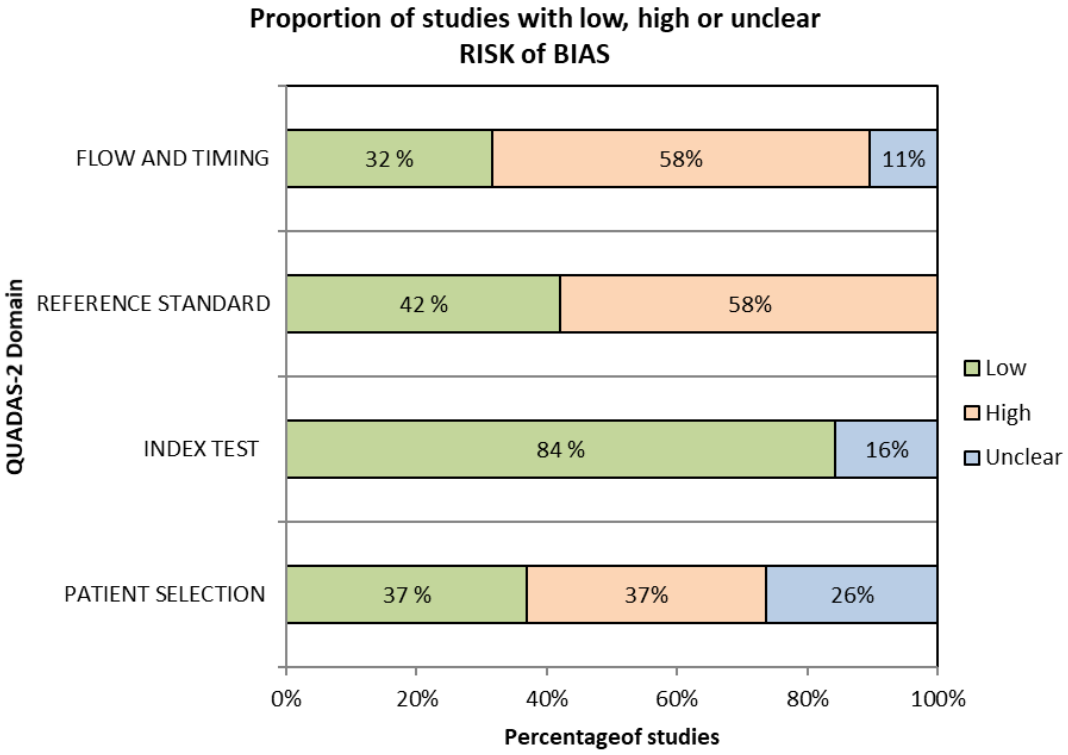
6.5.1 Quality Assessment

To assess the risk of bias and applicability for each study that have met the inclusion criteria, the primary and secondary author utilized the QUADAS-2, blindly and independently, as the preferred quality assessment tool. Procedures of every study included in this systematic review were described and scored for the possible risk of bias in relation to each and every domain of the quality assessment tool which include the patient selection domain, index test domain, reference of standard domain, flow and timing of the tool domain. Items that were unclear to the authors were clarified by contacting the author of the study however, in cases were no clarification was obtained, the item was marked as "unclear". The results of the scores of each article was presented in the tables and graphs below. Table 13 and 14 show the total and percentile scores for risk of bias of each study, for each domain of the assessment score.

Table 13: QUADAS-2 Results for Risk of Bias

	AUTHOR & YEAR OF PUBLICATION	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND
TEMPERATURE AND PRESSURE COMBINED	Morley et al. (2001)	Unclear	Low	Low	Low
	Maluf et al. (2001)	Low	Low	Low	Low
	Najafi et al. (2017)	Low	Low	Low	Low
	Rescio et al. (2018)	Unclear	Low	Low	Unclear
	Rescio et al. (2020)	High	Low	Low	High
IN-SHOE PRESSURE	Ferber et al. (2013)	Low	Low	Low	Low
	Lee et al. (2019)	Low	Low	High	Low
	Najafi et al. (2017)	Low	Low	High	High
	Ostadabbas et al. (2012)	Unclear	Low	High	High
	Shu et al. (2010)	Unclear	Low	Low	Low
	Price et al. (2016)	High	Unclear	High	High
	Guo et al. (2012)	High	Low	High	High
	Wang et al. (2015)	High	Unclear	High	High
IN-SHOE TEMPERATURE	Reyzelman et al. (2018)	Low	Low	Low	High
	Lugoda et al. (2018)	High	Low	High	High
	Sandoval-Palomares et al. (2016)	High	Low	High	High
	Coates et al. (2016)	High	Low	High	High
	Ming et al. (2019)	Low	Low	High	High
	Shoureshi & Albert (2006)	Unclear	Unclear	High	Unclear

Table 14: Bar chart showing the percentage of studies scoring high, low or unclear



With regards to the patient selection domain, 37% of the studies scored low risk of bias; 26% did not give clear description of patient population recruited and 37% of the studies had a very small sample size (n=17) and thus scored high-risk of bias. With regards to the index test domain 84% of the studies scored low risk of bias. The reference standard domain showed that 58% of the studies scored high-risk of bias on the use of a reference standard where 42% (low risk) reported the use of an appropriate reference standard. Lastly, with regards to the flow and timing domain, only 32% of the studies reported adequate flow and timing of the study (low risk of bias).

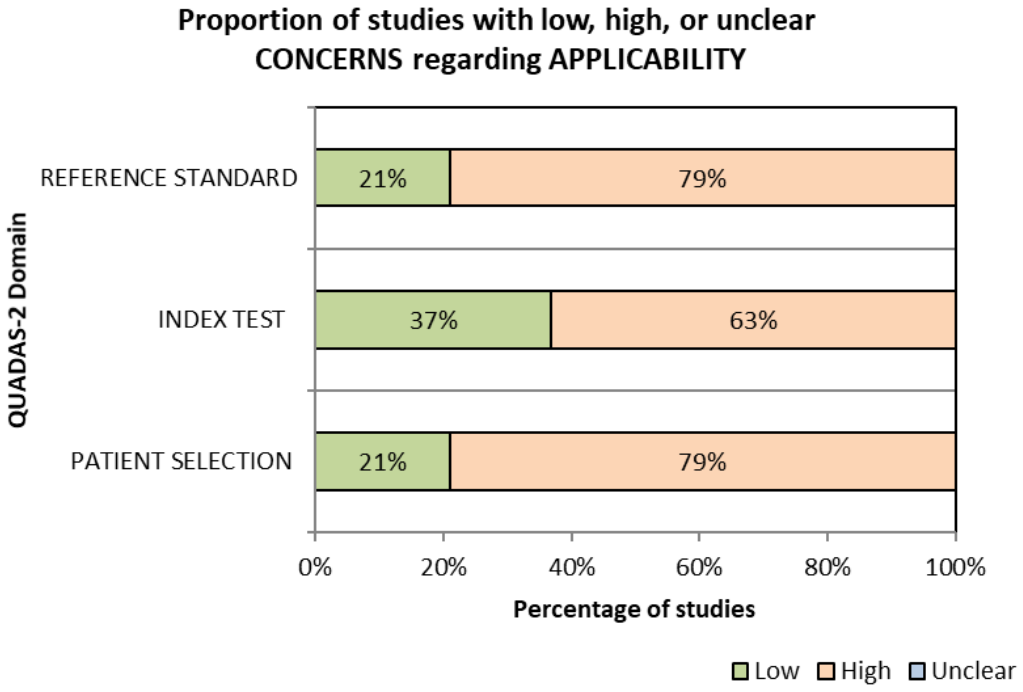
Table 15 and 16 below show the total scores for the risk of applicability of each study, for each domain of the assessment score. A high percentage of the studies scored high-risk of applicability in terms of patient selection (79%), index test (63%) and reference standard (79%). As these studies were conducted on healthy participants and recruited small sample sizes that averaged to n=17 participants furthermore, some of the studies did not specify the patient population recruited in the study. With regards to the applicability of the index test domain, the majority of the studies utilized an in-shoe device able to read and measure pressure only or temperature only and not in a combined form. Lastly, over 50% of the studies did not report the use of a reference

standard, or utilized a non-in-shoe device as a reference standard, to determine the validity of their device.

Table 15: QUADAS-2 Results for Risk of Applicability

	AUTHOR & YEAR OF PUBLICATION	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD
TEMPERATURE AND PRESSURE COMBINED	Morley et al. (2001)	High	Low	High
	Maluf et al. (2001)	High	Low	High
	Najafi et al. (2017)	Low	Low	Low
	Rescio et al. (2018)	High	Low	Low
	Rescio et al. (2020)	High	Low	Low
IN-SHOE PRESSURE	Ferber et al. (2013)	High	High	High
	Lee et al. (2019)	High	High	High
	Najafi et al. (2017)	Low	Low	High
	Ostadabbas et al. (2012)	High	High	High
	Shu et al. (2010)	High	High	High
	Price et al. (2016)	High	High	High
	Guo et al. (2012)	High	High	High
	Wang et al. (2015)	High	High	High
IN-SHOE TEMPERATURE	Reyzelman et al. (2018)	Low	Low	Low
	Lugoda et al. (2018)	High	High	High
	Sandoval-Palomares et al. (2016)	High	High	High
	Coates et al. (2016)	High	High	High
	Ming et al. (2019)	Low	High	High
	Shoureshi & Albert (2006)	High	High	High

Table 16: Bar chart representing the percentage of studies scoring the applicability to this review



6.5.2 Participant Characteristics

This systematic review looked at which patient population was the validation and/or reliability testing of the devices were carried upon. In total, 15 out of 19 studies conducted their investigations with the help of human participants of which, 3 studies recruited healthy individuals (Maluf et al., 2001; Sandoval-Palomares et al., 2016; Coates et al., 2016), 6 studies did not specify their patient population or any involvement of participants at all (Ferber et al., 2013; Price et al., 2016; Lugoda et al., 2018; Rascio et al., 2020), 5 studies were conducted on patients living with diabetic neuropathy (Shoureshi & Albert, 2006; Najafi et al., 2017; Reyzelman et al., 2018; Lee et al., 2019 Ming et al., 2019) and finally, 1 study was conducted on patients living with diabetes mellitus (Najafi et al., 2017). Though the studies by Ferber et al. (2013), Price et al. (2016), Lugoda et al. (2018) and Rascio et al. (2020) did not specify whether or not their participants lived with diabetes mellitus, were healthy or had any other medical condition, the aim of these studies was to validate or confirm the reliability of their device in view of diabetic foot ulcer prevention.

Overall, 14 out of 19 studies included in this systematic review reported to have recruited an average of 11 participants, with the exception of the studies conducted by

Ming et al. (2019), who reported to have conducted their research on 300 participants living with diabetic neuropathy and Shoureshi and Albert (2006) who reported to have conducted their research on 60 participants also living with diabetic neuropathy. None of the studies included in this systematic review reported to have calculated and determined the sample size of the population being investigated through power calculation analysis. The magnitude of sample size plays a fundamental role, in providing precise and accurate conclusions (Nayak, 2010). A small sample size may not be powerful enough to distinguish between measurements of true or surrogate exposures this leads to false negative results and type II errors which inability reject the null hypothesis (Nayak, 2010). In simple words, a small sample size may not be powerful enough to permit the researcher to generalise the results to the true population being studied.

From the studies that have specified the mean age of their participants, it was concluded that the mean age of participants of the included studies was equivalent to 38.54 years (Maluf et al., 2001; Shu et al., 2010; Guo et al., 2012; Ostadabbas et al., 2012; Ferber et al., 2013; Coates et al., 2016; Najafi et al., 2017; Lee et al., 2019; Reyzelman et al., 2018). Some studies did not report specific mean ages of their participants but reported an age range between 18 to 85 years of age (Sandoval-Palomares et al., 2016; Najafi et al., 2017; Ming et al., 2019).

Unfortunately, the majority of studies did not report their inclusion (n=10) and exclusion criteria (n=11). The remaining studies included participants who had diabetic peripheral neuropathy (n=4) walked unaided and have had a past history of ulceration for the past 18 months (n=5). The exclusion criteria varied; namely history of amputation, inability to ambulate, other gait impairments, foot deformity, Charcot foot, inflection and arthropathy, active tumour and participation in other studies. An overview of the identified in-shoe pressure and/or temperature devices is given in table 17 below.

Table 17: An overview of identified temperature and pressure sensing devices

Category		Authors	Device	Manufacturer	Type of sensor	Qty.	Sensor Placement	Size (cm)
Primary Studies	Temp. & Pressure Combined	Morley et al. (2001)	In-shoe Sensor Pod	Paromed	Resistive	4	med., cent., lat.MTH; heel	n/a
		Maluf et al. (2001)	Multisensory Data Acquisition Device	Paromed	Resistive	4	MTH1,3,5; heel	2.55x2.05
		Najafi et al. (2017)	SmartSox	Novinoor LLC	Fibre optic FBGs	5	hallux; MTH1,5; midfoot; heel	<0.03
		Rescio et al. (2018)	Smart Insole	Self designed	FSR & Maxim	8	hallux; MTH1-5; midfoot; heel	n/a
		Rescio et al. (2020)	Temperature/pressure sensors in PU	Self designed	n/a	8	not specified	n/a
Secondary Studies	Pressure	Ferber et al. (2013)	SurroSense Rx™ Insole	Orpyx Medical Tech. Inc	Resistive	8	heel; lat.foot; MTH1; MTH5; hallux; lat.toes	n/a
		Lee et al. (2019)	Pedar® X	Novel	n/a	99	hallux; med.ff, lat.ff; midfoot; heel	n/a
		Najafi et al. (2017)	SurroSense Rx™ Insole	Orpyx Medical Tech. Inc	n/a	8	MTH; lat.foot; heel; hallux; lat.toes	n/a
		Ostadabbas et al. (2012)	FlexiForce force sensors between 2 insoles	not specified	n/a	5	toes; MTH1-3,5; heel	2.54
		Shu et al. (2010)	Insole with embedded pressure sensors	not specified	Resistive	6	forefoot; heel	n/a
		Price et al. (2016)	Medilogic/Pedar/Tekscan	not specified	Resistive/capacitive	n/a	not specified	n/a
		Guo et al. (2012)	Insole with embedded piezoelectric sensors	not specified	piezoelectric	8	lat., med.heel; MTH1-5	1x2x0.8
		Wang et al. (2015)	FreeWalker	Self designed	n/a	8	D2; MTH1,3,5; lat.midfoot; heel	0.5
	Temperature	Reyzelman et al. (2018)	Siren Diabetic Socks	Siren Care Inc	n/a	6	hallux; MTH1,3,5; midfoot; heel	n/a
		Lugoda et al. (2018)	Temperature-sensing yarns	Murata	NTC thermistor	16	n/a	0.087x0.153
		Sandoval-Palomares et al. (2016)	Temperature/humidity sensors in insole	Sensirion	SHT15	5	forefoot; midfoot; hindfoot	5x7x3
		Coates et al. (2016)	HYT271 sensors	Ardunino Nano	capacitive	4	heel; MTH1,5; hallux	n/a
		Ming et al. (2019)	Medixfeet Insole®	Thoris Technologies	n/a	6	hallux; MTH1,3,5; lat.midfoot; heel	n/a
		Shoureshi & Albert (2006)	Smart insole for diabetics	Self designed	Fenwal thermistor	7	MTH; heel; hallux	0.165; 0.241

6.5.6 Randomization

Reporting of whether or not the sample selection was random is fundamental as randomization controls whether the measurements of true exposures differ from the measurements of surrogate exposures with respect to any variable, known or unknown to the researcher, that might influence the results. In other words, randomization promotes comparability between two studied entities, and allows for a probabilistic basis for an inference from the concluded results (Rosenberger & Lachin, 2002).

Although 15 studies have recruited participants, only 4 have reported randomization of their sample population. The remaining studies (n=11) have not clearly reported whether their participant selection was random or not.

6.5.7 Comparison to Reference Standard

A reference standard refers to the best test or method of diagnosing or measuring something that is currently available. It is the "gold standard" technique, method, or instrument against which the index test is compared to.

In this systematic review, 11 out of 19 studies selected have validated their results against a reference standard (Morley et al., 2001; Maluf et al., 2001; Shu et al., 2010; Ferber et al., 2013; Price et al., 2016; Coates et al., 2016; Reyzelman et al., 2018; Lugoda et al., 2018; Rescio et al., 2018; Ming et al., 2019; Rescio et al., 2020). It is empirical to point out that, as of yet, a "gold standard" device that measures both foot plantar pressures and temperatures concurrently is not available. In view of this, it is understandable why comparison had to be performed with two individual reference standards; that is, a reference standard for measuring pressure and another for measuring temperature. It was noted that studies by Morley et al. (2001) and Maluf et al. (2001), reported only one pressure measuring reference standard, against which their in-shoe temperature and pressure measuring device was validated. Table 18 and 19 outlines the number of studies which utilized a reference standard to validated their results.

Table 18: Table showing the reference standard used for device with combined pressure and temperature

	Author & Year	Index Test	Reference Standard	Manufacturer
Combined Pressure and Temperature	**Morley et al. (2001)**	In-shoe Sensor Pod	FSCAN	Tekscan Boston
	Maluf et al. (2001)	Plastazote insert fitted with 4 sensors	FSCAN	Tekscan Boston
	Najafi et al. (2017)	SmartSox	FSCAN / Fluke Ti25 (IR Thermal Camera)	Tekscan Boston / Fluke Corporation
	Rescio et al. (2018)	Smart Insole	aluminum plate with accurate temperature gradient control/BTS Pwalk platform	NS
	Rescio et al. (2020)	Temperature and pressure sensors between polyurethane-based layers	Baropedometry Pwalk platform/FEA simulations using Comsol Multiphysics	NS

Table 19: Table showing the reference standard used for device that read in-shoe pressure and in-shoe temperature

	Author & Year	Index Test	Reference Standard	Manufacturer
In-shoe Pressure	**Ferber et al. (2013)**	SurroSense Rx™ Insole	Pedar X®	Novel
	Lee et al. (2019)	Pedar® X	n/a	n/a
	Najafi et al. (2017)	SurroSense Rx™ Insole	n/a	n/a
	Ostadabbas et al. (2012)	FlexiForce force sensors between 2 shoe insoles	n/a	n/a
	Shu et al. (2010)	Insole with embedded pressure sensors	Pedar X®	Novel
	Price et al. (2016)	Medilogic/Pedar/Tekscan	TruBlue Device	NS
	Guo et al. (2012)	Insole with embedded piezoelectric sensors	n/a	n/a
	Wang et al. (2015)	FreeWalker: pressure+gyroscope+accelerometer	n/a	n/a
In-shoe Temperature	**Reyzelman et al. (2018)**	Siren Diabetic Socks	thermostatic water bath + mercury thermometer	Zhejiang Jinbo Electronic Co. Ltd.
	Lugoda et al. (2018)	Temperature-sensing yarns	NTC thermistor in an Ecotherm™ Chilling/Heating Dry Bath	Murata
	Sandoval-Palomares et al. (2016)	Temperature + humidity sensors in insole	n/a	n/a
	Coates et al. (2016)	HYT271 sensors	PT104 Pico Technology	NS
	Ming et al. (2019)	Medixfeet Insole®	Standard routine care	n/a
	Shoureshi & Albert (2006)	Smart insole for diabetics	n/a	n/a

6.6 Outcome Measures

6.6.1 Type and Size of Sensing Devices

As previously mentioned, a "gold standard" for the simultaneous measurement of both in-shoe pressure and temperature parameters has not yet been established. This systematic review has only identified 3 studies that have developed and validated a device that is able to read and measure in-shoe plantar pressures and foot skin temperatures contemporarily simultaneously (Morley et al., 2001; Maluf et al., 2001; Najafi et al., 2017). For instance, the SmartSox device by Novinoor LLC was validated in a study by Najafi et al. (2017). This device was reported to incorporate fibre optic sensors based on Fibre Bragg Gratings (FBGs) which were reported to measure less than 0.03cm, made of weightless, thin and highly flexible silica, and wrapped in plastic.

The speciality of these types of sensors is that they are able to reflect specific wavelengths of infrared light. Morley et al. (2001) and Maluf et al. (2001) presented a device which used a resistive type of hydrocell sensor originally developed by Paromed. This device was reported to be able to read temperature and pressure simultaneously. Though the study by Morley et al. (2001) failed to specify the size of the Paromed senor, Maluf et al. (2001) reported to have used a sensor that measured 2.55cm by 2.05cm in dimension. As shown in Table 20 below, the most popular type of sensors were mostly resistive sensors of which among the favourites were balanced resistive bridges, Resistance Temperature Detectors (RTDs), Force Sensing Resistors (FSRs) and thermistors. Other choices of sensors included capacitive and piezoelectric sensors measuring.

Table 20: Table showing the type of sensor used per study

Type of Sensor	Type of measurement	No. of Studies
Balanced resistive bridges; RTD*	Pressure; Temperature	1
Resistive not specified	Pressure	4
Fibre optic based on FBGs	Temperature and pressure	1
Force Sensing Resistor (FSR); Maxim (MAX30205)*	Pressure; Temperature	1
Capacitive not specified	Temperature	2
Piezoelectric	Pressure	1
Murata NTC thermistor	Temperature	1
SHT15	Temperature and humidity	1
capacitive	Temperature	1
MC65F103B thermistor and Fenwal (NTC) thermistor	Temperature	1
**A combination of*		

The ability of a sensor to accurately detect pressure change is highly dependent on the size of the sensor used (Ostadabbas et al., 2012). The size of sensor also plays a fundamental role in terms of portability, in-shoe fitting and comfort during clinical and research assessments. For instance, in the study by Pataky et al., (2000) and Ostadabbas et al., (2012), small-sized pressure sensors were reported to underestimate the pressure forces acting upon them furthermore, due to their small size, the user might find it difficult to place the sensor well to receive the peak pressure (Ostadabbas et al., 2012). Though large sensors are more likely to contain the peak pressure, and thus better at detecting pressure change, the pressure readings may still result to be a significant under-estimation of peak pressure (Pataky et al., 2000; Shu et al., 2010; Ostadabbas et al., 2012).

The recommended sensor size is that of 0.5cm by 0.5cm or greater. Sensors of a smaller size are recommended to be used in form of an array (Razak et al. 2012). Furthermore, bulky instrumentation in gait analysis may bring inconvenience and discomfort during clinical assessment influencing the patient's natural walk. In this systematic review, 11 of the selected studies failed to specify the size of the sensor used. With regards to temperature sensors, the recommended size to avoid

measurement errors as much as possible was that of 0.87 in diameter (Lugoda et al.,2018). Table 21 below, summarizes the reported sensor sizes.

Table 21: Table showing the type of index test per study

Authors	Index Test	Type of sensor	Sensor Size (cm)
Morley et al. (2001)	In-shoe Sensor Pod	Pressure=balanced resistive bridges; temperature=resistive RTD	not specified
Maluf et al. (2001)	Plastazote insert fitted with 4 sensors	Resistive	2.55 by 2.05
Najafi et al. (2017)	SmartSox	Fibre optic based on FBGs	<0.03
Rescio et al. (2018)	Smart Insole	FSR & Maxim	not specified
Rescio et al. (2020)	Temperature & pressure sensors between PU based layers	FSR & Maxim	not specified
Ferber et al. (2013)	SurroSense Rx™ Insole	Resistive	not specified
Lee et al. (2019)	Pedar® X	not specified	not specified
Najafi et al. (2017)	SurroSense Rx™ Insole	not specified	not specified
Ostadabbas et al. (2012)	FlexiForce force sensors between 2 shoe insoles	not specified	2.54
Shu et al. (2010)	Insole with embedded pressure sensors	Resistive	not specified
Price et al. (2016)	Medilogic/Pedar/Tekscan	Resistive/capacitive/resistive	not specified
Guo et al. (2012)	Insole with embedded piezoelectric sensors	piezoelectric	1 by 2 by 0.8
Wang et al. (2015)	FreeWalker	not specified	0.5
Reyzelman et al. (2018)	Siren Diabetic Socks	not specified	not specified
Lugoda et al. (2018)	Temperature-sensing yarns	Murata NTC thermistor	0.087 by 0.153
Sandoval-Palomares et al. (2016)	Temperature and humidity sensors embedded in insole	SHT15	5 by 7 by 3
Coates et al. (2016)	HYT271 sensors	capacitive	not specified
Ming et al. (2019)	Medixfeet Insole®	not specified	not specified
Shoureshi & Albert (2006)	Smart insole for diabetics	MC65F103B thermistor and Fenwal (NTC) thermistor	0.165 and 0.+C47+A

6.6.2 Number & Placement of Sensors

This systematic review also looked at the number of sensors used per study and at which anatomical landmark were these or the sensor/s placed. It was identified that the most common anatomical landmark at which the sensor/s was placed coincided with the medio-plantar and the lateral aspect of the 1st metatarsal head and the plantar aspect of the heel (Table 22).

Table 22: Table showing the anatomical landmarks used for sensor placement per study

Anatomical Landmark	Number of studies
Medial MTH	12
Lateral MTH	12
Central MTH	7
Heel	16
Hallux	9
Midfoot	7
Lateral Toes	3
not specified	2

Studies reported that placement of sensors was based on previously ulcerated sites or sites which were identified to have elevated peak plantar pressures which corresponded to the medio-plantar and the lateral aspect of the 1st metatarsal head and the plantar aspect of the heel (Shu et al., 2009; Ostadabas et al., 2012; Ferber et al., 2013; Najafi et al., 2017; Rescio et al., 2018). Guo et al. (2012), and later Wang et al. (2015), reported to have distributed the pressure sensors throughout the plantar aspect of the foot as the authors wanted to quantify the highest pressures applied to each region of the foot as they occur during foot contact.

Like in the study by Ferber et al. (2013), Rescio et al. (2018) positioned 8 pressure sensors over the anatomical landmark that corresponded to the medio-lateral aspect of the heel, 1st to 5th Metatarsal head, midfoot and hallux. In addition to the pressure sensors, a temperature sensor was added at each site (Rescio et al., 2018). The SurroSense Rx system by Orpyx Medical Technologies (Najafi et al., 2012) and the device developed by Guo et al. (2012) both comprised of 8 pressure sensors in total. The device developed by Shu et al. (2009) comprised of 6 sensors, while that of Ostadabbas et al. (2012) had 5 sensors in all. The highest number of sensors identified where thoses of Pedar X by Novel which incorporated a total of 99 sensors which were built in an array throughout the plantar aspect of the foot (Lee et al., 2019).

The studies by Price et al. (2016) and Lugoda et al. (2018) did not report to have involved any participants in their investigations and thus anatomical placement of sensors was not relevant to these studies. The remaining 5 studies reported to have used an average of 6.4 sensors however, the choice for having selected the reported anatomical landmarks was not reported.

Table 23 below summarises the overall number of sensors used per device.

Table 23: Table showing number of sensors used per device

Authors	Index Test	Number of Sensors (per foot)
Morley et al. (2001)	In-shoe Sensor Pod	4
Maluf et al. (2001)	Plastazote insert fitted with 4 sensors	4
Najafi et al. (2017)	SmartSox	5
Rescio et al. (2018)	Smart Insole	8
Rescio et al. (2020)	Temperature & pressure sensors between PU based layers	8
Ferber et al. (2013)	SurroSense Rx™ Insole	8
Lee et al. (2019)	Pedar® X	99
Najafi et al. (2017)	SurroSense Rx™ Insole	8
Ostadabbas et al. (2012)	FlexiForce force sensors between 2 shoe insoles	5
Shu et al. (2010)	Insole with embedded pressure sensors	6
Price et al. (2016)	Medilogic/Pedar/Tekscan	not specified/99/not specified
Guo et al. (2012)	Insole with embedded piezoelectric sensors	8
Wang et al. (2015)	FreeWalker	8
Reyzelman et al. (2018)	Siren Diabetic Socks	6
Lugoda et al. (2018)	Temperature-sensing yarns	16
Sandoval-Palomares et al. (2016)	Temperature/humidity sensors embedded in insole	5
Coates et al. (2016)	HYT271 sensors	4
Ming et al. (2019)	Medixfeet Insole®	6
Shoureshi & Albert (2006)	Smart insole for diabetics	7

6.6.3 Presentation of the Device

Figure 31 below shows that a great proportion of the selected studies presented their device as an insert or insole which fitted within the subject's footwear. A small selection of studies has created temperature and/or pressure sensitive socks or yarns which might be used as a wearable textile in future research.

One single study designed their device in the form of a pod, described as four combined hydrocell pressure and temperature sensors encased in a plastic enclosure that measures 16.8cm by 8.5cm by 3.5 cm (Morely et al., 2001). The device was designed to fit comfortably over the insole of the subject's footwear.

Another study presented their device in a very raw form described as 3 individual pressure sensors and 1 temperature sensor, wired to a micro-USB connector for flexibility and robustness (Coates et al., 2016). The sensors and microcontroller were attached directly onto the subject's foot with adhesive tape (Coates et al., 2016).

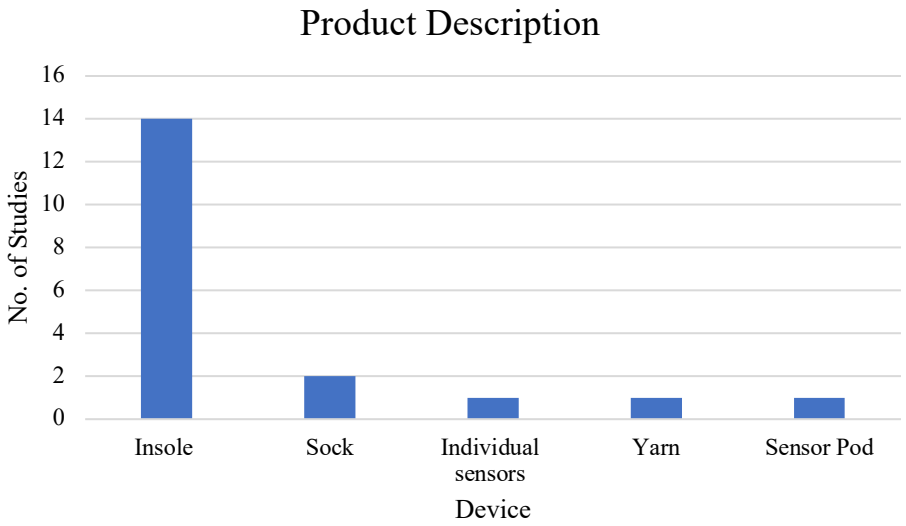


Figure 31: Graph showing the commonest type of device design used

6.6.4 Validity and Reliability Assessment

Having a valid and reliable device is very essential if it is to be introduced in a clinical setting. A reliable device is one which is able to give the consistent results over time, across subjects and across different users. A valid device is one which is able to measure what it was designed to measure or monitor, and for that measurement to correspond well to the actual measurements. The value of the validity results increases when the results of the index test are compared to a reference standard in the validation study. In this systematic review nearly all studies (n=19) were able to validate their pressure and/or temperature sensing device however, only a handful (n=7) compared it against a reference standard. Moreover, with regards to reliability this systematic review has identified that out of 19 studies, only 6 studies have reported to have tested their device for its reliability.

Combined in-shoe pressure and temperature sensing devices

The In-shoe Sensor Pod (Morley et al., 2001) and the Plastazote insert by Maluf et al. (2001), both devices design to measure in-shoe temperature and in-shoe pressure, were found to have a high correlation between the Fscan system, which served as a reference standard in both studies (Maluf et al., 2001; Morely et al., 2001). It is important to highlight that the pressure data collected in these studies were taken over a single step. Moreover, no reference standard for the temperature sensing device was reported to have been used in the study by Morely et al. (2001). Unlike Morley et al. (2001), in the study by Maluf et al. (2001), the use of a reference standard for temperature was reported. Though the data recorded showed lower values compared to the criterion values, the overall results showed a high correlation between the index test and reference standard for the measurements of in-shoe temperatures. Both the in-shoe Sensor Pod (Maluf et al., 2001) and the Plastazote insert (Morley et al., 2001) proved reliably in measuring both pressures and temperatures over time. Maluf et al. (2001) reported that the In-shoe Sensor Pod was able to produce outcomes remained consistent between temperatures of 20-35 degrees Celsius, over a period of 8 hours of use.

Another device that was found to have high correlation with its reference standard was the SmartSox device that was investigated by Najafi et al (2017). In their study, the SmartSox device was tested for its validity against the FScan system which as in the study by Maluf et al. (2001) and Morley et al. (2001) served as reference standard. Results of their study concluded that the SmartSox system was accurate in detect changes in in-shoe temperature and pressure measurements with minimal cross talk. Finally, the study by Rascio et al. (2018) also confirmed the validity of their in-shoe temperature and pressure system as it showed good level of performance and high accuracy in detecting pressure and temperature.

In-shoe pressure sensing devices

In the study by Ferber et al. (2013), the index test was found to have good correlation when compared against its reference standard (Pedar X by Novel). Specifically, only 2 out of 8 sensors were reported to have had poor correlation. The authors reported that the accuracy of a sensor was noted to be depended on the placement of the sensor and on the line of travel and velocity of movement of the center of pressure of the individual being assessed. For this study, it was apparent that the longer the center of pressure remained focused on a specific area, such as the hindfoot and the 1st Metatarsal Head, the more accurately the sensor was able to read the pressure. Shu et al. (2010) reported to have obtained similar results as Ferber et al. (2013), where their index test was able to measure pressure change just as well as the reference standard. The authors further reported that adding an additional sensor at the hallux and midfoot may improve the accuracy of the device.

In the study by Price et al. (2016), the validity and repeatability of the Pedar X, the Fscan and the Medilogic system were quantified across a range of applied pressures and durations. Results of this study demonstrated the most accurate measurements in terms of contact area were delivered by the Medilogic system and that the highest average errors were delivered by the Fscan system possibly because the sensors are embedded within a thin plastic film which might have created cross-talk between the material and the sensors (Price et al., 2016). The Medilogic and Pedar system are made of a soft foam material which could have given a more balanced distribution of the load subjected to it (Price et al., 2016). It was also noted that the Pedar X device tended to give varied pressure measurements depending on the size of insole whereas the pressure readings read by the Medilogic and Tekscan systems remained constant irrelevant to the size of insole (Price et al., 2016). Lastly, this study showed overall good repeatability for all 3 commercial in-shoe pressure devices especially for pressure readings that were above 100kPa (Price et al., 2016). The lowest repeatability for peal pressures across the entire insole was that of the Fscan system (Price et al., 2016).

The study by Guo (2012) validated a piezoelectric based, self-designed, in-shoe pressure sensing device during standing and walking. Moreover, their device was deemed reliable when tested both indoors and outdoors with pressure readings corresponding to the actual clinical measurements of the participant (Guo 2012). Another 8-pressure sensor in-shoe pressure device, the FreeWalker, was also validated in a study by Wang et al. (2015). The authors of the study reported good validation results which confirmed the device as accurate in measuring plantar foot pressure and motion sequences in real time with a data transmission of up to 20 meters (Wang et al, 2015).

Despite the good validation results reported by Pataky et al., (2000), Ostadabbas et al., (2012), Guo (2012) and Wang et al. (2015), none of these studies reported the use of a reference standard to compare and confirm that the pressure readings measure by the index test correspond to those of an already established and validated device.

Lee et al. (2019) conducted a test-retest reliability study which confirmed that their in-shoe pressure device was able to reliably measure all peak plantar pressures. The study was conducted on patients living with diabetes mellitus with previous history of diabetic foot ulceration and results demonstrated good reliability especially when measuring the medial forefoot of a non-ulcerated foot, the heel area of a non-ulcerated foot and the lateral forefoot of both ulcerated and non-ulcerated feet (Lee et al. 2019). The study also highlighted that patient with a history of plantar diabetic foot ulceration exhibited higher peak plantar pressures over the hallux and forefoot regions compared to non-ulcerated feet. No statistical difference was reported between the previous history of foot ulceration and no history of foot ulceration for the midfoot and heel region (Lee et al. 2019).

In-shoe temperature sensing devices

The in-shoe temperature device investigated by Sandoval-Palomarez et al. (2016) was validated for its ability to measure in-shoe temperature change for over 8 continuous hours. In this study, the use of a reference standard to confirm that the temperature

readings measure by the index test correspond to those of an already established and validated device, was not reported.

The Siren Diabetic Socks were tested for their reliability in measuring in-shoe plantar foot temperatures in view of diabetic foot ulcer prevention. Results of the study confirmed the device to be accurate and reliable in measuring in-shoe temperature changes that range from 20°C-40°C results which corresponded to those of the reference standard (Reyzelman, A.M. et al., 2018).

6.6.5 Responsiveness

By definition, responsiveness is the ability of a device to detect changes in a specific measurement of interest over a period of time and within the concept being measured (Mokkink et al., 2010; Terwee, 2014). Though it may sound similar to validity, responsiveness is deemed as part of validity, where validity is set over one time point, responsiveness is set over different time points that change over time (Husted et al., 2000; Terwee, 2014). The assessment of longitudinal validity has been suggested as a measure for responsiveness as to date there is no consensus on the best method to prove responsiveness of a device (Husted et al., 2000). This systematic review highlighted that none of the included studies tested for responsiveness or longitudinal validity of their device thus, responsiveness of the index could not be determined for this systematic review.

Simple validation testing on the devices, as reported in studies included in this systematic review, resulted effective in detecting changes in-shoe pressure and temperature measurements. These devices show potential for further research and they can be used to early detect pre-ulcerative inflammation and ulcer development (Sandoval-Palomares et al., 2016; Coates et al., 2016).

6.7 Meta-Analysis

Meta-analysis is a quantitative approach of combining the results of a number of scientific studies and it is performed to provide more precise, statistical evaluation of the measurement effect of an investigation. For meta-analysis to be conducted,

homogeneity (equality) of study outcomes is key (Haidich, 2010). In this systematic review, meta-analysis could not be performed as there was a variety in participant characteristics and type of devices used.

6.8 Discussion

Local health care economy is currently sustaining a great burden due to the high rate of diabetic foot ulceration which often lead to higher risk of infections, hospital admissions and amputations (Cuschieri, 2020; Schembri et al., 2021). Monitoring of predictive factors such as inflammation, and pressure re-distribution off the ulcerated area, help in preventing recurrence of plantar ulceration (Armstrong et al., 2017; Bus et al., 2013; Ulbrecht et al., 2014).

As previous, similar systematic reviews stated, the role of skin temperature and plantar pressures in the causation of diabetic foot ulcers has only been investigated in a limited number of studies (Bus, 2016; Jones, Bibb, Davies et al., 2020). Bus (2016) reported that contemporary technological device that are being developed to predict the development of diabetic foot ulceration by monitoring foot pressures are encouraging however, further improvement and clinical validation is required (Bus, 2016). The authors Jones, Bibb, Davies et al. (2020) reported that diabetic foot ulcer prediction remains clinically difficult to predict ulcer risk factors such as temperature and pressure are not being monitored together as a whole (Jones, Bibb, Davies et al., 2020). In agreement to what these reviews have stated, in this systematics review, study results of all included studies have shown that only 19 studies have conducted validation tests on their device and that only 5 of these 19 studies tested in-shoe devices that had a combination of both temperature and pressure sensors. A great variation in the methodological approach in between studies including patient medical history and sample size was also noted. Despite these included studies based their research on the validation of a device to predict diabetic foot ulceration by monitoring in-shoe pressure and/or in-shoe temperatures, only 25% of these studies conducted their study on participants living with diabetes mellitus. Fifteen per cent (15%) of the remaining studies included in this systematic review conducted their research on healthy

participants, and 30% did not specify the medical history of their participants. Finally, another 20% of the selected studied did not include participants in their validation studies.

As previously mentioned, the outcomes of a validation study, are considered as more valid when compared to a reference standard. In this review, only 11 studies compared their index test to a reference standard. All studies from the first category (*n*=5), device that can measure pressure and temperature concurrently, validated their index test against a reference standard however, only 3 out of those 5 had a reference standard for both the temperature and pressure sensor to compare it with. Due to the lack of an already established "gold standard" device that measures in-shoe plantar temperatures, studies validated their in-shoe temperature sensor in against a temperature sensing device that was too bulky or in-flexible to fit within footwear such examples include mercury thermometer and the infrared thermal camera.

Studies investigating the longitudinal validity of an in-shoe temperature and/or pressure sensing device were not found thus, responsiveness of the device could not be determined in this review. It was also disappointing to find that only 6 studies have performed reliability testing on the index test and that these tests were conducted on small sample sizes (mean *n*=17) and despite focusing their study on diabetic foot ulcer prevention, only 2 studies included participants living with diabetes mellitus.

The most common limitation identified throughout this review is power consumption and limited capacity of data sampling and storage during data collection. Devices were noted to have a high energy expenditure depleting the battery life exponentially. This effected how long the system could be used wirelessly during the collection of data. It is possible that this high energy consumption is attributed to the high levels of frequency used to collect the data. A study suggested that by lowering the data collection frequency, the total energy consumption should reduce, preserving enough power to last a whole day (Morley et al., 2001). Despite the recommended sampling rate of at least 50Hz for data collection of dynamic plantar pressures, authors suggested that a data collection frequency of 4Hz is more than enough to acquire the necessary

data. Furthermore, studies suggested that data compression could be an adequate technique to lengthen the period, by over 8hrs of data recording and sampling (Morley et al., 2001; Ferber et al., 2013). Given that the data collection will be acquired through a lower frequency, the prolonged energy consumption will promote battery life and thus will prolong the length of time at which the data is collected. This will compensate and allow missing data points to be collected over multiple footsteps (Ferber et al., 2013).

Another factor that may have contributed to the slight variances in results between the index test and the reference standard (Ostadabbas et al 2012; Price et al., 2016), may be attributed to the difference in resolution and frequency of data collection. It is common knowledge that these differences are why studies cannot find a common ground on which to base a true pressure threshold that can specifically predict the development of diabetic foot ulceration.

Sensor size and placement was a very important outcome not to be overlooked. Common anatomical landmark for sensor placement included the metatarsal area particularly the first and fifth metatarsal head, hallux, the heel and the midfoot. The study by Ferber et al. (2013) have identified that sensors placed at anatomical areas over which the Center of Pressure (CoP) moved rapidly, the data of the index test exhibited poor correlation to the reference standard. Conversely, sensors placed at anatomical areas over which the CoP moved at a slower pace, both data collected by the index test and the reference standard correlated excellently. The larger the number of sensors place within an insole or device, the higher is the risk of sensor cross-talk (Price et al., 2016) leading to higher risk of errors. Furthermore, compared to small sized sensors, large sized sensors are more accurate to detect pressure change however, they predispose a higher risk of underestimating true peak pressures (Ostadabbas et al., 2012).

Material and size of insole also plays an important role in detecting pressure change. Ostadabbas et al. (2012) have identified that soft materials provide a more even distribution of pressure and increasing the contact area between the foot and sensors

thus altering the true estimate of peak plantar pressure. When using multiple sensors, it is possible that the resolution reduces with size of insole (Price et al., 2016).

6.9 Recommendations

Due to the low quality of evidence that was identified in this systematic review, more research on the longitudinal validity and reliability of the in-shoe devices that measure both plantar foot pressures and temperature presented in this systematic review is recommended. Ideally, the studies should be conducted on large randomized sample size that will accurately represent the diabetic population especially those considered at a high-risk of ulceration. Studies that test for longitudinal validity will be testing for responsiveness of their device which would help them better determine the accuracy of their device in detecting pressure and/or temperature change. Last but not least, a reference standard should be used in the studies so that the outcomes of the index test can be compared to the outcomes of an already established and validated device.

6.10 Conclusion

This systematic review aimed to provide a thorough analysis of current literature that relate to various technologies developed purposively to assess and monitor in-shoe plantar pressures, and in-shoe skin temperatures. Their evidence of validity, reliability and responsiveness was compared. A comprehensive understanding of their role as an identification technique for foot plantar ulceration and/or re-ulceration of the diabetic high-risk foot was identified.

Though further research is required in this field, current literature has paved the way to a new era where it is possible to predict pre-ulcerative inflammation and peak plantar pressures prior an ulcer develops. Through the development, validation and reliability testing of these devices research studies will be able to gather valuable information about the true relationship between in-shoe foot temperature and pressure and how they contribute to skin breakdown. With obtaining such information, a clinician will be able to predict the formation of an ulcer and provide treatment accordingly. The device can be used as part of the management plan for patients living

with diabetes mellitus who are prescribed with prescription orthoses and fill the gap for objective assessment for diabetic foot examination. Prescription insoles can be evaluated for their effectiveness at dispensing; and monitored for their effectives in relation to wear over time. The device could also be used to monitor the patient's adherence to offloading treatments often prescribed to treat ulceration. Another valuable purpose of such a device is that it can be programmed to send sensory feedback marking anatomical areas with peak pressure points, alerting the wearer that a possible modification of gait is due.

Exciting as it is, the current body of evidence is not sufficiently robust and further research is required.

Phase II

Chapter 7: Development and laboratory validation of the Prototype

7.1. Introduction

This chapter details the design, development and validation of the innovative, specifically designed, single-sensor, in-shoe pressure and temperature measurement device. This Chapter is divided into 3 sections (Figure 33). Part I presents the design and building process of the innovative, single-sensor in-shoe pressure and temperature measurement device; Part II describes the methodology of the laboratory static validation of the device and finally, Part III is a Pilot Study that involved the laboratory dynamic validation of the device.

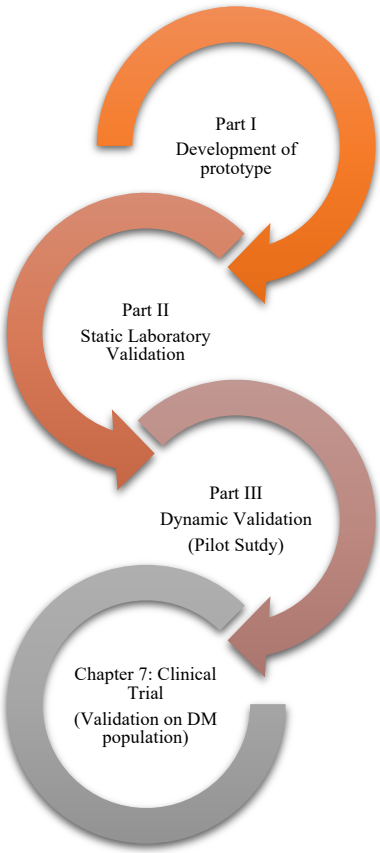


Figure 32: Flow chart highlighting the 3 sections that make up chapter 5.

To date, foot skin temperature and pressure data can be obtained separately using a thermographic camera and an in-shoe pressure device, a technique which can result as both expensive and time consuming. Thus, the main aim of this study was to develop an innovative, cost-effective, single sensor pressure and temperature measuring in-shoe device that can be used to continuously monitor the diabetic high-risk foot with the aim of reducing foot ulcerations.

7.2 Part I - Development of an innovative, single-sensor, in-shoe pressure and temperature mapping device

This section, Part I of Chapter 7, gives a detailed account of the thoughts and brainstorming processes that led to development of the innovative, single-sensor, in-shoe pressure and temperature measurement device. A detailed description of the design and architecture of the prototype device, choices of hardware and other technical details is presented. A detailed instructions manual on how to use the device can be found in Appendix 8.

7.2.1 The design and architecture of the prototype

As part of this research project, the hardware and software of an innovative, single-sensor, in-shoe pressure and temperature mapping device was developed with the help of two qualified and experienced Engineers. The aim was to create a device that could not only measure plantar pressure and temperature simultaneously but, was also a cost-effective alternative to the current gold standard devices which are costly (circa EUR 60,000) and that can be used in a clinical setting to evaluate plantar pressure in areas of interest during a consultation with high-risk patients. In view of this, a series of specifications were required in terms of design, technology and architecture to fulfil the aim of this project.

Aim: The aim of part I of phase II of this study was to develop an innovative, single-sensor pressure and temperature mapping device that is able to read and measure in-shoe skin temperature and in-shoe plantar pressures simultaneously in a specific area of interest.

Objectives:

- To develop the hardware of the innovative, low-cost, in-shoe single-sensor device able to measure plantar foot pressures and plantar foot skin temperatures simultaneously

- To develop the software of the innovative, low-cost, in-shoe single-sensor device able to measure plantar foot pressures and plantar foot skin temperatures simultaneously

7.2.1.1 General system architecture

The innovative, single-sensor, in-shoe temperature and pressure measuring devices has three main systems as shown in Figure 33. The first system relates to the low-cost device that can measure temperature and pressure data through a combination of pressure and temperature sensors. The second system is a mobile application that provides an interface to control and manage the device via the Bluetooth protocol and store the collected data in the database hosted on cloud servers. The third system is a multi-function web-based dashboard that displays collected data in the form of graphs and visualizations, and allows users to manage the system and perform operations such as, adding devices and users, searching/filtering of data based on user, date, device, amongst others.

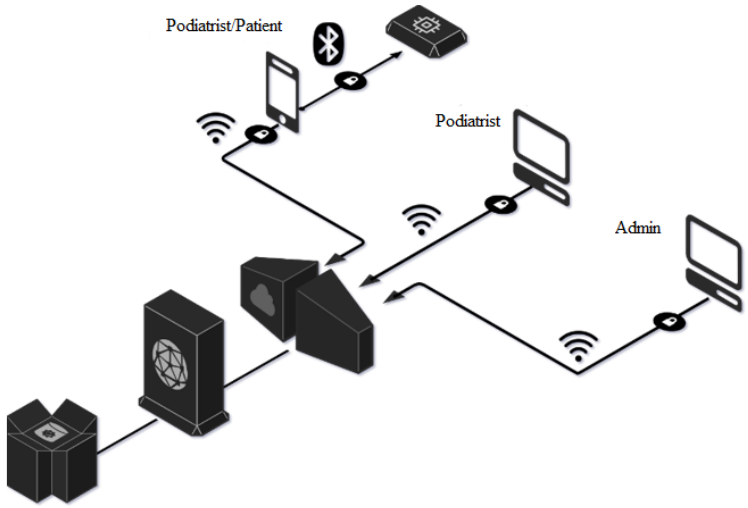


Figure 33: System architecture with all different user types.

7.2.2 General technical requirements

The specifications of this device were based on extensive research (Saliba Thorne, Gatt, DeRaffaele et al., 2021) which highlighted best sensors to be used based on the scientific and practical needs required to accomplish the development of the device. These requirements included (Razak et al., 2012):

- A pressure sensor able to measure low to high (0-1000 kPa) ranges of both pressure
- A temperature sensor able to quickly to respond to change in temperature (±1%) with a reading capacity of -55 to approx. 70°C
- Both sensors are thin and flexible to fit in tight spaces in footwear and to conform to the non-flat surfaces of the foot
- Both sensors are small enough so that the entire circuit of the device is small in size and lightweight.
- Both sensors had to read re-producible and repeatable data.
- The entire circuit of the device had to be wireless to avoid tangling of wires and to avoid wires from influencing the patient's gait
- Circuit requiring low power consumption so that the device could operate efficiently even after prolonged use.

7.2.1.2 General device architecture

When assembled, the device appears as a squarish, compact case that measures 60mm by 75mm by 10mm (Figure 34). The case of the innovative, single sensor, in-shoe pressure and temperature device was designed to host all the electrical components of the device which includes an operational amplifier, resistors, capacitors, and a microcontroller. The pressure sensor and the temperature sensor extend from the case of the device and are superimposed on each other so that they can be placed at a specific area within the shoe, while the case sits at the exterior of the shoe such as in the patient's pocket.

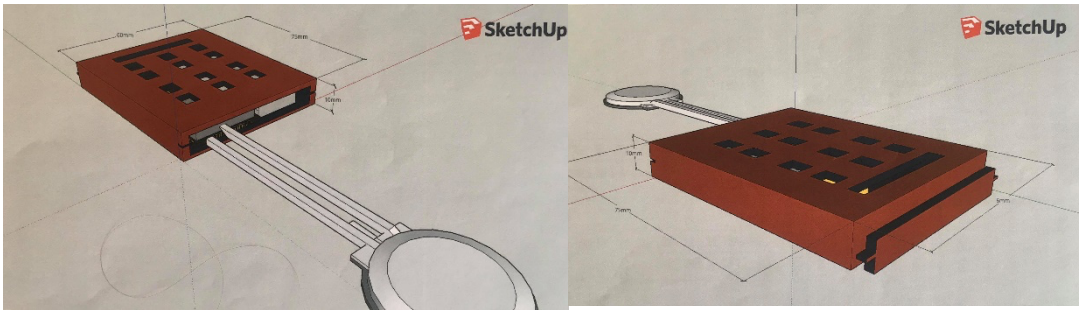


Figure 34: Image showing a sketch of the prototype prior development.

Figure 35 below, shows the photograph of the assembled prototype. This set-up allowed for comfort and did not influence the gait of the participant as it took minimal space within their footwear.

a) b)

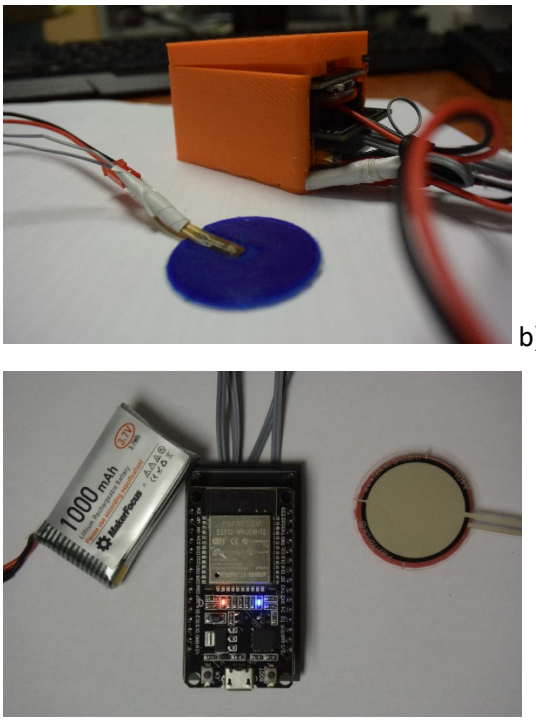


Figure 35: Photograph of the developed working prototype a) with a temporary finished casing; b) without casing.

7.2.2 Prototype Hardware

The total components of the prototype consist of 1 flexible pressure sensor, a temperature sensor and other electronic components such as an operational amplifier, resistors, capacitors, and a microcontroller.

The microcontroller

A microcontroller is a compressed microcomputer that controls the functions of embedded systems within a device (Figure 36). The microcontroller component of this prototype is of a consumer-grade ESP32 which offer a built-in BLE (Low Energy Bluetooth). The microcontroller also offers additional details including a dual-core Central Processing Unit (CPU), integrated Wi-Fi, a small footprint, has sufficient number of input/output ports and, it employs the Tensilica Xtensa LX6 microprocessor which is recommended for automated medical devices (Roos, 2019). The role of the microcontroller is to determine the data collection method, the sampling rate and the samples averaging count; and through the CPU, it handles the data collection from the sensors and transmits the data to a computer or mobile phone via Bluetooth.

Figure 36: Photograph of the ESP23 type of microcontroller used

The amplifier

A non-inverting operational amplifier (OpAmp) is an integrated circuit that produces an amplified output signal which is in-phase with the input signal (Singh & Singh, 2006) (Figure 37). This type of amplifier was selected for this project and it was

utilised to adjust the force range of the sensors. OpAmp circuit not only allows adjustment of the operation range, but also the sensitivity of the sensor (Singh & Singh, 2006). Hence, force range was adjusted by altering the reference voltage (VREF), and sensor sensitivity was adjusted by varying the value of the Feedback RC Resistor/Capacitor (RFEEDBACK, and C1). The dynamic range of this implementation is (VREF – VSUPPLY). The recommended value of VREF can be a square wave of up 5V with a 50% max duty cycle or between 0.25V – 1.25V DC. Lower values are recommended for VREF since it heavily influences the power consumption of the circuit.

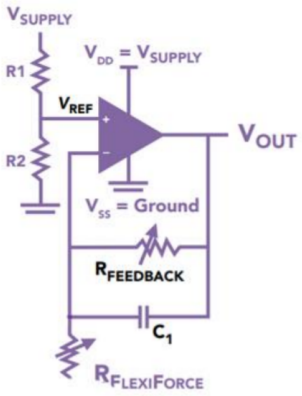


Figure 37: Image showing the implemented non-inverting OpAmp circuit.

Overall, this device can be set to collect data at a frequency that ranges between 50Hz to 75Hz. Furthermore, the overall developed Printed Circuit Board (PCB), features a compact size of 58x32mm with a modular design that can host up to four pressure sensors and up to 4 temperature sensors along with all the required components (Figure 38).

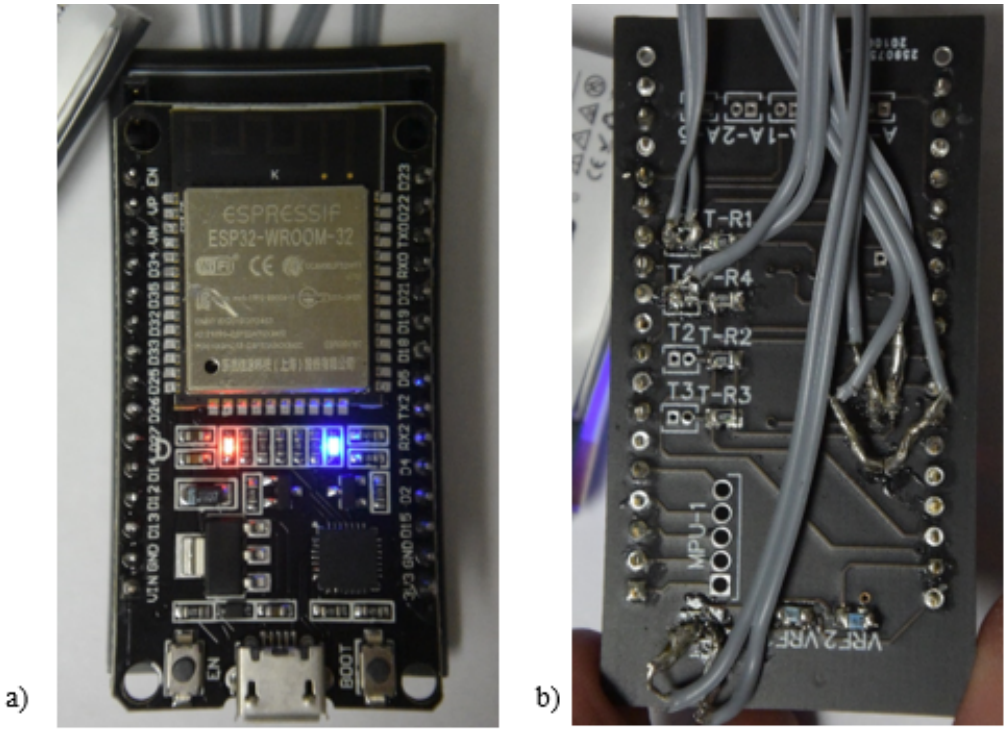


Figure 38: Photograph showing a close-up of the completed PCB from a) front b) rear view

Pressure Sensor

Based on the features and suitability of the pressure sensor, a Force Sensitive Resistor (FSR) type of pressure sensor was selected specifically, the FlexiForce™ A401 Sensor (Tekscan, Boston, MA). Like any other type of pressure sensing device, an FSR provides an electrical signal output which is directly proportional to the pressure input. Force Sensing Resistors are composed of a conductive polymer material that alters its resistance when a force or pressure is applied. Force-sensing resistors can be described as a thin film that is made of both an electrically conducting, and electrically non-conducting materials suspended in matrix (Figure 39). When pressure is applied, the particles are compressed against the electrodes. This causes a change in resistance within the film (Paredes-Madrid et al., 2017).

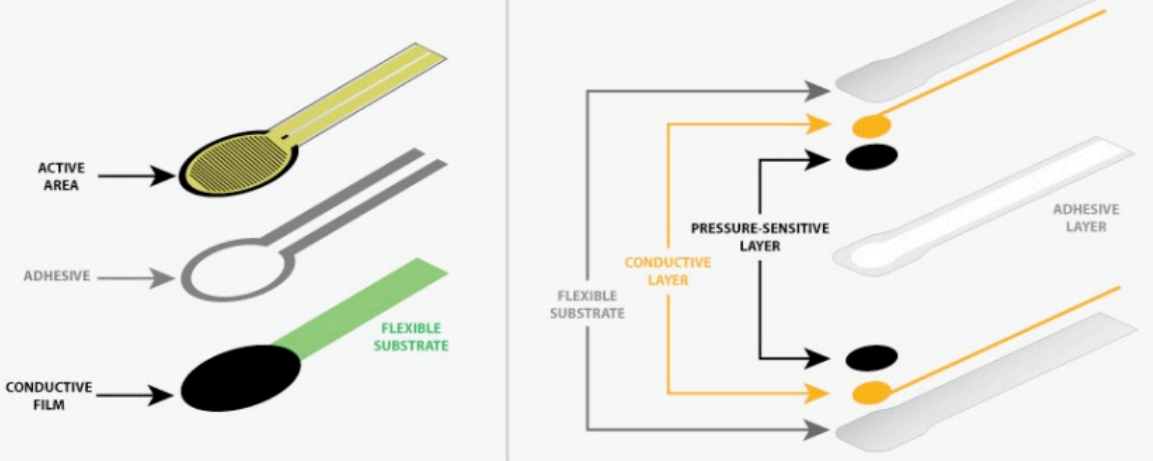


Figure 39: Image showing the components of an FSR pressure sensor (left) and the type of material that it is composed of (right) (Tekscan, 2019).

The A401 (Figure 40) is a resistor made from piezoresistive material used to measure mechanically generated stress "piezoresistive" manufactured by Tekscan™. This sensor is very thin with a sensing area of 25.4mm and a force range of 111N.

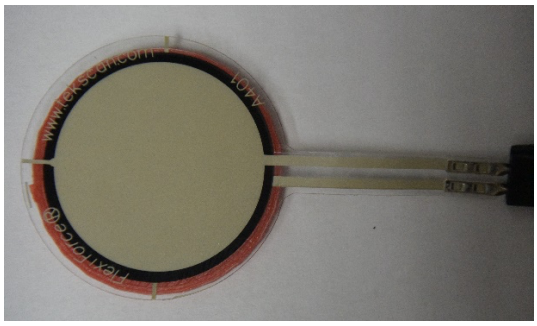


Figure 40: Photograph of the FSR used

The overall dimensions of this pressure sensor are equivalent to 0.203mm in thickness, 56.9mm in length and 31.8mm in length (Figure 41). This specific model features a linearity of ±3%, repeatability of ±2.5% of the full-scale drift of 5% per logarithmic time scale, and a response time of less than five µsec. Additionally, it can operate with measurement ranges of 0-1 lb and 0-7000 lb using the recommended circuitry (Refer to Appendix 9 for manufacturer data sheet).

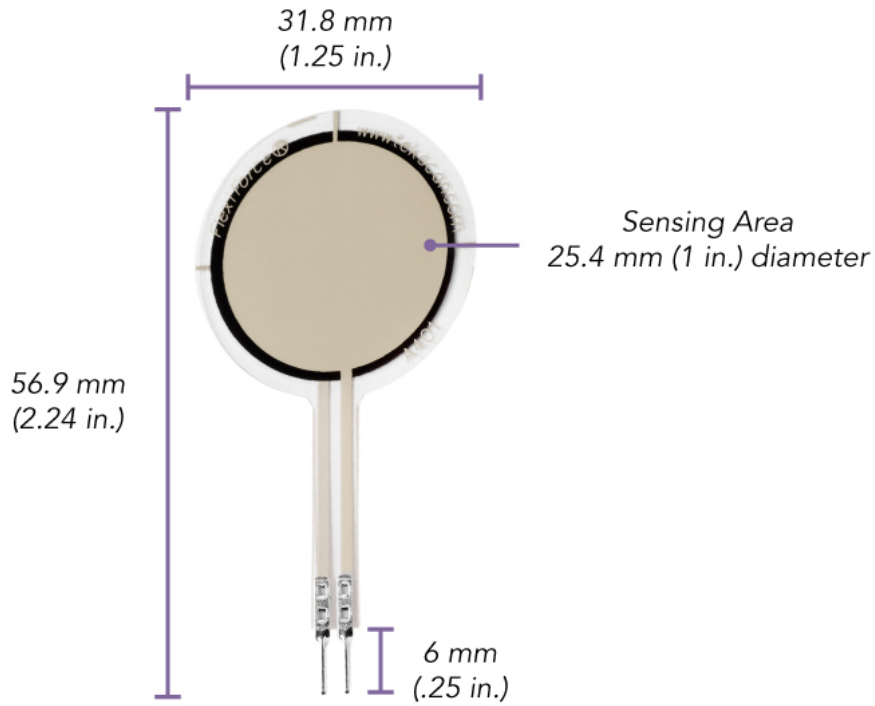


Figure 41: Image showing the dimensions of the FlexiForce™ A401 (Teckscan, Boston, MA)

Temperature Sensor

This temperature sensor selected for this prototype is a thermistor type of sensor. Thermistors are also a type of resistive sensors that are able to read low temperature ranges, durable, long-lasting, inexpensive and are accurate to the ± 0.2°C (Priest, 2004). The temperature sensor selected for this prototype is a 10 Kom thin-film Negative Temperature Correlation (NTC) thermistor specifically, the Semitec USA JT Thermistor, manufacture number 103JT-025 (Mouser Electronics Inc., 2022) (Figure 42).

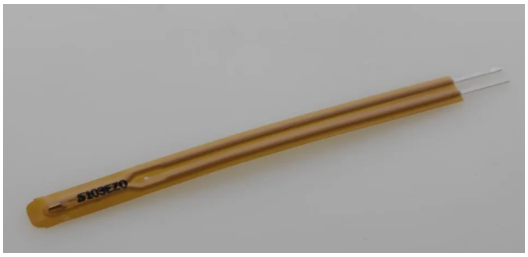


Figure 42: Image showing the Semitech USA JT Thermistor used in this PhD study. Retrieved from Mouser Electronics Inc. (2022).

This type of thermistor is reported to be a highly-accurate radial thermistor of dimensions equivalent to 500µm in thickness, and 11.5mm in length (Mouser Electronics Inc., 2022) (Figure 43).

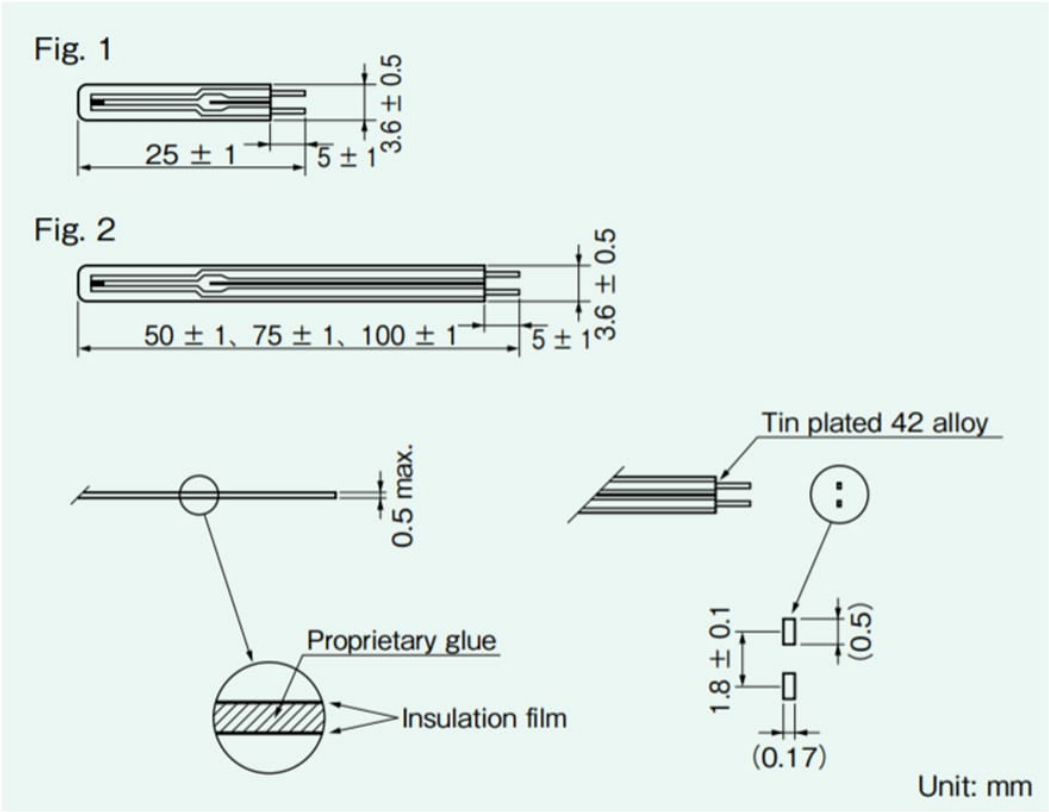


Figure 43: Image showing the dimensions of the Semitech USA JT Thermistor. Retrieved from Mouser Electronics Inc. (2022).

NTC thermistors are composed of thin layers of metallic oxides, binders and stabilizers that provide a higher resistance compared to conducting materials and lower resistance

compared to insulating materials, and thus are considered as semiconductors. What makes the device so accurate is the proportion of the composite materials that it is made up of, which determines the relationship non-linear between the temperature and the resistance of the device (Smis, 2017) furthermore, this sensor was ideal for this study as it is very thin, enough to fit into tight spaces such as between the foot and the shoe, without influencing the FSR pressure sensor that superimposes it (Figure 44). The selected sensor features a tolerance of 1%, an operation range between --50°C to +125°C, a Beta value of 3435K with a small form factor having a height of 0.5mm which makes it ideal for such embedded applications (Refer to Appendix 10 for manufacturer data sheet).

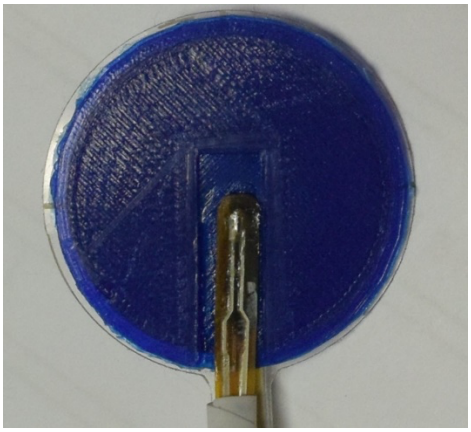


Figure 44: Photograph of the NTC thermistor used

The device is portable and compact enough to provide comfort while gathering the required data, objectively and effectively, from within the patient's footwear without interfering with the patient's normal gait (Figure 45).

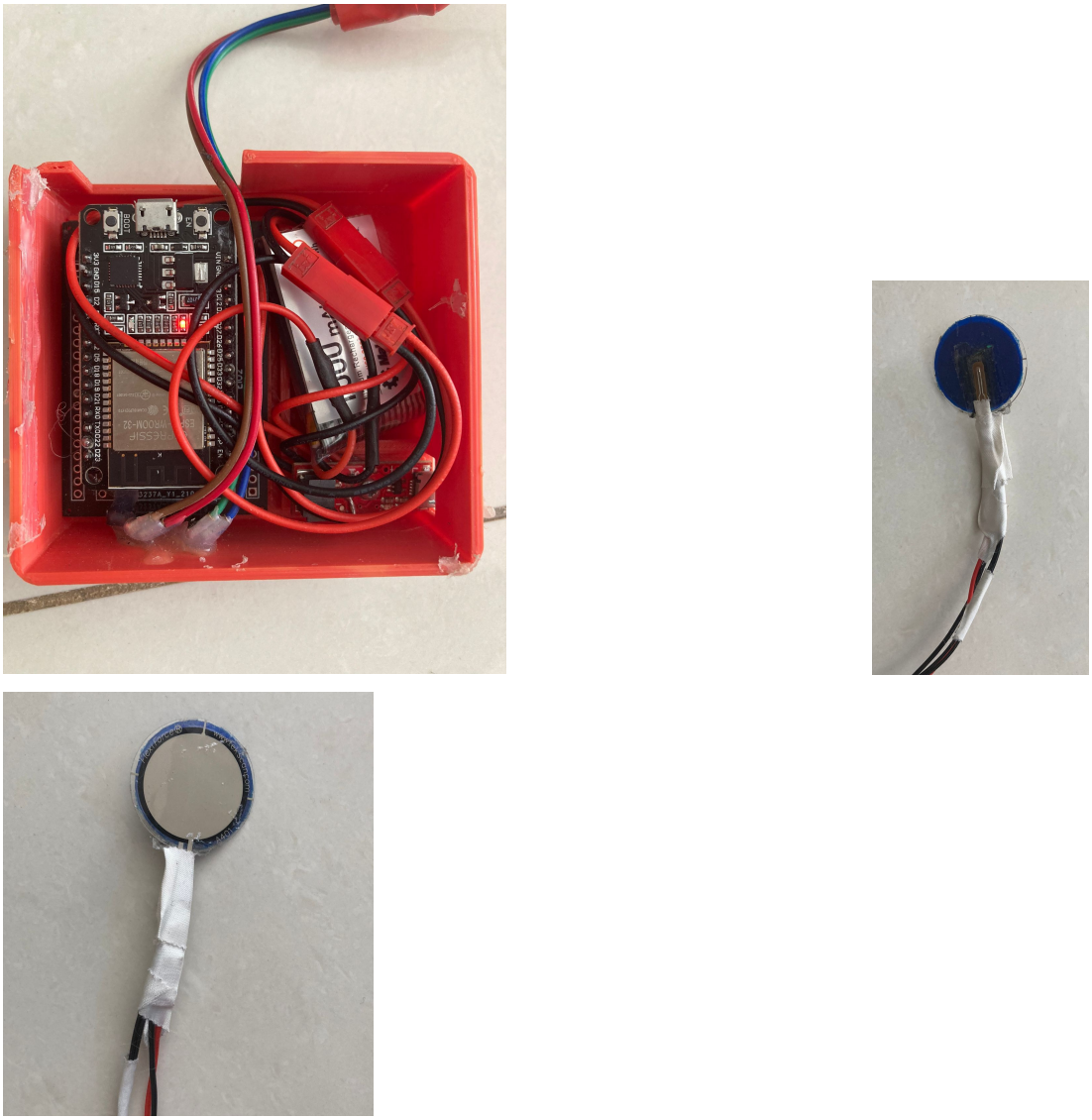


Figure 45: Photograph showing the final design of the prototype

The system is designed to employ a wireless approach to transmit the collected data to a personal computer on an online cloud which will be made accessible solely to the clinician (Figure 46). The system is also designed to communicate with a smart phone application via Bluetooth. This will permit the clinician to carry out the assessment in any setting of his/her choice be it clinical, laboratory or any other environment.

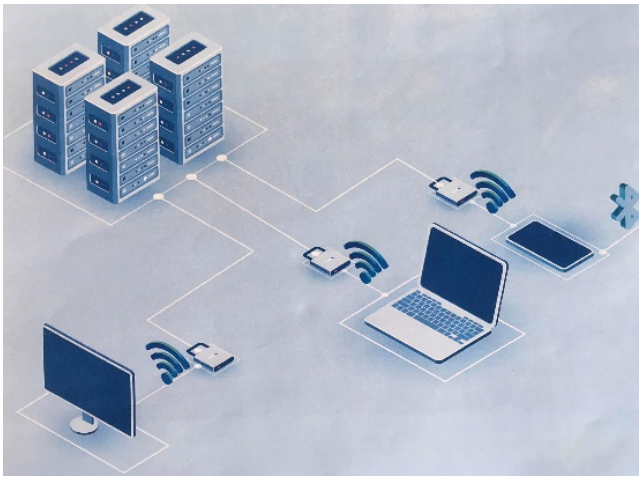


Figure 46: Image showing how the configuration of system

7.2.3 Prototype Software

Firmware

The role of the microcontroller is to set up the Bluetooth server to which the user can connect and send/receive data from. An authentication process will be prompted after which the microcontroller determines the data collection method, sampling rate and samples averaging count. Consequently, the CPU is responsible for handling data collection from the sensors and for transmitting the data to a connected mobile phone via Bluetooth. A differential encoding mechanism is used to optimize the power consumption by reducing the size of the data and most importantly to serve as a security feature by encrypting the data. This device can be set to collect data at a frequency that ranges between 50Hz to 75Hz.

Web-based dashboard

A web-based system was created so that the data collected can be accessed and visualized in the form of graphs and tables. Furthermore, the dashboard was programmed to allow the users to manage the overall system (Figure 10), this means

that the user can add, update, and delete users, devices, and admins. The web-based system interacts directly with the cloud Application Programming Interface (API) and the database. For those unfamiliar with the terms, an API is a computing terminology that describes the interaction between various software intermediaries (Groth et al., 2014).

The web-based system has two user types, admins and devices (Figure 47), where admins can control the entire system and manage users such as patients and clinician. A clinician's account can view the data related to a patient. The system was designed with scalability as one of its non-functional requirements. In other words, the system allows the clinician to have access to multiple patients' data. It will enable patient data to be shared with multiple clinicians, all of which are controlled by the admin users.

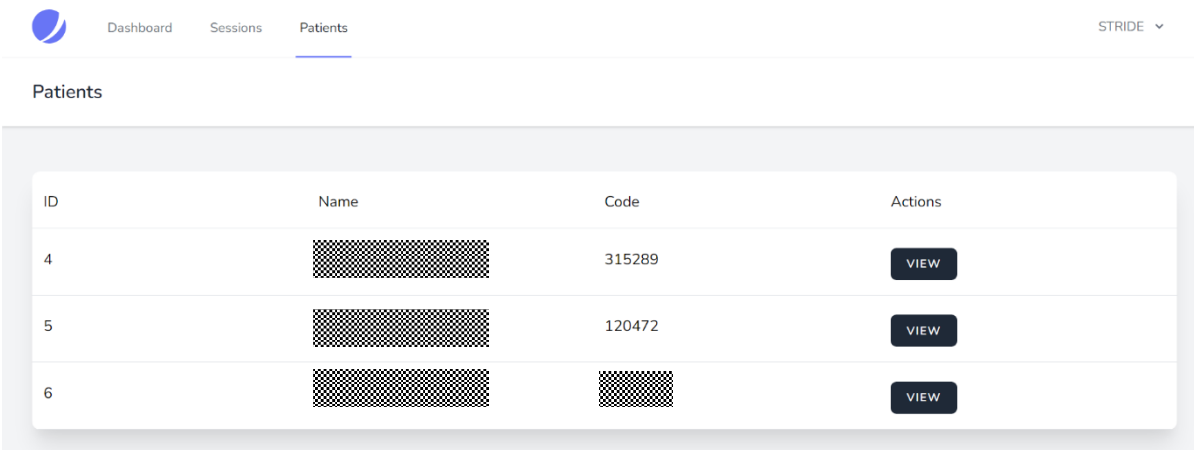


Figure 47: Image showing the admin and user's profile on the web-based system

Additionally, the admins can associate a specific device with a clinician or a patient and view the particular device's data (Figure 48). The system features several different functionalities such as email notifications and password reset via email and user email confirmation.

Figure 48: Image showing the dashboard of the web-based system

Smartphone application

A cross-platform mobile application (Figure 49) was developed using the React-Native framework, which allows targeting a broader audience group and removes any limitation related to what OS the host uses. The mobile application was designed to work as an intermediary connection point between the microcontroller and the server and remove any internet connectivity limitation and allow the system to work offline. The application serves two primary purposes, controlling and configuring the microcontroller and transmitting the data collected by the microcontroller to the cloud. The application uses two wireless communication protocols, Bluetooth, to establish a connection with the microcontroller and Wi-Fi to establish a connection over the internet to the cloud-based server. A two-way Bluetooth based communication channel allows the application to send configuration parameters to the microcontroller using an easy-to-use interface and receive the data collected by the microcontroller. Additionally, it encrypts and sends the data to the server if a connection is established successfully; if not, store the collected data in a locally hosted database until a connection is established.

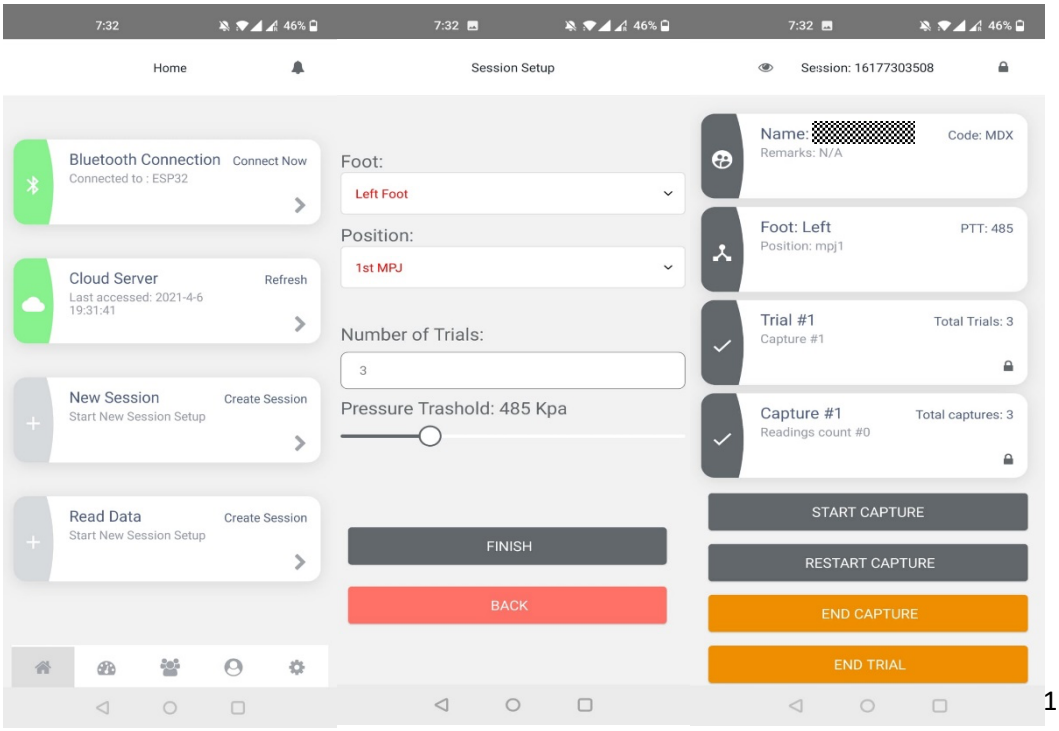


Figure 49: Image showing a screenshot of the mobile application where the user can customise the number of captures and trials

7.2.4 Data Transfer Interface

The system employs a wireless approach to transmit the microcontroller's data to the database hosted on the cloud (Figure 50). This is achieved using two wireless communication protocols (Figure 51). Initially, a connection is established between the mobile phone and the microcontroller via Bluetooth. The established connection allows the microcontroller to obtain several parameters that define how the microcontroller operates (polling or interrupt-based data collection style, sampling rate, noise reduction via averaging, count of samples to average). All configuration parameters can be manipulated manually from the device setting tab within the smart phone application. After a successful device configuration, the device will be ready to transmit the data to the smart phone application. The transmitted data is deferentially encoded for two main reasons, reducing power consumption during data transmission and adding a security layer to the transmitted data. Once the smart phone application receives the data, it encrypts the data to prepare the transmission to the server on the cloud. The application attempts to post encrypted data. In case of any failure, the data gets temporarily stored in a local database until a successful connection to the server is established.

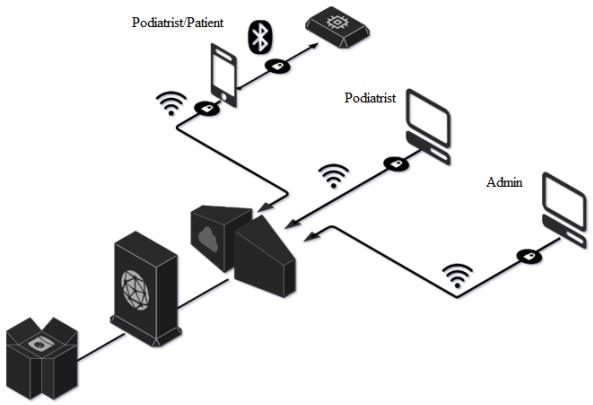


Figure 50: A diagrammatic image showing the transfer of data pathway created for this device

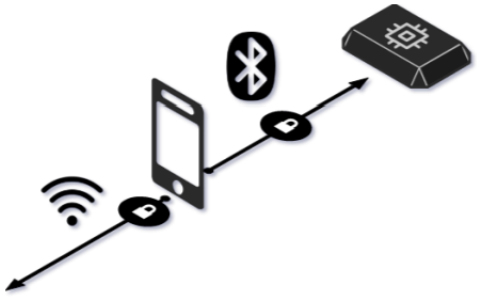


Figure 51: A diagrammatic image showing the two types of connections (Bluetooth vs Wi-Fi) employed in this device

7.2.5 Conclusion

The aim of this part of this study was to present the design and development of an innovative, cost-effective, single-sensor, pressure and temperature measuring in-shoe device that can be used to continuously monitor in-shoe temperature and in-shoe pressure within the shoe of the diabetic high-risk foot. The simplicity and compactness in the design of the device allows better fitting within footwear and targeted assessment of specific anatomical landmarks. Thus, allowing the device to be used as an alternative to the to the current costly and time-consuming technologies that are currently available with the ability of measuring both in-shoe plantar pressures and in-shoe plantar foot temperature simultaneously.

Once validated, this device will be the first to allow the conduction of a longitudinal study that compares laboratory-based results to real-time results in any field that relates to in-shoe plantar pressure and temperature assessment. It has the potential to measure pressure and temperature at a specific area of concern, and pre-empt the development of diabetic foot ulceration and provide treatment and advice accordingly. In doing so, complications such as ulcerations, hospitalization or even amputation could be predicted and hence avoided thus reducing the burden on healthcare costs.

The static laboratory validation of this innovative, low-cost, single-sensor, in-shoe pressure and temperature measuring device is described in the next section.

7.3 Part II – The Static laboratory validation of an innovative, single-sensor, in-shoe pressure and temperature mapping device

This section details the laboratory static validation of the innovative, single-sensor, in-shoe pressure and temperature mapping prototype.

7.3.1 The static validation process: aims and objectives

Static validation, also referred to as 'static verification', is a type of validation analysis performed on a tool or an instrument to determine the accuracy of the tool's performance and to detect potential measurement errors (Zelt et al., 2018).

Aim: The aim of this study was to determine static laboratory validation, of the innovative, single-sensor in-shoe pressure and temperature mapping device purposely developed to read and measure in-shoe pressure and in-shoe skin temperature.

Objectives:

- To establish static validation of the prototype
- To determine the presence of hysteresis
- To achieve linearity of data between prototype and reference standard.

All of the above were determined by testing the newly-developed single-sensor in-shoe pressure and temperature device with a known force, against the FScan™ in-shoe pressure mapping system by Tekscan™ which served as a reference standard in this study.

7.3.2 Methodology

The laboratory static validation of the newly developed, low-cost, single-sensor pressure and temperature device was conducted at the Biomechanics Laboratory at the Faculty of Health Sciences at the University of Malta. The data collection experiment used an Equilibration 'bladder calibrator' to create a known force over the F-Scan System from Tekscan™, and the newly developed prototype. Details of the experiment are explained below.

The F-Scan System

F-Scan System from Tekscan™, comprises of 960 sensor elements (sensels) arranged in a 16x6 rectangular grid, embedded between 2 thin sheets of polyester insoles, referred to as the FScan insert for the purpose of this dissertation. This system has a dynamic range of 1kPa-500kPa.

The prototype

As detailed in Section 7.2.1.1, the prototype device is an innovative, in-shoe, single-sensor, pressure and temperature sensor device. It consists of a squarish, compact case that is designed to sit out on the exterior of footwear. The device hosts the entire technical components which includes an operational amplifier, resistors, capacitors, and a microcontroller. The flexible FSR pressure sensor and the NTC temperature sensor extend from the case of the device and are superimposed on each other so that they can be placed at a specific area within the shoe, while the case sits at the exterior of the shoe such as in the patient's pocket.

Equilibration 'bladder calibrator'

The Tekscan™ Equilibration 'bladder calibrator' is a tool used to generate pressure and consists of two latex covered metal plates which are placed over and below the array of sensors. Through inflating the latex rubber, the calibrator applies constant pressures equally over all sensor cells and desired pressure levels are read off an attached pressure gauge (Armstrong et al., 2017).

7.3.2.1 Method

Pressure Sensor

As presented in section 7.2.2, a Force Sensitive Resistor (FSR) type of pressure sensor, specifically the FlexiForce A401, was used as pressure sensor for the innovative, single-sensor pressure and temperature measuring device. The A401 is a resistor made from piezoresistive material used to measure mechanically generated stress "piezoresistive" manufactured by Tekscan™.

The data collection experiment used the equilibration method to determine the presence of hysteresis, linearity of the pressure sensor and to determine static validation. This method is referred to as the equilibration method as it uses a calibration bladder, otherwise referred to as a pressure generator rig, to a known force over a pressure sensor. In this study Tekscan™ Equilibration 'bladder calibrator' was used to generate known pressures. This tool consists of two latex covered metal plates which are placed over and below the array of sensors (Figure 52). Through inflating the latex rubber, the calibrator applies constant pressures equally over all sensor cells and desired pressure levels are read off an attached pressure gauge (Murin et al., 2001).

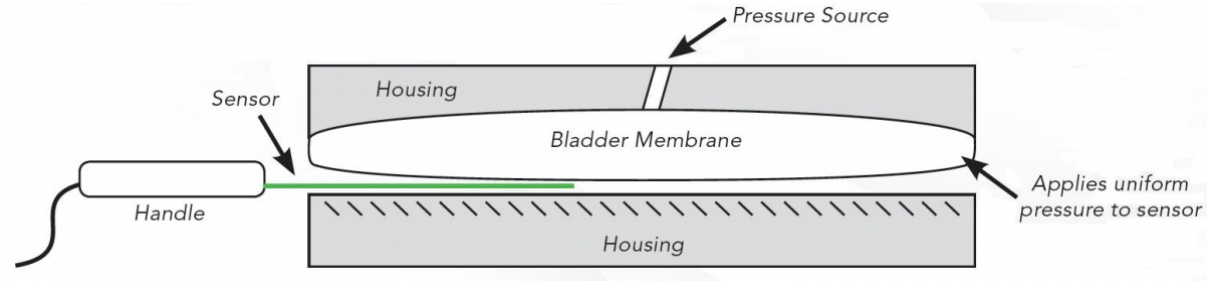


Figure 52: Image showing a representative diagram of how the equilibration bladder works. Retrieved from Tekscan (n.d.)

In clinical practice, accuracy of a diagnostic tool is empirical as inaccurate results are more likely to lead to misdiagnosis or biased clinical conclusions. To avoid this, a newly developed instrument or device is compared to what is known as a reference standard. A reference standard is an already established tool or instrument that is considered as the best available way of comparing results with (Naaktgeboren, de Groot, Rutjes et al., 2014). Not using a reference standard may lead to a phenomenon of research referred to as verification bias however, one must consider that a reference standard may not always be available (Naaktgeboren, de Groot, Rutjes et al., 2014). For instance, to date, reference standard for in-shoe temperature devices is not yet available. In this PhD study, the F-scan® system was used as a reference standard for the pressure sensor. It was used to record the pressure readings generated by the

pressure generator rig and, to establish a baseline for pressure readings recorded by the developed prototype.

The FScan insert, which hosts the sensors of the FScan in-shoe system, and the pressure sensor of the prototype were inserted between the two latex covered metal plates of the pressure generator rig. The latex rubber plates of the pressure generator rig were then inflated to give a specific pressure value, simultaneous and equally, over the sensors of the FScan in-shoe system and over the pressure sensor of the prototype (Figure 53). A total of 20 different pressure values were recorded with 100 samples each, for both the prototype and FScan in-shoe system.

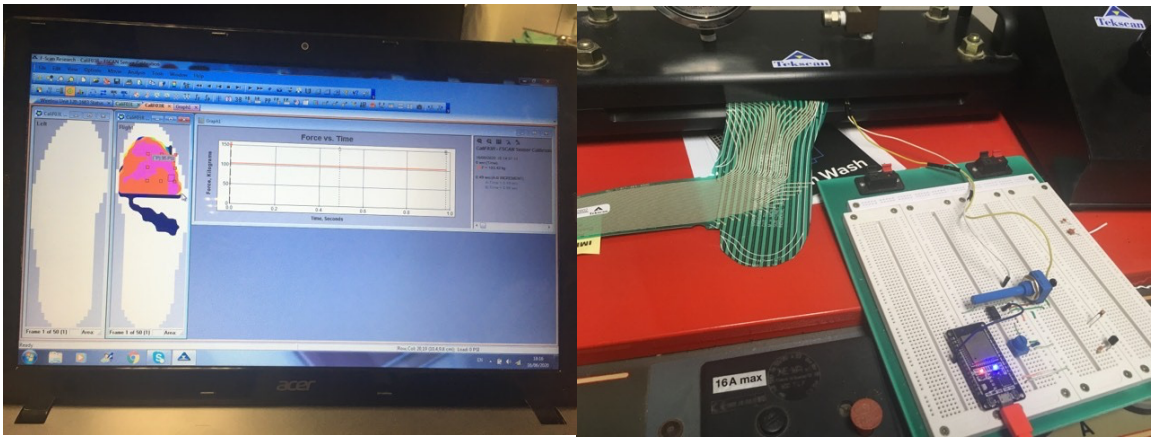


Figure 53: Photographs taken during the data collection showing pressure readings from the F-scan (left) and the set-up used during data collection (right)

Though many pressure sensors are tested and calibrated prior to they are released from the factory producing them however, the researcher felt the need to re-test the pressure sensor for hysteresis, pressure repeatability, and stability; and optimize the performance of the device were necessary, prior to using it on test subjects.

Method of how the presence of hysteresis was determined

Hysteresis, or hysteresis error, is defined as a measurement error given off by a pressure sensor due to a difference in pressure readings during loading and unloading

(Razak et al., 2012). It is possible that during equilibration, when a known pressure force is sensed by the pressure sensors being investigated, though it was being distributed equally over the external structure of the sensor material, internally the pressure distribution might very slightly in terms of direction. This may then lead to a lag in pressure readings when the device is being loaded and offloaded a phenomenon referred to as hysteresis (Mellodge, 2016). In the presence of hysteresis, the data plotted of the in-put signal versus that of the out-put signal would be represented by a characteristic curve as exemplified in Figure 16. Hysteresis error is calculated by determining the difference between in-put and out-put pressure values at 50% and/or at 100% of the pressure from the data plotted (Figure 54). It is typical to observe higher hysteresis error as the pressure increases from 0 to 50% as opposed to having the pressure reduced from 100% to 50% (Mayergoyz, 2003).

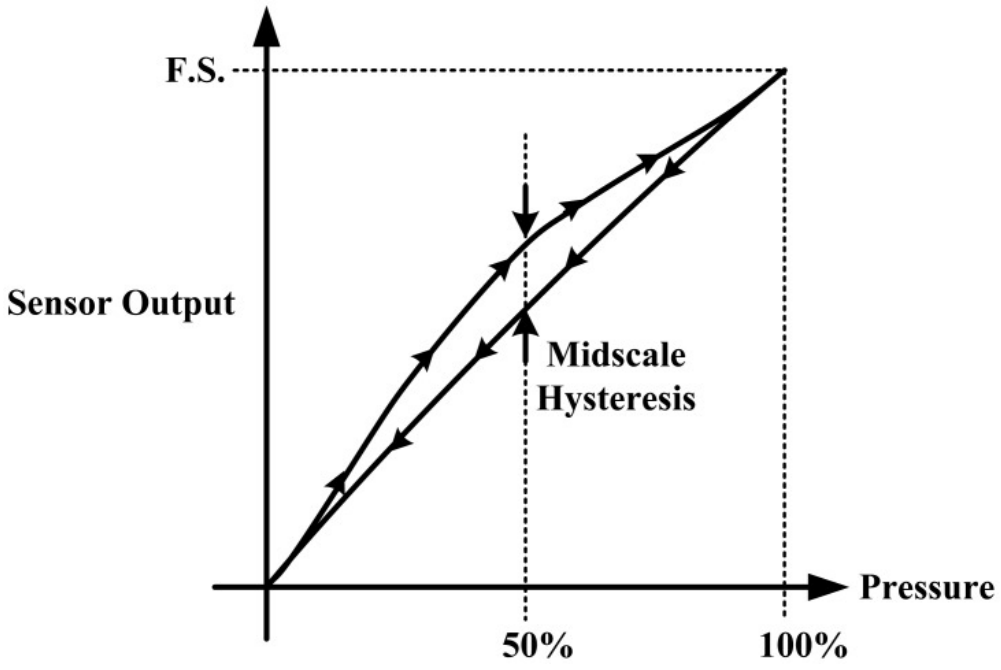


Figure 54: An example of hysteresis pressure curve. Adopted by Razak et al. (2012)

In this study, at 50% of pressure range, the sensor output signal of both the prototype and the FScan in-shoe system, was observed and recorded as the sensors were loaded

and unloaded with 20 different pressure values. These pressure values were recorded at 100 samples each for both the prototype and FScan in-shoe system. The pressure values generated were at 10 psi, 25 psi, 45 psi, 100 psi, 30 psi, 50 psi, 15 psi, 35 psi, 55 psi, 20 psi, 40 psi, 60 psi, 65 psi, 85 psi, 70 psi, 90 psi, 75 psi, 95 psi and 80 psi, in this specific order. Readings of both loading and unloading matched at that specific pressure range.

Method of how linearity was determined

Linearity is a reflection of how usable and accurate a sensor is. Linearity is defined as the proportional measure between the authentic values of a measurement to the output measurement of an instrument. When plotted, a linear data plot is represented by a straight line that crosses over output values ranging from 0 to 100% of the pressure scale values. Because pressure sensors measure stress over a slightly non-uniform area, they are naturally non-linear, giving a slightly curved output measurement which must be linearized to improve usability and accuracy (Beeby, 2004).
In this PhD study, linearity was determined by using the Best Fit Straight Line (BFSL) method and through a mathematical linear regression model. As for hysteresis, a total of 20 different pressure values were recorded with 100 samples each for both the prototype and FScan in-shoe system. The pressure values generated were at 10 psi, 25 psi, 45 psi, 100 psi, 30 psi, 50 psi, 15 psi, 35 psi, 55 psi, 20 psi, 40 psi, 60 psi, 65 psi, 85 psi, 70 psi, 90 psi, 75 psi, 95 psi and 80 psi, in this specific order. The data collected was then fitted in the best straight line possible.

<u>Temperature Sensor</u>

As presented in section 7.2.2, a 10 Kom thin-film Negative Temperature Correlation (NTC) thermistor was used as a temperature sensor for the innovative, single-sensor, in-shoe, pressure and temperature measuring device. Prior to static validation testing, the selected temperature sensor was tested for any faults through the use of a digital multimeter which is a special equipment used to measure resistance (Figure 55).

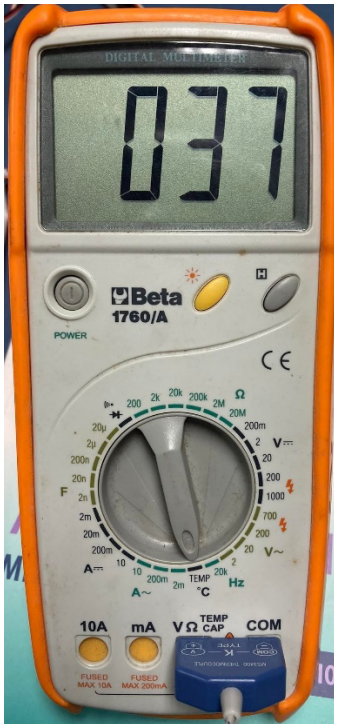


Figure 55: Image showing an example of the digital multimeter used.

As a general rule, as the temperature increases, the resistance of a thermistor is expected to decrease. At room temperature, the resistance of the selected thermistor marked equal to the fabrication value on the ohmmeter. Readings that markedly differ from the fabrication value often indicate a fault and thus the sensor would be considered as unreliable.

To validate that the selected sensor can provide accurate, repeatable, and fast readings in a practical environment another sensor was used to establish a base line and used to compare the reading from the selected sensor. For this validation, the DS18B20 one-wire digital sensor was used which reports degrees in Celcius with 9 to 12-bit precision with +- 0.5C accuracy. Both sensors were connected to a microcontroller and then exposed to a set of conditions at the same time to compare the desired characteristics (Figure 56).

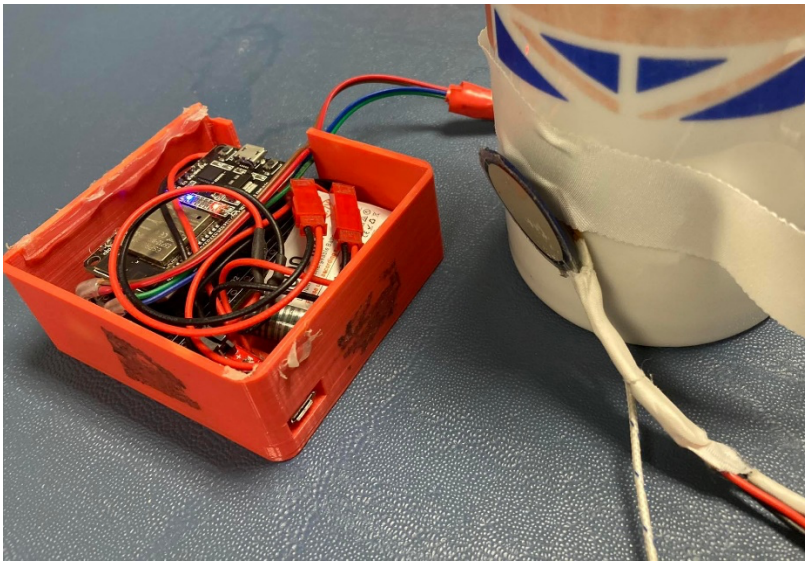


Figure 56: Set-up used during the validation process of the thermistor in the study.

Following this preliminary test, heat was applied to the thermistor by attaching in direct contact, together with a digital multimeter, it to a mug filled with boiled water (at 100°C) (Figure 56). The apparatus was set up in a room with a constant ambient temperature which was set to 25°C. The boiled water was then allowed to cool down naturally and the change in temperature of the boiled water was recorded by both the newly developed device and the multi-meter. The time taken (minutes) for the temperature to drop by 1 degree was recorded until the water reached a temperature of 25°C (the temperature corresponding to the ambient temperature). The resistance of the sensor was expected to decline steadily, within seconds following the application of heat. Again, failure to do so is indicative of a faulty sensor and thus unreliable to use. This technique also served as a calibration method for the temperature sensors that is, to convert factory coding into degrees Celsius.

7.3.3 Results

Pressure Sensor

After constructing the dataset, several operations were performed on it, such as exploratory data analysis, to gain insights and analyse the prototype's behaviour at

different pressure points. Additionally, pre-processing and data cleaning were performed to remove any anomalies detected within the recorded data to ensure the data's reliability and avoid any impacts that could be caused by any outliers.

Following the collection and pre-processing of the data, as discussed in the previous section (Section 7.3.2.1), to determine the linearity of the pressure sensor of the prototype, the data values collected were plotted to portray the output value patterns of the investigated pressure sensor. Figure 57, shows the average sensor reading per pressure value which, when plotted against the sensor reading mean, as expected, gave out a curved line (non-linear) as opposed to the straight line that is congruent to linearity.

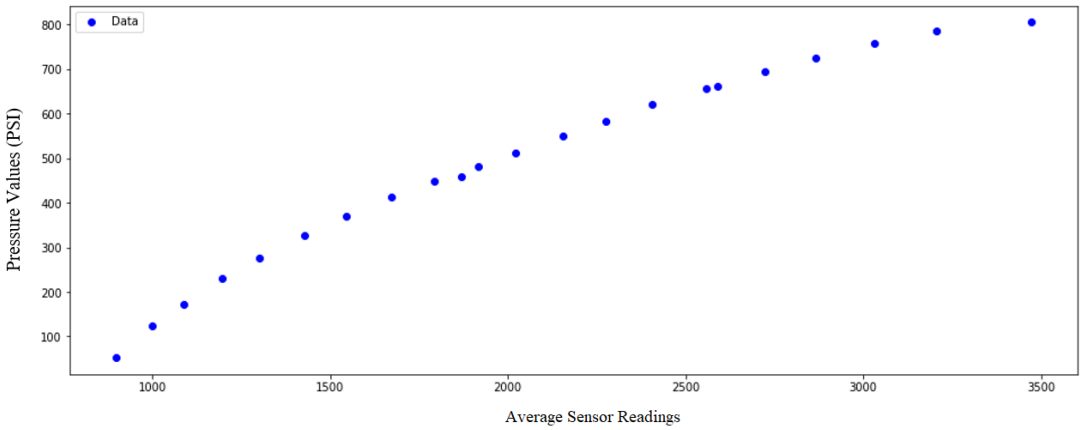


Figure 57: Image showing the average reading per pressure point of the cleaned dataset

To ensure sensor accuracy and counter the inherited variation in sensor characteristics, a linear regression-based technique was required to increase each sensor's trustworthiness. In this prototype, the Support Vector Regressor (SVR) was used with a polynomial kernel to fit the recorded data curve.

The SVR's initial score was significantly inaccurate, which led to using a hyperparameter tuning technique to optimize the algorithm and find the best

parameters to allow the SVR to fit the data. The Grid-Search algorithm was used in the hyperparameter tuning process. The best combination of parameters had a Mean Squared Error of 2.59 and a Root Mean Squared Error of 1.61. This process can be applied to each sensor individually to ensure maximum accuracy per sensor. Additionally, the coefficients used by each SVR are extracted and stored to be used later in a simple linear equation to convert raw readings to pressure values. Figure 58 below, shows the SVR fit for the data recorded in this experiment.

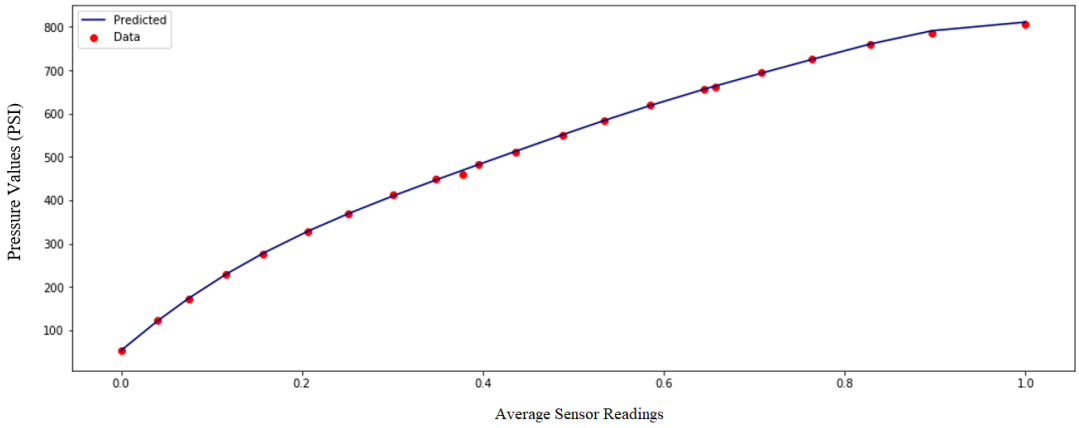


Figure 58: Image showing the SVR fit for the data recorded in this experiment

Temperature Sensor

The DS18B20 outperformed the selected sensor (the NTC thermistor) in accuracy. Results highlighted that though the selected sensor had an accuracy of +-0.5C to +-1.0C, it had a much faster response time which made it ideal for the application since. The value +-1.0C falls within the tolerance range for this application, and detecting spikes/increases in temperature is more valuable than determining the absolute temperature in this case.

7.3.4 Discussion

The aim of this study was to determine laboratory static validation of pressure and temperature from an innovative, single-sensor pressure and temperature monitoring

device specifically developed for the early detection of complications in high-risk foot. Results of this laboratory static validation study showed that the prototype displayed evidence of a good level of linearity when compared to the FScan® system that served as a reference standard in this experiment. This suggests that the new prototype functioned as required and at an equal level to that of an already validated and established in-shoe pressure system, the FScan® system.

This innovative, cost-effective, single-sensor in-shoe pressure and temperature monitoring device was designed to be used during normal daily activities as well as in a clinical setting. It was primarily developed to serve as a low-cost alternative to the currently available in-shoe pressure systems and costly barefoot temperature monitoring devices.

As stated in literature, daily monitoring of foot temperature can effectively identify local increases in skin temperature as pre-sign of foot ulceration (Mizzi & Falzon, 2018; Boulton et al., 2020). This is also pertinent to monitoring of any increase in plantar pressures (Frykberg et al., 2000; Bus et al., 2016; Lavery et al., 2016). The influence of the development of diabetic foot ulceration may be reduced through the monitoring of the pressures and temperature parameters of the high-risk foot (Frykberg et al., 2000; Bus et al., 2016; Lavery et al., 2016; Alahakoon, 2020). However, monitoring of both pressure and temperature parameters should be carried out in a valid and reliable manner if an objective diagnoses and timely intervention is to be achieved for the the prevention of ulceration of the high-risk foot (Bus et al., 2016; Wang et al., 2019).

In the literature, multiple research studies were identified to have developed in-shoe devices that were validated to measure temperature (Erdenechimeg et al., 2017; Hughes-Riley et al., 2017) and plantar pressure parameters (Gerlach et al. 2015; Lin & Seet, 2017; Rajala et al., 2017) however, only 5 studies were identified to have investigated the validity and reliability of an in-shoe device that can measure in-shoe temperature and pressure simultaneously (Saliba Thorne, Gatt, DeRaffaele et al.,

2021). It is important to investigate whether or not a device is valid and reliable as, reliability and validity indicate whether an instrument is consistent and accurate in detecting changes being observed (Scholtes, Terwee & Poolman,, 2011). Furthermore, once a device is validated and deemed as reliable, the practitioner using the device will be able to obtain and rely on objective measurements on which to base his/her clinical reasoning (Bus, 2016). Seeing the practitioner base their clinical decision on objective measurements may encourage his/her patient to comply and adhere to an especially tailored treatment (Najafi et al., 2019). On the other hand, unreliable diagnostic equipment might lead to delays in obtaining adequate results which are more likely to lead, in case of diabetes, to increased cases of ulceration and hospitalization (NHS Digital, 2019).

The type of information gathered from 2 previous studies conducted as part of this PhD project (Saliba Thorne et al., 2021) facilitated the design and development of an innovative, low-cost, reliable and valid, in-shoe pressure and temperature measuring device that can be used as an alternative to current technology to predict the risk of ulceration prior to tissue breakdown.

Having the capacity to read pressure and temperature simultaneously makes this device novel and, in the future, this may determine whether orthoses have any effect on the thermodynamic behaviour of the skin at previously ulcerated areas – a feature lacking in current commercial in-shoe devices. Furthermore, in the future, this innovative device may be used to determine the correlation, if any, between skin temperature and plantar pressures, and their role in the causation of diabetic foot ulcers amongst other foot-related pathologies.

7.3.5 Conclusion

The results of this study confirmed the static validity of the innovative single sensor, in-shoe pressure and temperature measuring device purposely developed to read and measure in-shoe temperature and pressures of the diabetic high-risk foot. Results showed that the data obtained from the prototype corresponded to the data obtained from the F-scan® in-shoe system which, in this study, served as a reference standard.

This makes the prototype equally effective in reading pressure parameters as the F-scan® in-shoe system. Furthermore, the prototype can also read in-shoe plantar skin temperature at the area of interest. Proving that the prototype is valid, allows the possibility of such an innovative device to be used as a low-cost alternative to current costly commercial in-shoe pressure mapping devices. The introduction of such a low-cost device, could change not only change clinical practice but could also change the notion of just relying on clinical evaluation.

The dynamic validation of the innovative, low-cost, single-sensor, in-shoe pressure and temperature measuring device will be introduced in the next chapter. This chapter will inform the reader on the steps taken to dynamically validate the prototype on health participants.

7.4 Part III – The dynamic laboratory validation of an innovative, single-sensor, in-shoe pressure and temperature mapping device.

The laboratory dynamic validation of the innovative, single-sensor, in-shoe pressure and temperature mapping prototype is described in the following sections. This study is published in Gait & Posture Journal. Cited as: Saliba Thorne, C., Gatt, A., DeRaffaele, C., Bazena, A., Formosa, C. (2022). Innovative single-sensor, in-shoe pressure and temperature monitoring device: A dynamic laboratory validation study. *Gait & Posture 100*,70-74. doi: 10.1016/j.gaitpost.2022.11.013 (Appendix 5).

7.4.1 The dynamic validation process: aims and objectives

Following static validation, dynamic validation was performed on the innovative, in-shoe pressure and temperature device. Dynamic validation is a type of validation testing that determines the behaviour, performance and accuracy of measurement of the device in a simulated, real-life scenario (Zelt et al., 2018). This study was important as it helped the researcher establish content validity, identify points for hardware and software improvements of the prototype and help gain an initial assessment of internal consistency. Thus, this dynamic validation study also served as the pilot study for this PhD project.

Aim: The aim of this study was to achieve dynamic validation, of the innovative, single-sensor in-shoe pressure and temperature mapping device purposely developed to read and measure in-shoe pressure and in-shoe skin temperature.

Objectives:

- To determine dynamic validation - to validate the newly-developed single-sensor in-shoe pressure and temperature device in a real-life scenario, on healthy participants against the FScan™ in-shoe pressure mapping system by Tekscan™ which served as a reference standard to this study.

7.4.2 Methodology

The aim of this study was to determine the dynamic laboratory validation, of the innovative, single-sensor in-shoe pressure and temperature mapping device in a real-life scenario, on healthy participants against the Flir® T630sc Thermographic Camera and the FScan™ in-shoe pressure mapping system by Tekscan™ which served as a reference standard to this study.

Prior to the commencement of this study, ethical approval was sought and granted by the Faculty of Health Sciences Ethics Board (FREC) and by the University of Malta Research Ethics Committee (UREC) (Appendix 11). Dynamic validation of the newly developed, low-cost, single-sensor pressure and temperature device was conducted at the Biomechanics Laboratory at the Faculty of Health Sciences at the University of Malta. In this study, the pressure results obtained via the prototype were compared to that of an already established and validated in-shoe pressure device, specifically the FScan in-shoe pressure system, originally developed by Tekscan™ which thus served as a reference standard tool. As for the temperature results obtained by the prototype, since to date, current technology has not yet established a "gold standard" in-shoe temperature device, a thermographic camera, the Flir® T630sc, was used as a reference standard device for temperature. The set-up of both the prototype and the FScan™ in-shoe system, was prepared with the help of 2 qualified and experienced

Engineers who also ensured seamless functioning of both hardware and software during data collection.

7.4.3 Method

Through a convenient random sampling technique, 5 healthy participants with no known physiological or biomechanical conditions and aged between 30 to 60, were recruited to participate in this study. The participants were given a pair of 100% cotton socks to ensure consistency when interpreting temperature measurements during data collection however, the participants were instructed to use their own lace-up sports shoes during data collection.

At the beginning of the data collection, the participants were instructed to lay supine, barefooted while wearing the provided cotton socks, for a total of 15 minutes in a pre-set ambient climate of 25 degrees Celsius (Roy, Boucher & Comtois 2006). This served as an acclimatization period prior to the collection of plantar temperature readings via the Flir® thermographic camera (Figure 59).

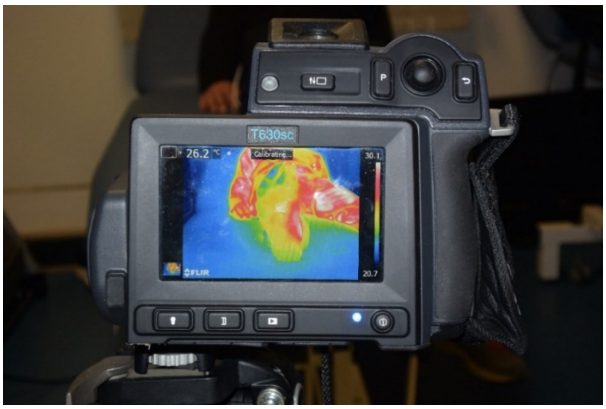


Figure 59: Photograph showing thermographic images of participant's right foot

The data collection proceeded with the set-up of the equipment (the FScan and the prototype) within the Rt shoe of the participants. To ensure that the pressure and temperature sensors of the prototype do not create a pressure point over the insole of the FScan™ system, they were embedded within a 3mm-thick simple foam insole (Figure 60). As shown in Figure 60, the temperature and pressure sensors of the prototype were positioned at an area that matched to the 1st metatarsophalangeal joint

(MPJ) of the right foot of the participant. Figure 61, shows how the equipment was worn by the participants during the data collection.

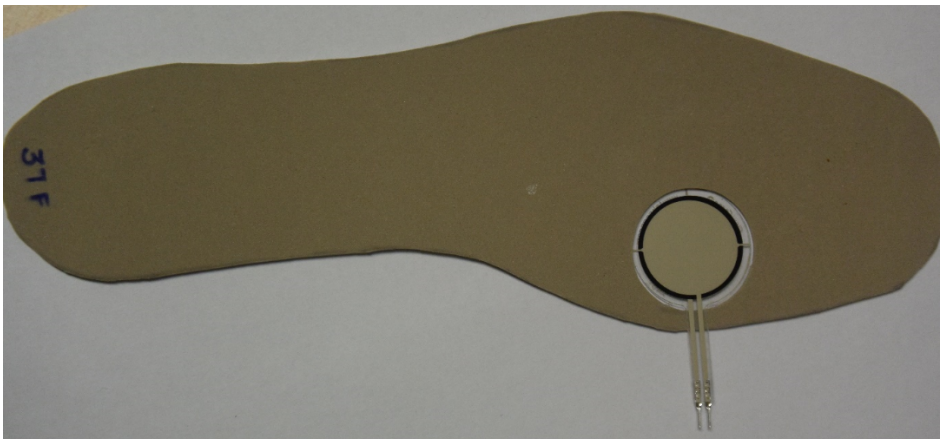


Figure 60: Photograph showing an example of simple insole used to hold the FSR sensor of the prototype over the FScan™ sensor insert

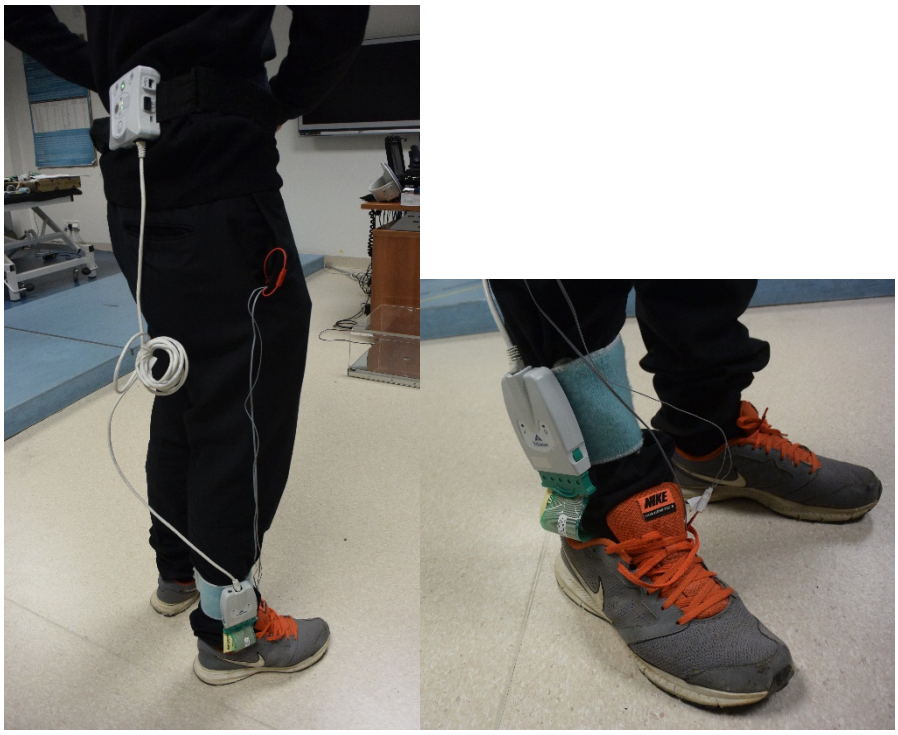


Figure 61: Photograph of the set-up of the FScan in-shoe system and prototype as worn by the participant during data collection

Point calibration was the calibration method of choice for the FScan™ system via the Tekscan™ software used to control the system. Point calibration is performed with the participant standing, in the case of this study, on his or her right foot while the system automatically calibrated the sensors based on the weight of the participant.

Following the set-up of the equipment on the participants, the participants were instructed to walk for 15-minutes, at a comfortable pace on an electric treadmill, to simulate mild physical exertion. During the walk, both temperatures and pressures parameters were recorded at 50Hz (50 readings per second) using the innovative single-sensor, in-shoe pressure and temperature measuring device and FScan™ system (Figure 62). Once the walk was completed, the barefoot thermographic image of the right foot was re-taken (utilizing the Flir® T630sc thermographic camera) to record any change in temperature at the plantar aspect of the participant's foot following the physical exertion. This procedure was repeated for all 5 participants.

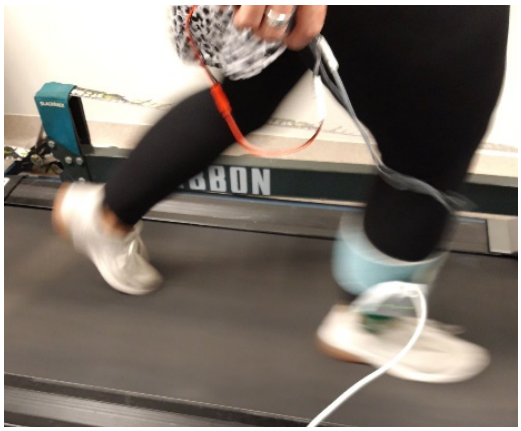


Figure 62: Participant walking at natural pace on treadmill wearing the prototype and FScan™ device

Figure 63 below provides the reader with a flow chart that summarizes the steps taken for the data collection of the dynamic validation testing.

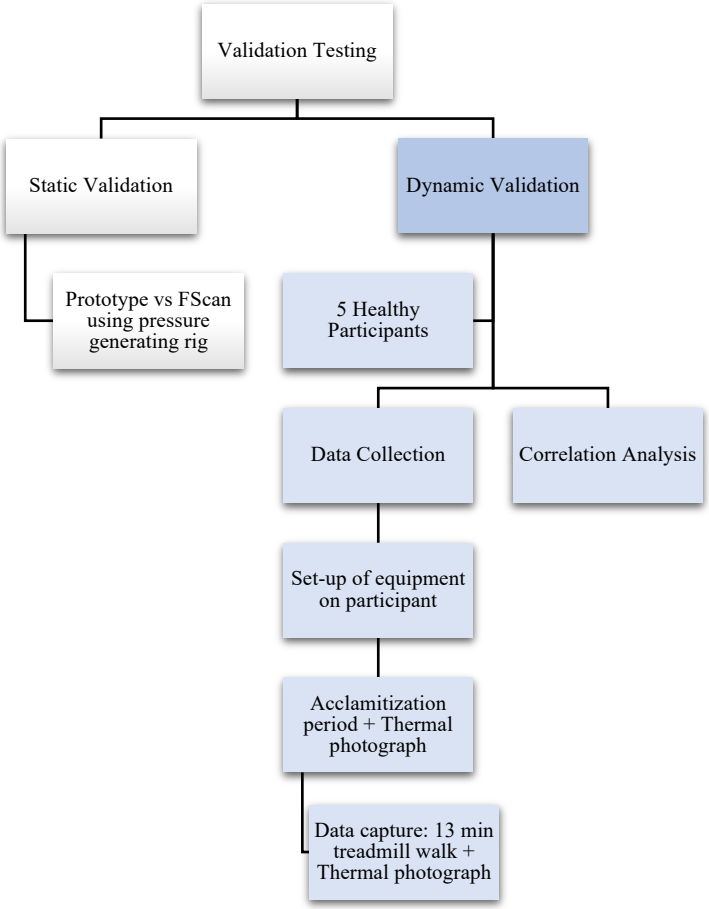


Figure 63: Flow chart summarizing the process taken to conduct dynamic validation testing.

7.4.4 Data extraction

Two datasets were collected during each trial. The raw readings were passed to the regressor, which returned the estimated KPa value. Several evaluations metrics were used to evaluate the performance of the modal. The selected methods were chosen to consider as per the industry standards.

 Mean Absolute Error: MAE is a straightforward metric that calculates the absolute difference between actual and predicted values.

$$\mathrm{MAE} = \frac{\sum_{i=1}^{n} |y_i - x_i|}{n}$$

 Mean Squared Error: MSE is the most used and straightforward metric with little change in mean absolute error. Mean squared error states that finding the squared difference between actual and predicted value. Results are interpreted as follows: the lower and closer to 0 the MSE value is, the more accurate the device is able to predict pressure readings.

$$\mathrm{MSE} = \frac{1}{n}\sum_{i=1}^{n}(Y_i - \hat{Y}_i)^2$$

 Root Mean Squared Error is the standard deviation of the residuals (prediction errors). Residuals measure how far from the regression line data points are; RMSE measures how to spread these residuals. It provides an estimate of how accurate the device is to read, in case of this study, pressure values. A perfect RMSD should read 0 however, since this rarely occurs, the lowest the value the more accurate are the results.

$$\mathrm{RMSD} = \sqrt{\frac{\sum_{i=1}^{N}(x_i - \hat{x}_i)^2}{N}}$$

 Root Mean Squared Logarithmic Error: This metric measures the ratio between actual and predicted values and takes the predictions and actual values log. Use this instead of RMSE if an under-prediction is worse than an over-prediction. The perfect score for RMSLE is estimated to be around 2.34.

$$\sqrt{\frac{1}{n}\sum_{i=1}^{n}(\log(x_i+1) - \log(y_i+1))^2}$$

 R Squared (R2): R2 score is a metric that tells your model's performance, not the loss in an absolute sense that how many wells did your model perform.

$$R^2 = 1 - \frac{RSS}{TSS}$$

 Adjusted R Squared: The disadvantage of the R2 score is that while adding new features in data, the R2 score starts increasing or remains constant but never decreases because it assumes that the variance of data increases while adding more data.

$$R_a^2 = 1 - \left[\left(\frac{n-1}{n-k-1}\right) \times (1 - R^2)\right]$$

 Pearson Correlation: is a measure of linear correlation between two sets of data. It is the ratio between the covariance of two variables and the product of their standard deviations; thus, it is essentially a normalised covariance measurement. The result always has a value between −1 and 1.

$$\rho_{X,Y} = \frac{\mathbb{E}[(X - \mu_X)(Y - \mu_Y)]}{\sigma_X \sigma_Y}$$

7.4.5 Results

7.4.5.1 Demographic data

From a total of 5 participants, 40% were females (*n*=2) and 60% were males (*n*=3). The mean age of the participants was that of 40.1 years of age with a mean weight of 72kg (Figure 64).

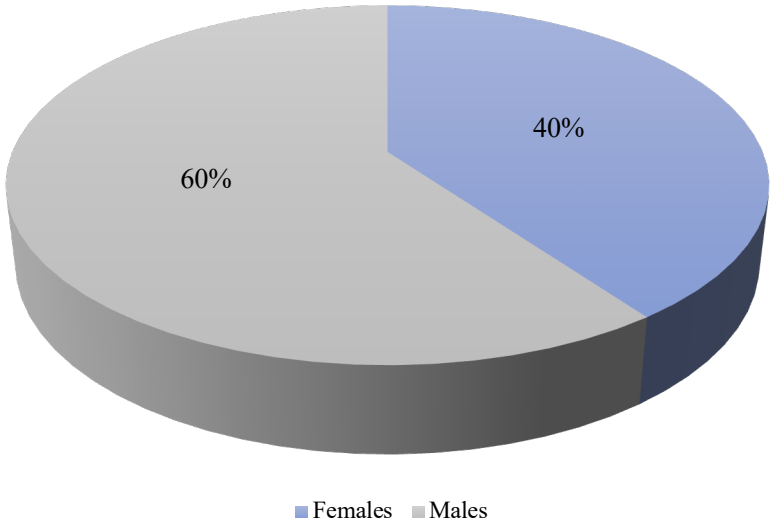


Figure 64: Pie chart representing the gender distribution of participants for this study

7.4.5.2 Correlation of Pressure Results between the Prototype and Reference Standard

Spearman's Rank Order Correlation (*rho*) was used in this study to describe the strength and direction of the linear relationship between the pressure values obtained via the prototype and the pressure values obtained via the FScan system which for the purpose of this study served as reference standard. The strength of relationship between variables can vary from: -1 which indicates a perfect negative correlation; to +1 which indicates perfect positive correlation; and where 0 shows no correlation (Parker, 2010).

The experimental results presented in Table 24 show that, in all 5 trials, there was a high correlation (0.801, 0.978, 0.813, 0.887, 0.944) in peak pressure readings between the prototype and the FScan system which for the purpose of this study served as a reference standard (Table 24).

Table 24: Table showing the correlation results for the pressure readings obtained from the FScan system and the Prototype device

ID	P Correlation	MAE	MSE	RMSE	RMSLE	R2	R2 ADJ
1	**0.801**	6.976	93.04	9.645	2.266	0.517	0.491
2	**0.978**	6.657	89.877	9.48	2.249	0.951	0.948
3	**0.813**	6.237	82.079	9.059	2.203	0.495	0.467
4	**0.887**	6.425	86.003	9.273	2.227	0.725	0.71
5	**0.944**	7.39	100.299	10.014	2.304	0.88	0.874

The correlation between the FScan system and Prototype device in terms of peak pressure readings was further confirmed by superimposing the peak pressure data readings of all (n=5) participants gathered from the FScan system to form one graph (Figure 65) and superimposing the peak pressure data readings of all (n=5) participants gathered from the prototype device into another graph (Figure 66). Comparison of the superimposed peak pressure data plots from the FScan and superimposed peak pressure data plots from prototype proved to be similar in pattern. This indicates that both devices are reading the peak pressure readings similarly. Individual data plots for each and every participant can be found in Appendix 12.

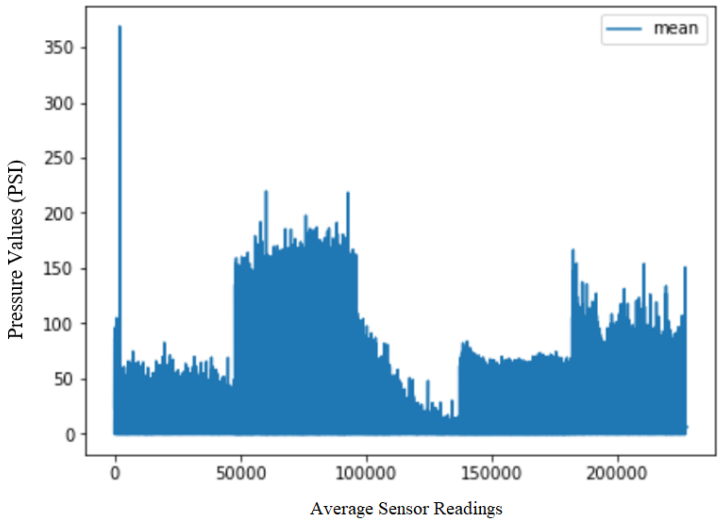


Figure 65: Pressure data of all 5 participants collected by the FScan system

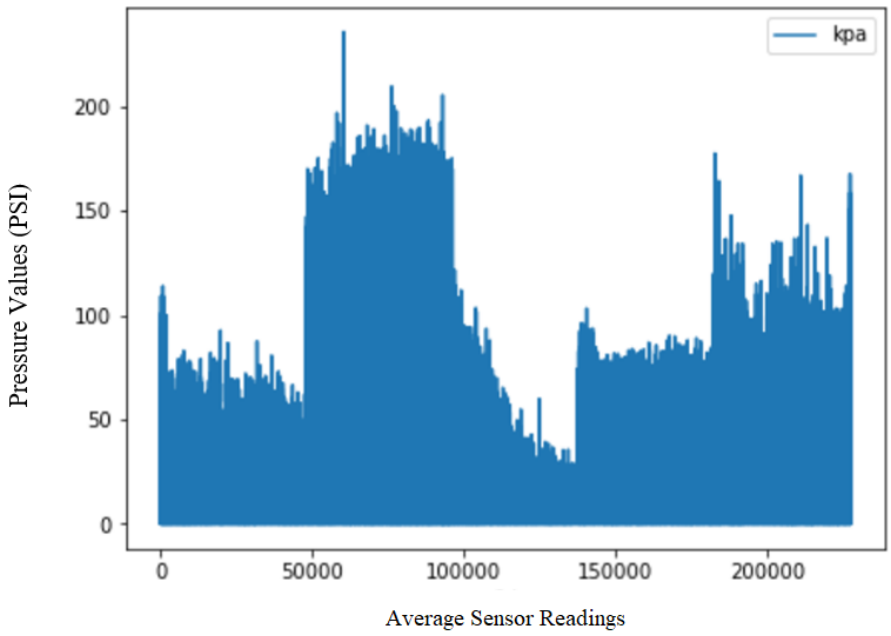


Figure 66: Pressure data of all 5 participants collected by the Prototype system

To further support the results obtained from the correlation analysis, test such as the Mean Absolute Error, the Root Mean Squared Error, Root Mean Squared Logarithmic Error, R Squared (R2), Adjusted R Squared were conducted to confirm accuracy of the prototype device, compared to the reference standard. Referring back to Table 24, interpretation of results for the Mean Absolute Error (around 7 in all 5 trials) and the Root Mean Squared Error (around 10 in all), show that the prototype device equivalence between the FScan and prototype device in predicting pressure readings. Though no exact value exists in predicting accuracy, when interpreting MSE and RMSE the lowest or closest to 0 the better the result. Interpretation of Root Mean Squared Logarithmic Error values obtained in this study are around 2.3 in all 5 trials, this also shows that the predictions made be the reference standard (FScan) and those made by the prototype are equivalent (Table 24). R Squared results of this study, show that the prototype was able to accurately read pressure values by 52% for patient 1, 95% for patient 2, 49% for patient 3, 72% for patient 4 and 88% for patient 5, compared

to the FScan system (Table 24), again, confirming that the equivalence of the prototype device to the reference standard.

7.4.5.3 Temperature

The experimental results presented in Table 25 below show that the average change of temperature read by the thermal cameral is equivalent to 3.7 °C with a Confidence Interval (CI) of 1.07 and Standard Deviation (SD) of 0.86. This shows that the overall distribution of the data values is spread out and thus vary from the actual mean.

Table 25: Barefoot temperature readings (thermal camera)

Participant	Sex	Age	Weight (Kg)	T_1	T_2	ΔT	SD	CI	RSD
1	F	53	70	28.8	32.1	3.3			
2	M	55	92	28.4	33.2	4.8			
3	M	26	60	26.8	30.8	4	0.86	1.07	23.17
4	F	32	70	26.5	30.4	3.9			
5	M	36	68	31.1	33.6	2.5			

The in-shoe temperature readings, presented in Table 26 below, showed that the average change of temperature read by the in-shoe temperature sensor is equivalent to 0.67°C with a confidence interval of 0.48. This means that the overall distribution of this data values is also spread out and thus varies to the mean.

Table 26: In-shoe temperature readings (Prototype device)

Participant	Sex	Age	Weight (Kg)	T_0	T_1	ΔT	SD	CI	RSD
1	F	53	70	14.33	14.88	0.55			
2	M	55	92	14.31	15.46	1.15	0.43	0.48	63.64
3	M	36	68	12.36	12.68	0.32			

The Relative Standard Deviation (RSD) was calculated to compare the variation in temperature distribution between the in-shoe temperature sensor and the thermal

camera. Results showed that measurements from the in-shoe temperature sensor had greater variation in temperature change between participants (63.64) as opposed to the measurements taken from the thermal camera (23.17) (Table 27). This information shows that both the in-shoe temperature sensor of the prototype device and the thermal camera show great data variation when reading temperatures. It also shows that, since the RSD value of the prototype is greater than that of the thermal camera, in-shoe temperature sensor of the prototype has an even larger data variation compared to that of the thermal camera.

Table 27: Table comparing the RSD results of each device used to measure temperature

	In-shoe temperature from prototype device	**Barefoot temperature from thermal cameral**
RSD	63.64	23.17

Furthermore, comparison of temperature data readings between the in-shoe temperature sensor and the in-shoe pressure sensor, showed a high correlation (0.87) between the 2 parameters (Table 28). Such results indicate that as pressure increases, so does the skin temperature at the affected area.

Table 28: Correlation analysis of in-shoe temperature vs. in-shoe peak pressure

Participant	**In-shoe Temp (ºC)**	**Pressure (kPA)**	**Pearson's Correlation Coefficient**
1	14.88	20	0.87
2	15.46	22	
3	12.68	19	

7.4.6 Discussion

Prevention of diabetic foot complications is empirical as these bring about a huge burden on the local health care system due to the increased need of treatment for infections, hospital admissions and amputation procedures (Armstrong et al., 2017;

Cuschieri, 2020). It is well known that diabetes, with or without the presence of comorbidities such as peripheral arterial disease and peripheral neuropathy, amplify pre-existing biomechanical anomalies that are often overlooked thus, over time, clinical signs tend to present themselves as persistent plantar wounds (Shavelson et al., 2011). Early identification of the clinical signs that can be used to predict ulcer development if highly important in the diabetic high-risk foot. Previous foot ulceration, callus formation, blistering and bruising of the skin are all strong predictors for foot re-ulceration, which are aggravated by biomechanical factors such as foot deformity and increased foot plantar pressures (Peters et al., 2007; Dubský et al., 2013; Waaijman, 2014).

The aim of this study was to determine the dynamic laboratory validation of the innovative, single-sensor in-shoe pressure and temperature mapping device on healthy participants. This device is innovative as it can read and measure in-shoe plantar pressure and in-shoe skin temperature simultaneously at one particular site.

Results from the laboratory dynamic validation experiment showed a high correlation between the in-shoe peak pressure readings gathered from the innovative, single-sensor, in-shoe pressure and temperature device and the FScan® in-shoe pressure system which in this study acted as a reference standard for pressure. To remind the reader, a reference standard refers to the best test or method of diagnosing or measuring something that is currently available. It is the "gold standard" technique, method, or instrument against which the index test is compared to (Santini & Eaton, 2022). Thus, test results confirm that the innovative, single-sensor, in-shoe pressure and temperature device is indeed able to read and measure in-shoe plantar pressures as effectively as the renowned, already established FScan® in-shoe pressure system by Tekscan. The difference between the 2 devices, besides the ability of the innovative, single-sensor, in-shoe pressure and temperature device to read temperature, is that the innovative, single-sensor, in-shoe pressure and temperature device has only one sensor and, compared to the FScan system, it is very user friendly and straight forward to use and interpret results, making it ideal in a typical busy clinical setting.

The innovative, single-sensor, in-shoe pressure and temperature device was also tested for its ability to read and measure in-shoe plantar pressures. As with the testing of the in-shoe pressure sensor, a reference standard was necessary for comparison of results. Following a systematic review of the currently available in-shoe temperature devices, it was concluded that as of yet, a "gold standard" device that measures both foot plantar pressures and temperatures concurrently is not available (Saliba Thorne, Gatt, DeRaffaele et al., 2021). In view of this, an already established, commercial thermal camera, Flir® T630sc, was used to compare temperature results. The laboratory dynamic validation test demonstrated that the overall distribution of the data values of both thermal camera and of the innovative, single-sensor, in-shoe pressure and temperature device, is spread out and thus vary from the actual mean. This means that readings from both devices have high variability from one reading to the next and/or from one participant to another. Elements in data collection that could have influenced this result include a) the physiological responses and thermoregulation of the human body across individuals differ and b) the sample size was too small.

The thermoregulation of a human body is controlled by the hypothalamus which sends and receives signals from skin in response to a change in ambient temperature (Mendoza & Griffin, 2010). This also occurs during exercise. The movement of the muscles generate heat and, through the hypothalamus, vasodilation of the peripheral capillaries occur. Heat from the body is then lost through conduction and/or radiation through the outer layer of the skin (Gonzalez et al., 2012). Sweat also plays an important role in thermoregulation as it serves as a cooling mechanism while it is evaporating (Osilla, Marsidi & Sharma, 2022).

The ability to have an efficient thermoregulation of the core body temperature and prevent overheating, is highly influenced by a number of factors and varies across individuals (Kenney & Munce, 2003). A review study by Kenny & Munce (2003) highlighted that, changes in physiological conditions and biochemistry of the human body, vascular perfusion, age, level of fitness, medication and chronic diseases such as neuropathy, heart disease and diabetes can have a major influence on the ability to

thermoregulate the core body temperature. This was also argued in a study by Takeda & Okazaki (2018). Thus, the more active and healthier a person is, the greater is his/her ability to release heat and control the core body temperature (Sanko, 2007).

With an RSD of 63.64 for the innovative, in-shoe pressure and temperature device and an RSD of 23.17 for the thermal camera, it was concluded that both devices show great data variation when reading temperatures. Moreover, since the RSD value of the prototype is greater than that of the thermal camera, in-shoe temperature sensor of the prototype was considered to have even larger data variation compared to that of the thermal camera.

These results could also have been influenced by factors such as physiological and demographic factors as the above-mentioned which vary across participants. Furthermore, the number of participants varied from the readings taken by the thermal camera (n=5) and those by the prototype (n=3) due to a malfunction of the sensor during data collection. In both cases, a larger sample size could have achieved a different result. The variation in RSD result could also be attributed to the difference in technique of reading temperature by both devices. The temperature sensor of the innovative, in-shoe pressure and temperature device is able to read temperature when in direct contact (through conduction) to the object under investigation, while the thermal camera is reads temperature through at a distance (through radiation).

Finally, the comparison of data between the in-shoe temperature sensor and the in-shoe pressure sensor, showed a high correlation between temperature and pressure. This showed that, as it was for long suspected, as pressure increases, localised skin temperature also increased (Houghton, Bower & Chant, 2013; Bus, 2015; Ena, Carretero-Gomez, Arevalo-Lorido et al. 2020).

The benefit of having a validated single-sensor device lies within the fact that it can be used by the clinician during routine visits to monitor in-shoe temperature and pressure at any specific area of interest such as a formerly ulcerated anatomical site or an area that is showing pre-ulcerative indications. The innovative, single-sensor in-

shoe pressure and temperature measuring device was developed to provide the clinician with a low-cost alternative to the current commercially available, expensive, in-shoe pressure systems and barefoot temperature monitoring devices. This prototype is unique as it is purposively designed to read in-shoe plantar pressure and in-shoe skin temperature simultaneously, a feature which similar current commercial technology is lacking.

As demonstrated in various studies, off-loading and pressure re-distribution off the ulcerated area indeed help in preventing recurrence of plantar ulceration (Bus et al., 2013; Ulbrecht et al., 2014, Armstrong et al., 2017). Considering the huge impact of foot orthoses on foot offloading, and the wide variety of manufacturing choices, inappropriate designs may increase the risk of ulceration (Armstrong et al., 2017). With the introduction of this innovative, single-sensor, in-shoe pressure and temperature device on the market, the clinician would be able to check whether the prescribed offloading device is actually effective in reducing excessive pressures over the area of interest. The clinician may use this device to modify and re-distribute pressures if found necessary on the same day of dispensing the offloading device. It is stated in the literature that there is a greater chance of achieving better outcomes in offloading an at-risk area when assisted by proper technology to confirm current pressures and temperature readings of the high-risk foot.

Clinical assessments of prescription orthoses done with the help of technology, not only permits the practitioner to obtain objective, precise and reliable measurements, but also helps the practitioner to understand how he/she can adapt or make modifications to orthoses to best achieve foot plantar pressure reduction and avoid re-ulceration (Bus et al., 2004, Hsi et al., 2005, Mueller et al., 2006, Koenraadt et al., 2012, Paton et al., 2012, Ibrahim et al., 2013). The quality and effectiveness of foot orthoses prescribed for the diabetic high-risk foot is thus empirical for the prevention of diabetic foot ulceration and/or re-ulceration.

7.4.7 Limitations of the Study

Like any other study, this study came with its own limitations. Though this study validated a ground breaking and innovative in-shoe device that can measure temperature and pressure simultaneously, this study recruited a small sample size (n=5) of healthy individuals of which 2 participants had to be eliminated when considering temperature data. It would have been ideal to validate this device in a much larger sample size to provide more robust results.

7.4.8 Conclusion

Results from this study show positive correspondence of data between the prototype and the reference standard. This suggests that the innovative single-sensor pressure and temperature device was equally able to measure pressure to the currently available technology. Thus, the authors area confident that the prototype can be used as a low-cost alternative to costly commercial devices. Furthermore, a high correlation between increase in peak plantar pressure and raise in skin temperature was also confirmed showing a strong relationship between 2 predictors of diabetic foot ulcer formation.

Due to this feature of measuring both temperature and pressure at the same time, the single sensor, in-shoe pressure and temperature device is anticipated to be a significant instrument for the prevention and management of the diabetic high-risk foot and associated ulcerations. As of yet, this is the first, single sensor, in-shoe pressure and temperature monitoring device that has been developed and validated showing high correlation results when compared to already commercially established devices. The results of this study were published in the Gait & Posture journal doi: 10.1016/j.gaitpost.2022.11.013 (Appendix 5).

Despite these promising results, further investigation on the use of the innovative single-sensor pressure and temperature device in the diabetic high-risk population is still recommended. In view of this, Phase III of this dissertation consisted of a clinical trial involving participants living with diabetes mellitus that was conducted to further investigate the relationship between pressure and temperature and diabetic foot ulcer development. This clinical trial is presented in the following chapter (Chapter 8).

Chapter 8: The Clinical Trial

8.1 Introduction

In this chapter, the methods employed for Phase III of this study are described. Details on the location of the study, ethical considerations, study population, data collection process, outcome measures and planned statistical analysis were portrayed.

As part of Phase III of this research project, this study evaluated whether a single sensor pressure/temperature mapping device can be used as an adjunct assessment method to the current standard care in the prevention of diabetic foot ulceration/re-ulceration by assessing the effectiveness of offloading devices provided to patients as part of the standard local diabetic foot care management plan.

This study employed a quantitative type of methodology that revolved around a post-positive philosophical perspective. The data collection was conducted in scenarios that mimicked real clinical setting to ensure a realistic application of the proposed care plan.

8.2 The Local Standard Diabetic Foot Care Management

As detailed in Chapter 1, the current, standard, local diabetic foot care management plan follows the IDF screening guidelines for the management of the diabetic foot (IDF, 2020). This management plan consists of 3 levels of screening at which the patient is categorised as either at high-risk or low-risk of developing foot ulceration/amputation.

At all levels of screening, the patient is assessed by his or her Podiatrist for his or her dermatological status, and for his or her neurological and vascular status with the help of the 10g monofilament and a doppler (at screening level 1) or dopplex ultrasound (at screening level 2 and 3) which are tools to determine the presence of neuropathy and ischaemia respectively. Based on the vascular and neurological findings, the patient is then categorised as high-risk or low-risk of developing diabetic foot complications.

With regards to biomechanics, the only form of biomechanical assessment performed in in the current diabetic foot care management plan is the observation of visible deformities of the diabetic foot being examined. In cases of history of ulceration, amputations or signs of ulceration/re-ulceration such as erythema, haematomas and hyperkeratotic lesions, especially in the presence of foot deformities such as prominent plantar metatarsal heads and fat pad atrophy, the patient is provided with offloading devices such as prescription orthoses, to offload the at-risk areas. The effectiveness of the prescribed offloading device, pre- and post- dispensing, is determined through visual observation and clinical experience of the clinician.

8.3 Research Question, Aims and Objectives

Does monitoring through a single sensor pressure/temperature mapping device help in preventing ulceration/re-ulceration in a diabetic high-risk population when compared to standard clinical care?

Aims: To compare the outcome of the application of a single sensor pressure/temperature monitoring device to standard clinical protocols only in the prevention of diabetic foot ulceration and re-ulceration.

Objectives:

- To evaluate current offloading devices utilizing the innovative, single-sensor, in-shoe pressure and temperature measuring device to ensure 30% pressure reduction of the original peak plantar pressure at a previously ulcerated site.
- To determine whether using the single sensor pressure/temperature device as an adjunct to standard protocol clinical care for the management of diabetic foot ulceration/re-ulceration is effective in reducing the number of active re-ulcerations compared to the standard care alone.
- To determine the number of re-ulceration cases between the experimental and control group

- To establish any correlation between peak plantar pressure and peak plantar temperatures in the diabetic high-risk foot.

8.4 The Philosophical Influence on the Study design

The overarching aim of this PhD was to determine whether the application of the innovative, single-sensor, in-shoe pressure and temperature measuring device can be used as an objective and low-cost clinical tool, in the prevention of diabetic foot ulceration and re-ulceration.

Various decisions on the development of the research design and methodology had to be taken. To do so, the researcher followed the Research Onion by Saunders et al. (2009) as show in Figure 67 below.

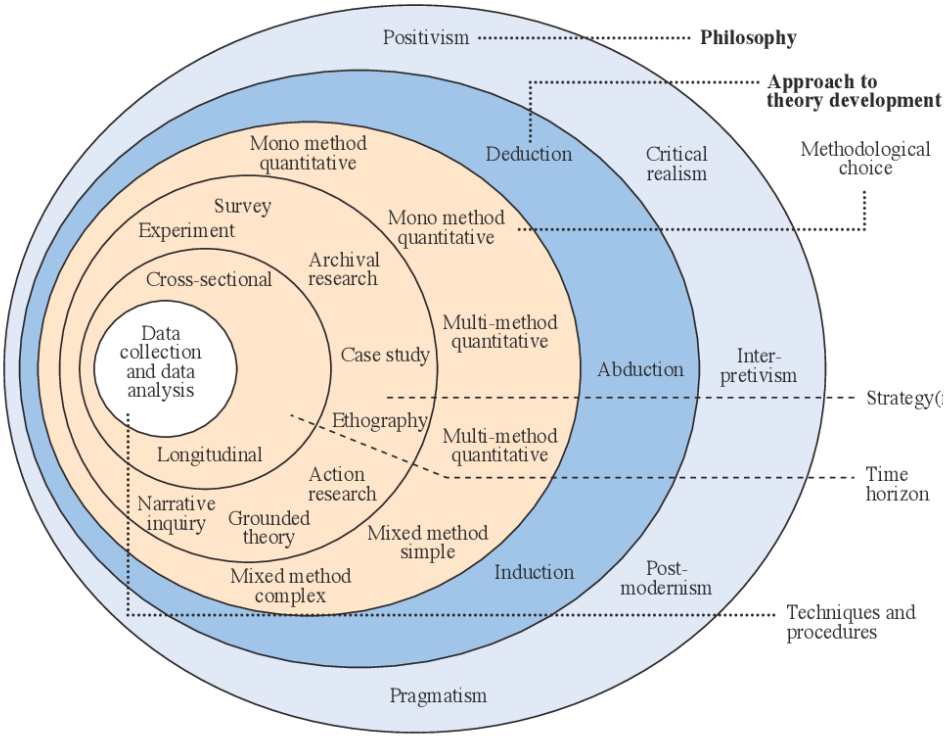


Figure 67: Research onion by Sauders (2009)

This PhD study was inspired by a post-positive epistemological approach and observed a deductive reasoning to its theory development. A matched parallel (non-crossover), prospective experimental clinical trial was selected.
Such study design was used to identify which patient management was best for the patient through fair comparison, in such case, between a new management protocol (the integration of the innovative, single-sensor, in-shoe pressure and temperature measuring device to the standard diabetic foot care protocol) and an existing standard diabetic foot care protocol (Nichol, Bailey & Cooper, 2010).

In this research study, the study design involved two groups of the same patient population; an experimental group, who were assessed for their peak plantar pressures and skin temperature, using the single-sensor, in-shoe pressure and temperature measuring device, before and after orthoses prescription; and a control group who were managed with the standard diabetic foot care protocol. Such design allowed the researcher understand whether using the innovative, single-sensor, in-shoe pressure and temperature measuring device as an adjunct to the standard diabetic foot care protocol, was indeed more effective than the current diabetic foot care protocol being implied within the local health care (Hariton & Locascio, 2018). Having used a Matched-pairs design for matching the participants prior to the commencement of the clinical trial, an element of randomisation was allowed. This provided the research with unbiased results as matched participants were equally and randomly distributed into the 2 groups. This study was longitudinal in nature as patients were reviewed every 4 months over a period of 1 year to assess any signs of re-ulceration. A detailed account of this clinical trial is discussed in the following sections.

8.5 Ethical Considerations

Prior to the commencement of this clinical trial full ethical approval was sought. A written request from the Data Protection Officer at Mater Dei Hospital and the Lead consultant of Diabetes & Endocrine Department affiliated with the Hospital from which patients were recruited (Mater Dei Hospital) was attained so that the researcher

was able to access patient data, and to recruit participants from the department. Permission to access both equipment and biomechanics laboratory available at the Faculty of Health Sciences, University of Malta was obtained from the Head of Podiatry Department at the Faculty of Health Sciences. Ethical approval was granted by the University Research Ethics Committee (University of Malta) on the 26 October 2020 (Appendix 11).

As in accordance with the Declaration of Helsinki, the researcher

- Preserved the participant's identity by using identification codes instead of personal identification information
- Stored data under lock and key or password protected (encrypted format)
- Destroyed data which was identifiable to the participants once the study was completed
- Allowed participants to choose freely whether or not to participant in this study and to stop their participation at any point of the study
- Fully informed the participants about what the study entailed and why their participation was of significance.

8.6 Methods

8.6.1 Study Design

The aims and objectives of this study primarily focused on the overall impact of using the innovative device as an adjunct to the standard diabetic foot care protocol, when compared to the standard diabetic foot care protocol on its own. A matched parallel (non-crossover) clinical trial with a prospective experimental design, was deemed as the best suited methodology for this investigation. Parallel clinical trials involve two independent treatment arms in which case, the experimental group and the control group, where each group is given a different type of treatment such as, the use of the

device as an adjunct to standard clinical care protocol versus the standard clinical care protocol only (Nair, 2019).

Initially, a pure randomised trial was planned however, due to the complexity of the patient population recruited, and the number of factors that may have influenced re-ulceration, a matched subject design was employed in this study. Matching of participants prior to an investigation helped in reducing the chances of influential and cofounding variables that may influence the outcomes of a study (Nestor & Schutt, 2015). Since randomisation is important to eliminate selection bias and accidental bias (Suresh, 2011), a matched-pair design was employed. This type of matching design allows for the combination of matching and random assignment of participants to a treatment arm giving the researcher greater control to detect statistical difference between the groups (Nestor & Schutt, 2015). As explained in more detail in Section 8.6.5, matched-pair designs, ensured that all subjects were equivalent to each other before being randomly introduced to either the experimental group or the control group. Matching of participants was based on age and gender, duration of diabetes, presence of neuropathy, presence of neuro-ischaemia or presence of ischaemia. This design also helped improve the comparability of participants thereby increasing the validity of the cause-and-effect relationship within the trial.

8.6.2 Study site

Potential participants that fitted within the pre-set inclusion criteria (as detailed in Section 8.6.7) were recruited, via an intermediary, from the Diabetic Foot Clinic at the Outpatients Department of the local hospital. The data collection was then conducted at the Biomechanics and Gait Lab at the Faculty of Health Sciences, University of Malta.

8.6.3 Study Population

In this study, the inclusion criteria for the study population entailed participants, male or female, living with type II diabetes mellitus with a past history of, one or more,

plantar foot ulceration. Only participants who already owned prescription orthoses, intended to offload previously ulcerated sites, were considered as potential participants.

8.6.4 Sample size and Power Calculation

The most common approach to data collection in a research study is sampling which is a term used to describe the selection of participants to be measured within the study (Garson, 2012). The choice of participants that make up the sample of a research study, determines the extent at which the results of the study may be generalized to the general population being studied (Garson, 2012). This means that preceding data collection, a clinical researcher should ensure that the selected sample size has enough power to represent the general population being studied (Serdar, Cihan, Yücel & Serdar, 2020).

In order to achieve generalizability of a study, it is ideal that the sample size of the study is determined through a sample power calculation analysis to ensure that the sample size is large and representative enough. The Power calculation analysis considers the population size (the actual size of the population being studied), the margin of error (confidence interval), the confidence level (generally at 95% with a Z-Score of 1.96) and the standard deviation (generally of 0.5) (Smith, 2013). The sample size is estimated using the following formula (Smith, 2013):

$$Sample\ Size = \frac{(\mathrm{Z-score})^2 * \mathrm{StdDev} * (1 - \mathrm{StdDev})}{(\mathrm{margin\ of\ error})^2}$$

Malta is rated to have 42.300 people affected with diabetes mellitus (IDF, 2020). It is estimated that 15% of patients living with diabetes mellitus develop foot ulceration at least once in their lifetime (Gershater et al., 2011; McEwen et al., 2013; Martins-Mendes et al., 2014; Yazdanpanah et al., 2018; Vassallo, Gatt, Cassar et al., 2021).

The general population size of people living with diabetes mellitus is that of 42.300 of which 15% have experienced a foot ulcer at least once in their life. Considering a confidence level of 95%, with a confidence interval of 7.99%, the estimated sample

size for this study resulted to be that of 150 participants. The sample size was calculated using a power analysis calculator (CRS, 2012).

8.6.5 Sample matching

As described in Section 8.5.3, in this study, the study population consisted of participants living with type II diabetes mellitus with a past history of one or more plantar foot ulceration (who already owned prescription orthoses intended to offload previously ulcerated sites). Participants were specifically selected based on their history of having a previous ulceration as previous ulceration is considered to be one of the strongest predictors of re-ulceration (Armstrong et al., 2017). This statement was exemplified in studies buy Dubský et al. (2013) and Bus et al. (2013) in which 40% of patients with previous ulceration experienced a recurrence within that same year of resolution of their previous ulcer.

Due to the complexity of the study population being investigated, and the number of factors involved that can influence the outcomes of this study, matching participants was deemed necessary to eliminate the chances of having differences between participants and to avoid as much as possible the presence of confounding variables. In this study, a Matched-pairs design was employed to allow the combination of randomisation of participants to either the experimental group or the control group (Nestor & Schutt, 2015). Matched-pairs design consists of matching participants based on one or more key characteristics and is best indicated in studies that investigate two treatment conditions as described in this study, standard diabetic foot care protocols versus using the innovative, single sensor, in-shoe pressure and temperature measuring device as an adjunct to standard diabetic foot care (Nestor & Schutt, 2015).

In this study, identified participants were matched based upon characteristics including age and gender, duration of diabetes, presence of neuropathy, ischaemia or neuro-ischaemia. These characteristics were specifically selected as the absence or presence of neuropathy, ischaemia and neuro-ischaemia, age range and gender determine the

level of risk of ulceration and ulcer healing in an individual (Shahbazian, Yazdanpanah, & Latifi, 2013, Armstrong, Boulton & Bus, 2017; Shi et al., 2021).

Precision matching was used to match participants based on gender, presence of neuropathy, presence of ischaemia and presence of neuro-ischaemia. Frequency distribution matching was used to match participants according to age range (for example, referring to this study, a male participant with a history of diabetic foot ulceration that fell within the age range of 50 to 60 years of age, living with neuropathy was paired with another male participant, also with a history of diabetic foot ulceration and neuropathy, and that fell within the same age range).

Once matched participants were identified, one participant was randomly assigned to the control group while the matched participant was assigned to the experimental group (Figure 68).

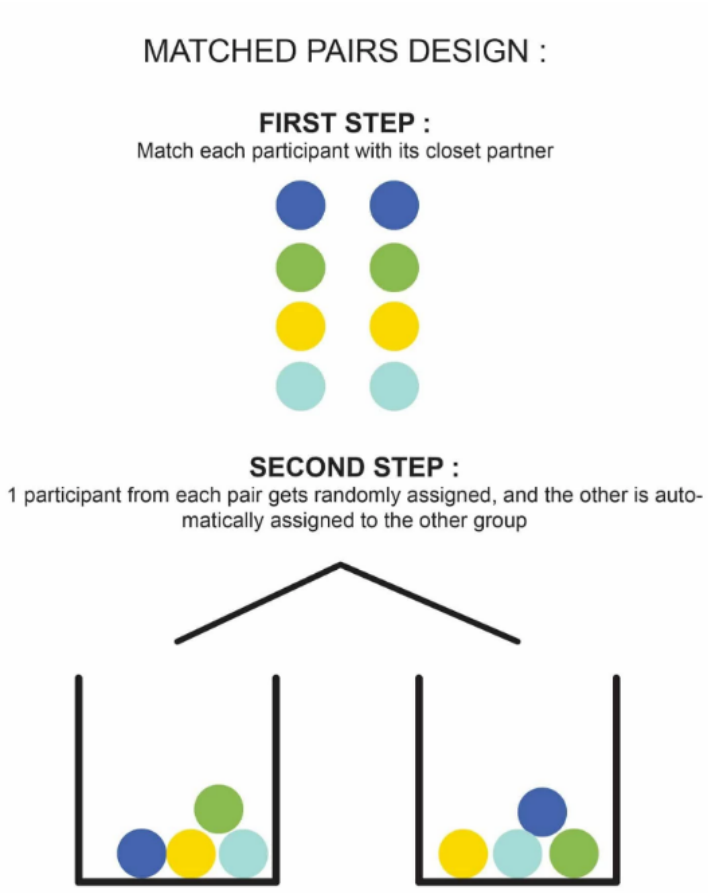


Figure 68: Visual aid to explain the steps taken to group assignment of participants. Retrieved from Voxco (2021).

Key variables such as presence of neuropathy, ischaemia and neuro-ischaemia may predispose the individual to different levels of at-risk of ulceration as represented in Figure 69 below (IDF, 2020).

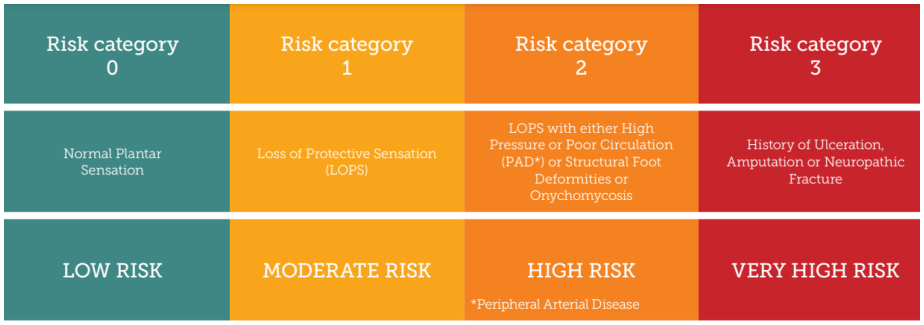


Figure 69: IDF guidelines on the risk categories of the diabetic foot. Retrieved from IDF (2018).

Following the IDF guidelines on risk categorization, individuals living with diabetes mellitus with no history of ulceration and no co-morbidities such as neuropathy, ischaemia or neuro-ischaemia are referred to as 'healthy' patients living with diabetes, and are categorised as low-risk. Individuals living with neuropathy are categorized as moderate risk as they unable to detect pain and thus, the expected biomechanical compensatory mechanisms in response to pain do not occur, predisposing the individual to higher risk of ulceration compared to people living with diabetes with no co-morbidities (Alam et al., 2017; Pop-Busui et al., 2017; Gatt, Hampton & Formosa, 2020). In the presence of ischaemia, excessive pressure and/or friction predisposes the skin to severe damage and tissue breakdown. The lack of blood supply to the lower limb, brought about by ischaemia, deprives the wound from oxygen and from receiving reparative nutrients causing delayed wound healing, infection and ultimately amputation predisposing the individual to an even higher risk. In the presence if neuropathy and ischaemia as co-morbidities, referred to as neuro-ischaemia, the consequences tend to be more grievous as the rate of tissue breakdown is faster and ulcer healing is more complicated (Edmonds, Manu & Vas, 2021). Thus, the IDF guidelines categorize these individuals to be at a very high risk of diabetic foot complications (IDF, 2008).

The use of a Matched-pairs design helped the researcher improve the comparability between subjects (Balzer et al., 2015). Matching the participants according to age, gender, duration of diabetes, presence of neuropathy, ischaemia and neuro-ischaemia avoided at-risk category bias which might have influenced the reason for re-ulceration

during the investigation. However, some disadvantages were also identified with using the Matched-pairs design. Having matched subjects signifies that in cases where a participant withdraws from the study or in cases of death of a participant, the corresponding/matched participant had to be eliminated from the trail putting a strain on the sample size. Another disadvantage identified was the difficulty in finding and matching subjects according the key characteristics selected especially during the COVID-19 pandemic (detailed in Section 8.5.8). During the recruitment stage, high-risk patients were socially isolating and were particularly avoiding hospital visits. This made both matching and participant recruitment very difficult which ultimately affected the sample size. Lastly, though Matched-pair design provides strong comparability and validation, the researcher is well aware that other, unidentified, confounding variables, could still have influenced the outcomes of the study (Moore, 2010; Bordens & Barrington Abbott, 2014). This will be discussed in more detail in the limitations of the study in Section 8.8.3.

8.6.6 Recruitment

As described in section 8.4, permission to recruit participants from the Diabetic Foot Clinic at the Outpatients Department of the local hospital was obtained. An experienced Podiatrist, specialised in diabetes foot care, working in this clinic was contacted and ask to act as an intermediary during the recruitment stage of this study in preparation for the data collection stage. The role of this experienced Podiatrist as the intermediary, was to help provide and identify potential participants that fitted the inclusion criteria and acted as middle person between the participant and the researcher to inform the potential participant about the study and invite him/her to participant in this study. Potential participants were identified based on characteristics such as living with type II diabetes mellitus, having a past history of plantar ulceration, living with peripheral neuropathy, neuro-ischaemia or ischaemia. Once potential participants gave their informed consent to have their information forwarded to the researcher to participate in this study, the potential participants were contacted via a telephone call for an appointment to participate in the clinical trial.

During the first visit, Time 0 (T_0), the researcher met the consenting participants to discuss in detail the nature of this study and their role as a participant, as discussed in more detail in Section 8.8.8. Participants were also informed that their participation was completely voluntary and that they could withdraw from the study at any point should they wish to do so as this would not affect their right to receive any future treatment care. This was also explained in writing, in form of the information sheet (Appendix 13) and the consent form (Appendix 14), that was handed to the participants prior to commencement of the study.

At Time 0 (T_0), the researcher ensured that the participant fitted the inclusion criteria (Section 8.8.7). At this stage, the following demographics were collected as detailed in the Data Assessment Sheet (Appendix 15).

- Age
- Gender
- Duration of Diabetes Mellitus
- Prescence of neuropathy, obtained from participant's medical record
- Prescence of ischaemia, obtained from participant's medical record
- Prescence of Neuro-ischaemia obtained from participant's medical record
- BMI: height and weight
- Most recent HbA1c levels, obtained from participant's medical record
- Site of previous ulceration

An in-depth biomechanical assessment was also performed which consisted of the following:

- Assessment of the Foot Posture Index (FPI)
- Assessment of the foot type
- Prescence of Hallux limitus or Rigidus
- Assessment of 1st ray position
- Limb length discrepancy
- Ranges of Motion of the knee joint, ankle joint, subtalar and midtarsal joint

Once the desired population sample was gathered, the participants were matched based on age range, gender, presence of neuropathy, presence of ischaemia and presence of neuro-ischaemia. One participant from the matching pair was allocated randomly to the experimental group while the other member of the same pair was assigned to the control group as previously portrayed in Section 8.6.5. This was repeated for the rest of the participants. The recruiting of participants initiated in June 2021 and was completed by August 2022.

Once all participants were assigned to either the experimental group or the control group a 3-week observation period was dedicated at Time 0 to observe both the control group and the experimental group for any re-ulcerations whilst under the current, local, standard diabetic foot care described in Section 8.2. This observation period served to give participants from both groups equal chance to re-ulcerate/not ulcerate under the same treatment. This period also served to demonstrate, through the clinical trial, whether cases of re-ulceration could be reduced with the introduction of the innovative, single-sensor, in-shoe pressure and temperature measuring device, used as an adjunct to standard diabetic foot care.

8.6.7 Inclusion and Exclusion Criteria

Inclusion criteria:

- Adults living with type II diabetes mellitus with history of plantar ulceration
- Categorized as high-risk of ulceration
- Have already been prescribed with prescription orthoses

Exclusion criteria:

- Subjects living with musculoskeletal pathologies such as Rheumatoid arthritis, Osteoarthritis, history of major amputations, and neuromuscular diseases.
- Subjects that were making use of walking aids such as crutches, wheelchairs and prosthesis.

8.6.8 Data Collection Procedures

Though the targeted patient population to be recruited was that of 150 participants, due to a number of difficulties listed below, the total number of participants recruited in the clinical was limited to 88 participants.

Limitations encountered during the recruitment processes included:

- Restrictions pertaining to the recent global COVID-19 pandemic: locally, there was a period of social distancing and many patients including high-risk patients refrained from attending to hospital appointments. This made the recruitment process much slower and more difficult than predicted especially with a Matched-pairs design. Several high-risk patients refused to attended to appointments at the local hospital due to risk of pandemic exposure this made identifying potential participants very difficult. Furthermore, due to the pandemic many potential participants refused to participate in the study. Only a few numbers of participants were unable to reach.
- Matching of participants was very difficult but crucial for the study as it helped the researcher minimise confounding variables.
- A number of participants were lost to follow-up as they withdrew their participation during the first or second visit. Reasons for withdrawal from the study included that the 20-minute walk on treadmill that was necessary to complete the trial was too intensive and fatiguing and fatiguing for the participants, and the fact that it had to be repeated in all the 3 visits did not encourage them.
- A number of participants refused to participate for personal reasons (reason was not disclosed).

Thus, in view of these difficulties, the recruitment and follow-up process were terminated with a final sample size of 88 matched participants living with Type II diabetes mellitus with a history of ulceration and who already have been prescribed custom-made hospital orthoses were recruited from the Diabetic Foot Clinic at the Outpatients Department at a local hospital. The participants were recruited with the

help of an experienced Podiatrist from the Diabetic Foot Clinic who acted as an intermediary during the recruitment stage of the study. The 88 recruited participants were grouped into 44 pairs. Table 29 represents the total visits arranged with the participants from first day of recruitment to the final visit.

Table 29: Diagram representing the total visits planned for the participants from first day of recruitment to the final visit.

<table>
<tr><td>Time 0 | Month 1-2
Recruitment Phase</td><td colspan="2">Informed consent & data collection of demographics
Matching of participants (n=88)

Control Group (n=44) | Experimental Group (n=44)</td></tr>
<tr><td>Start of Clinical Trial

Time 0 | 3-weeks
(T_0)
Observation period</td><td colspan="2">Both Control Group and Experimental Group were monitored for any cases of re-ulceration under standard diabetic foot care only</td></tr>
<tr><td>Start of the Experiment

Visit 1 | Month 4
(V1)</td><td>Control Group (n=44)

Standard clinical care

No orthoses alterations were provided

Monitored for re-ulceration</td><td>Experimental Group (n=44)

Set-up of the innovative, single sensor, in-shoe pressure and temperature measuring device on participant

Data capture using the innovative device: 10-minute walk without orthoses on a treadmill

5 minutes rest</td></tr>
</table>

		Data capture using the innovative device: 10-minute walk with orthoses on a treadmill Correction of orthoses where was needed – done at OPU. Monitored for re-ulceration
Visit 2 | Month 8 (V2) Follow-up period	Same with visit 1	
End of Trial **Visit 3 | Month 12** (V3)	Same with visit 1	

At Time 0 (T_0), the participants read the information sheet and together with the researcher, went through their role as participants in this study and were given a chance to ask any questions and to clarify any unclear aspects concerning their participation in the study. Following recruitment, matched participants were randomly assigned to either the experimental group or the control group. Also at Time 0, a 3-week observation period was dedicated to observe both groups, the control group and the experimental group, for any re-ulceration whilst still under the same standard diabetic foot care. To remind the reader, the standard diabetic foot care given at the Diabetes Outpatients Clinic consisted mainly of observation of foot deformities and assessment of pedal ranges of motion, neurological and vascular examination of the diabetic foot. Visual observation and clinical experience are used to determine the efficiency of the prescribed offloading devices.

Following the observation period at Time 0, a series of 3 appointments, referred to as Visit 1 (V1), Visit 2 (V2) and Visit 3 (V3), were set every 4 months to monitor both groups for re-ulceration and to assess the experimental group for pressure and

temperature measurements as will be explained in more detail in Section 8.6.8.1 and 8.6.8.2.

8.6.8.1 Data Collection Process for the Control Group

Participants in the control group (*n*=44) received standard diabetic foot care by their Podiatrist at the Diabetic Foot Clinic and continued to receive standard care as was required till the end of the trial. The standard diabetic foot care consisted mainly of observation of foot deformities and assessment of pedal ranges of motion, neurological and vascular examination of the diabetic foot. Visual observation and clinical experience were used to determine the efficiency of the prescribed offloading devices.

The control group was reviewed by the researcher every 4 months from the first assessment for a total of 3 visits. This was done to observe whether any of the participants have re-ulcerated or developed any other foot complication such as amputation within that year. The involvement of the researcher here, was purely observational. In this group, no form of intervention or diagnostic tests were performed by the researcher so not to influence the outcomes of the current standard diabetic foot care given in the local hospital to all patients living with diabetes mellitus.

8.6.8.2 Data Collection Process for the Experimental Group

For the experimental group (*n*=44), the area of interest (previous site of ulceration) was assessed for peak pressure and temperature readings utilizing the innovative single-sensor pressure and temperature mapping device designed specifically for this study. On the day of their appointment (V1), these participants were asked to bring with them their sports shoes/prescription footwear and their prescription orthoses. The single-sensor in-shoe pressure and temperature measuring system was set up by embedding the sensor of the device within a 3mm thick simple insole, made of a soft foam material, customized to the size of each participant. The sensor was positioned at an area on the simple insole that corresponded to the pre-ulcerated site of each participant.

The sensor of the innovative device was inserted within the participants own shoes first without their orthoses and asked to walk, at a self-selected speed, on a treadmill for 10 minutes. The in-shoe pressure and temperature parameters were recorded. Following 5 minutes of rest, the single-sensor device embedded within the simple insole, was superimposed over the participant's orthoses and inserted within the shoe. The participant was then asked to walk again on a treadmill for another 10 minutes were the in-shoe pressure and temperature parameters were recorded. This process was repeated every 4 months for a total of 3 visits till the end of the trial to ensure that the orthoses were still effective in pressure reduction and to monitor cases of re-ulceration.

The aim of evaluating the orthoses was to determine whether there was indeed a significant (>30%) plantar pressure reduction with the patient's already prescribed orthoses. In those cases where the prescription orthoses were found they were not offering the required amount of pressure reduction, the Orthotist working at the Orthotics and Prosthetics Unit who originally designed the offloading devices was contacted to adapt and modify the orthoses until the desired pressures were obtained. According to the literature, in diabetes, the ideal peak plantar pressure should not exceed <200kPa (Bus et al., 2020).

8.6.9 Outcome Measures

The outcome measures of interest pertaining to this clinical trial consisted of the following:

- Skin temperature readings at site of previous ulceration
- Peak plantar pressures at site of previous ulceration
- To evaluate whether there was a significant (>30%) plantar pressure reduction with the patient's already prescribed orthoses
- To evaluate whether or not the experimental group re-ulcerated more/less compared to the control group whose offloading devices were not assessed for reduction of pressure at the site of interest.
- The correlation between peak plantar pressure and peak plantar temperature.

8.7 Statistical Analysis

All data analysis was conducted using IBM SPSS Statistics 28.

Independent sample t-test was used to confirm that the participants were actually matched in terms of age and duration of DM (Appendix 16).

Simple mathematical calculations were used to calculate the number, percentage and standard deviation of the data collected including the age, gender, and medical history of the sample population.

Nominal data collected to investigate whether there was a statistically significant difference in number of re-ulceration cases between the experimental group and the control group, was tested using the Cochran's Q-test. This helped the researcher determine the relationship between the two clinical methods as will be described in more detail in Section 8.7. The Cochran's Q-test is especially recommended, to be used instead of Chi-squared test, when the data has paired and/or repeated measures such as a pre-intervention and post-intervention. The data of this PhD study relates to this test as this study investigates the presence or absence of active re-ulceration in both the experimental group and the control group at 3 or more time points.

The correlation between peak plantar pressure and peak skin temperature parameters was determined by first assessing the data for its normal distribution through the Kolmogorov–Smirnov test. Since the data was determined as having an abnormal distribution that is, non-parametric in nature, Spearman correlation analysis was used to determine the strength of the relationship between the 2 variables, peak plantar pressure and skin temperature. As a correlation analysis test, Spearman's Rank Order Correlation (*rho*) is used to describe the strength and direction of the linear relationship between two variables. This test is particularly indicated for continuous categorical or ranked level data. The strength of relationship between variables can vary from -1 which indicates a perfect negative correlation, to + which indicates perfect positive correlation where 0 shows no correlation (Parker, 2010).

8.8 Results

8.8.1 Descriptive analysis of demographic data

A total of 88 participants, of which 80% (*n*=70) were males and 20% (*n*=18) were females, with mean age of 68 years (*p*=0.895), accepted to participate in this clinical trial and thus were recruited, matched and randomly assigned to either the experimental group (*n*=44) or the control group (*n*=44). The distribution of neuropathic, ischaemic and neuro-ischaemic feet was as follows: 34% of the participants (*n*=30) presented with neuropathic feet, 23% of the participants (*n*=20) presented with ischaemic feet and 43% of the participants (*n*=38) presented with neuro-ischaemic feet.

The demographic data of the experimental and control group showed mean HbA1c levels of 7.39mmol/mol for the experimental group and 9.43mmol/mol for the control group with a mean duration of diabetes of 19 years for both groups (*p*=0.887). The mean BMI scores for experimental group fell within the overweight category (28 kg/m^2) whereas the mean BMI scores of the control group fell within the obese category (30kg/m^2). The most common site of ulceration resulted in the hallux for both the experimental group (*n*=15) and the control group (*n*=12) followed by 2nd MPJ and 1st MPJ.

8.8.2 Need for intervention

This analysis was conducted for the experimental group only, as only the participants within the experimental group were assessed with the innovative, single-sensor, in-shoe, pressure and temperature measuring device for in-shoe pressure and temperature changes vis-à-vis the effectiveness of their offloading device.

Following the assessment of peak plantar pressures and peak plantar temperatures using the innovative single sensor, in-shoe pressure and temperature measuring device, orthoses which were identified not to be achieving the required amount of pressure reduction (30% off of the original pressure that is, the pressure identified without orthoses) where referred to the orthotist working at the Orthotics and Prosthetics Unit

of the local hospital to have the orthoses modified or renewed depending on the necessity. This was carried out for every participant until the desired pressure reduction was achieved. Table 30 below shows a few examples of the types of modifications that were required.

Table 30: Table showing examples of modifications carried out on orthoses identified as not achieving the required amount of pressure reduction.

Orthoses design	Modification required
Full-length simple insole, no apparent posting, EVA medium to low density	A medial rearfoot post added to control overpronation
Full-length EVA medium density with double winged cut out	The double winged-plantar cover was replaced with a Plantar Metatarsal Pad so to elevate the 2nd metatarsal, straighten the 2nd MPJ and thus decrease pressure at D2
Accommodative, 2 superimposed simple insoles (made of Grey poron)	Full-length, medium density orthoses with the addition of reverse Morton's Extension and a metatarsal bar to further reduce pressure under the 1st metatarsal head and support the metatarsals
Full-length with a 1st metatarsal cut out filled with diabetic poron which was slightly worn out and almost detached from the insole	Renewal of same design
Full-length insoles with a perforation that corresponded to the 3rd MPJ Rt	A u-shaped plantar cover was incorporated within the orthoses itself
Full-length simple insole made of EVA	Addition of a 1st metatarsal cut out
Full-length with a cut-out filled with poron corresponding to the 1st MPJ	Renewal of orthoses keeping the full-length, medium density design and adding a 1st metatarsal cut out to offload the 1st MPJ
Full-length with the addition of a double winged plantar cover bilateral.	The double winged plantar cover changed to a u-plantar cover to offload the 2nd MPJ Lt foot
Full-length, low density simple insoles, no posting. Marked indentation noted on insoles, corresponds to 2nd MPJ bilateral.	Full-length, medium density EVA orthoses with the addition of a u-shaped plantar cover, to offload 2nd MPJ bilateral
Simple insoles, made out of soft foam, with no posting.	Full length, medium density EVA with the addition of a 1st ray cut out
Simple insole made of low-density material, no posting	Medium density material with the addition of a medial rearfoot post bilateral
Full-length with the addition of a metatarsal dome	The metatarsal dome was removed and instead the plantarflexed 1st ray was corrected through a 2-5 metatarsal bar

A simple count of the number of interventions required to achieve at least 30% reduction of the original pressures at previous sites of ulceration revealed that at V1, 27.3% of participants required orthoses modification, 29.5% of participants at V2 and 9.1% at V1 (Table 31, Figure 70) required more modifications to their orthoses to ensure that the recommended pressures/offloading was reached with the use of the orthoses.

Table 31: Table showing the frequency of orthoses modification in the experimental group

		Frequency	Percent (%)
T_0	Observation Period No modification required	44	100
V1	No modification required	32	72.7
	Modification required	**12**	**27.3**
V2	No modification required	31	70.5
	Modification required	**13**	**29.5**
V3	No modification required	40	90.9
	Modification required	**4**	**9.1**

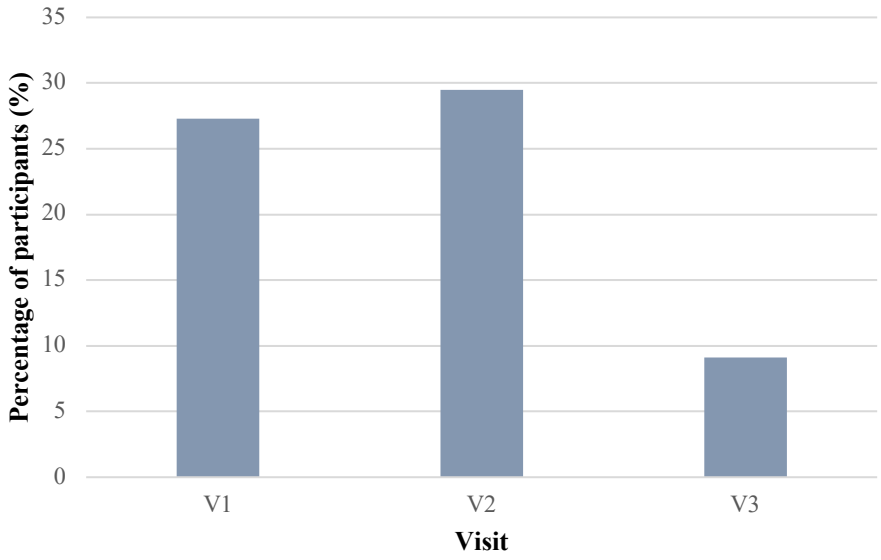


Figure 70: A bar chart representing the number of interventions required per visit in the experimental group

The below bar graph (Figure 71) shows how often a participant required modification to his/her prescription orthoses during the trial since a 30% pressure reduction was not achieved. Results showed that, 54% (*n*=24) of the participant population required no intervention to their prescription orthoses, 30% (*n*=13) required an intervention only once, 11% (*n*=5) of the participant population required an intervention twice during the trial and, 5% (*n*=2) of the patient population required an intervention at all 3 visits.

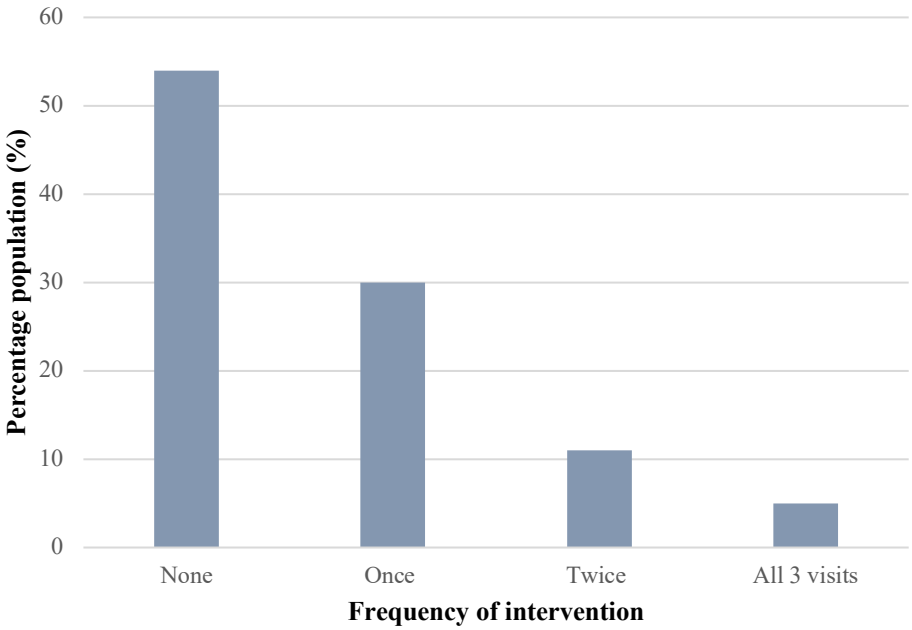


Figure 71: Bar chart showing how often participants required orthoses modification

8.8.3 Recurrence of ulceration during the clinical trial

During the trial, the researcher evaluated whether or not the experimental group had more or less onsets of re-ulceration cases compared to the control group who were not assessed and followed-up for the efficiency of their offloading devices during the study period. This information helped determine whether or not the innovative, single-sensor, in-shoe pressure and temperature measuring device was indeed useful in preventing re-ulceration by closely monitoring prescription offloading devices prescribed to high-risk patients and adjusting the offloading device accordingly.

Observation period at Time 0

As detailed in the previous sections, both the experimental and control group presented with no ulceration at the Time 0 of recruitment (T_0). However, following the 3-week observation period, 6 participants from the experimental group were noticed to have re-ulcerated and another 16 participants were observed to have re-ulcerated from the control group. Both groups were still under the standard diabetic foot care which relied

on visual observation and clinical experience to determine the offloading capability and effectiveness of the prescribed offloading device. This demonstrates that the standard diabetic foot care currently provided in the hospital was not sufficient to prevent re-ulceration as will be discussed in Section 8.8.

Comparison of re-ulceration across, visits and between groups

In order to determine the efficacy of treatment intervention following the use of the innovative, single-sensor, in-shoe pressure and temperature measuring device for assessing and monitoring peak plantar pressure and peak plantar temperatures of the participants during the trial, the data for the experimental group was analysed for changes in ulceration from V1 to V2, from V2 to V3. Simple mathematical calculations were used to calculate the number and percentage of the observed re-ulceration cases during the trial period that is, at T_0, V1, V2 and at V3.

Results show that overall, the control group showed more cases of active re-ulceration compared to the experimental group across all visits (Figure 72). Moreover, results showed that at the end of the trial, that there were 4 cases of amputations in the control group whereas the experimental group experienced none.

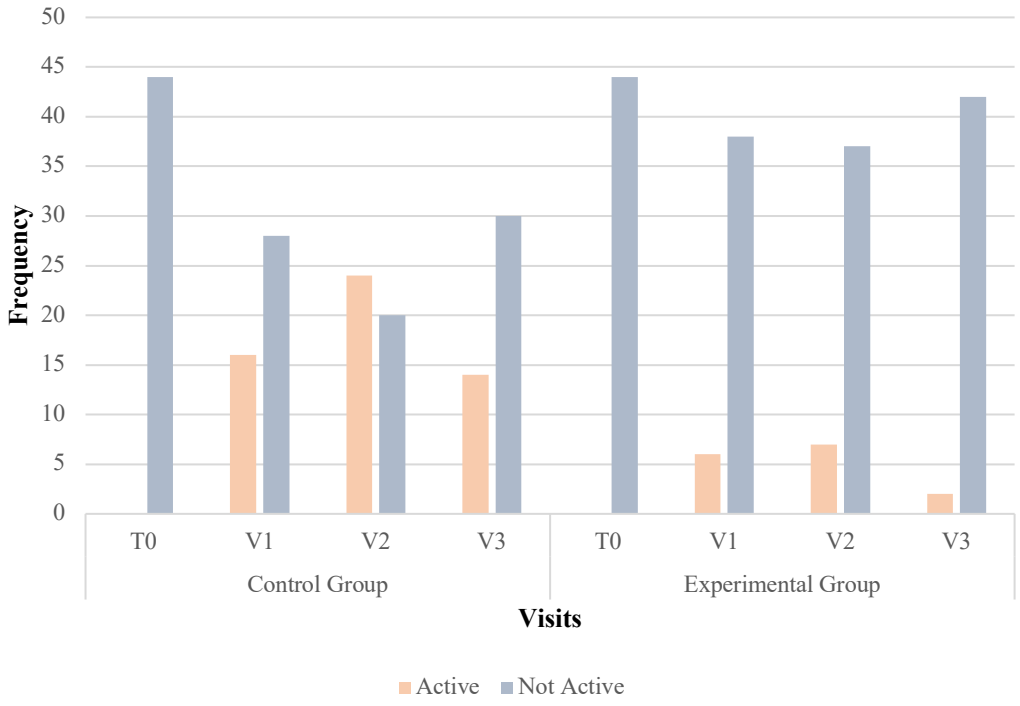


Figure 72: Bar graph showing the comparison of re-ulceration presentation across visits between groups

Table 32 below, provides a visual representation of the cases of re-ulceration presented in both the experimental group and the control group across all 3 visits. In this table, the phrase 'Not active' represents a participant who was in remission at that point in time. This means that, he/she had no active ulceration at that point in time. Conversely, the word 'Active' represents a participant who have experienced re-ulceration at that point in time. Finally, the word 'Amputation' represents a participant who his/her re-ulceration failed to heal to the point that he/she required an amputation. This table shows that the control group showed more cases of "Active" re-ulceration through all 3 visits compared to the experimental group where "Active" re-ulceration cases were sparse across all 3 visits. Furthermore, at the end of the trial (V3) 4 participants had to undergo an amputation due to complications related to their re-ulceration.

Table 32: Table providing a visual representation of cases of re-ulceration presented in both groups

	Control Group					Experimental Group				
	ID	T_0	V1	V2	V3	ID	T_0	V1	V2	V3
Neuropathy Category	1C	Not active	**Active**	**Active**	**Active**	1E	Not active	Not active	Not active	Not active
	2C	Not active	Not active	**Active**	Not active	2E	Not active	**Active**	Not active	Not active
	3C	Not active	**Active**	Not active	Not active	3E	Not active	Not active	Not active	Not active
	4C	Not active	**Active**	Not active	Not active	4E	Not active	Not active	Not active	**Active**
	5C	Not active	Not active	**Active**	**Active**	5E	Not active	Not active	Not active	Not active
	6C	Not active	Not active	Not active	Not active	6E	Not active	Not active	Not active	Not active
	7C	Not active	Not active	Not active	Not active	7E	Not active	**Active**	Not active	Not active
	8C	Not active	**Active**	Not active	Not active	8E	Not active	Not active	**Active**	**Active**
	9C	Not active	**Active**	Not active	Not active	9E	Not active	Not active	Not active	Not active
	10C	Not active	**Active**	Not active	**Active**	10E	Not active	Not active	Not active	Not active
	11C	Not active	Not active	not active	Not active	11E	Not active	Not active	Not active	Not active
	12C	Not active	Not active	**Active**	Not active	12E	Not active	Not active	Not active	Not active
	13C	Not active	Not active	**Active**	Not active	13E	Not active	Not active	Not active	Not active
	14C	Not active	Not active	Not active	Not active	14E	Not active	Not active	**Active**	Not active
	15C	Not active	Not active	Not active	Not active	15E	Not active	Not active	Not active	Not active
Neuro-ischaemic Category	16C	Not active	Not active	**Active**	Not active	16E	Not active	Not active	Not active	Not active
	17C	Not active	Not active	**Active**	**Amputation**	17E	Not active	**Active**	**Active**	Not active
	18C	Not active	Not active	**Active**	**Active**	18E	Not active	Not active	Not active	Not active
	19C	Not active	**Active**	Not active	Not active	19E	Not active	Not active	Not active	Not active
	20C	Not active	**Active**	**Active**	**Amputation**	20E	Not active	Not active	Not active	Not active
	21C	Not active	Not active	**Active**	Not active	21E	Not active	**Active**	**Active**	Not active
	22C	Not active	**Active**	**Active**	**Active**	22E	Not active	Not active	Not active	Not active
	23C	Not active	Not active	**Active**	Not active	23E	Not active	Not active	Not active	Not active
	24C	Not active	Not active	**Active**	Not active	24E	Not active	Not active	Not active	Not active
	25C	Not active	**Active**	**Active**	**Amputation**	25E	Not active	Not active	Not active	Not active
Ischaemic Category	26C	Not active	Not active	**Active**	Not active	26E	Not active	Not active	Not active	Not active
	27C	Not active	Not active	**Active**	Not active	27E	Not active	Not active	Not active	Not active
	28C	Not active	**Active**	Not active	**Active**	28E	Not active	Not active	Not active	Not active
	29C	Not active	Not active	**Active**	**Amputation**	29E	Not active	Not active	Not active	Not active
	30C	Not active	Not active	Not active	Not active	30E	Not active	Not active	Not active	Not active
	31C	Not active	Not active	**Active**	Not active	31E	Not active	Not active	Not active	Not active
	32C	Not active	Not active	Not active	Not active	32E	Not active	**Active**	Not active	Not active
	34C	Not active	Not active	Not active	Not active	34E	Not active	Not active	Not active	Not active
	35C	Not active	Not active	Not active	**Active**	35E	Not active	Not active	Not active	Not active
	36C	Not active	Not active	**Active**	Not active	36E	Not active	Not active	Not active	Not active
	37C	Not active	Not active	Not active	**Active**	37E	Not active	Not active	Not active	Not active
	38C	Not active	Not active	Not active	Not active	38E	Not active	Not active	Not active	Not active
	39C	Not active	**Active**	**Active**	**Active**	39E	Not active	Not active	Not active	Not active
	40C	Not active	Not active	**Active**	Not active	40E	Not active	**Active**	**Active**	Not active
	41C	Not active	**Active**	**Active**	Not active	41E	Not active	Not active	**Active**	Not active
	42C	Not active	**Active**	**Active**	**Active**	42E	Not active	Not active	Not active	Not active
	43C	Not active	**Active**	**Active**	Not active	43E	Not active	Not active	Not active	Not active
	44C	Not active	**Active**	Not active	Not active	44E	Not active	Not active	**Active**	Not active

If we break down re-ulceration cases according to visits and refer Table 33 below, it can be observed that at V1, 72.7% participants (n=16) from the control group were observed to have re-ulcerated of which 6 were participants living with neuropathy, 4 were participants with neuro-ischaemia and 6 were participants living with ischaemia. Only 27.3% participants (n=6) from the experimental group were observed to have re-ulcerated at V1 of which 2 were participants living with neuropathy, 2 were participants with neuro-ischaemia and 2 were participants living with ischaemia.

Table 33: Table showing the status of re-ulceration cases across the experimental and control group.

				Group		
				Experimental Group	Control Group	Total
Prescence of Ulcer						
Not Active	Visit	T_0	Count	44	44	88
			Percentage	50.0%	50.0%	100.0%
		V1	Count	38	28	66
			Percentage	57.6%	42.4%	100.0%
		V2	Count	37	20	57
			Percentage	64.9%	35.1%	100.0%
		V3	Count	42	30	72
			Percentage	58.3%	41.7%	100.0%
Active	Visit	V1	Count	6	16	22
			Percentage	**27.3%**	**72.7%**	100.0%
		V2	Count	7	24	31
			Percentage	**22.6%**	**77.4%**	100.0%
		V3	Count	2	14	16
			Percentage	**12.5%**	**87.5%**	100.0%

An interesting observation is that within 4 months, the cases of re-ulceration increased at V2 particularly for the control group in which the count increased by 8 participants who had also re-ulcerated in addition to the previous count. Thus, from the control group, the total participants who re-ulcerated increased to 77.4% participants at V2. One must remind the reader that participants from the control group were not being monitored with the innovative, single-sensor, in-shoe, pressure and temperature

measuring device and thus, the need, if any, for modifications of prescription orthoses was determined solely through clinical experience and visual observation by the Podiatrist as per the standard diabetic foot care protocol provided to date in the Diabetes Clinic at the local hospital.

A dramatic shift in cases of re-ulceration and ulcer resolution was observed in the experimental group when comparing V1 to V3. A 15% of ulcer resolution was noted in the experimental group were from a count of 6 re-ulceration cases (27.3% of participants), the cases dropped to 2 participants only (12.5%) by the end of the trial. This implies that, being followed with the innovative, single-sensor, in-shoe, pressure and temperature measuring device as an adjunct to the current standard diabetic foot care protocol, which helped inform the researcher with regards to the orthoses modification required to provide better offloading, the majority of the presented re-ulceration in the experimental group healed successfully. Conversely, though the number of cases of re-ulceration improved from V2 to V3, when comparing V1 to V3 within the control group, it was observed that with the current standard diabetic foot care protocol on its own, the cases of active re-ulceration had only resolved by 5%. From count of 16 re-ulcered cases, the number of cases only dropped to 14 cases (87.5%). Moreover, 4 of these active re-ulceration cases (from the control group) led to amputation by the end of the trial. No amputations were sustained in the experimental group.

Cochran's Q-Test to determine statistical significance

In this section, the researcher sought to determine whether there was a change in proportion in amount of re-ulceration within the experimental group, across 3 time-points that is, (i) prior to the trial, (ii) during the trial and (iii) by the end of trial.

To answer this question the researcher employed the Cochran's *Q*-Test as the statistical test of choice. The Cochran's *Q*-Test is an extension of the McNemar test which is a non-parametric test used to verify whether the proportion of success of a specific treatment is the same between groups at different time points (Shoukri, 2004). The

Cochran's *Q*-Test, differs from the McNemar test as it investigates the differences amongst 3 or more, matched set of time points rather than between 2 time points (Greenland & O'Rourke, 2008).

When presented with paired or repeated measures research designs, Cochran's *Q*-Test is considered a better suited statistical approach compared to the traditional Chi-square test (Pallant, 2020). The Cochran's *Q*-Test, as the Chi-square test, also base its analysis on Chi-square distribution however, the generated probability result indicates a variation across studies rather than across individuals which makes this test ideal to verify pre-test/post-test studies.

Cochran's *Q*-Test assumes that the data collected is categorical and has a non-parametric distribution (Pallant, 2020). Thus, the Cochran's *Q*-Test was conducted to evaluate any statistically significant difference in amount of re-ulceration at 3 different time points i.e., at V1, V2 and V3 for the experimental group who were assessed with the single-sensor, pressure and temperature measuring device and who had their orthoses modified wherever necessary by the Orthotist at the Orthotics and Prosthetics Unit at the local hospital.

Cochran's *Q*-Test results for the experimental group:

As demonstrated in the table below (Table 34), the Cochran's *Q*-test concluded that there was a statistically significant difference (p=<0.014) in number of active re-ulcerations across visits for the experimental group and thus the alternative hypothesis was accepted.

Table 34: Table showing the showing the p-value results following Cochran's Q-test analysis for the experimental group

Null Hypothesis	Test	Sig.	Decision
The distributions of Re-ulceration at T_0, Re-ulceration at V1, Re-ulceration at V2 and Re-ulceration at V3 are the same.	Related-Samples Cochran's Q Test	.014	Reject the null hypothesis.

This statistically significant difference in number of re-ulcerations is particularly evident comparing T_0 to V1 (p=0.016), T_0 to V2 (p=0.005), V2 to V3 (p=0.044). However, there was no statistically significant difference when comparing T_0 to V3 (p=>0.421), V1 to V2 (p=0.687), V1 to V3 (p=0.107) (Table 35).

Table 35: Table showing the pairwise comparison in re-ulceration cases across visits for the experimental group

	Test Statistic	Std. Error	Std. Test Statistic	Sig.	Adj. Sig.
Re-ulceration at V2 – Re-ulceration at V1	.023	.056	.403	.687	1.000
Re-ulceration at V2 – Re-ulceration at V3	-.114	.056	-2.013	**.044**	.264
Re-ulceration at V2 – Re-ulceration at T_0	.159	.056	2.819	**.005**	.029
Re-ulceration at V1 – Re-ulceration at V3	-.091	.056	-1.611	.107	.643
Re-ulceration at V1 – Re-ulceration at T_0	.136	.056	2.416	**.016**	.094
Re-ulceration at V3 – Re-ulceration at T_0	.045	.056	.805	.421	1.000

As summarized in Table 36, this implies that between the observation period at Time 0 and Visit 1, from 0 cases of re-ulceration there was a total of 6 observed re-ulceration cases (27.3% of the experimental group population) which brough about a statistically

significant difference (p=0.016). No statistically significant difference was observed between V1 and V2 as the number of re-ulceration cases increased by only one case (n=7) making up 22.6% of the experimental group population. Between V2 and V3, another statistically significant result was observed as the number of re-ulceration cases (n=7) reduced to only 2 cases of re-ulceration (12.5% of the experimental group population).

Table 36: Table showing a summary of change in re-ulceration cases across visits for the experimental group

Re-ulceration cases Visit comparison	*p*-value	Number of cases
T_0 to V1	**.016**	From 0 to 6
V1 to V2	.687	From 6 to 7
V2 to V3	**.044**	From 7 to 2
T_0 to V3	.421	From 0 to 2
T_0 to V2	**.005**	From 0 to 7
V1 to V3	.107	From 6 to 2

Finally, no statistically significant difference was observed between Time 0 (n=0) (p=0.421) and V3 (n=2) and V1 and V3 (p=0.107) as the number of re-ulceration cases was very close from one time-point to the other. This implies that the use of single-sensor, in-shoe pressure and temperature measuring device as an adjunct to the standard diabetic foot care helped in reducing the number of cases close to 0 when compared to the control group where 14 cases were still active or sustained an amputation by the end of the trial.

Cochran's *Q*-Test results for the Control Group:

As demonstrated in the table below (Table 37), the Cochran's *Q*-test concluded that there was a statistically significant difference (p=<0.001) in re-ulceration cases at all visits for the control group and thus the alternative hypothesis was accepted.

Table 37: Table showing the showing the p-value results following Cochran's Q-test analysis for the control group

Null Hypothesis	Test	Sig.	Decision
The distributions of Re-ulceration at T_0, Re-ulceration at V1, Re-ulceration at V2 and Re-ulceration at V3 are the same.	Related-Samples Cochran's Q Test	<.001	Reject the null hypothesis.

This statistically significant difference in number of re-ulcerations is particularly evident comparing T_0 to V1 (p=<0.001), T_0 to V2 (p=<0.001), T_0 to V3 (p=<0.001), V1 to V2 (p=0.039), V2 to V3 (p=0.022). However, there was no statistically significant difference when comparing V1 to V3 (p=0.819) (Table 38).

Table 38: Table showing the pairwise comparison in number of re-ulcerated cases across visits for the control group

	Test Statistic	Std. Error	Std. Test Statistic	Sig.	Adj. Sig.
Re-ulceration at V2 – Re-ulceration at V1	.205	.099	2.065	**.039**	.234
Re-ulceration at V2 – Re-ulceration at V3	-.227	.099	-2.294	**.022**	.131
Re-ulceration at V2 – Re-ulceration at T_0	.568	.099	5.735	**<.001**	.000
Re-ulceration at V1 – Re-ulceration at V3	-.023	.099	-.229	.819	1.000
Re-ulceration at V1 – Re-ulceration at T_0	.364	.099	3.671	**<.001**	.001
Re-ulceration at V3 – Re-ulceration at T_0	.341	.099	3.441	**<.001**	.003

As summarised in Table 39 below, this implies that between the observation period at T_0 and V1, from 0 cases of re-ulceration there was 16 observed cases of re-ulceration which brought about a statistically significant difference (p=0.001). A statistically significant difference (p=0.039) was observed between V1 and V2 as the number of re-ulceration cases increased by 8 cases (n=24). Between V2 and V3, another statistically significant result was observed as the number of re-ulceration cases, from 24, reduced to 14 cases of re-ulceration.

Comparing T_0 to V3, a statistically significant difference (p=<0.001) was observed as the difference in number of cases from the start (n=0) of the trial to the end of the trial is still high (n=14). Finally, no statistically significant difference (p=0.819) was observed between V1 (n=16) and V3 (n=14) as the number of re-ulceration cases is very close from one time-point to the other. This implies that using the current standard diabetic foot care brought only the resolution of 2 cases of re-ulceration. Furthermore, 4 participants from the control group had to undergo an amputation secondary to complications associated with their re-ulcered lesion.

Table 39: Table showing a summary of change in re-ulceration cases across visits for the control group

Re-ulceration cases Visit comparison	*p*-value	Number of cases
T_0 to V1	**>.001**	From 0 to 16
V1 to V2	.039	From 16 to 24
V2 to V3	**.022**	From 24 to 14
T_0 to V3	**>.001**	From 0 to 14
T_0 to V2	**>.001**	From 0 to 24
V1 to V3	.819	From 16 to 14

8.8.5 Correlation Analysis for Pressure and Temperature Parameters

As an additional investigation to this PhD project, the researcher explored the relationship between in-shoe peak plantar pressure and in-shoe peak plantar temperature under 2 scenarios. The first scenario investigated the correlation between peak plantar pressure and peak plantar temperature data that was taken while participants walked for 10 minutes while wearing their orthoses. The second scenario investigated the correlation between peak plantar pressure and peak plantar temperature data that was taken while participants walked for 10 minutes without their orthoses. In both scenarios the data readings were taken at 3 different time points referred to as Visit 1 (V1), Visit 2 (V2) and Visit 3 (V3).

Before the data relating to peak plantar pressure and peak plantar temperature was analysed for any correlation, it was checked for the violation of assumptions of linearity that might ultimately influence the final correlation result. Thus, the data was screened for extreme outliers and for linearity. This determined through the use of scatterplots which ultimately determined the subsequent correlation analysis tests used. The hypothesis for this investigation is as follows:

H_1: The distribution of both pressure and temperature values is normal

H_0: The distribution of both pressure and temperature values is not normal

Preliminary analysis for correlation

A scatterplot was generated to identify outliers and to check for the violation of assumptions of linearity that influence correlation analysis. The scatterplot was also used to give a preliminary insight on the nature of relationship between the 2 variables being investigated.

Extreme data outliers that were identified within the dataset were eliminated as these may have influenced the correlation analysis. The final scatterplot of the cleaned dataset was generated, as presented below, and the distribution of data points were inspected (Figure 73 and 74).

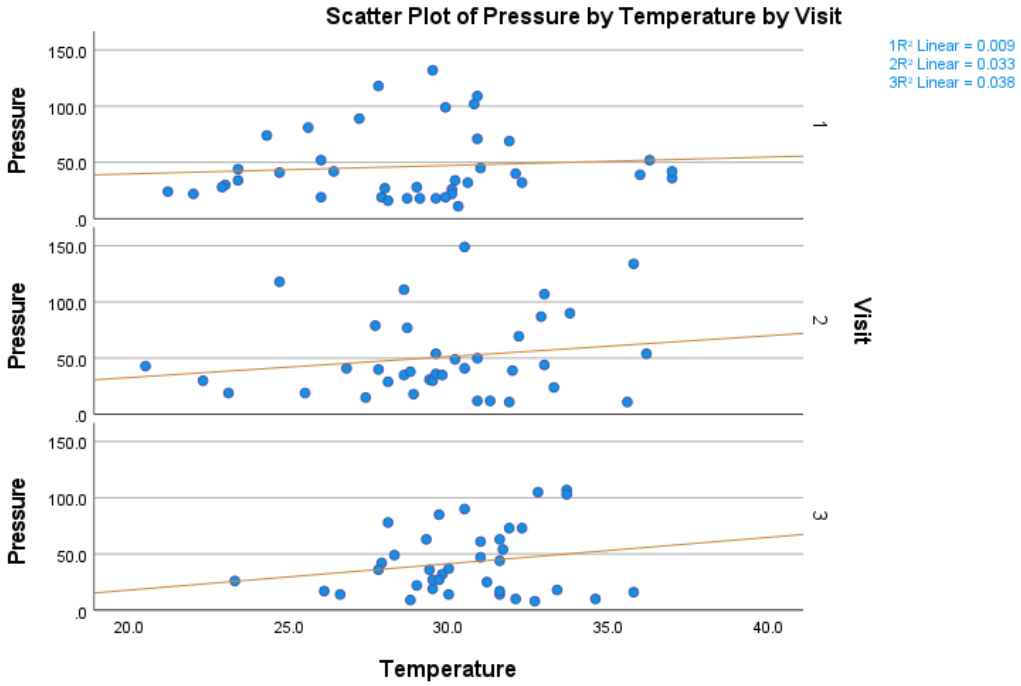


Figure 73: Scatterplot of pressure vs temperature per visit. Data was taken while participants wore their orthoses

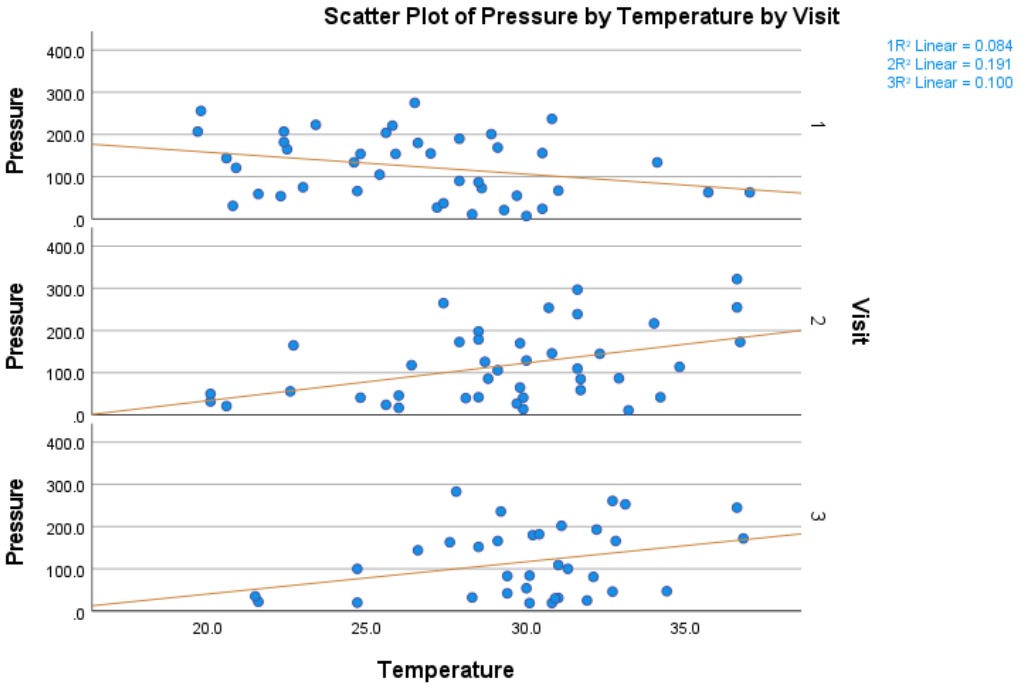


Figure 74: Scatterplot of pressure vs temperature per visit. Data was taken while participants walked without their orthoses

In a dataset that has a linear distribution, its datapoints should be neatly arranged in a narrowly-cylindrical-shaped distribution (Pallant, 2020). The datapoints distribution of the generated scatterplots as displayed in Figure 73, taken while the participants walked while wearing their orthoses, can be described as loosely spread from across each other. Similarly, the datapoints distribution of the generated scatterplots as displayed in Figure 74, which were taken while the participants walked without their orthoses, though still described as loosely spread from across each other, they appear to have a closer distribution to each other as compared to the dataset with orthoses. Both scenarios indicate a non-linear relationship which generally point to a very low correlation or no correlation.

The aim of correlation analysis is to determine the strength and direction of a linear relationship between 2 variables under investigation. Due to the nature of the dataset of this study, as it violates the assumption of correlation analysis with having a non-linear distribution, the Spearman Rank Order Correlation (*rho*) was best indicated to test the strength of the relationship between pressure and temperature.

As in Pearson's correlation analysis, the Spearman Rank Order Correlation analysis considers values from 1 to -1 where the positive sign indicates a positive correlation and a negative sign indicates a negative correlation. The number behind the sign indicates the magnitude and thus the strength of relationship between the 2 variables. Results of data scoring 1 or -1 indicates a perfect correlation that is, values from one variable can predict the values of the other variable however, data scoring 0 indicates no significant relationship between variables. In this study, values between 0 and 1 were interpreted following the guidelines proposed by Hemphill (2003) which were based the revision of Cohen guidelines (1988) (Gignac & Szodorai, 2016) (Table 40). It is important to highlight that were correlation analysis applies, the level of statistical significance presented, highly influenced by sample size, only indicates the level of confidence the researcher should have in the results obtained (Pallant, 2020).

Table 40: Interpretation of correlation values (Hemphill, 2003).

Interpretation	***r* result**
Small correlation	<0.20
Medium correlation	0.20 to 0.30
Large correlation	>0.3

Correlation Results for Scenario 1 (with orthoses)

Results investigating the relationship between peak plantar pressure and peak plantar temperature show a small positive correlation between peak plantar pressure and peak plantar temperature at V1 (n=40, r=0.155, p=0.339), V2 (n=38, r=0.191, p=0.252) and V3 (n=38, r=0.054, p=0.746) (Table 41, 42 and 43). Results of scenario 1 thus imply that at all 3 time-points, data collected for peak plantar pressures seem to have a very small influence on the data gathered for peak plantar temperature of which, as indicated by the level of significance, a low level of confidence should be assumed on these results.

Table 41: Correlation results for scenario 1 at V1 with orthoses

			Temperature	Pressure
Spearman's rho	Temperature	Correlation Coefficient	1.000	**.155**
		Sig. (2-tailed)	.	.339
		N	40	40
	Pressure	Correlation Coefficient	**.155**	1.000
		Sig. (2-tailed)	.339	.
		N	40	42

Table 42: Correlation results for scenario 1 at V2 with orthoses

			Temperature	Pressure
Spearman's rho	Temperature	Correlation Coefficient	1.000	**.191**
		Sig. (2-tailed)	.	.252
		N	38	38
	Pressure	Correlation Coefficient	**.191**	1.000
		Sig. (2-tailed)	.252	.
		N	38	41

Table 43: Correlation results for scenario 1 at V3 with orthoses

			Temperature	Pressure
Spearman's rho	Temperature	Correlation Coefficient	1.000	**.054**
		Sig. (2-tailed)	.	.746
		N	38	38
	Pressure	Correlation Coefficient	**.054**	1.000
		Sig. (2-tailed)	.746	.
		N	38	42

Correlation Results for Scenario 2 (without orthoses)

Results of scenario 2 show that at Visit 1 (n=41, r= -0.284, p=0.072), and Visit 3 (n=34, r=0.277, p=0.113) the data collected for peak plantar pressures seem to have a medium negative and a medium positive influence on the data gathered for peak plantar temperature respectively (Table 44, 45 and 46). As indicated by the level of significance, a low level of confidence should be assumed on these results. Results for visit 2 show a larger positive correlation between peak plantar pressure and peak plantar temperature with a stronger level of confidence (n=41, r=0.375, p=0.016) (Table 45).

Table 44: Correlation results for scenario 2 at V1 without orthoses

			Temperature	Pressure
Spearman's rho	Temperature	Correlation Coefficient	1.000	**-.284**
		Sig. (2-tailed)	.	.072
		N	41	41
	Pressure	Correlation Coefficient	**-.284**	1.000
		Sig. (2-tailed)	.072	.
		N	41	41

Table 45: Correlation results for scenario 2 at V2 without orthoses

			Temperature	Pressure
Spearman's rho	Temperature	Correlation Coefficient	1.000	**.375***
		Sig. (2-tailed)	.	.016
		N	41	41
	Pressure	Correlation Coefficient	**.375***	1.000
		Sig. (2-tailed)	.016	.
		N	41	41

Table 46: Correlation results for scenario 2 at V3 without orthoses

			Temperature	Pressure
Spearman's rho	Temperature	Correlation Coefficient	1.000	**.277**
		Sig. (2-tailed)	.	.113
		N	34	34
	Pressure	Correlation Coefficient	**.277**	1.000
		Sig. (2-tailed)	.113	.
		N	34	35

The following section presents a detailed discussion of these findings in view of current literature. An in-depth evaluation of the results related to the use of the innovative, single-sensor, in-shoe pressure and temperature measuring device and

ulcer recurrence, and its clinical relevance to the care of the diabetic high-risk foot will be presented. The clinical implication pertaining to the results in context to the non-linear relationship between pressure and temperature will be also discussed.

8.8 Discussion

The purpose of this study was to compare the outcome of the application of the innovative, single sensor in-shoe pressure and temperature monitoring device to standard clinical protocols in the prevention of diabetic foot ulceration and re-ulceration. This study also investigated the correlation between in-shoe peak plantar pressure and in-shoe peak plantar temperature in high-risk diabetic population.

Observations from this study showed that when using the single-sensor, in-shoe pressure and temperature measuring device as an adjunct to the standard diabetic footcare, participants had higher ulcer resolution compared to relying to the standard diabetic foot care alone. Results of this study also showed a small positive correlation between peak plantar pressure and peak plantar temperature when observing participants walking with their orthoses. When observing the correlation analysis for peak plantar pressure and peak plantar temperature for participants walking without their orthoses, a medium to strong correlation could be observed.

The following sections present a detailed discussion of these findings in view of current literature. An in-depth evaluation of the results related to the use of the single-sensor, in-shoe pressure and temperature measuring device and ulcer recurrence and its clinical relevance to the care of the diabetic high-risk foot will be presented. The clinical implication pertaining to the results in context to the non-linear relationship between pressure and temperature will be also discussed.

8.8.1 Re-ulceration and the need of the innovative, low-cost, single-sensor, in-shoe pressure and temperature measurement device

The purpose of this study was to determine the efficacy of the innovative, single-sensor, in-shoe pressure and temperature measuring device on a targeted population specifically high-risk individuals living with type II diabetes mellitus with previous foot ulceration and making use of prescription orthoses.

The efficacy of prescription orthoses, following the evaluation utilizing the innovative, single-sensor, in-shoe pressure and temperature measuring device for assessing and monitoring peak plantar pressure and peak plantar temperatures of the participants during the trial, was determined by observing changes in number of re-ulcerations presented in the experimental group across 3 time points that is, from V1 to V2, from V2 to V3. These results were compared to the results a control group, who were not monitored with the single-sensor, in-shoe pressure and temperature measuring device. This helped determine whether the introduction of the innovative, single-sensor, in-shoe pressure and temperature measuring device as an adjunct monitoring device to the current standard diabetic foot care clinical protocol currently provided to all patients living with diabetes mellitus helps in preventing re-ulceration in the high-risk diabetic foot.

In this study, an observation period was planned deliberately to help the researcher portray the reality of the current situation with regards to the outcomes of just relying on visual observation of clinical signs of ulceration and on clinical experience to determine the efficiency of the prescribed offloading devices, in view of diabetic foot ulcer prevention and prevention of diabetic foot re-ulceration, as per standard diabetic foot care protocol.

Results from this study showed that during the observation period, prior to start of the actual clinical trial, 27.3% (n=6) of the participant from the experimental group were observed to have re-ulcerated at the same site of their previously recorded ulceration. A higher percentage of re-ulceration that amounted to 72.7% (n=16) of the control

group population was also observed at the same site of their previously recorded ulceration. It is important to highlight that this presentation of re-ulceration occurred while both groups were still under the current standard diabetic foot care.

These results highlighted the fact that the current standard diabetic foot care protocol may not be sufficiently effective in preventing recurrence of foot ulceration in high-risk patients living with type II diabetes mellitus. It is very likely that since the current standard diabetic foot care protocol relies solely on visual observation of clinical signs related to ulcer development, and clinical experience to determine the efficiency of the prescribed offloading devices, increased foot plantar pressures and raised skin temperatures, as causative factors for diabetic foot ulceration and re-ulceration, are not being monitored and thus they are being overlooked (Bus, 2012). The presentation of erythema, swelling, and bruising amongst others factors, to predict skin changes as signs of re-ulceration (Saliba Thorne at al., 2021) may have led to these numbers of re-ulceration cases in such a short period of time (3 weeks). This is a great indication that there is a urgent need of early recognition of the causative factors of ulceration if prevention of re-ulceration is to be achieved. Quoting Smith-Strøm et al. (2017) "*Time is tissue*", therefore to wait for such predictors to become visible to the naked eye may too late to prevent the development of pre-existing or new ulceration and this could be detrimental to a high-risk patient (Smith-Strøm et al., 2017).

The reason for the unbalanced presentation of re-ulceration cases between groups could not be explained, as all participants were matched in terms of age, gender, duration of diabetes, presence of neuropathy, presence of ischaemia and presence of neuro-ischaemia, prior to their random assignment to either the control group or the experimental group. Moreover, the demographics of the participants were very similar in both groups with mean HbA1c levels of 7.39mmol/mol for the experimental group and 9.43mmol/mol for the control group with an average duration of diabetes of 19 years for both groups. The mean BMI scores for experimental group fell within the overweight category (28 kg/m^2) whereas the mean BMI scores of the control group fell within the obese category (30kg/m^2). Since age and gender and co-morbidities

such as neuropathy, ischaemia and neuro-ischaemia have a large influence on the at-risk of ulcer formation, matching participants according to these characteristics helped in eliminating the differences between the control group and experimental group thereby increasing the statistical sensitivity of the investigation. However, the researcher is conscious that matching of participants can never be perfect. No matter how careful the matching was carried out, the biological variety within subjects might have influenced the outcomes of this study (Bordens & Barrington Abbott, 2011).

The focus of the study however, was to determine whether with the introduction of the innovative, single-sensor, in-shoe pressure and temperature measuring device, as an adjunct to the current standard diabetic foot care protocol, helped in reducing the number of re-ulceration cases presented following the observation period in this study.

Results from this clinical trial concurred with the statement by Bus (2016), were the author advocated that offloading and pressure re-distribution tend to have better outcomes when assisted by proper technology such as in-shoe pressure mapping devices. This statement was confirmed in this clinical trial since participants from the experimental group who were monitored for the effectiveness of their offloading device by monitoring their in-shoe peak plantar pressures and peak plantar temperatures utilizing the innovative, low-cost, single-sensor, in-shoe pressure and temperature measuring device, while receiving the current standard diabetic foot care, and who had their offloading device modified where and when necessary, had better outcomes in terms of ulcer resolution compared to the control group, who only received the current standard diabetic foot care.

In the experimental group, a dramatic shift in cases of re-ulceration and ulcer resolution was observed when comparing the number of re-ulceration cases at the start of the trial (V1) which amounted to 27.3% (n=6) of participants, to the end of the trail (V3) which amounted to 12.5% (n=2) of participants. As demonstrated in the results achieved from the Cochran's Q-test a statistically significant difference in number of active re-ulcerations across visits for both the experimental group (p=<0.014) and the control group (p=<0.001) was confirmed. Further exploration of the Cochran's Q-test

results pertaining to experimental group showed that a statistically significant difference, when comparing Time 0 to V3 (p=0.421) and V1 and V3 (p=0.107), was not achieved as the number of re-ulceration cases was very close from one time-point to the other. This implied that the use of single-sensor, in-shoe pressure and temperature measuring device as an adjunct to the standard diabetic foot care helped in reducing the number of cases very close to 0 when compared to the control group, where 14 cases were still active and 4 cases sustained an amputation by the end of the trial.

Conversely, a thorough analysis of the Cochran's Q-test results pertaining to control group, showed that, while no statistically significant difference was found in number of re-ulceration cases when comparing V1 to V3 (p=0.819), a statistically significant difference in re-ulceration cases was particularly evident when comparing T_0 to V3 (p=<0.001). These results implied that by the end of the trial, relying only on the current standard diabetic foot care protocol had not managed to reduce the number of re-ulceration cases close to 0 and that the small change, of only 2 cases of healed re-ulcerations brought about during the trial, can be still considered high as no statistically significant difference was confirmed between V1 (n=16) and V3 (n=14).

Despite the efforts of clinicians to prevent ulceration and re-ulceration in the diabetic high-risk foot, the situation of having a high rate of ulcer recurrence seems to be an international problem (Aldana & Khachemoune, 2020). Bus et al. (2013), similarly to this clinical trial, investigated the outcomes of improving prescribed custom-made footwear using in-shoe pressure measurement technology compared to standard care that consisted of non-improved footwear designs.

One-hundred-and-seventy-one neuropathic patients with diabetes mellitus, with a recently healed plantar foot ulcer were enrolled in this study who were randomly assigned to the either the intervention group or the control group. The intervention group had their custom-made footwear assessed every 3 months, with in-shoe pressure technology to make sure that at least 20% peak pressure relief was being achieved and

maintained throughout the study. Both groups were monitored for re-ulceration. Though no significant difference (p=0.48) in ulcer recurrence was observed between the groups, results showed that participants who undergone orthoses modification throughout the study fared better (only 38% of re-ulceration) than the control group (44.2% of re-ulceration) as they exhibited less cases of re-ulceration.

Zwaferink et al. (2020), advocate for the implementation of objective and scientific-based approaches to determine the design and improvement of an offloading device in view of plantar pressure relied and diabetic foot ulcer prevention. As in their study, a 90% success rate of reducing plantar pressures via offloading device was achieved when the offloading device were assessed via an in-shoe pressure mapping device, which guided necessary modifications and improvements of the offloading design, following dispensing (Zwaferink et al., 2020).

Another interesting aspect highlighted in the results of this clinical trial is that nearly half (46%) of the participants in the experimental group needed orthosis modification, at least once during the trial, since their orthoses were identified as not achieving a minimum of 30% reduction of the original peak plantar pressure at the site of their previous ulceration as suggested in the literature (Bus et al., 2020). In this study, original peak plantar pressure is defined as an area of peak plantar pressure that corresponds to the area of previous ulceration while not wearing an offloading device designed to offload that same area. The concern raised with these results is that the standard diabetic foot care, in which orthoses are just observed visually for their effectiveness, is failing to objectively determine whether the prescribed offloading device is actually beneficial and affective.

In this clinical trial 30% of participants in the experimental group required a modification to their orthoses only once, 11% of participants required a modification twice and 5% of participants required a modification of their orthoses 3 times, once every visit, since this required more than one adjustment in order to reduce the peak pressure areas as targeted. The majority of these participants did not present with the typical clinical signs of ulcer development, such as erythema, warmth, callosities and

so forth (Baig et al., 2022), and their orthoses were in mint condition. In spite of this, the orthoses of these patients were not achieving 30% pressure reduction as advised by international guidelines (Bus et al., 2020) thus, modification of their orthoses was necessary. This highlighted the fact that by just relying on visual observation it is very difficult to determine whether the required offloading is being achieved.

In the guidelines on the prevention of foot ulcers in persons with diabetes, it is recommended that peak pressure areas that exceed <200kPa (measured with a $2cm^2$ pressure sensor) at the site of previous ulceration should be reduced by 30% or more in order to prevent re-ulceration (Bus et al., 2020). The use of valid and reliable technology, such as in-shoe pressure systems, to achieve the targeted pressure relieve off of previously ulcerated areas in the high-risk foot, has been highly recommended, especially to determine the design and efficacy of the offloading device (van Netten et al., 2018). Thus, these statements concur with the results of this clinical trial which suggest that monitoring patients with the innovative, single-sensor, in-shoe pressure and temperature measuring device, as an adjunct to the current standard diabetic foot care protocol, informed the modifications relevant to the offloading device to an improved design which ultimately helped reduce the number of re-ulceration cases.

8.8.2 Correlation between pressure and temperature parameters

In this clinical trial, given the very limited research on the correlation between pressure and temperature in view of diabetic foot ulcer development (Bus et al., 2016; Jones, Bibb, Davies et al., 2020), the correlation between in-shoe peak plantar pressure and in-shoe peak plantar temperature, at previously ulcerated sites, with and without orthoses, was also investigated. The necessity to measure plantar skin temperature in the diabetic high-risk foot emerged from the concept that with repetitive excessive pressure, specific areas in the foot become warmer, sometimes weeks before the underlying tissue breaks down (Bus, 2013; Armstrong et al., 2017; Mizzi & Falzon, 2018; Gatt et al., 2018; Mifsud et al., 2022).

This study is first of its kind to have investigated the strength and direction of a linear relationship (correlation) between pressure and temperature, in the diabetic high-risk foot, in which measurements of pressure and temperature were taken in-shoe and in real-time, and in the absence and presence of an offloading device. Correlation analysis from this clinical trial showed a small positive correlation between peak plantar pressure and peak plantar temperature when observing participants walking with their orthoses and a medium to large correlation when observed walking without their orthoses implying that the excessive pressure that was imposed over a specific area of the skin initiated an inflammatory process thereby raising the skin temperature over that same area.

Although Yavuz et al. (2014) utilized a non-contact infrared thermal camera and a custom-built barefoot pressure-shear plate, to measure skin temperature and plantar pressures, on a healthy non-diabetic population, despite the differences in study methodology, a positive correlation between pressure and temperature was confirmed which was congruent with the results of this clinical trial were an in-shoe pressure and temperature device was used.

El-Nahas and colleagues, (2018) investigated the correlation between pressure and temperature in view of diabetic foot ulcer prevention using a sock incorporating pressure and temperature sensors referred to as 'Smart Socks' (Najafi et al., 2017; El-Nahas et al., 2018). Similar to the study by Yavuz et al., (2014), this study was also conducted on healthy non-diabetic participants however, a positive correlation between in-shoe pressure and in-shoe temperature was also confirmed (El-Nahas et al., 2018).

In the cross-sectional study presented by Qin et al. (2021), 2,014 diabetic feet were investigated for increased temperature areas over observed hyperkeratotic lesions via thermographic imaging. Peak pressure measurements were taken with an in-shoe pressure mapping device however, the participants were asked to stand over the in-shoe insert barefoot in a static position. Similar to the results obtained from this clinical trial, a positive correlation between pressure and temperatures was also confirmed.

This correlation was especially observed in participants with higher peak plantar pressures who had higher temperature readings over the corresponding site of lesion (Qin et al., 2021).

The results of this clinical trial also support the results obtained in a recently published, local study (Perren et al., 2021). The study by Perren et al., (2021) utilized non-contact infrared thermal cameral and barefoot pressure mapping to investigate the correlation between temperature and pressure in the diabetic high-risk foot. A total of 24 participants living with diabetes mellitus, together with 24 healthy controls, were asked to walk at self-selected speed, over a treadmill for 15 minutes. Plantar temperatures were then read off from 5 regions of the plantar aspect of the foot via a thermal camera. Peak plantar pressures were taken soon after via a High-Resolution (HR) Mat (by Tekscan, Boston, MA, USA). Results of this study also showed a positive correlation between pressure and temperature which was especially evident in participants living with diabetes mellitus.

Despite the differences identified in the above mention studies to this clinical trial, all results of the different studies seem to concur that as pressure increases, the skin temperature also increases in healthy participants (Yavuz et al. 2014; Wang et al. 2018; Jimenez-Perez et al., 2021) but more importantly this was also observed in the diabetic high-risk foot (Wang et al. 2019; Jimenez-Perez et al., 2021; Perren et al., 2021) with and without the use of prescription offloading devices. It can thus be concluded that with the help of emerging technology, such as the innovative, single-sensor, in-shoe pressure and temperature measuring device, the correlation between pressure and temperature can be used to early predict diabetic foot ulcer development.

8.8.3 Strengths and Limitations of the Study

Sample Size

Due to a number of hinderances as mentioned in Section 8.8.6, and due to the limited time period available for this clinical trial to be conducted, the targeted participant population to be recruited in this clinical trial could not be reached and thus, the total number of participants recruited was limited to 88 participants. The small sample size, not only may have influenced the representation of the general diabetic population but it may also have affected the strength of the statistical significance of the results obtained from the Cohran's Q-test analysis and Spearman's Rank Order Correlation Analysis as both tests are influence by the sample size. However, despite this limitation, results still showed a positive correlation between pressure and temperature parameters. Furthermore, this study was first to explore the correlation between in-shoe pressure and in-shoe temperature readings, in real-time, within the shoe, in both the presence and absence of an offloading device and in the high-risk diabetic population.

Matching

Due to the limitations encountered in recruiting participants, the participants were not matched according to their HbA1c. It is well known that elevated HbA1c levels predispose the individual to a higher risk of ulceration and may delay wound healing (Christman et al., 2011) however, given the limited time period available to conduct the trial, matching the participants according to HbA1c levels in addition to age, gender, duration of diabetes, presence of neuropathy, presence of ischaemia and presence of neuro-ischaemia would have further reduced the sample size.

Re-ulceration rate

The observation period at T_0 was intentionally planned to observe the amount of re-ulceration in both groups while still receiving standard care. The researcher is aware that the unexpected imbalance in amount of re-ulceration between the experimental

group and the control group at T_0 may be seen as a statistical bias, since the control group had disadvantage over the control group in terms of re-ulceration numbers at the start of the study. The researcher here would like to remind the reader that the purpose of this study was to evaluate whether or not the use of the single-sensor, in-shoe pressure and temperature measuring device could be used as an adjunct, monitoring mechanism, to the standard diabetic foot care in the prevention of re-ulceration and ulcer resolution throughout the duration of the entire clinical trial.

Furthermore, matching of participants in this study helped in compensating for any undetected confounding variables within subjects that might have created bias and influenced the overall outcomes of this study (Nestor & Schutt, 2015). Having employed a Match-pairs design, full randomisation was not possible during the assignment of participants to the groups (Nestor & Schutt, 2015).

Influential factors on temperature readings

Another possible limitation identified in this study is that the innovative, single-sensor, in-shoe pressure and temperature measuring device was designed to measure pressure and temperature parameters, at a single targeted area only. Though the role of pressure and temperature in view of ulcer development is still a relatively new concept and is still being investigated, other parameters such as humidity and shear stress are also hypothesised to contribute to tissue breakdown (Armstrong et al., 1998; Jones, Bibb, Davies et al., 2020; Maluf et al., 2001). Moreover, it is also hypothesised that pressure, temperature, humidity and shear stress have a combined influence on the integrity of the skin and together they all play a major role in ulcer development (Maluf et al., 2001). Though current technology does not allow for simultaneous measurement all these 4 parameters, different studies provided evidence for a combination of these parameters (Jones, Bibb, Davies et al., 2020).

Though this clinical trial could have considered other variables that could have influenced temperature change, this study was first to measure temperature and pressure parameters in real time, inside the shoe (in-shoe), with and without

prescription orthoses and on participants living with diabetes mellitus. Furthermore, the primary aim of this study was to identify whether the use of the innovative, single-sensor pressure and temperature measuring device as an adjunct to standard diabetic foot care practice is actually beneficial in preventing re-ulceration and/or complications of diabetic foot. This aim was fully achieved in this study.

8.9 Conclusion

The purpose of this study was to compare the outcome when using an in-shoe single sensor pressure and temperature device to standard clinical diabetic foot care protocols to monitor the diabetic high-risk foot in view of ulceration and re-ulceration prevention. Locally, the standard care plan for the high-risk foot comprises the provision of off-loading devices, including foot orthoses and its monitoring, based on clinical experience and observation, to off-load previously ulcerated areas together with the monitoring for vascular or dermatological complications.

With the help of advancements in technology, the innovative, in-shoe, single-sensor, pressure and temperature measuring device was designed and developed to provide the clinician with the ability to pre-empt the development of foot ulceration and re-ulceration. This device was first of its kind to integrate clinical practice and patient management with new technology, which today is becoming more and more popular amongst both clinicians and patients.

With careful monitoring diabetic foot complications, and amputations, could be avoided as highlighted by the results of this clinical trial. The positive results of this clinical trial should encourage a change in clinical practice by not just relying on clinical experience and visual observation to determine the efficacy of an offloading device but instead rely on objective, evidence-based assessments. By doing so, the financial burden on healthcare costs could be alleviated if complications are to be reduced or avoided.

In light of confirming a correlation between in-shoe pressure and in-shoe temperature during ambulation, this device may also serve as a foundation tool to further investigate this phenomenon in both laboratory setting, and during the patient's at-home and daily activities.

Chapter 9 – Concluding Discussion

9.1 Introduction

This dissertation presented the background literature related to the importance of monitoring foot plantar pressures and plantar skin temperature assessment in view of foot ulcer development and prevention of re-ulceration in the diabetic high-risk foot. It also presented a series of investigations which led to the development of an innovative, single-sensor, in-shoe device that is able to read pressure and temperature simultaneously. The overarching aim of this PhD project was to determine whether the application of this device could be integrated to current standard diabetic foot care practice, as an objective and low-cost clinical tool, in the prevention of diabetic foot ulceration and re-ulceration. Locally, the standard care plan for the high-risk foot comprises of providing off-loading devices, including foot orthoses, to off-load previously ulcerated areas and to monitor for vascular and/or dermatological complications together with offering standard diabetic foot care.

This chapter provides the reader with a collection of all the investigations and findings conducted as part of this PhD dissertation. The clinical relevance of these findings and how this research may contribute to the advancement in the management of patients at-risk of ulceration and/or re-ulceration are discussed through the post-positivist perspective. This chapter also portrays how findings from this research could translate into a change in clinical practise. Lastly, the limitations pertaining to this PhD dissertation, and recommendations for future research are also highlighted.

9.2 The Philosophical Context

The conception of this project, which was to develop an innovative, low-cost, single-sensor, in-shoe pressure and temperature measuring device, was based on observing the local prevalence rate of lower limb amputations secondary to resilient ulceration, in individuals living with diabetes mellitus. This research project was inspired by the post-positive perspective theory, the *Theory of Scientific Revolution* and the *Paradigm Shift* from the work by Thomas Kuhn (Kuhn, 1996). As detailed in Chapter 4, the

Theory of Scientific Revolution describes that when a new scientific concept is introduced, it is very likely to remain within the same state of advancement for a period of time until it no longer serves its purpose, or it is challenged. The theory further explains that once this concept is challenged by another new scientific concept, the progress of its scientific research becomes linear and that it can only be accepted to be called scientific, if it advances through the 4 phases of science namely, the *Pre-paradigmatic Stage*, the *Normal Science*, the *Paradigm Shift/Crisis Stage* all which ultimately lead to the final stage that is the stage of *Scientific Revolution*. In a nutshell, when an already established scientific concept is challenged, which if applied to this PhD project would correspond to the current local standard diabetic foot care practices, it goes through the latter described stages. From a new concept a Paradigm is created that undergoes a series of scientific investigations to determine whether or not, the new proposal is more effective than the already established concept. If the new concept is proven to be less effective than the already established concept, that concept remains until it is challenged again. However, if the flaws within an already established theory are identified and proven, then the new theory brings about a change; what Kuhn refers to as *Scientific Revolution*.

9.2.1 Identifying the need for change in the health care setting

Despite the efforts that the local health care system is employing to prevent diabetic foot ulceration, we are still facing a disproportionate number of individuals who experience serious diabetic foot ulceration which often leads to lower limb amputation (Mizzi & Falzon, 2018; Grima et al., 2018). Due to the increase in number of ulcer recurrence the researcher questioned whether current management to prevent ulcerations is adequate and questioned whether a change in clinical practice is needed.

As presented in Chapter 3, a local scoping study investigated the referral and management pathways for in-depth biomechanical assessment and barefoot pressure assessment of patients living with diabetes mellitus within the local health care system. Results of this study showed that the current standard diabetic foot care assessment techniques focus mostly on the vascular and neurological aspect of the foot and little

attention is given to the biomechanical aspect of the high-risk foot. Moreover, clinicians determine the design and effectiveness of the prescribed offloading device through visual observation and clinical experience and the observation for the classic clinical signs of ulceration. Furthermore, the concept of utilizing in-shoe foot pressure mapping prior and following prescription of foot orthoses is not yet available within the local health care setting. Foot orthoses are being prescribed with the intention to reduce plantar pressures but the evaluation of their true effectiveness, to date, again relies only on the clinical judgement, expertise and observational skills of the experienced clinician. The local standard diabetic foot care plan is largely accepted within the local health care system and from a post-positive, Kuhnian perspective, this is the established scientific concept which is considered in the *Normal Science* Stage.

Questions have been raised whether this already established scientific concept is still effective in preventing or reducing the number of diabetic foot re-/ulceration cases. Early identification of the initial pathological changes, such as of deep tissue damage, may be difficult to observe when relying simply on visual observation and clinical experience. Furthermore, an estimation of plantar pressures and temperature monitoring cannot be conducted without the use of technology. Waiting to observe clinical signs of ulceration may be too late and detrimental to the high-risk foot (Smith-Strøm et al., 2017). As detailed in Chapter 2 (Literature Review), both excessive pressure and increased skin temperature are deemed as important causal components in the development of diabetic foot ulceration both relating to joint mobility and structural foot deformities (Fernando, et al., 2016; Bus, 2016; Armstrong et al., 2017). Moreover, the literature review highlighted that there is a correlation between skin temperature and plantar pressures in the causation of diabetic foot ulcers however, their role has only been investigated in a limited number of studies (Bus, 2016; Jones et al., 2020).

Currently the advancements in technology allows for the objective clinical measurement of pressure and temperature using devices such as the in-shoe pressure

systems and thermal cameras, for the early identification of tissue breakdown in the high-risk foot (Armstong et al., 2017; Astasio-Picado et al., 2018; Gatt et al., 2019; Perren et al., 2021). Nonetheless, due to relative high costs that the use of such devices entails not only to purchase the equipment, but also the time required during clinical consultation to perform the assessments, leaves clinicians reluctant to use especially since the use of such devices is time consuming (Saliba Thorne et al., 2021). This is unacceptable since the measurement of these parameters, particularly plantar pressures, in clinical environments have been proven to be a vital contribution to determine the pathomechanics of the abnormal foot and record treatment progression (Hessert et al., 2005).

The inspiration behind the development of this device was to provide a compact, low-cost and efficient alternative device which is able to pre-empt the development of diabetic foot ulceration and re-ulceration following a concern of whether the high recurrence rate of re-ulceration may be attributed to the fact that despite the healing of an ulcer, causative factors for ulceration such as foot deformity and increased foot plantar pressures and temperatures are still present and are not currently being promptly addressed (Bus, 2012). This is clearly suggestive of anomalies within the management care of these high-risk patients. From a Kuhnian perspective, here the researcher identified anomalies within the local current standard diabetic foot care which is the current established scientific concept. The identification of such anomalies brought about a *Paradigm Shift* or a *Crisis* where the established concept was being questioned for its effectiveness. For this purpose, a new scientific concept was introduced in order to help improve and hopefully bring about change in clinical perspective. Thus, as detailed in Chapter 6 (Development and laboratory validation of the Prototype), an innovative, single sensor, in-shoe pressure and temperature measuring device was developed to continuously monitor the diabetic high-risk foot for changes in localized in-shoe plantar pressure and temperature with the aim of reducing foot ulcerations and/or re-ulcerations. This device is first of its kind to integrate clinical practice and patient management with new technologies that are

nowadays becoming more popular and frequently used. The ultimate goal of such an innovation is to help preserve functional lower limbs of the high-risk diabetic population.

9.3 The proposal of a new diabetic foot care management plan

As previously described in Chapter 1, the role of the Podiatrists in both Primary and Tertiary Sector comprises of screening the diabetic foot (Diabetic Foot Screening) for any signs of risk factors that can lead to diabetic foot complications such as poor vascular perfusion and ulceration. The current diabetic foot care management plan guides the Podiatrists as follows.

At initial consultation, also referred to as Level 1 screening, the patient is assessed by his or her Podiatrist for his or her dermatological status using visual observation and clinical experience, and for his or her neurological and vascular status with the help of the 10g monofilament and a doppler ultrasound which are tools to determine the presence of neuropathy and ischaemia respectively. Based on the clinical findings, the patient is then categorised as high-risk or low-risk of developing diabetic foot complications.

Patients which are categorised as low risk are given a yearly review. This means that the dermatological, vascular and neurological assessment are repeated every year. In cases where the patient is categorised as high-risk, by identifying a neurological or vascular problem, the patient is referred for further assessment (Level 2 screening) where an in-depth vascular assessment using the Dopplex ultrasound to perform Ankle Brachial Pressure Index (ABPI) and Toe Brachial Pressure Index (TBPI) is carried out.

Following an in-depth vascular assessment, if an immediate risk of diabetic foot complication is identified the is referred to a consultation with a Vascular Surgeon at the local hospital (Level 3 screening) otherwise, if the limb is identified as having no immediate risk, then the patient is monitored regularly at Level 2 assessment.

It is very evident that the current diabetic foot care management plan, is overlooking an important influential factor of diabetic foot ulcer development. The foot function and morphology of the lower limb, in other words lower limb biomechanics, is heavily disregarded in the current diabetic foot care management plan and this is evident throughout all the levels of screening. Biomechanics is only and lightly mentioned at level 1 of screening where the Podiatrist is guided to fill the dedicated screening form, DH140 form (Appendix 1), where the podiatrist is instructed to tick the absence or presence of apparent visible deformities of the diabetic foot being examined, in the risk categorization section, at the end of the form. It is also important to highlight that, unlike for the neurological and vascular problems, the current diabetic foot care management plan does not guide the clinician what to do when foot deformities are identified.

It is concerning that in a scoping study conducted as part of this dissertation, it was identified that high risk patients with diabetes mellitus are not referred for a comprehensive biomechanical examination and barefoot pressure mapping, at the local Podiatric Biomechanics Clinic (Saliba Thorne et al., 2021). In this study, it was identified that diabetic high-risk patients are only examined biomechanically when they are referred to the Orthotics and Prosthetics Unit prior to the prescription of an offloading device such as orthoses generally secondary to an identified foot deformity that is suspected to produced increased plantar pressures and/or secondary to a previous history of ulceration and/or amputation (Saliba Thorne et al., 2021). Currently, for the high-risk diabetic foot, the clinical decision of whether or not the prescribed offloading devices are actually reducing peak plantar pressures at previously ulcerated sites or at sites at risk of ulceration is purely based on visual observation and clinical experience (Saliba Thorne et al., 2021). Locally, this may be due to the fact that the adequate technology is not yet available due to various reasons including, equipment is both costly and time consuming to use (Saliba Thorne et al., 2021).

The results of this clinical trial highlight the need for change in the current diabetic foot care management plan if better outcomes in terms of ulceration and re-ulceration

prevention are to be achieved. It is empirical that a comprehensive biomechanical assessment with the help of technology, to provide objective measurements of parameters such as pressure and temperature which cannot be measured through visual observation, are introduced as part of the diabetic foot care management plan.

New proposed plan

In order to provide a change or improvement to the current existing diabetic foot care management plan, this research proposes an innovative way for the management of the diabetic high-risk foot following the results of the studies conducted as part of this dissertation. The development of the new proposed diabetic foot care plan was the 4th objective of this dissertation and it is presented as a pocket guide for the clinician below.

Level 1 Screening

Current diabetic foot care protocol

Dermatological Assessment

- Patient is screened for dermatological lesions and/or conditions
- Including: Hyperkeratotic lesions, fungal, bacterial or viral infections, psoriasis, eczema, oedema, fissures, xerosis and maceration.
- Nail pathologies including: onychomycosis, onychogryphosis, onycholysis and nail involution

Tools required: Visual observation & Clinical experience

Vascular Assessment

- Pt is asked for signs of Intermittent Claudication (IC) and/or Rest Pain
- Assessment of pedal pulses and waveforms

Tools required: Dopper Ultrasound

Neurological Assessment

- Assess neural sensitivity to light touch

Tools required: 10g monofilament

New addition to the current diabetic foot protocol

Biomechanical Assessment

- Ranges of Motion of the hip, knee, ankle, midtarsal joint, subtalar joint, 1st and 5th ray and finally the 1st metatarsophalangeal joint
- Foot Posture Index: determine the foot posture through a set of pre-determined criteria
- Determine the prescence and absence of Leg Length Discrepancy Detemine the overall body posture
- Assess strength and stretching capabilies of muscles and tendons
- Assess and diagnose any aches and pains
- If present, relate any dermatological lesions to the patient's biomechanical profile
- Assess footwear
- Asses offloading device, including orthoses, if any

Tools required: Visual observation & Clinical experience

Prescription of offloading devices

- Assess dynamic in-shoe pressure and in-shoe temperature parameters to identify peak plantar pressures and raise in plantar skin temperature that corresponds to the area that is bearing the load.
- Design, manufacture and modification of offloading devices should be guided by technology that is able to read in-shoe plantar pressures and in-shoe plantar temperatures either simultaneously (which is ideal) or using separate devices
- Prescription orthoses should be monitored using in-shoe technology that is able to read pressure and temperature to assess the efficacy of the offloading device and make sure that the device is truely reducing excessive peak pressure areas.

Tools required: Single-sensor, in-shoe pressure and temperature measuring device

Level 2 Screening

Current diabetic foot care protocol

Dermatological Assessment

- Patient is screened for dermatological lesions and/or conditions
- Including: Hyperkeratotic lesions, fungal, bacterial or viral infections, psoriasis, eczema, oedema, fissures, xerosis and maceration.
- Nail pathologies including: onychomycosis, onychogryphosis, onycholysis and nail involution

Tools required: Visual observation & Clinical experience

Vascular Assessment

- Assessment of pedal pulses and waveforms
- Ankle Brachial Pressure Index (ABPI)
- Toe Brachial Pressure Index (TBPI)

Tools required: Dopplex Ultrasound

Neurological Assessment

- Assess neural sensitivity to light touch

Tools required: 10g monofilament

New addition to the current diabetic foot protocol

Biomechanical Assessment

- Ranges of Motion of the hip, knee, ankle, midtarsal joint, subtalar joint, 1st and 5th ray and finally the 1st metatarsophalangeal joint
- Foot Posture Index: determine the foot posture through a set of pre-determined criteria
- Determine the prescence and absence of Leg Length Discrepancy Detemine the overall body posture
- Assess strength and stretching capabilities of muscles and tendons
- Assess and diagnose any aches and pains
- If present, relate any dermatological lesions to the patient's biomechanical profile
- Assess footwear
- Asses offloading device, including orthoses, if any

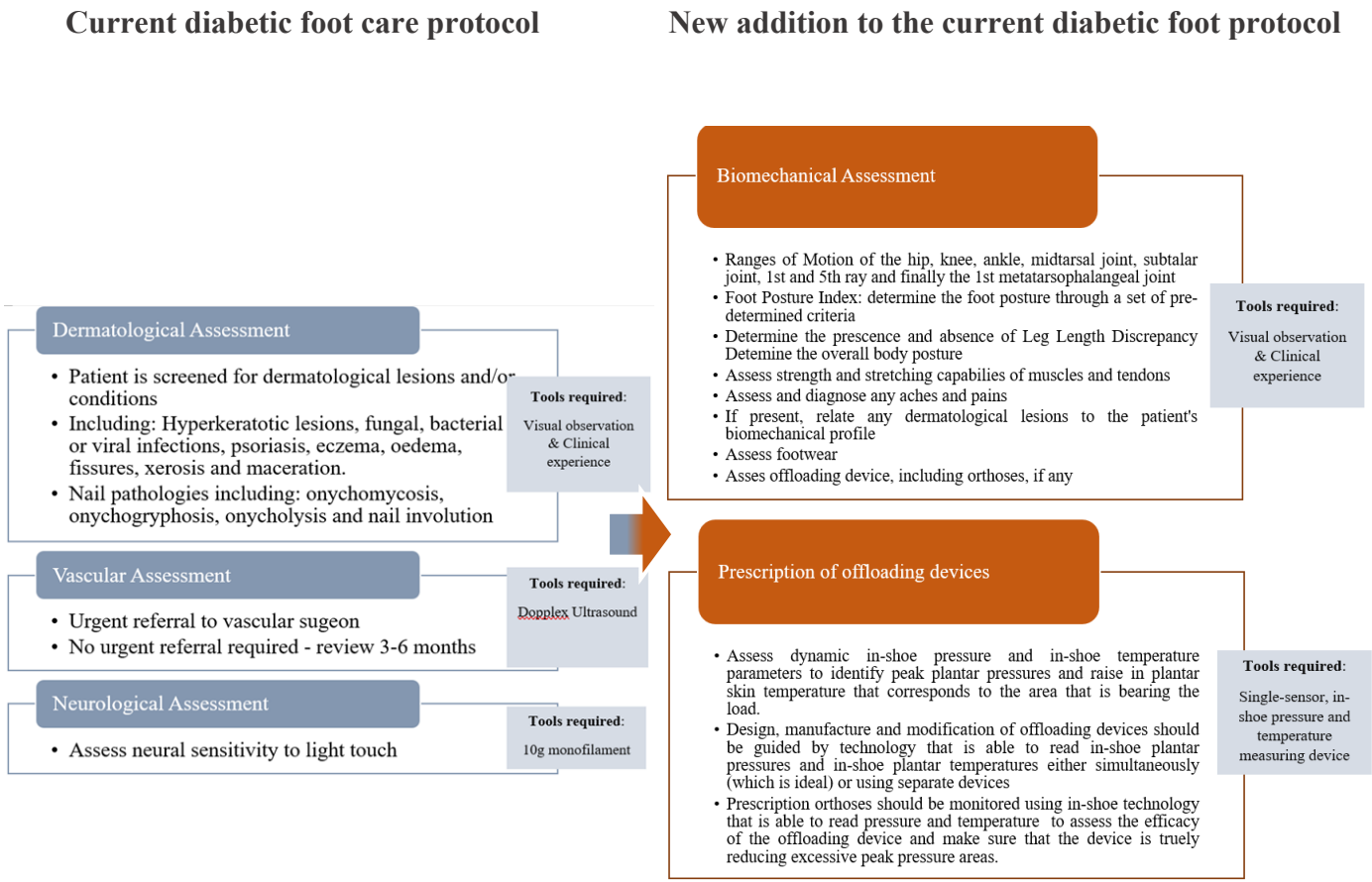
Tools required: Visual observation & Clinical experience

Prescription of offloading devices

- Assess dynamic in-shoe pressure and in-shoe temperature parameters to identify peak plantar pressures and raise in plantar skin temperature that corresponds to the area that is bearing the load.
- Design, manufacture and modification of offloading devices should be guided by technology that is able to read in-shoe plantar pressures and in-shoe plantar temperatures either simultaneously (which is ideal) or using separate devices
- Prescription orthoses should be monitored using in-shoe technology that is able to read pressure and temperature to assess the efficacy of the offloading device and make sure that the device is truely reducing excessive peak pressure areas.

Tools required: Single-sensor, in-shoe pressure and temperature measuring device

Level 3 Screening



The new diabetic foot care management plan amalgamates the concept of using technology to provide objective measurements and monitoring of risk factors, such as temperature and pressure, related to diabetic foot ulceration. In other words, the aim of the newly proposed diabetic foot care management plan is to integrate a detailed biomechanical assessment of the lower limb, with the help of in-shoe pressure and temperature measurements, as part of the current screening protocol which includes neurological and vascular assessments conducted at level 1, level 2 and level 3 screening program of the current diabetic foot care management plan.

As detailed in the literature review (Chapter 2), there are various types of in-shoe pressure systems that can be used to detect in-shoe pressure changes and other more sophisticated and innovative devices that are still being developed and validated as reported in the Systematic Review (Chapter 6) which was registered under PROSPERO (CRD4202183322) (Appendix 3) and published in the Diabetes and Clinical Practice Journal (Appendix4). In-shoe temperature measurement, is still a new concept and is proving to be slightly more challenging since commercial in-shoe temperature devices are still not available however, with regards to plantar pressure devices, sophisticated and innovative devices have been developed and validated (Martín-Vaquero et al., 2018; Saliba Thorne et al., 2021).

This research presented the development and validation of an innovative, cost-effective, single-sensor, in-shoe pressure and temperature measuring device that can read and measure pressure and temperature simultaneously and in-real time, in both laboratory and clinical setting which can be used as a low-cost alternative to the currently available expensive commercial devices mentioned above. As confirmed in the clinical trial, this device, when used as an adjunct to standard diabetic foot care, provided better clinical outcomes in reducing the incidence of re-ulceration when compared to the provision of current standard diabetic foot care management only.

This device is being encouraged to be utilized in clinical practice to identify excessive peak plantar pressure areas and any rise in localised skin temperatures at areas of interest, and to determine the efficacy of the already prescribed offloading devices (whether or not the device is truly achieving the targeted amount of pressure reduction of an area deemed at-risk of ulceration or at an area at risk of re-ulceration). The innovative, single-sensor, in-shoe pressure and temperature measuring device, can also

be used to guide the design and manufacture of an offloading device before and after dispensing.

A strong liaison with Orthotics and Prosthetics Unit is proposed where the Podiatry Department and the Orthotics and Prosthetics Unit could work hand in hand to determine the need, the design and the manufacturing of the offloading device/orthoses. This will also be applicable to follow-up cases to help determine the efficacy of the prescribed offloading device and to determine the need and choice of modification of the offloading device/orthoses. Detailed instructions of how to use the innovative, low-cost, single sensor, in-shoe pressure and temperature measuring device can be found in Appendix 8.

The compendium of the new diabetic foot care management plan also includes a detailed biomechanical assessment as suggested in the literature which consists of assessment of Ranges of Motion (RoM) of the main pedal joint which include the hip, knee, ankle, midtarsal joint (MTJ), subtalar joint (STJ), 1st and 5th ray and finally the 1st metatarsophalangeal joint (MPJ). It will also consist of the assessment of the foot posture via a set of pre-determine criteria as dictated by the Foot Posture Index (FPI) which is an established reliable and validated tool (Yang et al., 2022). Furthermore, assessments to identify presenting aches and pains, presence or absence of Leg Length Discrepancy (LLD), overall body posture during stance and assessments to identify the strength and stretching capabilities of muscles and tendons are to be included.

The current standard diabetic foot care plan is overlooking lower limb biomechanics, an important aspect which has a large impact on diabetic foot ulcer development. It currently relies on visual observation and clinical experience to assess the efficacy of prescribed offloading devices in view of ulcer and re-ulceration prevention. The reluctance to invest in technology, which has been reported and evidenced in numerous studies as being beneficial to save the high-risk foot (Singh et al., 2005; Bus, 2016; Armstrong et al., 2020), is leading to a great healthcare expenditure for the care of diabetic foot, including hospitalization and high amputation rates, which in reality could be avoided as has been shown in this study (Boulton et al., 2005; Rocchiccioli

et al., 2005; EHIS, 2008). A study by Armstrong et al. (2020) emphasized the need for new technology that can be used to help reduce the severity and healing period of diabetic foot ulceration by pre-empting signs of tissue breakdown as early as possible. The authors argue that with the introduction of such technology, diabetic foot complications such as ulceration and amputations can be avoided thereby decreasing the high mortality rate due to diabetes. People who undergo major lower limb amputations are estimated to live no longer than 5 years post intervention (Laverly et al., 2010; Morbach et al., 2012; Huang et al., 2018) and due to this, mortality associated with diabetic foot amputations have been rated second to lung cancer (Armstrong et al., 2020).

As shown in Chapter 8, this new proposed concept of managing the high-risk diabetic foot with the innovative, single sensor, in-shoe pressure and temperature measuring device resulted in better prognostic outcomes, indicating that this device may be a viable tool for the prediction of ulcer prevention in the high-risk foot. The cost-effectiveness, reliability and validity of this device makes it an ideal alternative to the currently available expensive commercial devices which can be used to monitory in-shoe plantar pressures and in-shoe temperatures. Furthermore, the simplicity and compactness in the design of the device allows for better fitting within footwear and targeted assessment of specific anatomical parts of the foot.

9.4 Impact of the PhD Investigation on Diabetic Foot Management

This project addressed a national problem. With Malta having a high prevalence rate of diabetes (>10%, circa 40,000 patients), a high prevalence rate of lower limb amputations is also observed. It is estimated that 120 major lower limb amputations are being performed each year due to diabetic foot complications (Cassar, 2020). This project is in line with the National Health System Strategy for Malta (2014-2020) and the Malta's Smart Specialisation Strategy (2021-2027) whereby the Maltese government is urging towards working in a safe and sustainable healthcare system for all. The National Health System Strategy builds on the solid foundation strategy that

health care systems should be a sustainable one and providing the best access to health for our population through prevention, efficiency and better use of available resources in order to deliver best patient care in the health sector. Strengthening prevention is key to the maintenance of a healthy population an aspect, that this project proposed and believed to be achieved by the early identification of foot disease and thus prevent foot morbidity such as amputations and mortality following severe lower limb complications.

Having the innovative, low-cost, single-sensor, in-shoe pressure and temperature measuring device validated and tested for its potential use to measure in-shoe pressures and temperature parameters at targeted anatomical landmarks in the high-risk foot, it can now also address both the EU and the global priority of managing the diabetic high-risk foot. Having a global population which is expected to rise by 592 million by 2035, diabetes will also affect the annual prevalence for nontraumatic lower limb amputations in persons living with diabetes mellitus which is estimated to be between 2.1 and 13.7 per 1000 individuals (Armstrong et al., 2017). Furthermore, it is estimated that the mortality rate associated with diabetic lower limb amputation ranges from 13% to 40% at 1 year, 35% to 65% at 3 years, and 39% to 80% at 5 years (Armstrong et al., 2017).

This research hopes to inform health care service managers as to how an innovative single sensor pressure and temperature device could be introduced in the healthcare system, as an alternative to the high-cost in-shoe pressure systems currently commercially available which, however, are not being utilized in our hospitals due to their high cost and time-consuming application. Having developed and validated the single sensor in-shoe pressure and temperature device for its effectivity, it can be safely introduced as part of the diabetic foot health services. This device has the potential to be an ideal tool to help the clinician determine whether the orthoses being prescribed, as part of the standard treatment and of the offloading strategy for the prevention and management of the high-risk foot, are being indeed effective in managing high plantar pressures to prevent ulceration/re-ulceration. Furthermore, this device can also help in

the monitoring of skin temperature vis-à-vis ulcer formation, a perspective never taken into consideration to date in clinical care. This device can help the clinician identify early stages of inflammation, caused by excessive and repetitive plantar pressures, through temperature monitoring to prevent skin damage and re-ulceration.

9.5 The Contribution to Knowledge

Having developed and validated the integration of this single-sensor, in-shoe pressure and temperature measuring device, as an effective method of assessing the efficacy of prescription orthoses for the diabetic high-risk foot, Intellectual Protection (IP) for this device will be sought. Once Intellectual Protection will be achieved, the device will be made commercially available as an innovative, cost-effective, easy-to-use product which has been developed and validated to simultaneously measure in-shoe pressure and in-shoe temperature at anatomical landmarks of interest.

The compactness and simplicity of the device, together with its ability to fuse 2 major predictors of ulceration (pressure and temperature), makes this device ideal to serve as a stepping stone that shed light on new information pertaining the relationship and integration between plantar pressure and skin temperature measurement in the diabetic high-risk foot. This topic often is overlooked and barely explored especially in the in-shoe environment, yet it is an extremely vital perspective in the prevention of diabetic foot ulceration (Bus et al., 2020) together with the application of an innovative method for fusion of temperature and pressure assessment in order to manage the diabetic foot.

This research hopes to improve the knowledge and the skills, related to in-shoe temperature and pressure measurements, of researchers and in the future various clinicians who could start making use of this innovative device in their clinical practice, by introducing them to the latest technologies in connection to the fusion of foot pressure mapping and temperature measurements in the diabetic high-risk feet. It is hoped that following the recommendations from this research, new technologies that are nowadays becoming more popular and frequently used, such as online clouds and mobile applications, will be integrated to the clinical practice and patient management.

Such innovations could make data more accessible for the clinician in any setting of choice being clinical, laboratory or any other environment thus improving patient care. This innovative device is perceived to highly encourage both clinicians and patients to start relying on objective measurements rather than traditional subjective measurements which could hopefully lead to decreased cases of ulceration, hospitalization and amputations, thereby reducing healthcare costs.

Last but not least, this research served as an opportunity for a collaboration between the Podiatry Department and Engineering Department at the University of Malta, where experiences, knowledge and awareness on how the diabetic foot can be preserved were shared between the professionals involved in this project.

9.6 The Impact of the Research on End-users, Society and Future Research

As previously mentioned, the ultimate goal of this research was to help preserve functional limbs in the high-risk foot by identifying whether the integration of an innovative, low-cost, in-shoe, single-sensor pressure and temperature measuring device is effective for assessing pressure and temperature as predictors of diabetic foot ulceration/re-ulceration.

Apart from being user-friendly and low-cost, this device was especially designed to permit portability. The simplicity and compactness in the design permit the researchers, clinicians and patients to monitor, in real time, in-shoe pressure and temperature of the foot within the shoe during daily activities and identify signs of tissue breakdown and pre-ulcer development, in various settings and daily activities. It can also provide the researcher or clinician with information about compliance to prescribed activities by monitoring the quantity and quality of pressure patterns that are characteristic during a specific activity. Furthermore, continuous monitoring of in-shoe pressure and temperature has the potential to further improve and facilitate early detection of tissue breakdown by observing trends over time rather than a single static threshold (greater potential to report consistent and clinically relevant measures).

This low-cost device can be used to indicate an increase in plantar pressure and a rise in plantar skin temperature which could serve as a prediction of the development of diabetic foot ulceration at an early stage hence, patient management can be then implemented to prevent ulceration or re-ulceration from occurring. This could reduce the risk of ulcer complications such as inflammation and amputations, safeguarding the patient's quality of life. Furthermore, due to the predicted reduced cases of ulceration, a reduction in healthcare costs could also be foreseen. Such costs may include active ulcer management that cover dressings and medicinal, surgical procedures (both minor and major), and hospitalizations. Furthermore, through objective measurements, this low-cost device could be used to determine the efficacy of prescribed orthotic fabrication and other offloading devices being used as treatment modalities to reduce peak plantar pressures in the diabetic foot management. Thereby it could change clinical practice and change the notion of just relying on clinical evaluation. The researcher is confident that this change will help in preventing ulceration and re-ulceration cases which will ultimately reduce cases of hospitalization, amputations and healthcare costs.

This project will inform future studies on the correlation between increased in-shoe plantar pressures and increased in-shoe local skin temperature and their role in tissue damage and diabetic foot ulcer development. It will encourage clinicians for objective assessment of foot biomechanics, insole prescription and objective treatment/management plan for the purpose of routine diabetic foot inspection. It hopes to offer a long-term, continuous monitoring of in-shoe plantar pressures and in-shoe temperature, during daily activities to help identify an objective, evidence-based pressure/temperature threshold vis-à-vis ulcer development. It could also serve as a means to compare lab-based results with real-life results creating the foundations for an objective and reliable home-monitoring device within this field.

Other researchers might be inspired to use this technology and to further explore its potential within both clinical and non-clinical environments and for further research. Researchers might wish to use this device to explore and investigate other areas of

interest such as footwear and orthotic fabrication, rheumatology, sports and rehabilitation to mention a few. Thus, this project is also expected to have an interdisciplinary advancement as, though targeted for Podiatrists, both the device and the application software associated with it has been created to provide access and facilitate use for any Allied Health Professional, Clinicians and Researchers interested in the field of clinical biomechanics and foot pressure and temperature measurements.

As with any other product on the market, refining and further development of the innovative, low-cost, single-sensor, in-shoe pressure and temperature measuring devices will be needed. Studies such as Patient Public Involvement (PPI) or Focus Groups, whereby several key stakeholders including Physiotherapists, Orthotists, Policy makers and Podiatrists will provide the researcher with their positive and negative feedback on the device and henceforth put forward their recommendations for aspects that require improvement and/or changing.

9.7 Dissemination of Findings

The researcher will continue to disseminate the knowledge and information obtained through this research to the general public, clinicians, policy makers and researchers, through social media and other activities such as articles in the Times of Malta, Think Magazine, Science in the City; local and international conferences, journal publications, poster presentations and lectures, both locally and internationally. Each investigation of the PhD study was published in International, peer reviewed journals throughout the project thus fulfilling the 4th objective of this PhD which sought to create a compendium on the application of a low-cost, single-sensor, device to measure in-shoe pressure and temperature simultaneously to encourage its use in clinical practice, as presented at the beginning of this dissertation (page v).

It is expected that this research will generate future research opportunities which will in turn be published creating a cascade of publishable material that could be shared among researchers and healthcare professionals to help manage the diabetic high-risk foot.

Awareness about the following topics will be raised to the general public, other Health Care Professionals and policy makers:

- The complications of diabetic foot ulcerations and the financial burden these complications bring on the Health Care System.
- The benefits of managing the diabetic foot by monitoring parameters such as plantar pressures and monitoring temperatures.
- The benefits of integrating a new clinical protocol in the management of the diabetic foot using innovative devices such as this innovative, single-sensor, in-shoe pressure and temperature measuring device.

An interactive web page was set up to present detailed information on innovative, single sensor, in-shoe pressure and temperature measuring device. The contents of this web page include a full description on the design and architecture of the innovative device; the uses and application of the innovative device; the instructions manual of the innovative device; literature, research and publications related conducted on the device. The reader can access this website via the following web address: www.stride-me.com

9.8 Strengths and limitations of the PhD

Although the limitations of each study were discussed in the relevant chapters, below are some biases related to the overall research. Smith & Noble (2014) defined bias as the tendency to focus on a particular interest, or to pose unfair judgement for or against a particular area of interest which leads to a deviation from the truth. Bias can be found at any stage including during data collection, data analysis and data interpretation (Pannucci & Wilkins, 2010). Acknowledging and understanding bias is very important in research as bias influences the validity and reliability of a study and may lead to misinterpretation of results of a study and its complete elimination is near to impossible (Smith & Noble, 2014). The 3 types of biases acknowledge in this research are selection bias, information bias and confounding bias (Fox & MacLehose, 2022).

Selection bias

To involve all the individuals with the characteristics of interest, such as diabetes, in a study is very difficult as it requires time and funding (Turner, 2020). In view of this, a representative sample of the population of interest is recruited. To ensure that the sample is indeed representative and that findings associated with the sample, can be generalised to the rest of the population, the researcher must provide every subject equal opportunity to be included in the study (Turner, 2020) this is referred to as Sampling Randomisation (Suresh, 2011).

In this study, though random sampling would have been preferred, the age, gender, duration of diabetes and the presence of characteristics such as neuropathy, ischaemia or neuro-ischaemia puts the subject at different risk of re-ulceration (IDF, 2020; Shi et al., 2021). In view of this, matching of participants was deemed necessary to eliminate potential bias and eliminate confounding variables that may have brought imbalance between the control group and the experimental group (Bordens & Barrington Abbott, 2014). To instil a sense of randomisation in the study, a matched-pair design was employed in this study where matched pairs of participants were randomly assigned to either the control group or the experimental group (Nestor & Schutt, 2015). The combination of matching and randomisation, provided this research with a balanced distribution of subjects at low risk of re-ulceration, subjects at intermediate risk of re-ulceration and subjects at high-risk of re-ulceration within the entire sample and thus, improving comparability between groups (Balzer et al., 2015). The researcher acknowledges that the presence of other, unidentified confounding variables may still have influenced the outcomes of the study (Moore, 2010, Bordens & Barrington Abbott, 2014).

To minimise selection bias and ensure generalisability, the selection of participants to be measured within this research was determined through a specified sample size calculation which considered the population size, the margin of error (confidence interval), the confidence level and the standard deviation (Smith, 2013). Giving that the general population size of people living with type II diabetes mellitus was that of 42.300 and considering a confidence level of 95%, with a confidence interval of 7.99%,

the estimated sample size for this study resulted to be that of 150 participants. However, having matched the subjects lead to cases where a participant had to be eliminated from the study as his/her matched subject withdraw from the study or died during the study. In addition to this, matching participants and the fact that this study was carried out during a pandemic (COVID-19) recruiting and matching participants proved very difficult. This ultimately affected the final sample size to a total of 88 participants.

Information bias

Information bias presents as any deviance from the truth that is derived from collecting, recalling, recording or handling information during a study (Althubaiti, 2016). To minimise information bias as much as possible, it was made sure that the appropriate study designs were chosen and systematic data collection protocols were employed in each and every study that make up this research (Bankhead, Spence & Nunan, 2019).

Though it was not possible to avoid over-stressing, under-reporting and non-disclosure of information from participants during this research, the researcher strived to avoid misinterpretation bias and recall bias by recording the interviews using a digital voice recorder. This helped the researcher record truthful amounts by not missing out on any information conveyed during the study or by letting his or her personal views influence the interpretation of the results. Furthermore, the standard and validated device such as the FScan® in-shoe system, Flir® thermographic camera, digital thermistor, and ultimately the innovative, single-sensor, in-shoe pressure and temperature measuring device were used to measure and collect data prospectively. Medical records were also utilized to ascertain medical history and to verify inclusion criteria of participants.

Confounding bias

Confounding bias is caused when a particular factor gives false association between a different variable and its outcome leading to false conclusions (Lambert, 2011). For a factor to be considered as confounding, it must be associated with the outcome and be considered as a risk-factor (Fox & MacLehose, 2022). Influential factors that can be considered as confounding in this research, included age, gender, presence of

neuropathy, presence of ischaemia or presence of neuro-ischaemia, as each of these factors predisposes the individual to a different level of risk of re-ulceration (Shi et al., 2021). As previously mentioned, confounding bias was minimised by matching participants according to latter mentioned factors to create a balanced distribution of subjects which were at low risk of re-ulceration (neuropathy), subjects at intermediate risk of re-ulceration (ischaemia) and subjects at high-risk of re-ulceration (neuro-ischaemia) (IDF, 2020) within the entire sample and thus, improving comparability between groups (Balzer et al., 2015).

Unidentified confounding variables may have influenced the outcomes of this research (Bordens & Barrington Abbott, 2014) however, the participants recruited were not denied access to hospital visits that would provide them with conventional therapies.

Chapter 10 - Conclusion

This PhD dissertation sought to investigate whether an innovative, specifically-developed low-cost, single-sensor, in-shoe pressure and temperature measuring device, can be used for the prevention of diabetic foot re-ulceration. Outcomes of this research indicated a great need for change or improvement within the current diabetic high-risk foot management in view of re-ulceration.

This PhD was completed through a number of studies that helped answer the research question. Prior to the commencement of the main study, 2 scoping studies were conducted to explore and gain insight on the local management and local referral pathway of the high-risk diabetic foot. These studies also gave a numerical perspective on the number of high-risk patients living with diabetes mellitus that were being referred for an in-depth biomechanical examination in view of ulcer prevention. Findings of these studies highlighted the need for better awareness of local healthcare professionals with regards to the importance of biomechanics and the assessment of plantar foot pressures and their role in ulcer development. Points of concerns were also raised in terms of patient management of the diabetic high-risk foot where offloading and ulceration is concerned. This instigated the need for a change or improvement in the current clinical biomechanical related management of the diabetic foot in which the patient and in turn the health care system could holistically benefit.

The third study consisted of a comprehensive systematic review where its findings helped to shed light on the existing literature related to the various technologies used to read and measure in-shoe plantar pressures and in-shoe skin temperatures. Findings from this study concluded that, in terms of validity and reliability of in-shoe pressure and temperature devices being developed, the current body of evidence was not sufficiently robust and further research was required.

These studies informed the researcher on the design, architecture and development of an innovative, single-sensor, in-shoe device that can measure both pressure and temperature simultaneously. The intention was to build a device that can serve as a

low-cost alternative to the current expensive and time-consuming technology. This innovative device was built on the functioning characteristics of devices identified in the systematic review and based on the recommendations given by participants from the scoping studies. Laboratory validation of this device was conducted in 4th and 5th study conducted as part of the PhD project and clinical validation was achieved in the main study.

Findings of the clinical trial, which is the 6th study conducted as part of this PhD research, demonstrated that participants who were monitored with the innovative, low-cost, single sensor, in-shoe pressure and temperature measuring device, as an adjunct to the standard diabetic foot care management protocol, and who undergone orthoses modification based on the observations with the device, fared better than the control group as they exhibited less cases of re-ulceration. These results exemplify the need for change in the current diabetic foot care management plan if better outcomes in terms of ulceration and re-ulceration prevention are to be attained. It is empirical that a comprehensive biomechanical assessment with the help of technology, to provide objective measurements of parameters such as pressure and temperature which cannot be measured through visual observation, are introduced as part of the diabetic foot care management plan.

This clinical trial also proved clinical validity for the innovative, low-cost, single sensor, in-shoe pressure and temperature measuring device. It also highlighted a correlation between in-shoe skin temperature and in-shoe pressure during ambulation in individuals living with diabetes mellitus which is congruent to findings of similar studies conducted on the topic (Bus, 2016; Seixas et al., 2018; Gatt et al., 2018; Jones, Bibb, Davies et al., 2020; Perren et al., 2021). However, this PhD also highlighted that, considering this astounding, empirical discovery, research studies exploring this phenomenon in the diabetic high-risk foot is still lacking and at its prime, especially were the in-shoe environment is concerned.

As previously emphasized, cases of diabetic foot ulcerations are increasing at an astounding rate, both locally and internationally (NHS, 2018; Cuschieri & Mamo,

2014; Grima et al., 2018; Aldana & Khachemoune, 2020; Armstrong et al., 2020; Schembri et al., 2022), and they are leaving a marked impact on the individuals, putting a great burden on the local healthcare system (Cuschieri & Mamo, 2014; Armstrong et al., 2020). Having identified anomalies within the current standard diabetic foot management, this PhD proposed a new management approach that was validated in both a laboratory scenario and in a clinical trial involving the concerned patient population. It is now up to the clinician to strive for a *Scientific Revolution* and seek objective methods to assess the high-risk foot. Introducing this innovative, low-cost, single sensor, in-shoe pressure and temperature measuring device as an adjunct to the standard diabetic foot care management plan, is not only expected to have better outcomes in ulcer prediction, ulcer resolution and prevention of amputations, but it is also expected to reduce the economic burden on the health care system.

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Appendix 1 | DH140

Diabetic Assessment Form

Name:		ID:	Date:
DM type: 1 ☐ 2 ☐	Year at Onset:	Treatment: ☐ diet ☐ oral ☐ insulin	
☐ Controlled ☐ Poor Control ☐ H/O Poor Control		☐ smoker ☐ H/O smoking	

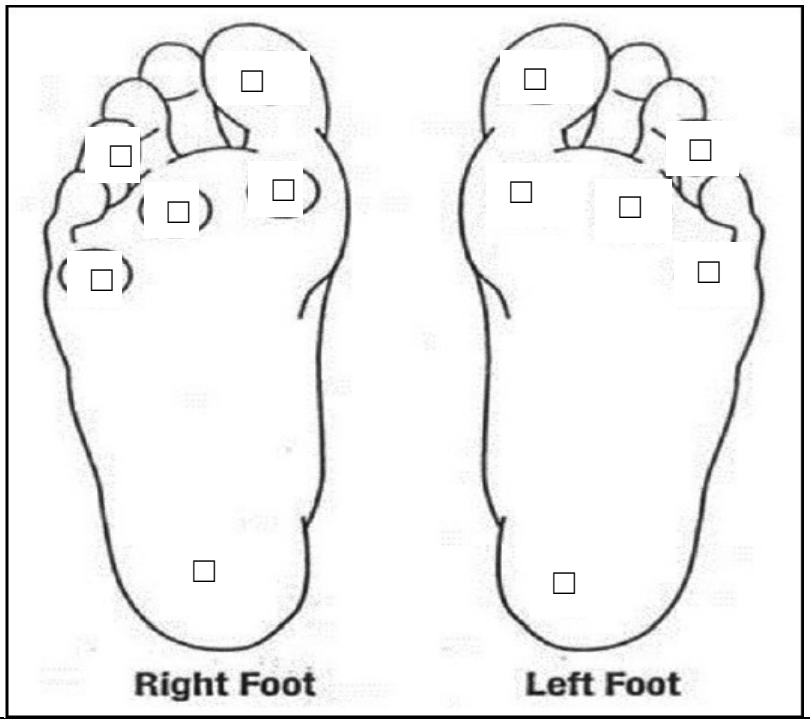
Medical history	**Medications**
☐ Cardiovascular disease	☐ Anti-Coagulants
☐ Nephropathy	☐ Statins
☐ Retinopathy	☐ Anti-hypertensives
Current Symptoms	☐ Thyroid medications
Intermittent Claudication? ☐ Yes ☐ No	☐ Anti-Depressants
Rest Pain? ☐ Yes ☐ No	☐ Immuno-suppressive drugs
Foot Ulcers? ☐ Yes ☐ No Location:	☐ Diuretics
Amputation? ☐ Yes ☐ No Location:	☐ Other:
Other:	

Foot Examination	
Nail Pathology:	**Dermatological:**
☐ Onychogryphosis	☐ Hyperkeratosis
☐ Onychomycosis	☐ Fungal infections
☐ Oncholytic	☐ Bacterial infections
☐ Involuted	☐ Viral infections
☐ Onychcryptosis	☐ Psoriasis ☐ Eczema

☐ Other:	☐ Fissures ☐ Xerosis ☐ Maceration
	☐ Oedema
	☐ Other:

Vascular examination stage 1	
Right foot:	**Left foot:**
Dorsalis pedis	**Dorsalis pedis**
☐ Triphasic	☐ Triphasic
☐ Biphasic	☐ Biphasic
☐ Monophasic	☐ Monophasic
Posterior tibial:	**Posterior tibial:**
☐ Triphasic	☐ Triphasic
☐ Biphasic	☐ Biphasic
☐ Monophasic	☐ Monophasic
Notes:	

Sensory foot examination: 10g Monofilament Neuropen
(Tick box = points felt)



Footwear assessment:
Does the Patient need any orthotics/ inserts:
Advice:

Risk categorisation	
Low risk patient – all of the following:	High risk patient – one or more of:
☐ Intact protective sensation	☐ Loss of protective sensation
☐ No severe deformity	☐ Severe foot deformity
☐no prior foot ulcer ☐No amputation	☐ History of foot ulcer
☐ Pedal pulses present	☐Weak pedal pulses ☐ Absent pedal pulses

Summary : ☐ Neuropathy ☐ PVD ☐H/O ulceration/ amputation ☐Low risk

Management Plan:

☐ Refer for vascular assessment

☐ Refer for neurological assessment

☐ No referral required

☐ Other:

Suggested Review Date:	Podiatrist:

Appendix 2 | Publication for Scoping Studies

Detailed Status Information

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Manuscript Type	Original Article
Special Section	Topics in Podiatric Medical Education
Corresponding Author	Claire Saliba Thorne (University of Malta)
Contributing Authors	Alfred Gatt , Cynthia Formosa
Conflict of Interest	I certify that all financial and material support for this research and work are clearly identified in the manuscript. Details regarding this support have been fully outlined in my cover letter. This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.
Abstract	BACKGROUND: Studies have shown that personal and economic reasons determine whether clinicians utilize diagnostic technology in their routine clinical biomechanical practice. This study aimed to identify the biomechanical management plan of local clinicians in relation to management of the diabetic high-risk foot and to investigate whether diagnostic technology is being used to determine the effectiveness of dispensed prescription orthoses in view of ulcer prevention. METHODS:A mixed-methodological approach was adopted in this study. A retrospective quantitative study was also conducted to access records of patients attending the Biomechanics Clinic at a local health. Outcomes of interest included the number and percentage of patients attending the biomechanics clinic, source of referral to this clinic, age and gender of patients, clinical diagnosis, management plan and referral pathway. Following a Phenomenological approach 4 experienced clinicians, working in the Private, Primary and Tertiary Health Sector were interviewed. Thematic Analysis was used to analyze and interpret data. RESULTS: Only low-risk patients living with diabetes mellitus were referred for a comprehensive biomechanics examination, of which, the majority of cases were referred by Podiatrists. There was no record of diabetic high-risk patients being referred for a detailed biomechanical assessment within the health service. This study also confirmed that, due to the expenses and laborious work involved when using diagnostic technology to assess foot pressures, interviewed clinicians based their treatment plan and tested the efficiency of dispensed offloading devices, on clinical experience and visual observation only. CONCLUSIONS: Waiting for signs of ulceration can be too late for the high-risk foot. A change in clinical practice is recommended where the integration of diagnostic technology, together with standard care, in view of ulcer prevention is warranted.
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Specialities	Biomechanics, Diabetes
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Digital Foot Technology in Ulcer Prevention and Re-ulceration: A Clinical Perspective.

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Abstract

Background

Studies have shown that personal and economic reasons determine whether clinicians utilize diagnostic technology in their routine clinical biomechanical practice. This study aimed to identify the biomechanical management plan of local clinicians in relation to management of the diabetic high-risk foot and to investigate whether diagnostic technology is being used to determine the effectiveness of dispensed prescription orthoses in view of ulcer prevention.

Methods

A mixed-methodological approach was adopted in this study. A retrospective quantitative study was also conducted to access records of patients attending the Biomechanics Clinic at a local health. Outcomes of interest included the number and percentage of patients attending the biomechanics clinic, source of referral to this clinic, age and gender of patients, clinical diagnosis, management plan and referral pathway. Following a Phenomenological approach 4 experienced clinicians, working in the Private, Primary and Tertiary Health Sector were interviewed. Thematic Analysis was used to analyse and interpret data.

Results

Only low-risk patients living with diabetes mellitus were referred for in-dept biomechanics examination, of which, the majority of cases were referred by Podiatrists. There was no record of diabetic high-risk patients being referred for a detailed biomechanical assessment within the health service. This study also confirmed that, due to the expenses and laborious work involved when using diagnostic technology to assess foot pressures, interviewed clinicians based their treatment plan and tested the efficiency of dispensed offloading devices, on clinical experience and visual observation only.

Conclusion

Waiting for signs of ulceration can be too late for the high-risk foot. A change in clinical practice is recommended where the integration of diagnostic technology, together with standard care, in view of ulcer prevention is warranted.

Introduction

International screening guidelines such as the IWGDF guidelines on the prevention of diabetic foot ulcer, recommend continuous monitoring of skin temperature of the diabetic foot, offloading of previously ulcerated areas or areas at risk of ulceration through the use of off-loading devices such as plantar paddings or foot orthoses[1]. Furthermore, offloading of peak plantar pressures is to be identified prior to the prescription of foot orthoses or bespoke footwear.

With the help of today's technology, plantar pressures can be easily identified through various pressure mapping devices. There are two types of pressure sensing devices these include the pressure distribution platforms and the in-shoe systems. Though both types of devices read pressures, the devices may vary in sensor sensitivity and configuration[2]. Pressure distribution platform systems consist of a flat, mat like device that is built from an array of pressure sensors, embedded within the floor particularly not to interfere with the patient's normal gait. Pressure platform are very easy to use and thus are the most popular in clinical settings. In an in-shoe system, the sensors are embedded within a thin and flexible insole-like sheet that can be inserted within the shoes[3]. This configuration, not only makes the device portable but, also ideal to measure the relationship between orthoses and the foot within the shoes, in different environment[4].

Despite the efforts being employed to prevent diabetic foot complications, an increasing number of diabetic foot ulceration, which often lead to lower limb amputation, cases are being recorded across the globe. It is reported that 8 to 10 non-traumatic amputations are attributed to diabetic foot ulceration where, 80% will develop a foot ulcer[5]. The annual prevalence for lower limb amputations secondary to diabetic foot ulceration is between 2.1 and 13.7 per 1000 individuals[6] which is associated with a mortality rate ranges from 13% to 40% at 1 year, 35% to 65% at 3 years, and 39% to 80% at 5 years[6]. Such a high recurrence rate may suggest that despite the healing of an ulcer, causative factors for ulceration are still persisting or not being accurately addressed[7].

This aim of this study was to determine the number of referrals pathways of patients living with diabetes mellitus that are referred for a diagnostic biomechanical examination within the Primary HealthCare sector prior and after prescribing foot orthoses or other offloading devices. Furthermore, to gain an understanding of how the high-risk foot is being managed within a specific healthcare system with regards to the biomechanical evaluation and identification of ulcer development from the perspective of local clinicians.

Methods

Ethical approval was sought from the Faculty Research Ethics Committee (FREC) and the University Research Ethics Committee (UREC) prior to the commencement of this study. As in accordance with the Declaration of Helsinki the identify of each participant was preserved by providing identification codes instead of personal identification information; the data collected was stored in an encrypted format. Participants were fully informed about what the study entails and why their participation is important and it was ensured that they understood that they were free to choose whether or not to participant in this study and could stop their participation at any point[8].

Study Design

A mixed-methodological approach was adopted in this study.

Study I

The first part of this study followed an observational retrospective study design that utilized a service evaluation approach. A service evaluation approach was used to provide the researcher with information on how the management of patients living with diabetes mellitus is progressing, in such case, within the Primary Care Services. A service evaluation approach can be defined as a systematic method that can be used to define current care and identify the standards that it is able to achieve[9]. A

retrospective analysis of records of new cases of patients living with type II diabetes mellitus attending to the Biomechanics Clinic at a local health center was conducted.

Locally, only one pressure platform is available in the public health services that can be used as a source for peak plantar pressure identification. This pressure platform technology is available at the Biomechanics and Gait Analysis Clinic, at the Podiatry department, at a local health center that falls under the local Primary Healthcare. The Biomechanics and Gait Analysis clinic is the only known clinic in the public health services to offer in-dept biomechanical examination of the lower limb that includes assessment of foot posture and kinematics of the knee joint, ankle joint and individual pedal joints of the foot; and barefoot plantar pressure analysis to identify barefoot peak pressure areas, utilizing a pressure platform/mat system. This service is offered to all Maltese and foreign citizens of any kind of medical background.

Data Collection

Records accessed dated between January 2019 and January 2020 as more recent data was not available due to temporary disruption of the service, due to restrictions related to COVID-19. Demographic data such as age and gender, source of referral, clinical diagnosis, and the biomechanical management plan of patients living with type 2 diabetes mellitus were of key interest. Data was recorded anonymously on an excel sheet. Data analysis was conducted using Microsoft Excel to calculate the number and percentage of patients attending the biomechanics clinic, source of referral to this clinic, age and gender of patients, clinical diagnosis, management plan and referral pathway.

Study II

The second part of this study followed a Phenomenological approach where 4 experienced clinicians, working in the Private, Primary and Tertiary Health Sector, were recruited through purposive sampling technique and interviewed. These participants were ideal for this study as each of them represented a clinician working within the Primary Health Sector, the Private Sector, and the Tertiary Sector of which,

one represented the Orthotics and Prosthetics Unit (OPU) and the other represented the clinicians working at the Diabetic Foot Clinic at the local hospital.

Open-ended interviews were used to obtain a perspective on how the diabetic high-risk foot is currently being managed from a biomechanical perspective and whether diagnostic technology is being integrated within clinical practice. No scales or instruments were used during these interviews that could have constrained the participants' opinions. Though a face-to-face interview would have been ideal so that the research could have noticed mannerisms and behaviour of the interviewed clinician, due to the current COVID-19 pandemic restrictions, the research had no choice but to carry out the interviews via a telephone calls as was preferred by the interviewed clinicians.

The data was then analysed using a Thematic Analysis approach where the data was organized into codes and themes in order to identify, analyse and report existing patterns among the different sectors available locally.

Interview Questions:

The open-ended question – As an experienced Podiatrist who works in the [Private Sector/Primary Health Care/Diabetic Foot Clinic/ OPU], what are your views on the biomechanical management of the high-risk diabetic foot in your clinic? Do you have any concerns and/or recommendation on how to improve or commend the service?

Question (Sub-question) – What are the advantages/disadvantages of using diagnostic equipment as part of your clinical management routine?

Probing questions used – "could you kindly explain what you mean by…"; "could you kindly elaborate on this aspect?"

Results and Discussion

Study I

Results of this study highlighted a low rate of referrals of patients living with diabetes mellitus to the Biomechanics Clinic. From a total of 965 cases that were retrieved, only 97 cases related to patients living with type II diabetes mellitus. of these 97 cases, there was an equal distribution of male versus female with an age range that ranged between 30 to 89 years of age. The majority of patients were referred to the biomechanics clinic by Podiatrists (65.6%) followed by Medical Doctors (26.6%). The reason for referral of all cases reflected to common biomechanical issues such as overpronation (18.6%), plantar fasciitis (9.3%) and Leg Length Discrepancy (LLD) (14.4%). Following a thorough examination, the majority of cases were observed to be referred to the Orthotics and Prosthetics Unit (OPU) as new cases for prescription of orthoses (58%) and as f/up cases for change of orthoses (10.3%). None of the referred cases were recorded as high risk or had diabetic foot complications such as active or previous history of ulceration. This means that within that 1-year timeframe, there is no record of diabetic high-risk patients being referred for a detailed biomechanical assessment and/or foot pressure mapping prior to the prescription of orthoses or post orthotic management within the primary care service.

Study II

The interviews showed that clinical management of patients living with diabetes mellitus differs from one case to the next as it highly depends on the situation at hand however, common factors between the Primary, Tertiary and Private sector have been identified. Sectors such as the Primary Health Sector, OPU and the Private sector receive a variety of patients including patients living with diabetes mellitus however, it was reported that only the OPU and Diabetic Foot Clinic reported cases of patients living with diabetes mellitus that are categorized as high-risk. All healthcare workers including medical doctors and surgeons can refer patients to these sectors. When it comes to management of the high-risk diabetic foot, the clinicians in the OPU and the Diabetic Foot Clinic Sector based their diagnoses and treatment on physical examination, visual observation and clinical experience. Only the clinician within the private sector reported the use of diagnostic technology. Results from this study also

showed that, although aware of the current diagnostic technology that could be used to reach objective clinical decisions, the clinicians divulged that, even if diagnostic technology such as the in-shoe pressure system is available, they are hesitant whether or not to include the tool within their daily clinical practise as they are too time-consuming. Furthermore, the interviewed clinicians speculated that such a system is not available within the health care service apart from the fact of being time-consuming to use during their clinical practice, the system is very costly to purchase and maintain.

The recommendations suggested by the interviewed clinicians included:

- "In-dept biomechanical examinations should be given more weight and thus introduced as part of the diabetic foot screening" – *Interviewee IV*
- "Low-cost alternatives to costly in-shoe pressure systems would provide an incentive even in the private sector, to invest in such equipment". – *Interviewee III*
- "Having a device that allows you to just look at the area of interest, I would be much more impressed"– *Interviewee III*
- "Having something that can determine whether the offloading capacity of a given orthotic is being effective it would be a great help" – *Interviewee II*

Discussion

This study provided detail on how many patients living with diabetes mellitus are being referred for in-dept biomechanical assessment at the only local public biomechanics clinic. It also provided evidence on the management pathway and clinical practices within the Educational, Primary and Tertiary Sectors form the perspective of local clinicians. It is of a great concern to note that the majority of the identified 97 cases were referred by Podiatrists for an in-dept biomechanical assessment. It is even of a greater concern to note that among these cases, there were no patients living with diabetes mellitus categorised as at high-risk of developing

diabetic foot complications; all cases registered were considered low-risk. Furthermore, no patients were referred following orthoses dispensing.

Monitoring and inspection of the diabetic high-risk foot is highly empirical as the diabetic lower limb is the primary site for diabetic foot complications[10]. It is common knowledge that diabetes imposes an amplification of pre-existing biomechanical anomalies that over time present themselves as persistent plantar wounds[11]. Thus, when a thorough biomechanical examination is not taken seriously or is disregarded, prescription orthoses and the overall treatment plan may prove inadequate for the patient[11]. Indeed, off-loading and pressure re-distribution was demonstrated to help in preventing recurrence of plantar ulceration[6] however, considering what a huge impact these offloading devices have on the high-risk foot, a better insight on the appropriate manufacturing of orthoses in high-risk patients is empirical as inappropriate designs increase the risk of ulceration[12]. Off-loading and pressure re-distribution has been found to have better outcomes when assisted by proper techniques and technologies such as in-shoe pressure mapping devices[13]. Prescription orthoses designed based on the results of barefoot plantar pressures are superior to foot orthoses designed on visual observation and clinical experience [12].

Conclusion

This study advocates for better awareness amongst healthcare professionals with regards to the importance of a biomechanical evaluation and awareness amongst these professionals with regards to referring more DM patients for in-dept biomechanical assessment and pressure mapping to early identify peak pressure areas. Furthermore, this study supports the integration of in-dept biomechanical examinations as part of the diabetic foot screening programs and recommends improvement in services with regards to ulcer prevention modalities.

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Appendix 3 | PROSPERO Registration for Systematic Review

Gmail

Claire Saliba Thorne <csal0013@gmail.com>

PROSPERO Registration message [183322]

CRD-REGISTER <irss505@york.ac.uk> Sun, Aug 30, 2020 at 7:02 AM
Reply-To: irss505@york.ac.uk
To: csal0013@gmail.com

Dear Ms Saliba Thorne,

We apologise for the delay in dealing with your registration, an ever-increasing number of applications has led to a backlog and substantial delays for some users.

PROSPERO is currently prioritising submissions related to COVID-19. To enable us to focus on these submissions, and to avoid additional delay, during the pandemic we will automatically publish submissions that have been waiting more than 30 days for registration.

This applies to your systematic review "Wearable in-shoe temperature and pressure systems to monitor the diabetic high-risk foot: Protocol for a systematic review and planned meta-analysis." which was published on our website on Jul 05, 2020.

The records will be published exactly as submitted, without review by the PROSPERO team, so the public record will indicate:

"To enable PROSPERO to focus on COVID-19 registrations during the 2020 pandemic, this registration record was automatically published exactly as submitted. The PROSPERO team has not checked eligibility"

Review owners have always been responsible for the quality and content of PROSPERO records, and high-quality well-written records will continue to speak for themselves.

Your registration number is: CRD42020183322

You are free to update the record at any time, all submitted changes will be displayed as the latest version with previous versions available to public view. Please also give brief details of the key changes in the Revision notes facility and remember to update your record when your review is published. You can log in to PROSPERO and access your records at https://www.crd.york.ac.uk/PROSPERO

Best wishes for the successful completion of your review.

Yours sincerely,

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PROSPERO is funded by the National Institute for Health Research and produced by CRD, which is an academic department of the University of York.

Email disclaimer: https://www.york.ac.uk/docs/disclaimer/email.htm

Other non-commercial resources that may be of interest
SRDR-Plus is a systematic review data management and archival tool that is available free of charge
http://srdrplus.ahrq.gov.

Appendix 4 | Publication for the Systematic Review

diabetes research and clinical practice 175 (2021) 108783

Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

Review

Digital foot health technology and diabetic foot monitoring: A systematic review

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ABSTRACT

Background: In diabetic foot ulceration, a correlation between pressure and skin temperature is suspected. The aim of this systematic review is to provide a more rigorous analysis of existing literature related to the various technologies used to read and measure both in-shoe plantar pressures, and in-shoe skin temperatures simultaneously.

Methods: A systematic review of the literature related to the topic was searched in database sources such as Medline OVID, Cochrane Library, PubMed, CONAHL, PROSPERO, and Elsevier. Outcome measures of interest included validity, reliability and responsiveness of in-shoe temperature and/or pressure mapping device used, and characteristics and quantity of sensors used, anatomical landmarks and statistical analysis used to interpret the data. Quality of evidence and risk of bias was evaluated using the QUADAS-2.

Results: Nineteen studies were identified and included in this review. The majority of studies used a small sample size (mean $n = 17$) and recruited healthy participants. All studies have shown excellent validity but only a few tested for the reliability of the device. None of the studies tested for responsiveness of the device. Quality assessment results scored high risk in view of 'patient selection', 'use of reference standard' and 'applicability', and low risk in view of 'use if index test' and 'flow and timing'.

Conclusions: The data outlined in this review confirms that further improvement, reliability testing and clinical validation of the developed systems is required despite the results of excellent performance in detecting changes of in-shoe skin temperature and pressure.

Contents

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https://doi.org/10.1016/j.diabres.2021.108783
0168-8227/

1. Introduction

1.1. Background

Diabetic foot ulcerations pose a great burden on health care economy due to the high risk of infection, hospital admissions and amputations. Several studies have reported that at least 40% of patients living with diabetes mellitus has experienced a recurrence within the same year of resolution of the previous ulcer [1–5]. This high recurrence rate may be attributed to the fact that despite the healing of an ulcer, causative factors for ulceration such as foot inflammation and increased foot plantar pressures are still present and not yet, or not being properly addressed [6]. Thus, ulcer preven-tion and prevention of ulcer recurrence is deemed of utmost importance in diabetic patient care [2].

Inflammation has a major role in the development of ulceration but is often overlooked. It is characterized by heat, swelling, erythema and pain however, of which the latter three are very difficult to grade [1,6]. Furthermore, in the presence of neuropathy, erythema and pain may be absent due to the loss of innervation of the sensory nerves. Thus, inflammation can be detected by measuring local skin temperatures [5,7]. With repetitive pressure, an inflammatory process is initiated, heating up the area of stress [2,8] that can last up to a week prior tissue break down and ulcer formation [9,10].

Studies by Armstrong et al. [11] and Houghton et al. [12] showed that patients with a history of ulceration exhibited increased local skin temperatures at their follow-up visits prior to re-ulceration. This further supports that skin temperature measurements can be used to predict forthcoming ulceration. A more recent study by Gatt et al. [10] reported that participants living with diabetes mellitus with and without neuroischaemic ulceration showed elevated skin temperature levels when compared to healthy participants. Ulcerated and non-ulcerated toes of the same foot were also compared of which no significant difference was found meaning that both ulcerated and non-ulcerated sites have equal risk of ulceration/re-ulceration [10].

Plantar pressure measurements are also considered to have clinical value to help improve prescription offloading devices and to reduce risk of re-ulceration in the diabetic foot. A systematic review and meta-analysis by Crawford et al. [13] have supporting evidence that plantar pressure mapping is a reliable method that can be used to detect high plantar pressures that are associated with the development of diabetic foot ulceration. This innovates footwear practice to a more data-driven approach [14]. Daily monitoring of foot temperature can effectively identify local increases in skin temperature as pre-sign of foot ulceration [8,15], which can significantly reduce the incidence of foot ulcers in high-risk patients if acted properly on [16]. This statement is supported in multiple clinical guidelines [17–19] but in order to usufruct of their clinical benefits and integrate them in the prevention of ulceration of the high-risk foot, reliability and validity of the measuring device should be established to ensure objective diagnoses and timely intervention [20,21].

Skin temperature assessment has been deemed safe as it is a contactless, non-invasive and a reliable technique thatcan be used to provide a quantified measurement of temper- ature change [21,22]. A study by Gatt et al. [23] and later by Buset al. [18] has observed that despite the positive outcomes in

validity and reliability of the use thermography as a diagnostic tool [24–26], skin temperature measurement has not yet been integrated in diabetic preventive care practices. This is possibly attributed to the expense of thermography equipment or because there is a lack of accurate findings when reporting the correlation between temperature, pressure and ulcer development [10].

In-shoe pressure devices are also deemed as valid and reliable in detecting plantar pressure changes within various footwear and during various activities [27–29] and are extremely recommended for the evaluation of footwear and orthotic design [18,30].

Various studies have introduced devices that were validated to measure temperature [31,32] and plantar pressure parameters [33–35] however very few studies have investigated the validity and reliability of devices that can measure in-shoe temperature and pressure simultaneously, and their role in the in the causation of diabetic foot ulcers [36,37].

In a systematic review conducted by Bus [37], plantar pressures have been proven to have an essential clinical value in view of reducing the risk of first ulceration and re-ulceration. Similarly, frequent monitoring of foot temperatures may be used to predict pre-ulcerative states by detecting a localized rise in skin temperature which is indicative of inflammation [37–40]. The review further argues that current technologies that are being developed to predict ulceration and monitor foot plantar pressures are promising however, further improvement and clinical validation is required [8]. Reliability and validity of an instrument not only indicates the consistency and high accuracy in detecting changes being observed [41], it also permits the practitioner to obtain and rely on objective measurements on which to base his/her clinical reasoning [37]. Furthermore, a patient might feel more encouraged to comply and adherence to a specifically tailored treatment [42]. Having unreliable diagnostic equipment might lead to delays in obtaining adequate results within may lead to increased cases of ulceration and hospitalization [43].

A more recent review [36] reviewed the risk predictors of diabetic foot ulcers in relation to the microclimate of the foot. The correlation between the microclimate characteristic of the foot and the prediction of diabetic foot ulcer was also discussed. Microclimate refers to the environment in which the foot is in and that includes temperature, pressure, humidity, shear and stress [36]. When seen holistically, the threshold of each of the latter components may be used to predict the development of diabetic foot ulceration [36] however, being a relatively new concept, little research is yet available [36]. From this review, the authors concluded that diabetic foot ulcer prediction remains clinically difficult to predict as risk predictors such as temperature and pressure are not being monitored together as a whole. The review has shown that the majority of studies focused on contralateral temperature (the comparison of temperature between the right and left foot), pressure and shear. A great variation in the methodological approach in between studies including sensor anatomical placements and resting time prior temperature readings was also noted.

This systematic review aimed to provide a more rigorous analysis of existing literature related to the various technologies used to read and measure both in-shoe plantar pressures, and in-shoe skin temperatures. The validity and reliability of the various technologies included in this systematic review are compared in order to achieve a comprehensive understanding of their use as diagnostic techniques for diabetic foot plantar ulceration and/or re-ulceration.

1. Methods

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines.

1.1. Literature search

Through preliminary searches related to the topic, key words were identified and formulated. Database sources such as Medline OVID, Cochrane Library, PubMed, CONAHL, PROSPERO, and Elsevier were searched with no restrictions except for literature published between the 2000–2020, on humans and to studies published in the English language. Literature search strategies were developed using medical subject headings (MeSH) and text words related to the topic (Fig. 1). Reference lists from each publication were screened for additional studies that match the inclusion criteria.

Draft Medline OVID search:

1. diabetes.af.
2. diabetes mellitus. af.
3. diabetic f??t. af.
4. type 2 diabetes mellitus. af.
5. type II diabetes mellitus. af.
6. diabetic f??t. af.
7. in-shoe pressure mapping. af.
8. in-shoe pressure measure*. af.
9. wearable pressure sensor*. af.
10. f??t pressure. af.
11. diabetic f??t pressure*. af.
12. f??t plantar pressure*. af.
13. diabetic f??t plantar pressure*. af.
14. peak plantar pressure*. af.
15. pressure time integral*. af.
16. foot ulcer*. af.
17. plantar foot ulcer*. af.
18. plantar wound*. af.
19. plantar foot wound*. af.
20. plantar ulcer*. af.
21. diabetic foot ulcer*. af.
22. re-ulcer*. af.
23. recurrent foot ulcer*. af.
24. temperature sensor*. af.
25. wearable temperature sensor*. af.
26. heat sensor*. af.
27. thermal sensor*. af.
28. 1 or 2 or 3 or 4 or 5 or 6 354
29. 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15

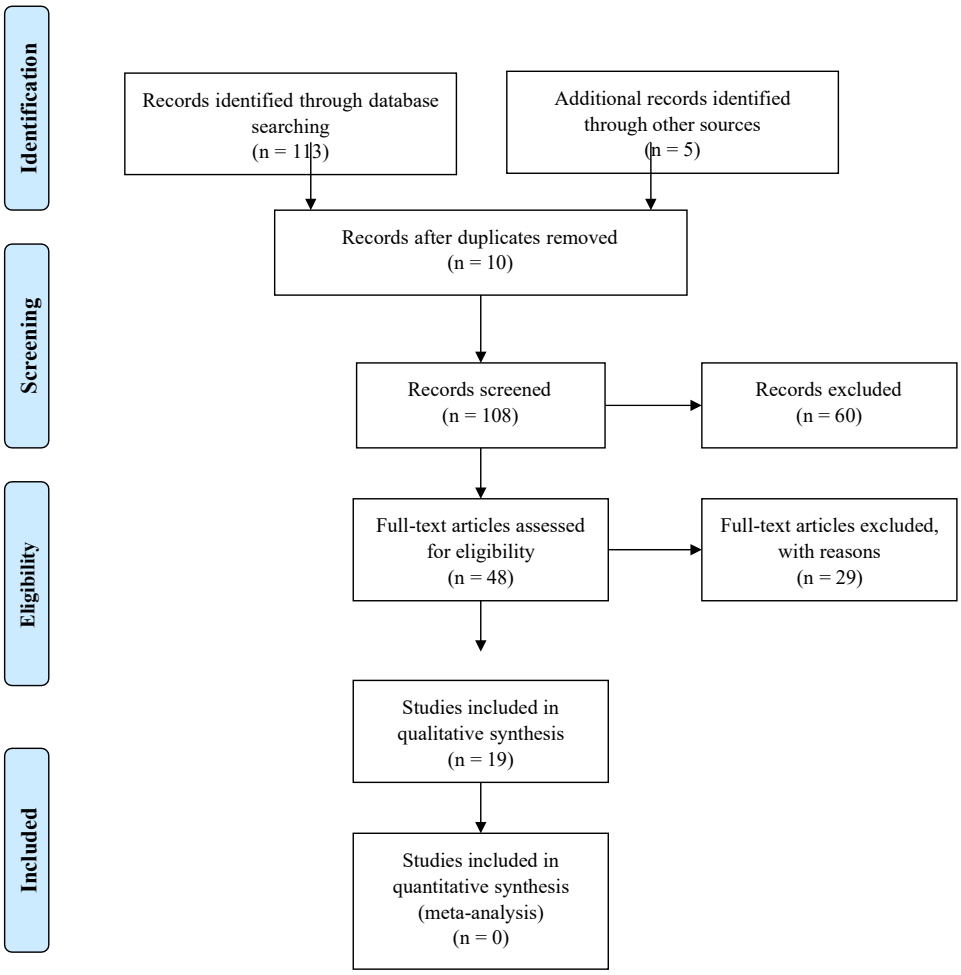

Fig. 1 – PRISMA Flow Diagram.

30. 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23
31. 24 or 25 or 26 or 27 4598
32. 28 and 29 and 30 and 31

1.1. Study eligibility criteria

In view of developing the search strategy, the research question of this systematic review was expressed using the PICOS framework as proposed by the PRISMA guidelines where, PICOS stands for Population, Intervention, Comparisons, Outcomes and Study design [44]. This systematic review sought to answer the research question below

What is the current evidence on the validity, reliability and effectiveness of in-shoe pressure and temperature systems and their role in the prevention of the diabetic high risk-foot ulceration/ re-ulceration?

2.2.1. Inclusion and exclusion criteria

The search strategy focused on studies that have conducted their research on human adults, male or female, aged 18 years or above and living with type II diabetes mellitus preferably with history of ulceration or are at risk of ulceration. All study designs related to the subject under investigation were included in this review.

Eligible articles that met the inclusion criteria needed to report on:

- The validity, reliability and responsiveness of in-shoe pressure mapping as clinical assessment techniques to identify the development of diabetic foot ulceration
- The validity, reliability and responsiveness of in-shoe temperature measurements as clinical assessment techniques to identify the development of diabetic foot ulceration
- The validity, reliability and responsiveness of a combination of in-shoe temperature measurement and in-shoe plantar pressure measurement used as clinical assessment techniques to identify the development of diabetic foot ulceration

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Studies were excluded from this review if they included overweight or obese participants, participants living with

musculoskeletal conditions or participants who walk aided, as these factors are known to alter gait and foot biomechanics.

2.2.1. Outcomes measures

Primary outcome measures of interest related to the diabetic foot included validity, reliability and responsiveness of the device used. Studies reporting the validity and reliability results of either in-shoe plantar pressure devices and/or in-shoe temperature measuring devices were included. Studies reporting whether or not an in-shoe pressure mapping device and/or in-shoe pressure temperature sensing device is accurate in determining pressure reduction and/or determining temperature changes within the shoe were also included. The search was focused on test–retest reliability that is, how well is the investigated instrument able to give consis- tent measurements over a number of tests and on longitudi-nal validity or treatment effects which is known to be a measure for responsiveness.

Secondary outcome measures of interest included type and size of pressure and/or temperature sensing devices used to detect in-shoe plantar pressures and/or in-shoe skin temperature changes; number and placement of sensors used and the specific anatomical landmarks at which the sensors were placed for investigation; and statistical analysis that have been used to report the integration of data and knowledge from different sources pertinent to the research topic.

2.3. Study selection

2.3.1. Selection process

All titles and abstracts were screened by the primary and secondary author independently against the inclusion and exclusion criteria. Full reports of titles and abstracts that met the inclusion criteria were obtained for a second screening against inclusion and exclusion criteria and reason for exclusion was documented. Disagreement between study selections were resolved through discussion.

2.3.2. Data collection process

Data was extracted independently by reviewers and it included the following:

- [redacted]nographic data of participants including age, gender, medical history, history of ulceration;
- [redacted]e, size and number of pressure sensing device;
- [redacted]nufacturer of sensor or device, anatomical placement of sensor, design of device, reference standard, trial design, population size;
- [redacted]itations of study;
- [redacted]ults and outcomes of validation and reliability studies.

Due to the limited number of results, the inclusion criteria had to be extended to studies that utilized the aforemen- tioned devices in a non-specified population (n = 3), or non- diabetic, healthy participants (n = 1). All of these studies wereincluded only if they related their investigations and resultsto the diabetic foot. After matching with the inclusion criteria, the full text of a total number of 19 articles was obtained [45–63]. For simplicity, studies were categorised into 3 groups, according to the sensor's ability to recognise temperature and/or pressure (Tables 1–3).

Table 1 shows 5 studies that have included a device that is able to measure both in-shoe pressure and temperature. Tablse 2 and 3 include studies that have utilized a device that is able to measure in-shoe pressure and in-shoe temperature respectively.

2.4. Risk of bias individual studies

QUADAS-2 was used to facilitate the assessment of risk of bias for each study that meets the inclusion criteria. QUADAS-2 is a quality assessment tool that covers four main domains namely patient selection, index test, reference of standard, flow and timing. This quality assessment tool was used independently and blindly by the primary and the secondary author, to assess the risk of bias and applicability for each study that have met the inclusion criteria. All four main domains of the tool were covered. For each domain, procedures from every study was described and a score on the possible risk of bias was given. In cases where an item was unclear, the authors were contacted for clarification. If clarification was not obtained, the item was marked as ''unclear". The final scoring results of each article was presented in Table 4.

3. Results

A total number of 113 trials were identified through a thorough literature search from databases as mentioned in sec- tion 1.2 with an addition of 5 articles that were obtained from secondary sources. All abstracts were examined andmatched with the inclusion and exclusion criteria of this sys- tematic review. The full text of a total number of 19 articles was obtained [45–63].

A total number of 29 studies were excluded from this study on the basis of using measuring techniques irrelevant to this systematic review such as, barefoot pressure mapping and barefoot, non-weight bearing thermographic cameras. Studies that have reported unrelated outcome measures, inadequate exclusion or inclusion criteria or lacked specific outcome measures from their results were also excluded from this review. Ten duplicate papers were also removed.

3.1. Validity and reliability assessment

Knowing the validity, reliability and responsiveness of a device is significant if it is to be introduced in a clinical setting. A device is said to be reliable when the outcome results remain similar with repeated testing over a period of time, across subjects, and across different users. Thus, reliability is the ability of a measure to remain consistent over time. It is common for reliability to be tested in test retest studies with intraclass correlation statistical analysis. Reliability testing was only conducted in 6 studies with most of the studies reporting small sample size (mean n = 17). Although the selected studies focused their investigations on improving techniques for the early identification of diabetic foot ulcers,

Table 1 – Characteristics of included studies that have used devices that measure in-shoe temperature and in-shoe pressure measurements simultaneously.

Study	Participant Characteristics				Index Test					Reference Standard	
Authors	*N*	Sex	Age	Disease Severity	Index Test	Type of sensor	No. of Sensors	Sensor Placement	Sensor Size (cm)	Reference Standard	Manufacturer
Morley et al. [45]	1	NS	NS	NS	In-shoe Sensor Pod	Resistive	4	MTH & heel	NS	FSCAN/not specified for temperature	Tekscan Boston
Maluf et al. [46]	4	Both	30	Healthy	Plastazote insert fitted with 4 sensors	Resistive	4	MTH & heel	2.55x2.05	FSCAN/Standard Mercury Thermometer	Tekscan Boston
Najafi et al. [47]	33	Both	58	DM	SmartSox	Fibre optic based on fiber Bragg gratings (FBGs)	5	Hallux, MTH, midfoot, heel	less than0.03	FSCAN/Fluke Ti25 (IR Thermal Camera)	Tekscan Boston /Fluke Corporation
Rescio et al. [48]	5	NS	NS	NS	Smart Insole	FSR & Maxim (MAX30205)	8	Hallux, MTH, midfoot, heel	NS	aluminium plate with accurate temperature gradient control/BTS Pwalk platform	NS
Rescio et al. [49]	n/a	n/a	n/a	n/a	Temperature and pressure sensors between polyurethane based layers	FSR & Maxim (MAX30205)	8	n/a	NS	Baropedometry Pwalk platform/FEA simulations using Comsol Multiphysics	NS

Key: NS = not specified, n/a = not available, MTH = metatarsal heads.

Table 2 – Characteristics of included studies that have used devices that measure in-shoe pressure measurements only.

Study	Participant Characteristics				Index Test						Reference Standard	
Authors	*N*	Sex	Age	Disease Severity	Index Test	Manufacturer	Type of sensor	No. of Sensors	Sensor Placement	Sensor Size (cm)	Reference Standard	Manufacturer
Ferber et al. [50]	10	Both	27.91	n/a	SurroSense Rx™ Insole	Orpyx Medical Technologies Inc	Resistive	8	Hallux, MTH, midfoot, heel	NS	Pedar X®	Novel
Lee et al. [51]	23	Both	56.7	DM	Pedar® X	Novel	NS	99	Hallux, MTH, midfoot, heel	NS	n/a	n/a
Najafi et al. [52]	17	NS	>18	DM	SurroSense Rx™ Insole	Orpyx Medical Technologies Inc	NS	8	Hallux, MTH, midfoot, heel	NS	n/a	n/a
Ostadabbas et al. [53]	11	Both	51	NS	FlexiForce force sensors between 2 shoe insoles	NS	NS	5	Lesser toes, MTH, Midfoot, heel	2.54	n/a	n/a
Shu et al. [54]	8	Male	31.3	NS	Insole pressure sensors	NS	Resistive	6	MTH & heel	NS	Pedar X®	Novel
Price et al. [55]	n/a	n/a	n/a	n/a	Medilogic/Pedar/Tekscan	NS	Resistive/capacitive /resistive	NS/99/NS	NS	NS	TruBlue Device	NS
Guo et al. [62]	3	Male	20	NS	Insole with piezoelectric sensors	NS	piezoelectric	8	MTH & heel	1x2x0.8	n/a	n/a
Wang et al. [57]	NS	NS	NS	NS	FreeWalker	Self-designed	NS	8	MTH, Heel Midfoot	0.5	n/a	n/a

Key: NS = not specified, n/a = not available, MTH = metatarsal heads.

Table 3 – Characteristics of included studies that have used devices that measure in-temperature measurements only.

Study	Participant Characteristics				Index Test						Reference Standard	
Authors	*N*	Sex	Age	Disease Severity	Index Test	Manufacturer	Type of sensor	No. of Sensors	Sensor Placement	Sensor Size (cm)	Reference Standard	Manufacturer
Reyzelman et al. [58]	35	Both	62	DM	Siren Diabetic Socks	Siren Care Inc	NS	6	Hallux, MTH, midfoot, heel	NS	thermostatic water bath +mercury thermometer	Zhejiang Jinbo Electronic Co. Ltd.
Lugoda et al [59]	n/a	n/a	n/a	n/a	Temperature-sensing yarns	Murata	Murata 10kX 100mW 0402 SMD NTC thermistor	16	n/a	0.087 × 0.153	NTC thermistor in Ecotherm™ Chilling/Heating Dry Bath	Murata
Sandoval-Palomares et al. [60]	2	Male	>18	Healthy	Temperature and humidity sensors embedded in insole	Sensirion	SHT15	5	MTH, Midfoot, Heel	5x7x3	n/a	n/a
Coates et al. [61]	16	Both	33.4	Healthy	HYT271 sensors	Ardunino Nano	capacitive	4	Hallux, MTH, midfoot, heel	NS	PT104 Pico Technology	NS
Ming et al. [62]	300	NS	18–85	DM	Medixfeet Insole®	Thoris Technologies GmbH	NS	6	Hallux, MTH, midfoot, heel	NS	Standard routine care	n/a
Shoureshi [63]	60	Both	33.3–66.8	DM	Smart insole for diabetics	Self-designed	MC65F103B thermistor and Fenwal thermistor	7	Hallux, MTH, midfoot, heel	0.165 cm and 0.241 cm	n/a	n/a

Key: NS = not specified, n/a = not available, MTH = metatarsal heads.

Table 4 – Table showing the results for QUADAS-2 Quality Assessment Tool.

		Bias				Applicability		
	Author & year of publication	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Temperature and pressure combined	Morley et al. [45]	Unclear	Low	Low	Low	High	Low	High
	Maluf et al. [46]	Low	Low	Low	Low	High	Low	High
	Najafi et al. [47]	Low	Low	Low	Low	Low	Low	Low
	Rescio et al. [48]	Unclear	Low	Low	Unclear	High	Low	Low
	Rescio et al. [49]	High	Low	Low	High	High	Low	Low
In-shoe pressure	Ferber et al. [50]	Low	Low	Low	Low	High	High	High
	Lee et al. [51]	Low	Low	High	Low	High	High	High
	Najafi et al. [52]	Low	Low	High	High	Low	Low	High
	Ostadabbas et al. [53]	Unclear	Low	High	High	High	High	High
	Shu et al. [54]	Unclear	Low	Low	Low	High	High	High
	Price et al. [55]	High	Unclear	High	High	High	High	High
	Guo et al. [56]	High	Low	High	High	High	High	High
	Wang et al. [57]	High	Unclear	High	High	High	High	High
In-shoe temperature	Reyzelman et al. [58]	Low	Low	Low	High	Low	Low	Low
	Lugoda et al. [59]	High	Low	High	High	High	High	High
	Sandoval-Palomares et al. [60]	High	Low	High	High	High	High	High
	Coates et al. [61]	High	Low	High	High	High	High	High
	Ming et al. [62]	Low	Low	High	High	Low	High	High
	Shoureshi [63]	Unclear	Unclear	High	Unclear	High	High	High
Total Scores	Low	37%	84%	42%	32%	21%	37%	21%
	High	37%	0%	58%	58%	79%	63%	79%
	Unclear	26%	16%	0%	11%	0%	0%	0%

only 5 studies reported that their participants were living with diabetes mellitus.

Validity is the ability of a tool to measure what it is intended to measure and for that measurement to correspond well to the actual measurements. It is common for validity to be based on the sensitivity and specificity of the device with correlation analysis statistical analysis and/or regression models. Reference standards are investigations or tools considered as the gold standard method of assessing the target condition. Results in validity studies, are deemed more valid when compared to a reference standard. All 19 studies included were able to validate their pressure and/or temperature sensing device but only 7 studies, out of the 19, compared their device against a reference standard.

3.1. Combined in-shoe pressure and temperature sensing devices

Compared to the gold standard Fscan pressure sensing system, in-shoe pressure and temperature sensing devices, such as the In-shoe Sensor Pod [45] and the Plastazote insert by Maluf et al. [46], were observed to have high correlation to the reference standard. Maluf et al. [46] reported that the data had comparable plots in both magnitude and duration of pressure changes before and after prolonged use of the investigated insert. In both studies, direct comparison of the pressure data was taken over a single step. It was also observed that comparison of the in-shoe temperature sensorof the index test, to a gold standard temperature sensing device was not reported in the study by Morley et al. [45]. While in the study by Maluf et al. [46], correlation analysis proved measurements of in-shoe temperatures, for both the index test and the gold standard thermometers, to correlate equally between them. Here, results showed that the data recorded was slightly lower than the criterion values possible attributed to the insulating effects of the Plastazote material of the insert.

Reliability for the In-shoe Sensor Pod was investigated and results showed that outcomes remain consistent between temperatures of 20–35 degrees Celsius, over a period of 8 h of use. Similar results have been reported in the study by Maluf et al. [46]. Thus, the overall both the In-shoe Sensor Pod and Plastazote insert can be deemed valid and reliable when assessing in-shoe plantar pressures and in-shoe temperatures during prolonged activities [45,46].

A high correlation between SmartSoxs and the FScan system as the refence standard was found by [47]. Secondary to the validation tests, SmartSoxs were reported to be accurate in detecting changes in in-shoe temperature and pressure measurements with minimal cross talk.

Validity testing of the in-shoe temperature and pressure system developed by Rascio et al. [48] showed good performance and a high level of accuracy in data acquisition for both temperature and pressure readings.

3.2. In-shoe pressure sensing devices

Compared to the reference standard (Pedar X by Novel), Ferber et al. [50] demonstrated accurate ability for the index test to measure in-shoe plantar pressures that are greater than32 mmHg. A good correlation was found between the index test and the reference standard for all sensors except for 2 out of 8 sensors which showed poor correlation. It has been noted that the accuracy of sensor readings is dependent on the location, line of travel and velocity of movement of the center of pressure of the subject. The longer the center of pressure remains in a particular region such as the hindfoot and first metatarsal head, the more accurate the reading of the sensor in this particular region [50,53]. Similarly, Shu et al. [54] showed that their 6 sensor, index test is able to reflect pressure change as the reference standard. The authors further reported that adding an additional sensor at the hallux and midfoot improved the accuracy of the device.

Price et al. [55] compared 3 commercially available in-shoe pressure mapping systems namely the Pedar X, the Fscan and the Medilogic system. The aim of this study was to quantify the validity and repeatability of these in-shoe pressure mapping devices across a range of applied pressures and durations. The overall results showed high variability between systems when measuring contact area during gait. The Medilogic system delivered the most accurate measurements of contact area while, the FScan system delivered the highest average errors amongst the three systems. This can be attributed to cross-talk between sensor and material of the top cover of the insole. FScan systems have larger number of sensors and the insole is made of a thin plastic film. A softer material such as the soft foam of the Medilogic and Pedar system gives a more even distribution of the load thus increasing the contact area of the subject's foot. Another factor pointed out was that as opposed to the Medilogic and Tekscan which remained consistent, the resolution (number of sensors per area) of the Pedar X device varied according to the size of insole.

Price et al. [55] demonstrated good repeatability of Pedar, Medilogic and Tekscan pressure systems especially for pressures exceeding 100 kPa. However, compared to the Pedar and Medilogic systems, the Tekscan system exhibited lower repeatability for peak pressures across the whole insole possibly secondary to intrinsic cross talk between sensors

The study by Ostadabbas et al. [53], quantified the importance of pressure sensor placement on the plantar surface of the foot. Results of the study showed that size of sensors play an important role in the ability of detecting pressure change. Small sensors tend to underestimate the forces acting on the foot and accurate positioning of such sized sensors on the area of peak pressure may prove difficult. Conversely, larger sensors are more likely to detect pressure change but there is a higher change of underestimation of peak plantar pressures. The authors reported that their results are consistent with results of other studies such as Pataky et al. [64]. Guo et al. [56] validated the function of the a piezoelectric based, self-designed, in-shoe pressure sensing device by recording pressures during standing and walking. Validation testing gave satisfactory results confirming the device's ability to record natural stance and dynamic plantar pressures. The insole with embedded piezoelectric sensors was also deemed reliable when tested both indoors and outdoors and that plantar pressure measurements corresponded accurately to the actual clinical measurements of the participant [56].

Another study presented the FreeWalker, an 8-pressure sensor insole, validated and proved to be accurate in measuring plantar foot distribution and motion sequence in real

time, transmitting data at a distance up to 20 m [57]. In all the latter three studies, comparison of the in-shoe pressure sensor of the index test, to a gold standard pressure sensing device was not reported.

A more recent, test retest reliability study concluded excellent reliability for all peak plantar pressure variables detected by the index test [51]. Test retest reliability testing results showed higher results for the medial forefoot of the non-ulcerated foot, heel area for the non-ulcerated foot, and lateral forefoot for both. Absolute reliability testing demonstrated reliability that exceeded 15% over the midfoot and 18.3% over the hallux in the previously ulcerated foot. Furthermore, compared to non-ulcerated feet, previously ulcerated feet exhibited higher peak plantar pressures over the hallux and forefoot regions. There was no statistical difference between the previously ulcerated and non-ulcerated foot for the midfoot and heel region [51].

3.1. *In-shoe temperature sensing devices*

Validation testing of the temperature sensing device by Sandoval-Palomarez et al. [60] demonstrated technical practicability and accuracy in detecting temperature change for over 8 continuous hours. The authors reported that during the study no technical issues or patient discomfort was observed. Despite the positive results, this study did not report the comparison of the in-shoe temperature sensor of the index test, to a gold standard temperature sensing device.

In a reliability study, Siren Diabetic Socks were proved highly accurate and reliable in measuring in-shoe plantar foot temperature ranging from 20 °C to 40 °C. A high conformity between the temperature measurements read by the Siren Diabetic Socks and those measured by the reference standard was established [58]. Furthermore, the clinical trial demonstrated that temperature measurements of the shod feet were consistent with the clinical status of the participant.

3.2. *Responsiveness*

Responsiveness is the ability of a tool to perceive changes in measurement over time. Responsiveness differs from validity as it replicates the validity outcomes that have changed. As of yet, there is no consensus on how responsiveness can be quantified but assessing measures of longitudinal validity has been suggested [65].

None of the included studies have followed a longitudinal validation methodology and thus responsiveness of the index tests could not be determined for this systematic review. However, based on the validation tests performed, all included studies have indicated that the developed systems showed excellent performance in in-shoe plantar temperature and/or pressure detection. Validation and reliability results demonstrated high accuracy to detect changes with minimal cross-talk [52]. Results also showed similar plots in scale and duration of pressure and/or temperature changes to the reference standard [46]. All systems are deemed reliablein having constant performance in both static and dynamic activities [54]. Wireless systems provided accurate up-to-date and remote data analysis [56,57].

3.3. *Type and size of sensing devices*

Throughout the literature search, only five studies have reported the use of a sensor that is able to read pressure and temperature simultaneously [45–47]. Najafi et al. [47] has presented the readers with a newly developed SmartSox device by Novinoor LLC that has an incorporated fibre optic sensor based on Fibre Bragg Gratings (FBGs). These sensors were reported to measure less than 0.03 cm are made of weightless, thin and highly flexible silica, wrapped in plastic. Their ability is to reflect back specific wavelengths of infrared light. Both Morley et al. [45] and Maluf et al. [46] used a resistive type of hydrocell sensor by Paromed, that is also able to read temperature and pressure simultaneously. The size of the Paromed senor was not specified by Morley et al. [45] however, Maluf et al. [46] reported it to be 2.55 cm by 2.05 cm in dimension.

Despite the fact that some studies failed to specify the type of resistive sensor (n = 4), a trend in the use of resistive sensors was noticed (n = 8). Among the favourites where balanced resistive bridges, Resistance Temperature Detectors (RTDs), Force Sensing Resistors (FSRs) and thermistors. Other choices of sensors included capacitive (n= 1) and piezoelectric sensors measuring (n = 1).

Size of sensor plays a fundamental role in terms of accuracy, portability, in-shoe fitting and comfort. In plantar pressure measurement, When measuring peak plantar pressures small sensors, due to their size, were noted to miscalculate the true total force since it is more difficult to place a small sensor at a specific anatomical landmark [66], larger sensors are more likely to measure the peak pressure in a respective area but the reading may still give significant underestimation of peak pressure [53] The recommended size of a pressure sensor is that of 0.5 cm by 0.5 cm or greater. Sensors of a smaller size are recommended to be used in form of an array to avoid miscalculation of forces [53].

When measuring temperature, it was found that size and distance of positioning the sensor determined the accuracy of a temperature measurement [53,59]. A temperature sensor of 0.87 in diameter and the use of insulating materials was recommended to reduce measurement errors however, no evidence of moisture, humidity, bending, compression and stretching influences was noted [59].

3.4. *Number & placement of sensors*

This systematic review has identified that the highest number of sensors used was that of 99 sensors [51,55] and 16 sensors [59]. The rest of the studies had an average of 6.4 sensors used. It was also identified that the medio plantar and lateral aspect of the metatarsal head (MTH) and the plantar aspect of the heel, were the preferred anatomical landmark for pressure and temperature sensor placement. The most common reason for selecting these particular anatomical landmarks was mostly based on previous ulceration sites and highest peak plantar pressure areas.

In a study by Rescio et al. [48], 8 sensors were positioned secondary to the highest peak pressure area determined in an *a priori* assessment of the foot. These areas of peak pres- sures were deemed as areas at a critical risk for ulceration.

It was reported that the position of sensors in this study was mirroring a previous study by Ferber et al. [50] where pressure sensors were positioned at the lateral medial aspect of the heel, 1st to 5th Metatarsal head, midfoot and hallux. Differently to the latter study, the researchers placed an additional temperature sensor close to the pressure sensor so as to monitor the main pressure point of the foot [48].

Najafi et al. [47] validated an 8-sensor smart insole, SurroSense Rx system by Orpyx Medical Technologies, and determined the sensor placement over regions considered to be the highest risk for plantar foot ulcer development.

Based on clinical research, Shu et al. [54] reported that 6 sensorswere adequate enoughforclinical integration. Bothstudies by Shu et al. [54] (n= 6 sensors) and Ostadabbas et al. [53] (n= 5 sensors) reported thattheexact locationsof these Pressure sensors were determined by denoting the highest areas of pressure. Areas of sensor placement for this study included the heel and 1st to 5th metatarsal heads [53,54] and toe area [53].

Conversely, Guo et al. [56] utilized 8 piezoelectric pressure sensors and distributed them throughout the plantar aspectof the foot as the author wanted to quantify the highest pres- sures applied to each region of the foot as they occur during foot contact. On a similar note, another study also had a sim- ilar number and distribution of sensors so that the special pressure distribution of the whole foot was extracted [57].

Having validated a conventional device, the Pedar X by Novel, Lee et al. [51] used 99 pressure sensors built in an array throughout the plantar aspect of the foot. The authors reported that the anatomical landmarks such as the hallux, medial forefoot, lateral forefoot, midfoot and heel were inves-tigated for peak plantar pressures whereas, the lesser toes data was excluded due to poor repeatability.

Two studies had no participants involved in their validation study thus anatomical placement of sensors was not relevant to them [55,59]. Five studies using an average of 6.4 sensors, have not reported their rationale for selecting that specific anatomical landmark.

3.1. *Statistical analysis of studies*

A proportion of the selected studies followed a test–retest research design with Correlation Analysis (n = 5) or Intraclass Correlation Coefficient being the statistical test of choice (n= 4). The remaining studies reported a variety of other statis-tical methods which were used to explore differences between groups, establish equality between variances or establish whether a variable is unequal across the range values of another variable. Other relied on visual analysis of pressure plots and continuous monitoring of temperature patterns.

3.2. *Quality assessment*

A quality assessment tool, the QUADAS-2, was used independently and blindly by the primary and the secondary author, to assess the risk of bias and applicability for each study that have met the inclusion criteria. The final scoring results of each article was presented in table 4. In the first domain, patient selection, 37% of the studies scored low risk of bias; 26% did not give clear description of patient selection and 37% scored high risk of bias as the sample size selected was too small (mean n = 17) to give adequately representational results. The second domain showed that majority of studies (84%) scored low risk of bias with regards to the use of the index test. The third domain showed that 58% of the studies scored high risk of bias with regards to the use of a refence standard where 42% (low risk) reported the use of an appropriate reference standard. With regards to the final domain, only 32% of the studies reported adequate flow and timing of the study (low risk of bias).

Where applicability is concerned, the majority of studies scored high risk of applicability in terms of patient selection (79%), index test (63%) and reference standard (79%). The majority of studies used a small sample size (mean n = 17) and recruited healthy participants. Others, did not specify the medical history of their participants. The index tests of the majority of studies did not use a combination of in-shoe temperature sensors and in-shoe pressure sensor but a selection of either or. Finally, over half of the studies failed to report the use of a reference standard and some of the studies that have used a reference standard chose a gold standard device that cannot be used in-shoe.

3. Discussion

This systematic review was first to provide a more comprehensive and rigorous analysis of existing literature related to the various technologies used to measure in-shoe temperature and in-shoe plantar pressures of the diabetic foot. To our knowledge, there are only two systematic reviews that have similarly evaluated the current technology used to identify skin temperature and plantar pressures in the causation of diabetic foot ulcers. Both reviews discuss the new developments and applications of plantar pressure and temperature measurement however, the reviews focused on studies that utilized infrared thermographic cameras that cannot be inserted within the shoe [36,37]. This systematic review, in addition to discussing the new technology and applications of plantar pressure and temperature measurement, looked into the validity, reliability and responsiveness of in-shoe pressure and/or in-shoe temperature measuring devices. This review also explored the type and size of sensing devices, number and placement of sensors, and the statistical analysis used in studies.

Data from the current review have shown that in general, existing combined in-shoe pressure and temperature sensing systems have high correlation results between the index test and the reference standard [45–48] and that they are accurate in detecting changes in in-shoe temperature and pressure measurements with minimal cross-talk [47]. Furthermore, the devices showed overall good performance and a high level of accuracy in data acquisition for both temperature and pressure readings as separate measurements [48]. The overall reliability of such devices was investigated and results showed that outcomes remain consistent between temperatures of 20–35 °C, over a period of 8 h of use [45,46]. Studies investigating the longitudinal validity of an in-shoe temperature and/or pressure sensing device were not found thus, responsiveness of the device could not be determined in this review. From the selected studies, this systematic review has also identified the

medio plantar and lateral aspect of the metatarsal head (MTH) and the plantar aspect of the heel, as the preferred anatomical landmark for pressure and temperature sensor placement. The most common reason for selecting these particular anatomical landmarks was mostly based on previous ulceration sites and highest peak plantar pressure areas.

Despite the fact that some studies failed to specified the type of sensor used, a trend in the use of resistive sensors was noticed. Among the favourites where balanced resistive bridges, Resistance Temperature Detectors (RTDs), Force Sensing Resistors (FSRs) and thermistors. Other choices of sensors included capacitive and piezoelectric sensors. However, we expected to find more detail on the size of sensors used for both pressure and temperature sensors. Knowing which size of sensor to use is important as size plays a fundamental role in terms of accuracy, portability, in-shoe fitting and comfort. It was stated that smaller sensors underestimate the total force and they may not be placed well to receive the peak pressure [53]. Larger sensors are more likely to contain the peak pressure but the reading may be a significant under-estimation of peak pressure [66]. The authors of these statements did not elaborate on these findings. It would have been very interesting to have read the explanation of this outcome. The authors of this systematic review still felt the need to include these results, despite of the lack of elaboration on these statements form the authors. It was felt that these findings should not to be overlooked and further investigated by other authors interested in this field of study is encouraged.

Regardless of these findings, the value of this information is restricted due to the overall low quality of evidence in relation to reliability and validity of devices that measure in-shoe temperature or in-shoe pressure or a combination of both mainly due to possible risk of bias in the studies included in this review. We had expected to find more studies that have utilized devices with combined in-shoe pressure and temperature sensors. We expected studies to investigate the validity and reliability of their device on a diabetic population rather than on healthy individuals. We were also disappointed to find that only six studies investigated the reliability of their device and that no studies have investigated its responsiveness.

Bias in patient selection was observed as the majority of studies recruited a rather small sample size which gave a mean number of 17 participants from fourteen out of the nineteen selected studies. The magnitude of sample size plays a fundamental role, even in validation studies especially while proving external validity. Precise and accurate conclusions can only be drawn with appropriately sized sample size [67]. None of the studies have reported power calculation analysis or a sample size calculation based on the population being investigated. The concern a small sample size imposes is that the results might not be sufficiently powerful enough to distinguish between measurements of true or surrogate exposures leading to false negative results and type II errors. Type II error is inability to reject the null hypothesis [67].

Although all included studies have oriented their investigation on the prediction of diabetic foot ulceration, only 25% of them included participants living with diabetes mellitus. The rest of the studies included healthy participants (15%) or did not specify their medical history (30%), another 20% of the selected studied did not include participants in their validation studies. This creates an issue with how really sensitive the device being tested is. Generally, studies recruiting participants diagnosed with the disease in question give more accurate diagnostic results as opposed to testing the sensitivity of the device on healthy or undiagnosed population [68].

It was positive to find that 84% of studies included in this review scored low risk of bias with regards to the use of the index. Results from index tests used were interpreted without the knowledge of the results of the reference standard. This helped in reducing the subjectivity of the index tests used [69]. However, high risk of bias was found in with regards to the use of a refence standard where only 42% of the studies reported the use of an appropriate reference standard. Negative correlations between the results of the index test and that of the reference standard are attributed to the index testas the reference standard is always assumed to be 100% sen-sitive [70]. Results have shown that only 11 out of 19 studies included in this review compared results from their device to a gold standard equivalent device. In those studies which assessed a device which combined both in-shoe pressure and temperature sensor only 3 validated their device with a gold standard reference which measured both temperature and pressure. It is common knowledge that results in validity studies, are deemed more valid when compared to an equivalent gold standard device. Due to the lack of appropriate reference standard, where temperature validation was implied, the index test was tested in a laboratory setting or in a static position and the reference standard used consisted of a device that was too bulky and/or not flexible to be inserted within the shoe. Such examples include the mercury thermometer and the infrared thermal camera. As of yet, a ‘‘gold standard” device that measures in-shoe plantar temperatures and/or in-shoe temperature and pressure concurrently is not available. Thus, it is understandable that the researchers here had to utilize the next best standard in order to compare the index test with.

Health care guidelines encourage improvement of diabetic foot care quality through the use of objective risk evaluations [17–19,71]. It is well proven that objective risk assessment of the diabetic foot can early identify the risk of ulceration and thus reduce ulcer development by 70% [38,39,72]. Despite the evidence that supports the use of currently available technologies used to measure in-shoe pressure and skin temperature, these technologies have not yet integrated in the routine diabetic care because they are deemed as inconvenient, time-consuming and expensive [47]. Researchers have been attempting to develop innovative in-shoe devices that measure both plantar pressures and skin temperature to provide an alternative to the current impractical technologies [37]. However, current evidence of a newly developed device that is able to measure in-shoe temperature and pressure simultaneously, is not robust enough to confirm the reliability and validity of the device. With repetitive pressure, an inflammatory process is initiated, heating up the area of stress [2,8] that can be detected from up to a week prior to tissue breakdown and ulcer formation [9,10]. Thus, a reliable and valid device would help in the early identification of ulcer development by objectively measuring peak plantar pressures, and by

detecting heat as a sign of inflammation through temperature readings on which the clinician can base his/her clinical reasoning [18]. Confirming the reliability and validity of these instruments is empirical as this would indicate that thedevice is indeed consistent and highly accurate in detecting the changes that are being observed [41]. This would highly encourage both clinician and patient to rely on such measurements and thus delays in obtaining adequate results are avoided leading to decreased cases of ulceration and hospitalization [43,47].

3. Limitation of this review

Due to the limited number of results, the inclusion criteria had to be extended to studies that utilized devices that are able to read in-shoe plantar pressure or in-shoe temperatures in a non-combined form. Studies with non-specified population, non-diabetic or healthy participants were also included due to the limited number of articles concerning the validation of in-shoe temperature and pressure sensing devices. All these studies were included only if they related their investigations and results/findings to the diabetic foot.

Due to the significant heterogeneity of the data collected, meta-analysis could not be performed in this systematic review. For meta-analysis to be conducted, homogeneity (equality) of study outcomes is key [14] and the studies selected in this review showed marked variety in participant characteristics and type of devices used.

4. Recommendations

Further research evaluating the longitudinal validity and reliability of in-shoe devices that measure both plantar foot pressures and temperature concurrently is required. Such research should involve a large randomized sample size that will accurately represent the diabetic population especially those considered at a high risk of ulceration. This means that the population of the study should consist of males and female living with diabetes. Future studies should also focus on longitudinal validity testing to obtain outcome measures such as responsiveness which would determine whether or not a device in accurate enough in detecting change in pressure and temperature measures. Studies should also include a reference standard which can be used to compare the outcomes of the index test.

5. Conclusion

The value of this study is that it provides a comprehensive understanding of the currently available technologies purposively developed to simultaneously measure in-shoe plantar pressures and temperature. The data outlined in this study agrees with similar reviews [36,37] that further improvement, reliability testing and clinical validation is required. The type of information gathered from this review, can be useful in identifying functioning characteristics of mentioned devices to develop an innovative, low cost, reliable and valid, in-shoe pressure and temperature measuring device that can be used as an alternative to current technology to predict the risk of ulceration prior to tissue breakdown.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix 5 | Publication for the Dynamic Laboratory Validation Study

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Innovative single-sensor, in-shoe pressure and temperature monitoring device: A dynamic laboratory validation study

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ABSTRACT

Background: Available technology to detect the 2 primary predictors of ulceration is not being used as it is deemed as costly and time-consuming. Thus, the aim of this study was to determine dynamic laboratory vali- dation, of an innovative, single-sensor in-shoe device that can read peak pressure and temperature simultaneously.
Research question: Can an innovative, newly developed, in-shoe pressure and temperature measuring device, detect and measure the in-shoe peak plantar pressures and skin temperature of healthy participants, as accuratelyas the reference standard?
Methods: Five healthy adult participants were recruited. The prototype was validated against the gold standard FScan™ in-shoe system for pressures and the Flir® T630sc thermographic camera for temperatures. Participants were asked to walk at a comfortable pace on an electric treadmill for 13 min. The prototype and the FScan in- shoe sensors™ were superimposed inside the shoe of the participant, with the prototype on top, to ensure direct contact with the area of interest. Two thermographic images were captured using the Flir® T630sc thermo- graphic camera, before and after the walk. During the trials, the participants wore 100 % cotton socks and their own sports shoes and pressures were recorded at 50 readings a second.
Results: The raw readings of pressure were passed to the regressor, which returned the estimated kPa value. Several evaluations metrics were used to evaluate the performance of the modal. The prototype gave equal re- sults to that of the gold standard, the FScan™ in-shoe system. With regards to temperature measurements, both devices gave similar readings.
Significance: This innovative single-sensor, in-shoe pressure and temperature monitoring device showed similar measurements of pressure to the FScan™ system and temperature measurements were equivalent to the Flir® T630sc thermographic camera. The authors are confident that the innovative, low cost, single-sensor, in-shoe pressure and temperature monitoring device can be used as an alternative to the costly available commercial devices that measure pressure and temperature separately to detect early signs of complications in the high-risk foot.

1. Background

The prevention strategy for diabetic foot ulcer development includes continuous monitoring of skin temperature, offloading of previously ulcerated areas, and offloading of areas at risk of ulceration through the use of off-loading devices such as plantar paddings or foot orthoses [1]. Furthermore, the International Working Group on the Diabetic Foot (IWGDF) guidelines recommend identifying peak plantar pressures aspart of the offloading management, prior to and following dispensing of prescription of foot orthoses or bespoke footwear [1].

Modern technology has provided the clinician with various pressure mapping devices with which in-shoe plantar pressure parameters can be easily identified[2]. In-shoe systems consists of an array of sensors embedded within a thin and flexible insole-like sheet that can be inserted within the shoes [2]. This configuration, not only makes the device portable but, also ideal to measure the relationship between or- thoses and the foot within the shoes, in different environment [3]. A recent study reported that clinicians do value the importance of using diagnostic technology to help them reach objective clinical decisions however, they argued that current available commercial in-shoe

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pressure systems cannot be included within their daily clinical practice as they are very costly to purchase and to maintain, and time-consuming hence relying their diagnoses only on clinical experience [4]. Hence, the aim of this study was to determine dynamic validation, of an innovative, single-sensor in-shoe pressure and temperature mapping device in a real-life scenario, on healthy participants against the Flir® T630sc Thermographic Camera and the FScan™ in-shoe pressure mapping system by Tekscan™ which served as a reference standard to this study. The idea is to create and develop an innovative, reliable and valid device would help in the early identification of ulcer development by objec-tively measuring peak plantar pressures, and by detecting heat as a signof inflammation through temperature readings on which the cliniciancan base his/her clinical reasoning. This could change clinical practice, and change the notion of just relying on clinical evaluation such as tactile examinations and observation of the skin where tissue damage is concerned.

1. Methodology

This research study questions whether the innovative, newly developed, in-shoe pressure and temperature measuring device, is able to detect and measure the in-shoe peak plantar pressures and skin temperature of healthy participants, as accurately as the reference standards.

The hypothesis of this study is as follows:

H_1: The mean data gathered via the innovative, single-sensor in-shoe pressure and temperature mapping device, positively corresponds to the mean data of the FScan system and the Flir® T630sc which served as reference standards for this study for pressure and temperature measurement.

H_0: The mean data gathered via the innovative, single-sensor in-shoe pressure and temperature mapping device, does not positively correspond to the mean data of the FScan system and the Flir® T630sc which served as reference standards for this study for pressure and temperature measurement.

1.1. Ethical considerations

Prior to the commencement of this study, ethical approval was sought and granted by the local Research Ethics Committee (Registra- tion Number: V_15062020 5784). Dynamic validation of the newly developed, low-cost, single-sensor pressure and temperature device was conducted at the state-of the art Biomechanics Laboratory. The data collection experiment used an in-shoe pressure system specifically the F- Scan System by Tekscan™ which served as a reference standard tool to which the prototype was compared. Unfortunately, to date, current technology has not yet established a "gold standard" in-shoe device that can measure both skin temperature and plantar pressures simulta- neously. For this reason, a thermographic camera, the Flir® T630sc, was used as a reference standard device for temperature.

1.2. Equipment used

1.2.1. The prototype

The prototype device consists of a squarish, compact case that is designed to sit out on the exterior of footwear. The device hosts theentire technical components of the device which consists of one flexible, piezoresistive Force Sensing Resistor (FSR) pressure sensor (A401 FlexiForce) and one 10Kom thin-film Negative Temperature Correlation (NTC) temperature sensor (DS18B20) including other required electronic components such as an operational amplifier, resistors, capacitors, and a microcontroller. The FSR used for this device features linearity of ± 3 %, repeatability of ± 2.5 % of the full-scale drift of 5 % per logarithmic time scale, and a response time of less than five µsec. The temperature sensor features a tolerance of 1 %, an operation range between — 50° and 90° Celsius, a Beta value of 3435 K with a small form factor having a height of 0.5 mm which makes it ideal for such embedded applications. Both pressure and temperature sensors extend from the main components of the device so that only the sensors are placed under the desired anatomical landmark on the plantar aspect of the foot.

1.3. The F-Scan system

F-Scan System (Research Software v. 6.11, Tekscan, Boston, MA) is a device designed to measure in-shoe pressures during standing orwalking. It comprises of 960 pressure sensing elements (sensels) ar- ranged in a 16 6 rectangular grid, embedded between 2 thin sheets of polyester insoles which is connected to a cuff unit. The sensing elements of this device work by changing their electrical resistance each time they are subjected to a force [5]. This change in resistance is then relayed to, and read by a computer which converts the readings to force readings. This system has a dynamic range of 1kPa-500kPa and is connected directly to a computer through a cable. Through various studies, the FScan system was found to be reliable for measuring in-shoe pressures [6,7].

1.4. Flir® T630sc thermographic camera

The Flir® T630sc is a thermographic camera reads infrared radiation through a thermal sensor, to create an image that depicts the thermal energy of an object. The thermal camera provides an image quality of 640 × 480-pixel infrared resolution with an accuracy of ± 1 °C [8].

1.5. Method

Five healthy adult participants, both males and females, aged between 30 and 55, with no known physiological or biomechanical conditions, were recruited by random sampling and voluntarily participated in this study. All consenting participants were asked to bring their own lace-up sports shoes. A pair of 100 % cotton socks was provided to each participant to ensure consistency when interpreting temperature measurements during data collection.

The participants were asked to lay in a supine position, barefooted, for 15 min in a pre-set ambient climate of 25 degrees Celsius (room temperature) for temperature acclimatization before the thermographic images of their socked feet were taken. Following this, the data collec- tion equipment was set up by embedding the sensor of the prototype within a 3 mm thick simple insole, made of a soft foam material, so that the sensor was levelled over the insole of the FScan™ system and to ensure that the sensor was not influencing the sensors of the FScan™ in- shoe system beneath it. These sensors were then placed within the shoe of the participant. The sensor of the prototype was positioned at an area on the simple insole that corresponded to the 1st metatarsophalangeal joint (MPJ) of the right foot of the participant.

Calibration of sensors of both the prototype and the FScan™ in-shoe system was conducted. The FScan™ system was calibrated using the point calibration mode [5] that is available in the Tekscan™ software of the system itself. This means that prior the actual data collection, the participant was asked to stand on his/her right foot while the system automatically calibrated the sensors based on the weight of the participant.

Once ensured that the set-up was complete, the participant was asked to walk at a comfortable pace (self-selected speed) on an electric treadmill for 15 min to represent mild physical exertion, during which both temperatures and pressures were recorded using the innovativesingle-sensor device. Upon completing the trial, the participants wereasked to lay again in supine position so that another barefoot thermo- graphic image of the right foot was taken using the Flir® T630sc ther- mographic camera. This was done to record any change in temperatureat the plantar aspect of the participant's foot following mild exertion. This procedure was repeated for all 5 participants.

1.1. Statistical analysis

1.1.1. Pressure

The data collection comprised of 5 trails, one trail for each partici- pant from which 2 datasets, one from the prototype and the other from the F-Scan system, were collected from each trial. Since the FScan fea- tures 960 individual pressure sensors throughout its insole, more than one sensor corresponded to the region of interest (ROI). A data grid was created to extract only the data from the region of interest (the 1st MPJof the right foot) the same area that corresponded to the area located under the single-sensor of the prototype. Values such as the minimum, maximum, mean, sum and median, were computed from the data grid. The mean value proved to be the closest to the readings recorded by the prototype.

The raw readings were passed to the regressor, which returned the data in the equivalent estimated KPa value. The Mean Absolute Error (MAE), Mean Squared Error (MSE), Root Mean Squared Error, Root Mean Squared Logarithmic Error, R Squared (R2), Adjusted R Squared and Pearson Correlation, were the evaluation metrics used to evaluate the performance of the modal.

1.2. Temperature

The data collection comprised of 5 trails, one trail for each partici- pant from which 2 datasets, one from the prototype and the other from the thermal camera, were collected from each trial. Due to an unpre- dicted malfunction, temperature data related to participant 4 and 5 hadto be eliminated. The Standard Deviation (SD), Confidence Interval (CI) and Relative Standard Deviation (RSD) were the were the evaluation metrics used to evaluate the performance of the modal. The Pearson's Correlation Coefficient use used to assess the relationship between in- shoe temperature and in-shoe pressure measurements.

2. Results

2.1. Demographic data

From a total of 5 participants, 40 % were females (n 2) and 60 % were males (n 3). The mean age of the participants was that of 40.1 years of age with a mean weight of 72 kg.

2.2. Pressure data

The experimental results presented in Table 1 show that, in all 5trials, there was a high correlation between the prototype and the FScan system which served as a reference standard. This is also evident in the data plot as show in Fig. 1 where the plotted values of the FScan correspond to those of the prototype.

2.3. Temperature data

The experimental results presented in Tables 2 and 3 show that the average change of temperature read by the thermal cameral is equiva- lent to 3.7 °C with a Confidence Interval (CI) of 1.07 and Standard Deviation (SD) of 0.86. This shows that the overall distribution of the data values is spread out and thus vary from the actual mean.

The in-shoe temperature readings showed that the average change of temperature read by the in-shoe temperature sensor is equivalent to 0.67 °C with a confidence interval of 0.48. This means that the overall distribution of this data values is also spread out and thus varies to the mean.

The Relative Standard Deviation (RSD) was calculated to comparethe variation in temperature distribution between the in-shoe temper- ature sensor and the thermal camera. Results showed that measurementsfrom the in-shoe temperature sensor had greater variation in tempera- ture change between participants (63.64) as opposed to the measure- ments taken from the thermal camera (23.17).

Furthermore, as shown in Table 4, comparison of data between the in-shoe temperature sensor and the in-shoe pressure sensor, show a high correlation (0.87) between the 2 parameters. Such results indicate that as pressure increases, so does the skin temperature at the affected area.

Table 1
Data grid showing the minimum, maximum, mean, sum and median of the data collected.

ID	P Correlation	MAE	MSE	RMSE	RMSLE	R2	R2 ADJ
1	0.801	6.976	93.04	9.645	2.266	0.517	0.491
2	0.978	6.657	89.877	9.48	2.249	0.951	0.948
3	0.813	6.237	82.079	9.059	2.203	0.495	0.467
4	0.887	6.425	86.003	9.273	2.227	0.725	0.71
5	0.944	7.39	100.299	10.014	2.304	0.88	0.874
6	0.946	6.737	89.992	9.486	2.249	0.877	0.87

3. Discussion

The aim of this study was to achieve dynamic validation, of the innovative, single-sensor in-shoe pressure and temperature mapping device on healthy participants. The novelty of this device, is that it was designed to read and measure in-shoe plantar pressure and in-shoe skin temperature simultaneously at a specific anatomical landmark of interest. Due to this ground-breaking feature of measuring both temperature and pressure at the same time, a feature which to date does not exist in any commercial in-shoe equipment, the device is anticipated tobe a key tool in diabetic foot ulcer prevention and management. In this study, this single sensor, in-shoe pressure and temperature measuring device has been validated dynamically in laboratory setting. In fact, results of this study showed that data gathered from the prototype, highly correlated to data gathered from the reference standards used in this study.

Another aspect that was explored in this study, was the correlation between in-shoe peak pressure and in-shoe peak temperatures during ambulation. Results of this study confirmed a correlation between peak plantar pressures and peak temperatures. It is common knowledge that excessive plantar pressures induce a stress on the superficial layer of the skin leading to maceration and detachment of the skin itself and that sustained loading on the skin further damages the skin enough to form an ulcer [9]. Skin temperature is a highly overlooked predictive measurement for foot ulceration as it is fairly new concept and the proper technology has not yet been introduced as part of the clinical assessment of the diabetic high-risk foot [10,11]. A correlation between pressureand skin temperature is suspected as prolonged pressure limits tissue perfusion and induces ischaemia, hindering the supply of nutrients and oxygen to the surrounding tissue. Results of this study showed a high Pearson's correlation value which indicates that as the pressure value increased, the in-shoe skin temperature at the same area of pressure also increased and, in this case, pressure and temperature increased at the same rate. A study by Houghton et al. [12] also observed a rise in local skin temperature secondary to induced pressure. Such results highlight the importance of the role of skin temperature in the development offoot ulceration and show that besides pressure, skin temperature can bea strong predictor for foot re-ulceration [12].

Another interesting point observed was that a high variability in temperature change was noted, this was especially evident in the data collected by the prototype device. Exposure to the environment (relevant to the thermal camera), physiological response to thermal conditions and presence of co-morbidities especially those which effect change in circulation of the blood[10] may contributed to this variability. Furthermore, the variation in data distribution related to the thermal camera could have been affected while the patient had to take time to sit and remove his footwear before the temperature reading was recorded. This was likely to influence the overall result.

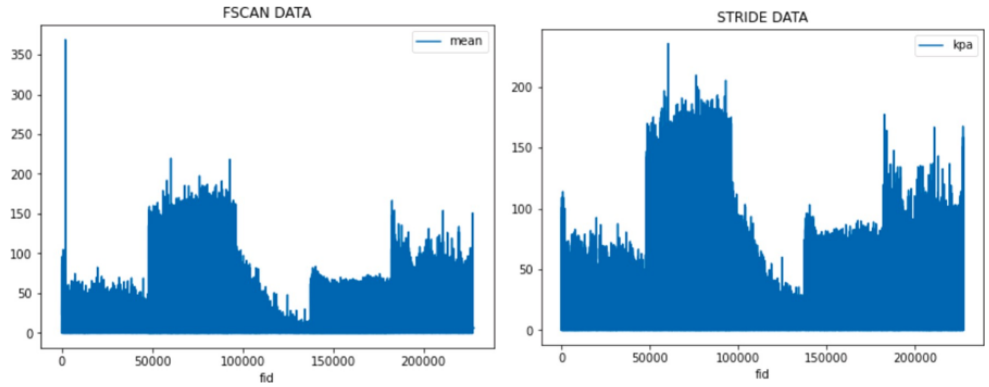

Fig. 1. Data plots showing the results of all 5 participants, FScan vs Prototype.

Table 2
Table showing the temperature readings measured by the thermal camera.

Participant	Sex	Age	Weight (Kg)	T_1	T_2	ΔT	SD	CI	RSD
1	F	53	70	28.8	32.1	3.3	0.86	1.07	23.17
2	M	55	92	28.4	33.2	4.8			
3	M	26	60	26.8	30.8	4			
4	F	32	70	26.5	30.4	3.9			
5	M	36	68	31.1	33.6	2.5			

Table 3
Table showing the temperature readings measured by the in-shoe temperature sensor.

Participant	Sex	Age	Weight (Kg)	T_0	T_1	ΔT	SD	CI	RSD
1	F	53	70	14.33	14.88	0.55	0.43	0.48	63.64
2	M	55	92	14.31	15.46	1.15			
3	M	36	68	12.36	12.68	0.32			

Table 4
Table showing the in-shoe pressure and in-shoe temperature readings.

Participant	In-shoe Temp (°C)	Pressure (kPA)	Pearson's Correlation Coefficient
1	14.88	20	0.87
2	15.46	22	
3	12.68	19	

The innovative, single-sensor pressure and temperature monitoring device was developed so that it can also serve as a low-cost alternative to the currently available costly in-shoe pressure systems and barefoot temperature monitoring devices. The benefit of having a validated single-sensor device can facilitate monitoring of temperature and pres- sure changes at targeted anatomical landmarks such as previously ul- cerated sites or sites showing pre-ulcerative indications, a feature which similar current commercial technology is lacking.

The quality and effectiveness of foot orthoses prescribed for the diabetic high-risk foot is also empirical for the prevention of diabetic foot ulceration and/or re-ulceration. This device can be used to assess the effectiveness of any in-shoe offloading device and modify and re-distribute pressures if found necessary on the same day of dispensing the offloading device. The study by Bus [1] advocates that it is more likely to achieve better outcomes related to pressure reduction when offloading and pressure re-distribution have been assisted by proper techniques and in-shoe technologies to confirm current pressures and temperature readings of the high-risk foot. If used correctly, the inno- vative, in-shoe to alleviate the burden imposed on the health care economy by early detecting signs of ulceration and provide treatment care accordingly.

1. Limitations of the study

Though this study validated a ground breaking and innovative in-shoe device that can measure temperature and pressure simultaneously, this study recruited a small sample size (n 5) of healthy individuals of which 2 participants had to be eliminated when considering temperature data. The selection of participant population was intentionally chosen as such as the researchers wanted to first test this device on healthy participants to ensure that no harm came to high-risk patients. Following the positive validation results of this study, this device will be now tested in an upcoming, larger clinical trial with different populations including the high-risk foot.

1. Conclusion

Results from this study show positive correspondence of mean data between the prototype and the FScan system and the Flir® T630sc which served as reference standards for this study for pressure and temperature measurement. This suggests that the innovative single-sensor pressure and temperature device was equally able to measure pressure and temperature as the FScan™ system and the Flir® T630sc Thermographic Camera which served as reference standards to the prototype in this study. Thus, the authors area confident that the prototype can be used as a low-cost alternative to costly commercial devices. Further studies on the use of the innovative single-sensor pressure and temperature device

on other populations including the high-risk foot will be conducted since this innovative device has the potential to determine in-shoe pressureand temperature parameters simultaneously - 2 risk known to be the cause of diabetic foot complications including ulcerations.

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Declaration of Competing Interest

This research did not receive any specific grant from fundingagencies in the public, commercial or not-for-profit sectors. The author confirm that it poses no conflict of interest.

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Appendix 6 | Medline OVID search

1. diabetes.af.

2. diabetes mellitus. af.

3. diabetic f??t. af.

4. type 2 diabetes mellitus. af.

5. type II diabetes mellitus. af.

6. diabetic f??t. af.

7. in-shoe pressure mapping. af.

8. in-shoe pressure measure*. af.

9. wearable pressure sensor*. af.

10. f??t pressure. af.

11. diabetic f??t pressure*. af.

12. f??t plantar pressure*. af.

13. diabetic f??t plantar pressure*. af.

14. peak plantar pressure*. af.

15. pressure time integral*. af.

16. foot ulcer*. af.

17. plantar foot ulcer*. af.

18. plantar wound*. af.

19. plantar foot wound*. af.

20. plantar ulcer*. af.

21. diabetic foot ulcer*. af.

22. re-ulcer*. af.

23. recurrent foot ulcer*. af.

24. temperature sensor*. af.

25. wearable temperature sensor*. af.

26. heat sensor*. af.

27. thermal sensor*. af.

28. 1 or 2 or 3 or 4 or 5 or 6

29. 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15

30. 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23

31. 24 or 25 or 26 or 27 4598

32. 28 and 29 and 30 and 31

Appendix 7 | QUADAS-2

Phase 3: Risk of bias and applicability judgments

QUADAS-2 is structured so that 4 key domains are each rated in terms of the risk of bias and the concern regarding applicability to the research question (as defined above). Each key domain has a set of signalling questions to help reach the judgments regarding bias and applicability.

DOMAIN 1: PATIENT SELECTION

A. Risk of Bias

Describe methods of patient selection:

- ❖ Was a consecutive or random sample of patients enrolled? Yes/No/Unclear
- ❖ Was a case-control design avoided? Yes/No/Unclear
- ❖ Did the study avoid inappropriate exclusions? Yes/No/Unclear

Could the selection of patients have introduced bias? **RISK: LOW/HIGH/UNCLEAR**

B. Concerns regarding applicability

Describe included patients (prior testing, presentation, intended use of index test and setting):

Is there concern that the included patients do not match the review question? **CONCERN: LOW/HIGH/UNCLEAR**

DOMAIN 2: INDEX TEST(S)

If more than one index test was used, please complete for each test.

A. Risk of Bias

Describe the index test and how it was conducted and interpreted:

- ❖ Were the index test results interpreted without knowledge of the results of the reference standard? Yes/No/Unclear
- ❖ If a threshold was used, was it pre-specified? Yes/No/Unclear

Could the conduct or interpretation of the index test have introduced bias? **RISK: LOW /HIGH/UNCLEAR**

B. Concerns regarding applicability

Is there concern that the index test, its conduct, or interpretation differ from the review question? **CONCERN: LOW /HIGH/UNCLEAR**

DOMAIN 3: REFERENCE STANDARD

A. Risk of Bias

Describe the reference standard and how it was conducted and interpreted:

- ❖ Is the reference standard likely to correctly classify the target condition? Yes/No/Unclear
- ❖ Were the reference standard results interpreted without knowledge of the results of the index test? Yes/No/Unclear

Could the reference standard, its conduct, or its interpretation have introduced bias? **RISK: LOW /HIGH/UNCLEAR**

B. Concerns regarding applicability

Is there concern that the target condition as defined by the reference standard does not match the review question? **CONCERN: LOW /HIGH/UNCLEAR**

DOMAIN 4: FLOW AND TIMING

A. Risk of Bias

Describe any patients who did not receive the index test(s) and/or reference standard or who were excluded from the 2x2 table (refer to flow diagram):

Describe the time interval and any interventions between index test(s) and reference standard:

- ❖ Was there an appropriate interval between index test(s) and reference standard? Yes/No/Unclear
- ❖ Did all patients receive a reference standard? Yes/No/Unclear
- ❖ Did patients receive the same reference standard? Yes/No/Unclear
- ❖ Were all patients included in the analysis? Yes/No/Unclear

Could the patient flow have introduced bias? **RISK: LOW /HIGH/UNCLEAR**

Appendix 8 | Instructions Manual for the Innovative, Single-sensor, In-shoe Pressure and Temperature Measuring Device

The user is advised to read the entire instructions manual to ensure seamless function of the device and avoid product malfunction.

1.1 General warnings and cautions

Hardware

Before using the single-sensor, in-shoe pressure and temperature measuring device, the user is advised to inspect the device for any signs of faults and defects especially if the device experienced excessive force from dropping. The user is also encouraged to avoid forceful pulling of the cords that connects the sensors to the main body of the device. In cases of visible damage to the device, the user is encouraged not to use the device as this may result in ineffective performance of the device.

If the user feels compelled to clean the device following use, it is strongly recommended to avoid water and other liquids as this may damage the device, including the sensors. A clean dry cloth can be used to wipe down the device.

Operational environment

The avoid damaging the sensors and device malfunction, the device should not be used to measure parameters in environments that exceed 60ºC for the pressure sensor and 90ºC for the temperature sensor, in both convection and conduction heat sources. Low temperatures below -40ºC should also be avoided when using the device.

The use of the device in wet environment should be strictly avoided as contact of the device to liquids, and/or immersion in water will damage the device.

Sensor replacement and battery re-charging

As per manufacturers indication, it is recommended that the Flex Force FSR pressure sensor is replaced after ≥ 3 million actuations to avoid data drift which is likely to lead to inaccurate measurements (Tekscan, 2016).

The device may require re-charging of battery following 8 hours of continuous use or following prolonged disuse.

Restrictions of use

The single-sensor, in-shoe pressure and temperature measuring device was designed and developed to provide non-invasive measurement of in-shoe pressure and temperature parameters for the high-risk diabetic foot. The device does not cause any discomfort nor harm to the individual and thus, the device poses no restrictions as safe to use in any patient category which includes the paediatric, geriatric, healthy adult, rheumatic and musculoskeletal patients and sports patient.

When assessing an ulcerated foot, for hygiene purposes and to avoid cross-infection, the user is recommended to avoid placing the sensors directly in contact to an unprotected wound bed. The user can opt to wait for the ulcer to heal prior to collect data or, cover the wound with a thin-layer of a breathable, non-adherent dressing. The sensors of the device can be placed over the thin dressing. In this scenario, temperature readings should not be affected. User should ensure that the dressing is well adhered to the patient's skin to avoid displacement of both dressing and sensors. User should also make sure that the dressing does not crease prior to and/or during data collection as this may result in increased pressure point.

The use of the device on highly exudative lesions should be avoided as a thin-layered dressing will not be enough to hold the discharge and thus, cross infection may still occur. Moreover, heavy exudate may damage the sensors of the device.

1.2 Purpose of the device

The single-sensor, in-shoe pressure and temperature measuring device was designed for the simultaneous measurement of in-shoe pressure and temperature parameters which are known to be predictors of ulceration in the diabetic high-risk foot.

This device was developed to provide the user with a low-cost and easy-to-use alternative to the currently commercially available pressure and temperature technologies.

1.3 Description of the device

The single-sensor, in-shoe pressure and temperature measuring device was developed by experienced engineers and it has been validated to be an excellent model for clinical use. The combination of portability, ease-of-use and functionality makes this device ideal for the measurement of both pressure and temperature at targeted anatomical landmarks within the shoe.

The wireless feature of this device permits the user to transmit the data collected to a personal computer on an online cloud which can be assessed solely by the user via the multi-purpose web-based dashboard. It also features the possibility to communicate with a smart phone application via Bluetooth permitting the user to carry out the assessment to the setting of choice such as clinical, laboratory or any other environment.

The device measures 60mm in width, 75mm in length and 10mm in height giving its case a squarish and compact ensemble which makes it ideal to fit inconspicuously in pockets (Figure 1). Within the case of the device, the entire electronic components are hosted. This includes an operational amplifier, resistors, capacitors, and a microcontroller. Both pressure and temperature sensors extend from it so that only the sensors are placed under the desired anatomical landmark on the plantar aspect of the foot.

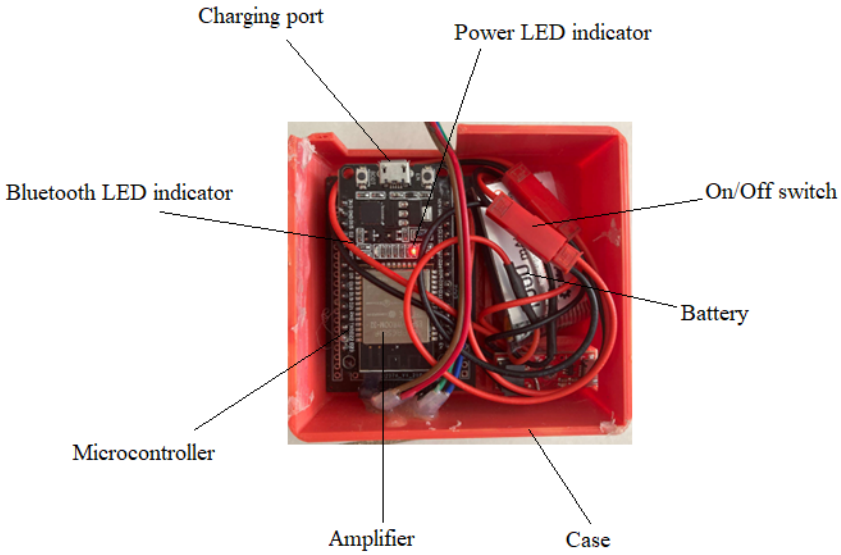


Figure 1: Components of the device

Microcontroller:

- Consumer-grade ESP32 microcontroller with a built-in BLE (Low Energy Bluetooth)
- Dual-core Central Processing Unit (CPU)
- Integrated Wi-Fi
- Input/output ports
- Employs the Tensilica Xtensa LX6 microprocessor which is recommended for automated medical devices
- Printed Circuit Board (PCB) is 58mm by 32mm in size and it can host up to 4 pressure sensors and up to 4 temperature sensors along with all the required components

Amplifier:

- Non-inverting operational amplifier (OpAmp) with a reference voltage (VREF) and sensor sensitivity of up to 5V with a 50% max duty cycle or between 0.25V – 1.25V DC

- This device can be set to collect data at a frequency that ranges between 50Hz to 75Hz

Pressure sensor:

- FlexiForce A401, Force Sensitive Resistor (FSR), manufactured by Tekscan™, which features a linearity of ±3%, repeatability of ±2.5% of the full-scale drift of 5% per logarithmic time scale, and a response time of less than five μsec. Additionally, it can operate with measurement ranges of 0-1 lb and 0-7000 lb using the recommended circuitry.

Temperature sensor:

- 10 Kom thin-film Negative Temperature Correlation (NTC) thermistor featuring a tolerance of 1%, an operation range between -50 and 90 degrees Celsius, a Beta value of 3435K with a small form factor having a height of 0.5mm which makes it ideal for such embedded applications.

Battery:

- 1000mAh 902540 3.7V Lithium Rechargeable Battery (MarkerFocus)

1.4 Operating instructions

The single-sensor, in-shoe pressure and temperature measuring device was developed with a plug-and-play design. This was intended to allow the user to ease-of-use and streamlined clinical approach. The device comes already assembled and calibrated and thus, no pre-operational preparations or device warm-up is required by the user before use.

1.5 Temperature and pressure sensor placement

To create a fusion of the 2 different sensors (pressure and temperature), and to avoid creasing of the sensors during use, a puck concept was introduced. The puck, consists

of a 1mm high, circular plastic disk onto which the pressure sensor is attached to it on one side, and the temperature sensor embedded within a 0.5mm engraving on the other side of the puck. Both temperature and pressure sensors extend out and away from the device so that they can be inserted comfortably within the shoe without hindering the normal gait.

The temperature and pressure sensor can be positioned over the desired area that requires investigation. The sensor puck can be embedded within a simple insole or placed directly against the skin keeping it in place via hypo-allergenic adhesive tape. For optimal temperature measurements, the temperature sensor must be placed in direct contact to the skin.

1.6 Connecting the device to the mobile application

A cross-platform mobile application was developed using React-Native Framework to allow compatibility with any mobile Operating System (OS). The purpose of this platform, was to serve as an intermediary connection between the device microcontroller and its server, enabling both online and offline operational facility.

From this platform, the user can adapt the parameters of the hardware of the device and create customized data collection protocols. Via a two-way Bluetooth based communication channel, the application can the pre-set configuration parameters to the microcontroller and receive the data collected by the microcontroller. The data is normally encrypted and sent from device to server on an online cloud however, should the connection between the device and server is lost, the data is programmed to be stored in a locally hosted database until connection is re-established. The device can be used by simply connecting the On/Off switch that is situated in the body of the device (Figure 2). Once connected, an LED indicator will turn on red. This indicates that the device is On and is ready to be connected.

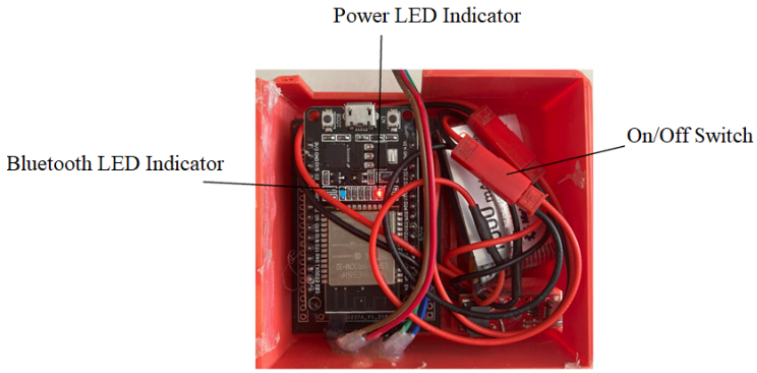


Figure 2: Power and Bluetooth LED indicator and On/OFF switch position

To connect the device to the mobile application, the 'Bluetooth Connection' tab can be tapped. Once the connection between the device and mobile application has been established, the 'Bluetooth Connection' tab will turn from blue to green, indicating the successful connection. On the device itself, a blue LED light will turn on, on the opposite to the power indication light (Figure 3).

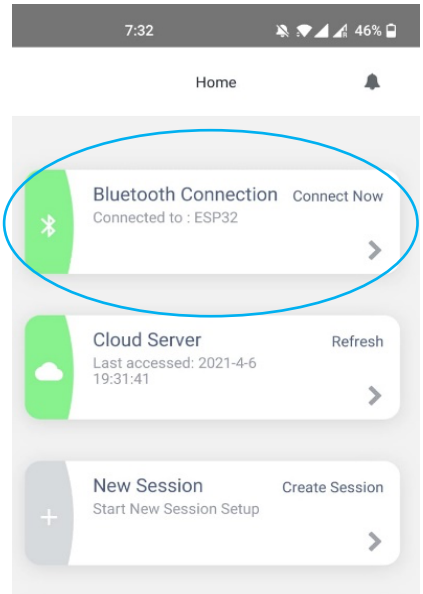


Figure 3: Screen shot of the mobile app of the device: Bluetooth connection

1.7 Starting a New Session

To create a new session, the user must ensure that a Bluetooth connection has been established between the device and the mobile application (Section 1.6). Once connected, the ‘New Session’ tab can be tapped to initiate the session (Figure 4).

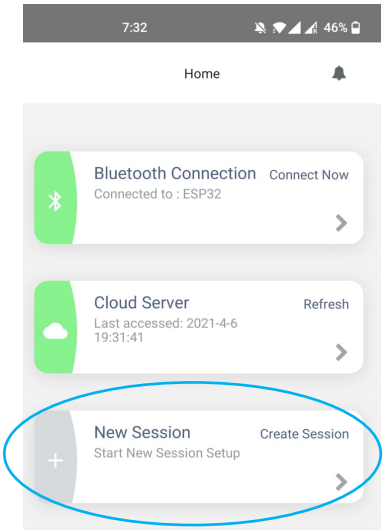


Figure 4: Screen shot of the mobile app of the device: new session

1.8 Setting configuration parameters

Once a new session is selected, the platform takes the user to the ‘Session Setup’ section where the configuration details are set up. This allows the user to instruct the device on which foot is to be assessed, which position was the sensors placed and the number of trials the user wishes to perform. It is important to note that the word ‘Trial’ here, represents a session. While the word ‘Capture’, represents a recording.

Once details of the session/trail are inserted, as per example in the picture below, the ‘Finish’ tab can be tapped. The user is then taken to the ‘Session’ page where the configuration details of the Trial are listed. To initiate the recording/capture of the trial the user has to tap on the ‘Start Capture’ tab. The session can be paused, un-paused and stopped any time during the trial by tapping on the respective tabs situated below the ‘Start Capture’ tab. The ‘End Capture’ tab allows the user to stop the current

recording/capture and move on to the successive capture. This is only permissible if more than one trials are selected beforehand in the ‘Session Setup’ section (Figure 5).

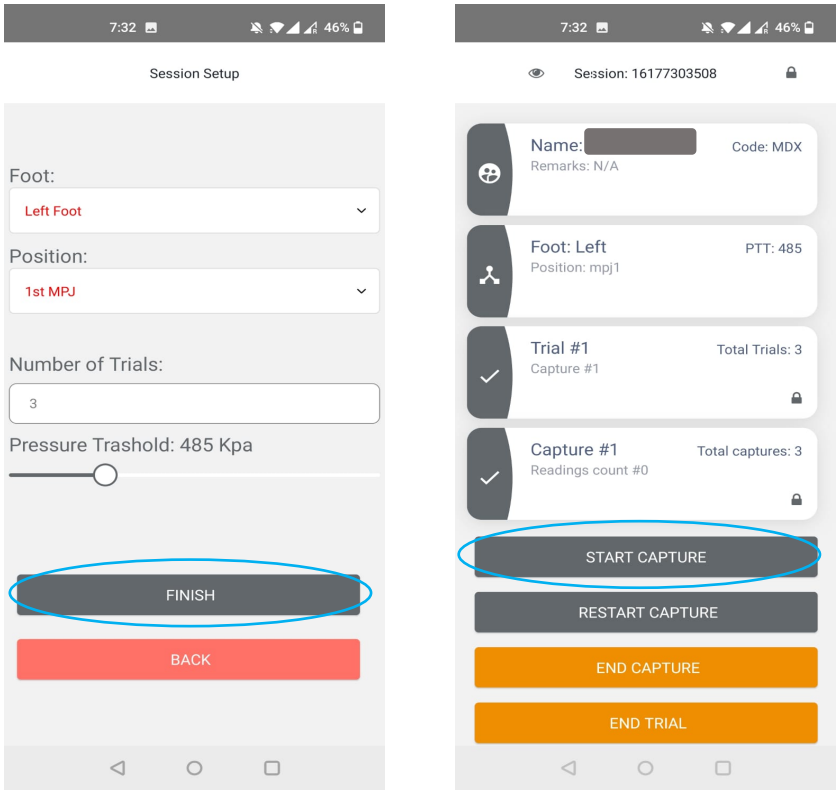


Figure 5: Screen shot of the mobile app of the device: Starting a capture

1.9 Ending and saving a session

To stop data collection, the ‘End Trial’ tab can be tapped. This will prompt the user to another section on the application. In this section, the user can add personal notes and comments, perhaps relating to the trial, in the free-text box provided. Once satisfied, the user can proceed to tab on the ‘Save and Continue’ tab. The data will be saved and stored in an encrypted format on a dedicated online cloud server which can be accessed via a web-based dashboard.

1.10 Accessing recorded data

The data recorded can be accessed by the user via a web-based dashboard that is directly connected to the Application Program Interface (API) of the online cloud where the data is stored. From this web-based dashboard, the user free to perform multiple tasks of which are listed below.

- Access data collected
- Visualize data collected in form of graphs and infographics
- Manage the overall system as desired
- Add and delete users if the system is being shared
- Update patient/client details
- Add other devices
- Add additional sensors
- Share data with other clinicians/users

The user can access the desired data in 3 ways: via user, via patient identification or else directly via sessions at the top right corner of the webpage. By selecting the 'Patients' tab, the user is presented with a list of patient records (Figure 6).

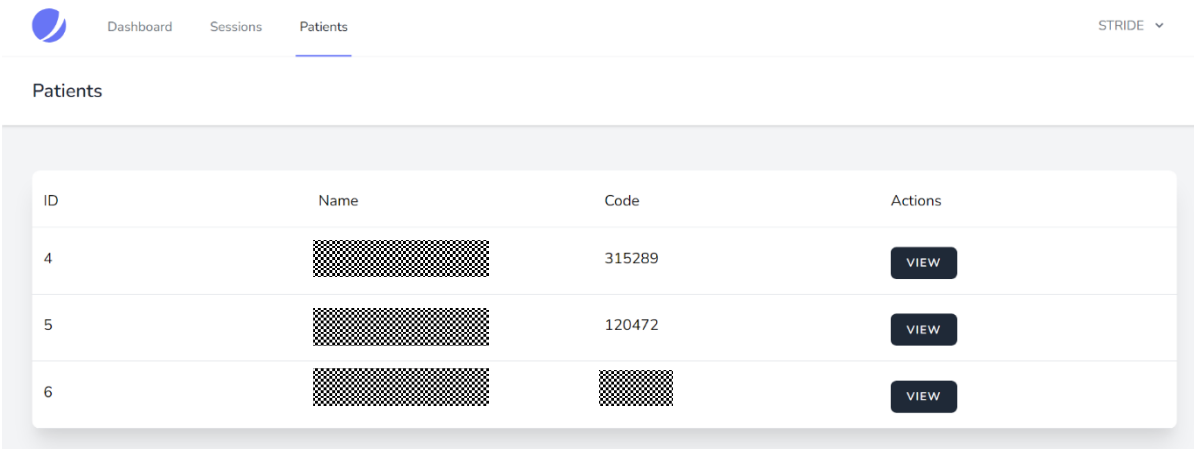


Figure 6: Screen shot of the web-based dashboard of the device: homepage

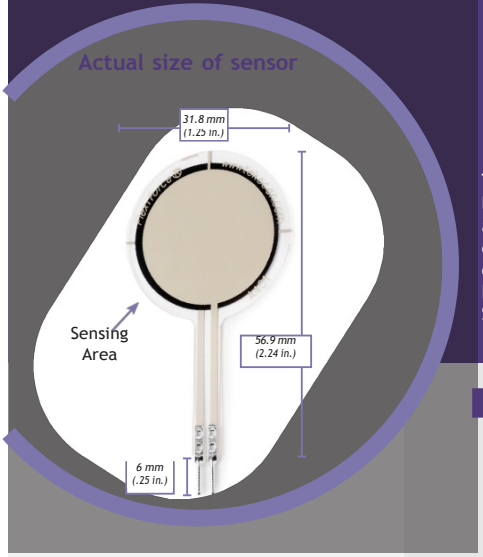
Once the patient of interest is identified, the user can click over view where he/she is presented with the list of sessions related to that particular patient. Each session can

be opened and the overall report be generated as exemplified in Figure 7. The user can save the report as PDF, share the report with his patient or colleagues and/or print as desired.

Back to the homepage, the ‘Sessions’ tab will display all the recordings of all patients in one page and in chronological order. Sessions can still be identified through session identification number and patient identification.

Figure 7: Screen shot of the web-based dashboard of the device: patient's report

Appendix 9 | Manufacturer's Details of Pressure Sensor Used in this Study



FlexiForce™

Standard Model A401

The FlexiForce A401 is our standard piezoresistive force sensor with the largest sensing area. It is available off-the-shelf for easy proof of concept and is also available in large volumes for design-in applications. The A401 can be used with our test & measurement, prototyping, and embedding electronics, including the FlexiForce Sensor Characterization Kit, FlexiForce Prototyping Kit, FlexiForce Quickstart Board, and the ELF™ System*. You can also use your own electronics, or multimeter.

Physical Properties

Thickness	0.203 mm (0.008 in.)
Length	56.9 mm (2.24 in.)**
Width	31.8 mm (1.25 in.)
Sensing Area	25.4 mm (1 in.) diameter
Connector	2-pin Male Square Pin
Substrate	Polyester
Pin Spacing	2.54 mm (0.1 in.)

Benefits

- Thin and flexible
- Easy to use
- Convenient and affordable

ROHS COMPLIANT

Sensor will require an adapter/extender to connect to the ELF System. Contact your Tekscan representative for assistance.

***Length does not include pins. Please add approximately 6 mm (0.25 in.) for pin length for a total length of approximately 32 mm (1.25 in).*

	Typical Performance	Evaluation Conditions***
Linearity (Error)	< ±3% of full scale	Line drawn from 0 to 50% load
Repeatability	< ±2.5%	Conditioned sensor, 80% of full force applied
Hysteresis	< 4.5% of full scale	Conditioned sensor, 80% of full force applied
Drift	< 5% per logarithmic time scale	Constant load of 111 N (25 lb)
Response Time	< 5µsec	Impact load, output recorded on oscilloscope
Operating Temperature	-40°C - 60°C (-40°F - 140°F)	Convection and conduction heat sources
Durability	≥ 3 million actuations	Perpendicular load, room temperature, 22 N (5 lb)
Temperature Sensitivity	0.36%/°C (± 0.2%/°F)	Conductive heating

***All data above was collected utilizing an Op Amp Circuit (shown on the next page).** If your application cannot allow an Op Amp Circuit, visit www.tekscan.com/flexiforce-integration-guides, or contact a FlexiForce Applications Engineer.

DS Rev I 062821

ISO 9001:2008 Compliant & 13485:2016 Registered

Tekscan™

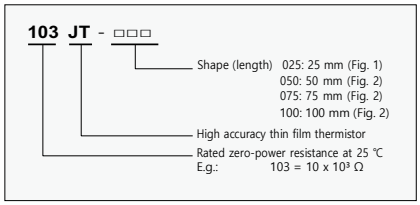
Appendix 10 | Manufacturer's Details of Temperature Sensor Used in this Study

Thin film thermistor

JT Thermistor

The JT series thermistor features high accuracy and a thickness of less than 500 µm. The JT thermistor also has excellent electrical insulation and can be safely used in environments where it might come in contact with electrodes.

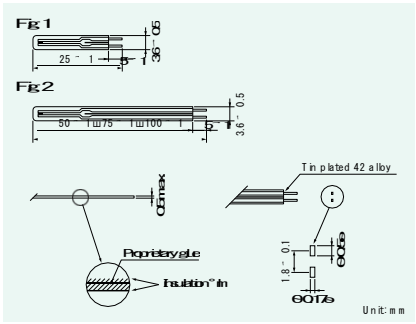
Product number explanation



Applications

Battery packs, battery chargers, IT equipment, mobile devices, LCDs, surface temperature sensors, high sensitivity air temperature sensors

Dimensions



Specifications

Product number	R_{25}[1]	R_{25} tolerance	'B value'[2]	Dissipation factor (mW/K)	Thermal time constant (s)[3]	Rated power at 25 K (mW)	Operating temperature range (K)
103JT	10kΩ	±1%	3435K±1%	approx.0.7	approx.5	35	−50 to 125
104JT	100kΩ		4390K±1%				

[1]: Rated zero-power resistance at 25 K [2]: B value calculated from rated zero-power resistance at 25 K and 85 K
[3]: Time required to reach 63.2% of temperature difference. Measured with sensor suspended in mid-air.

Reliability data

Item	Test conditions	Criteria
Resistance to soldering heat	5 s at 260 K	R ±1%
Solderability	2 s at 245 K Flux material: Rosin 25%, ethyl alcohol 75%	More than 90% soldered
Tensile strength (lead wire)	10 s at 1 N (orientation pull)	R ±1% and visual inspection
Termination bending	25 N, one time, 90 K	
Free fall	Three times natural fall to a sample board from 0.75 m height	
Voltage proof	100 VAC for one minute	Less than 1 mA
Insulation resistance	100 VDC	Over 100 MΩ
Dry heat	1000 hours at 125 K	R ±1%
Damp heat (under electrical load)	1000 hours at 40 K and 90% humidity Electrical load: 1 mADC	
Temperature cycle (one cycle)	100 cycles as below: 1. −25 K for 30 minutes 2. Room temperature for 3 minutes 3. 125 K for 30 minutes 4. Room temperature for 3 minutes	

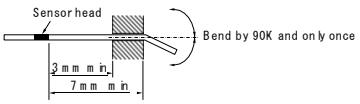
Caution

- If you plan pressing or pushing the thermistor against an object or inserting it into a tight space please contact SEMITEC sales staff.
- When soldering make sure to avoid contact of the hot part (over 150 ˚C) and the sensor, because this may melt the sensor film.
- When bending the sensor make sure to not apply force on the sensor head (minimum distance from sensor: 3 mm) when fixing it. Additionally, make sure to bend the lead wire with a minimum distance of 7 mm from the sensor head.

Resistance / temperature characteristics

Temperature (K)	Product number	
	103JT	104JT
−50	367.7	988.4
−40	204.7	452.2
−30	118.5	228.2
−20	71.02	119.1
−10	43.67	64.72
0	27.70	36.50
10	18.07	21.25
20	12.11	12.77
25	10.00	10.00
30	8.301	7.883
40	5.811	5.003
50	4.147	3.251
60	3.011	2.161
70	2.224	1.466
80	1.668	1.013
85	1.451	0.8433
90	1.267	0.7135
100	0.9753	0.5111
110	0.7597	0.3720
120	0.5984	0.2746
125	0.5331	0.2371
$B_{25/85}$	3433K	4390K

Unit: K (except)



Appendix 11 | Ethics Approval Documents

L-Università ta' Malta

Claire Saliba Thorne <claire.saliba-thorne.08@um.edu.mt>

UREC FORM V_15062020 5784 Claire Saliba Thorne

Ritienne Grima <ritienne.grima@um.edu.mt> 26 October 2020 at 06:26
To: Claire Saliba Thorne <claire.saliba-thorne.08@um.edu.mt>
Cc: Formosa Cynthia <cynthia.formosa@um.edu.mt>, Research Ethics HEALTHSCI <research-ethics.healthsci@um.edu.mt>

Thank you Claire.
I confirm that you have carried out the necessary amendments. You have approval on behalf of FREC and you may commence data collection.
Best wishes
[Quoted text hidden]
[Quoted text hidden]

Appendix 12 | Individual Data Plots of the Dynamic Laboratory Validation Study

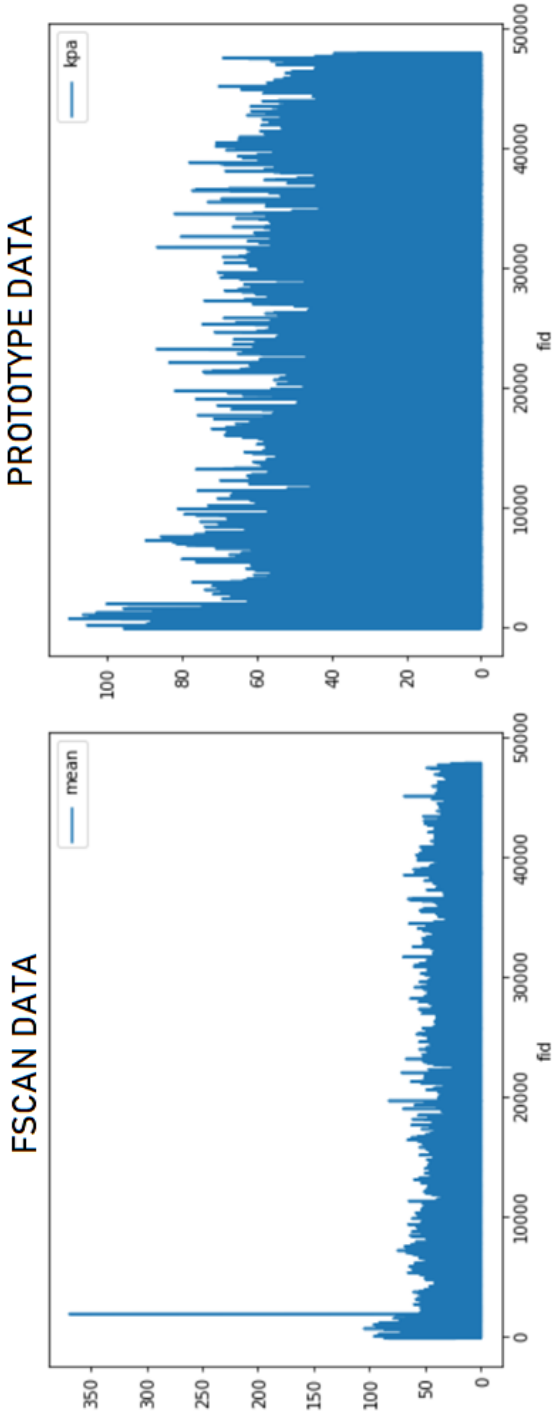


Figure 68: Data plots showing the results of the FScan vs Prototype for Trail 1 Participant 1

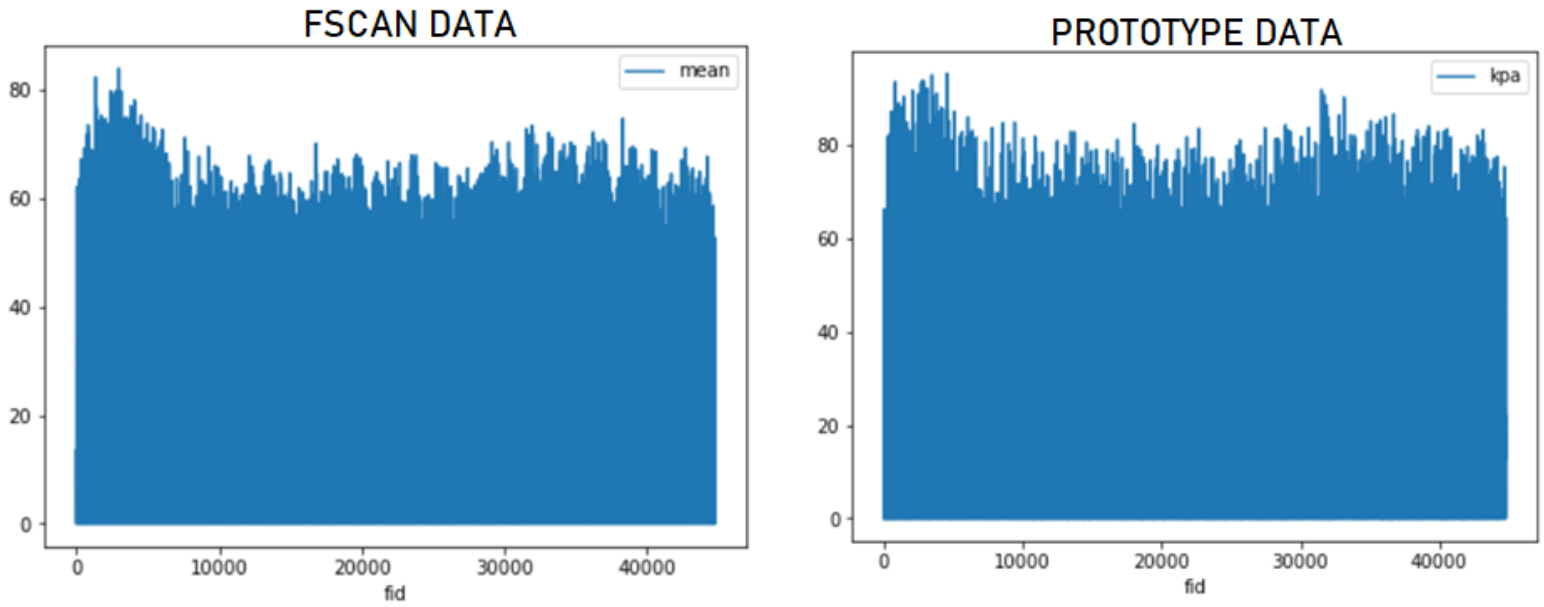


Figure 69: Data plots showing the results of the FScan vs Prototype for Trail 2 Participant 2

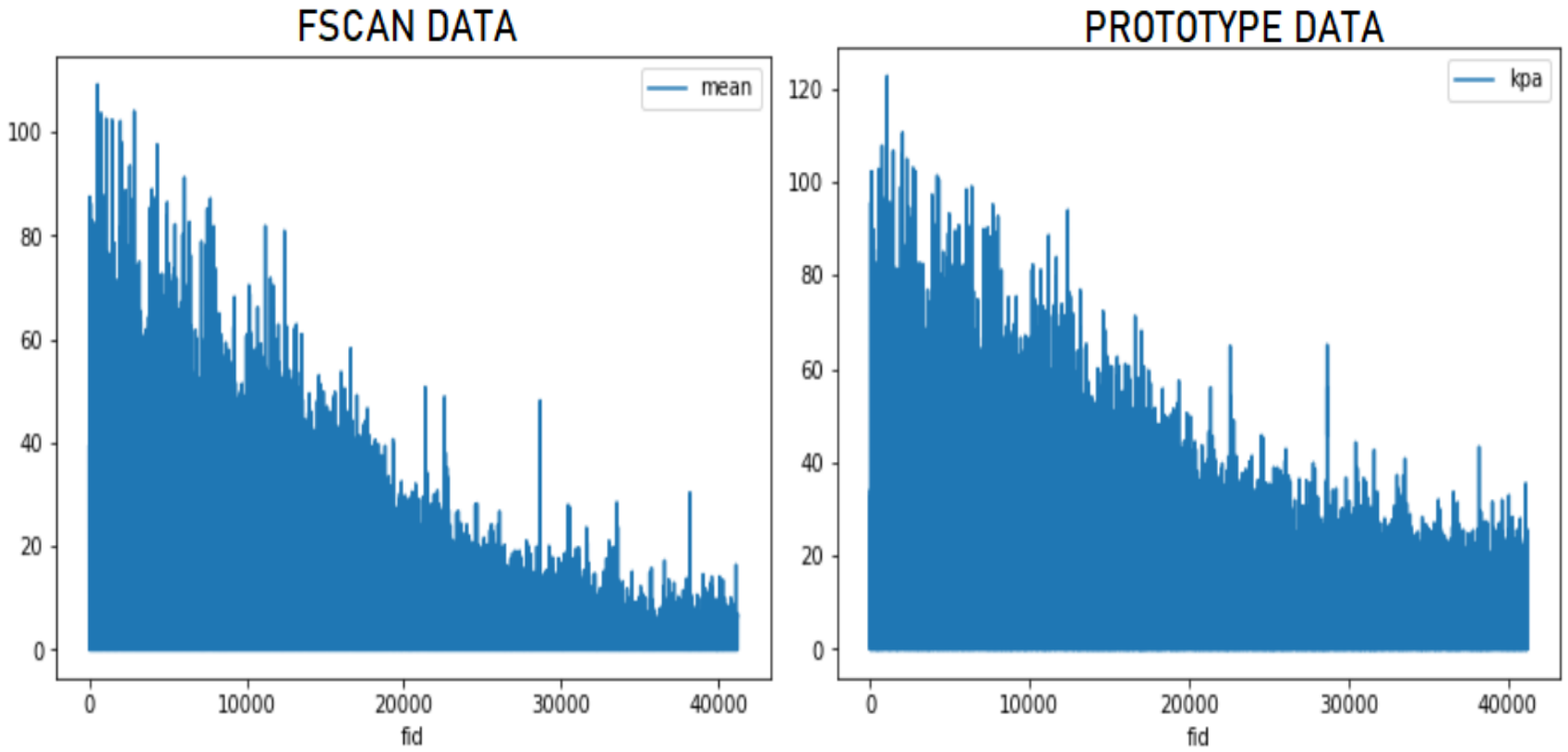


Figure 70: Data plots showing the results of FScan vs Prototype for Trial 3 Participant 3

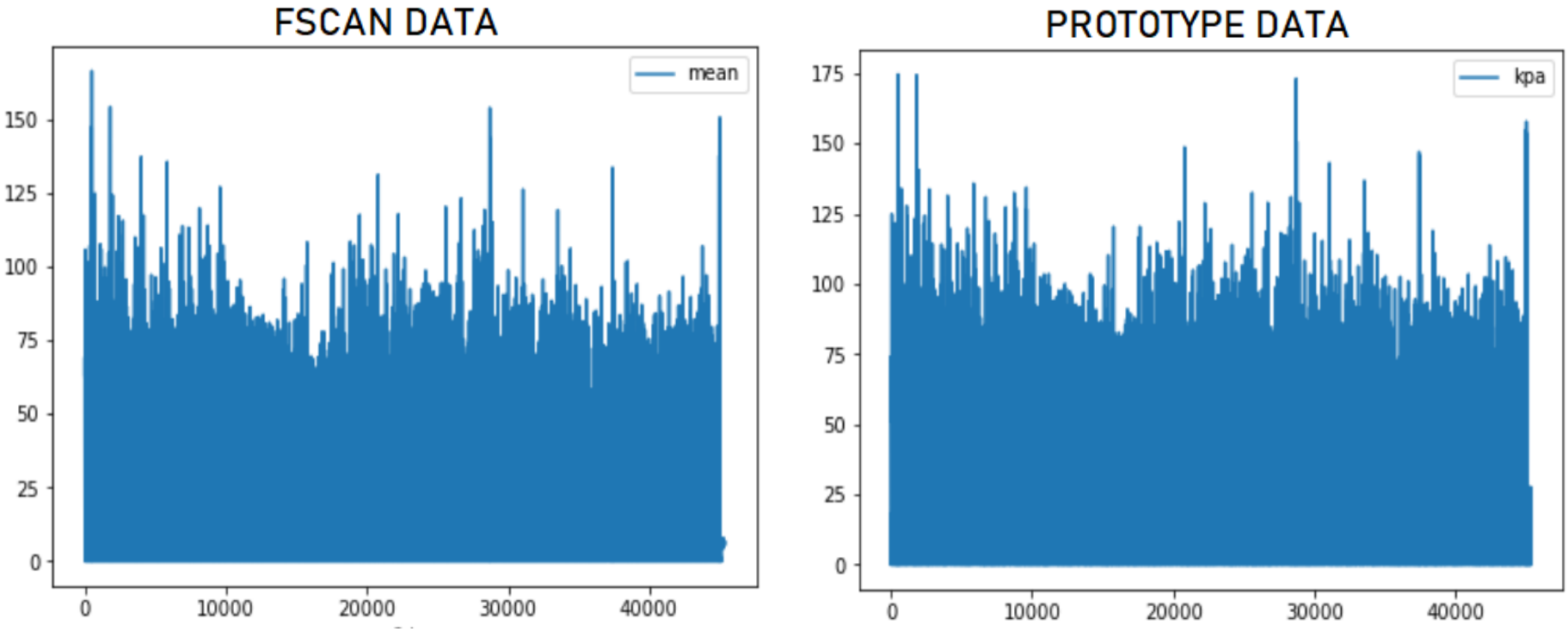


Figure 71: Data plots showing the results of FScan vs Prototype for Trial 4 Participant 4

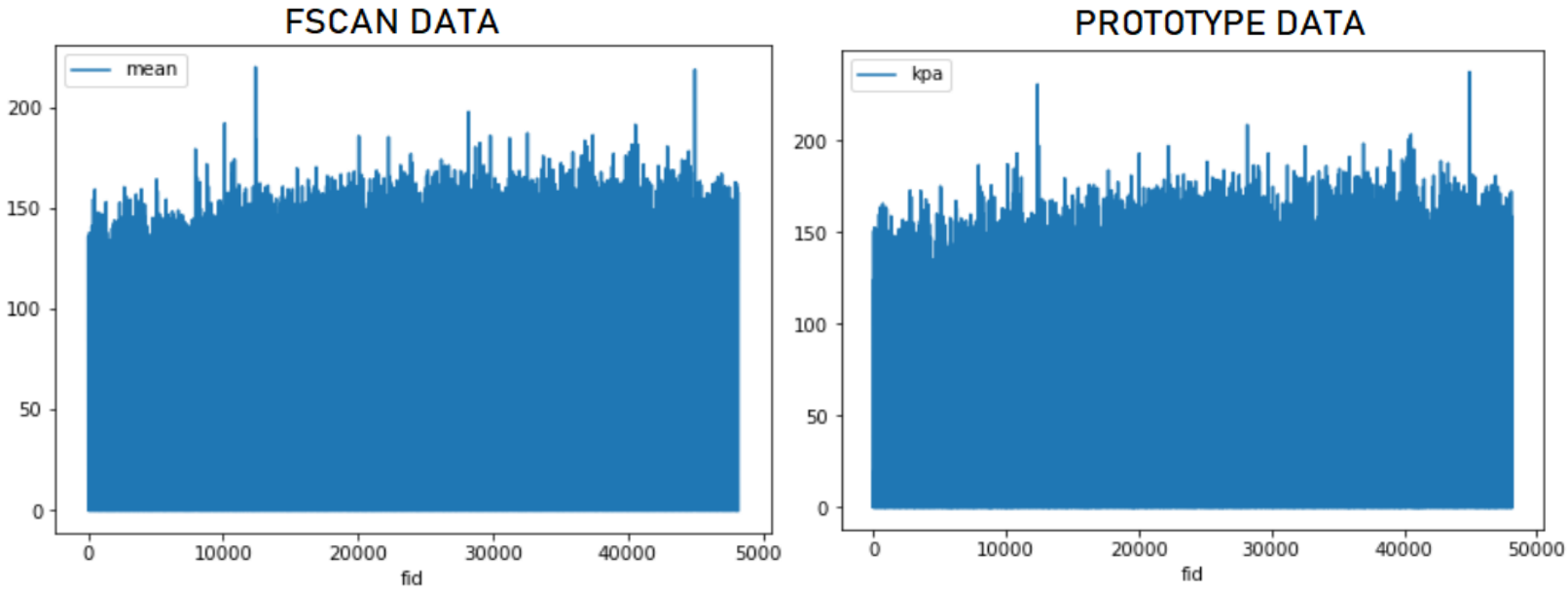


Figure 72: Data plots showing results of FScan vs Prototype for Trial 5 Participant 5

Appendix 13 | Information Sheet for Participants

L-Università ta' Malta

Participants` Information Sheet

Dear Participant,

My name is Claire Saliba Thorne and I am currently reading for a Doctor in Philosophy in Podiatry at the University of Malta. As part of my course requirements, I am conducting a research study entitled**,** *"Single sensor pressure and temperature mapping device for the prevention of diabetic foot re-ulceration"*. The aim of this study is to investigate whether a specifically designed pressure and temperature mapping system is effective in reducing ulceration and/or re-ulceration in a high-risk diabetic population, when compared with standard care currently being given. Your participation in this study would help us gain a better understanding about on how we can predict foot ulceration prior it forms by utilizing the aforementioned techniques. This will not only avoid the further diabetic foot complication but may avoid lower limb amputations and reduce the mortality rate. Any data collected from this research will be used solely for purposes of this study. Furthermore, all data collected from this research shall be used solely for the purpose of this study.

You are being invited to participate in a study which will investigate whether a specifically designed pressure and temperature mapping system is effective in reducing ulceration and/or re-ulceration in a high-risk diabetic population, when compared with standard care currently being given. If you agree to participate, you will meet the researcher once every 4 months for 1 year, at the Biomechanics Lab, Podiatry Department, Faculty of Health and at a time that is convenient for you, for approximately 1 hour.

During the visit I, as the researcher will ask some general questions about you, such as your age and general health status and will also require your permission to access your medical history. Should you choose to participate, you will be randomly assigned to one of the two groups. If you happen to be in the first group you will be monitored for any foot complications, every 4 months for over a period of 1 year, whilst receiving the planned standard care of that is usually provided by the hospital/health center.
If you happen to be in the second group, the pressures of the soles of your feet will be measured using a non-invasive, in-shoe pressure and temperature mapping device that was designed specifically for this study. Pressures and temperatures will be measured while you are walking across a 10-meter walkway at your comfortable pace, first without your already provided orthoses (insoles) than with orthoses. This will be done to check whether the orthoses provided to you are indeed reducing the pressure from the site of your previous ulcer. It is possible, that in cases where your orthoses are found not adequately reducing the amount of pressure, they will be adapted and modified (free of charge) until the desired pressures are obtained.

Last but not least, while measuring your plantar pressures, temperature readings will also be recorded via an embedded temperature sensor within the device. This will help us understand whether there is a correlation between skin temperature and ulcer formation. An information that will be valuable for preventing ulceration in the high-risk diabetic foot.

Like with the first group, participants allocated in the second group will also be monitored every 4 months for 1 year to check for any foot complication and further modification or change of orthoses where needed. Each visit should not take longer than 1 hour of your time. Temperature readings will continue to be recorded so that its relationship to ulcer formation will be investigated.

You are not obliged to participate in this study or to answer all the questions and you may withdraw from the study at any time without giving a reason. Furthermore, withdrawal from the study will not have any negative repercussions on you and any data collected will be erased. Data will be stored anonymously if it is impossible to

delete (e.g. if it has already been anonymized). Your responses will be not be audio recorded but the data will be written on the prepared record forms. I can assure you that confidentiality will be maintained throughout the study and that your identity and personal information will not be revealed in any publications, reports or presentations arising from this research. All data collected will be pseudonymized meaning that the data will be assigned codes and that this data will be stored securely and separately from any codes and personal data.

This data may only be accessed by the researcher. The academic supervisor/s and the examiners will typically have access to coded data only. There may be exceptional circumstances which allow the supervisor and examiners to have access to personal data too, for verification purposes. The coded data files will be stored on the researcher`s personal computer that is password protected and in an encrypted format. Any material in hard-copy form will be placed in a locked cupboard.
In the event that you feel distressed due to participation in this study the service of a healthcare professional, the Richmond Foundation, will be available to offer you counselling/psychological support at no financial cost on your part. Richmond Foundation can be contacted on freephone number 1770.

Participation in this study is completely voluntary and you are free to accept or refuse to take part without giving a reason. A copy of the information sheet and consent form will be provided for future reference. As a participant, you have the right, under the General Data Protection Regulation (GDPR) and national legislation that implements and further specifies the relevant provisions of said regulation, to access, rectify and where applicable ask for the data concerning you to be erased. Once the study is completed and the results are published, the data will be retained in anonymous form. Any personal details will be destroyed. This study has been approved by the Research Ethics Committee of the Faculty of Health Sciences at the University of Malta.

Thank you for your time and consideration. Should you have any questions or concerns do not hesitate to contact me on 99839623 or by e-mail claire.saliba-thorne08@um.edu.mt or my supervisors Professor Cynthia Formosa 23401838 or via email: cynthia.formosa@um.edu.mt or Dr Alfred Gatt 23401153 or via email alfred.gatt@um.edu.mt.

Yours Sincerely,

Claire Saliba Thorne
Researcher

Professor Cynthia Formosa
Research Supervisor

Appendix 14 | Consent Form for Participants

L-Università ta' Malta

Participants` Consent Form

"Single sensor pressure and temperature mapping device for the prevention of diabetic foot re-ulceration"

I, the undersigned, give my consent to take part in the study conducted by Claire Saliba Thorne. The purpose of this document is to specify the terms of my participation in this research study.

1. I have been given written and verbal information about the purpose of the study and all questions have been answered.
2. I understand that I have been invited to participate in a study, in which the researcher will ask questions, access my medical history and perform tests to investigate whether a specifically designed pressure and temperature mapping system is effective in reducing ulceration and/or re-ulceration in a high-risk diabetic population, when compared with standard care currently being given.
3. I am aware that the meeting will take approximately one hour. I understand that the meeting is to be conducted in at the Biomechanics Lab, Podiatry Department, Faculty of Health Sciences and at a time that is convenient for me.
4. I am aware that my responses will be not be audio recorded but the data will be written on the prepared record forms.
5. I am aware that the data collected will be coded and that this data will be stored securely and separately from any codes and personal data.
6. I am aware that the researcher is the only person who has access to this data. The academic supervisor/s and examiners will typically have access to coded

data only. There may be exceptional circumstances which allow the supervisor and examiners to have access to personal data too, for verification purposes.

7. I am also aware that the coded data files will be stored on the researcher`s personal computer that is password protected and in an encrypted format. Any material in hard-copy form will be placed in a locked cupboard and kept until results are published.
8. I am aware that my identity and personal information will not be revealed in any publications, reports or presentations arising from this research.
9. I also understand that I am free to accept, refuse or stop participation at any time without giving any reason. This will have no negative repercussions on myself and that any data collected form me will be erased. Data will be stored anonymously if it is impossible to delete (e.g. if it has already been anonymized).
10. I also understand that my contribution will serve to help in gaining a better understanding about on how foot ulceration can be predicted prior it forms by utilizing the aforementioned techniques. This will not only avoid the further diabetic foot complication but may avoid lower limb amputations and reduce the mortality rate.
11. Though no risks are associated with this study, if I feel distressed as a result of participation in this study the Richmond Foundation will be available to provide a counselling/psychological service at no financial costs on my part.
12. I understand that under the General Data Protection Regulation (GDPR) and national legislation that implements and further specifies the relevant provisions of said regulation, I have the right to access, rectify, and where applicable ask for the data concerning me to be erased.
13. I also understand that once the study is completed and results are published the data will be retained in anonymous form. Any personal details will be destroyed.
14. I will be provided with a copy of the information letter and consent form for future reference.

15. I have read and understood the points and statements of this form. I have had all the questions answered to my satisfaction, and I agree to participate in this study.

Participant: _____

Signature: _____

Date: _____

Claire Saliba Thorne	**Professor Cynthia Formosa**
Researcher	Research Supervisor
99839623	**23401838**
claire.saliba-thorne08@um.edu.mt	**cynthia.formosa@um.edu.mt**

Appendix 15 | Data Assessment Sheet Used to Obtain Demographics of Participants

Assessment Sheet

Identification Code: _____

General Information

Gender: Male/Female

Age: _____

Weight: _____ Kg

Height: _____m

Body Mass Index (BMI): _____

Medical History

Medical Conditions:

Medication:

HBA1c (within the year):

Biomechanics:

FPI: _____

Foot type: _____

Walks: unaided Yes/No Aided: Yes/No _____

Knee width: _____

Ankle width: _____

Limb Length: _____

Functional Hallux Limitus: Yes/No

Hallux Rigidus: Yes/No

Plantarflexed first ray: Yes/No

Foot Posture Index: Pronated/Supinated/Neutral

Joint Ranges of Motion (ROM):

Subtalar Joint (STJ) _____

Midtarsal Joint (MTJ) _____

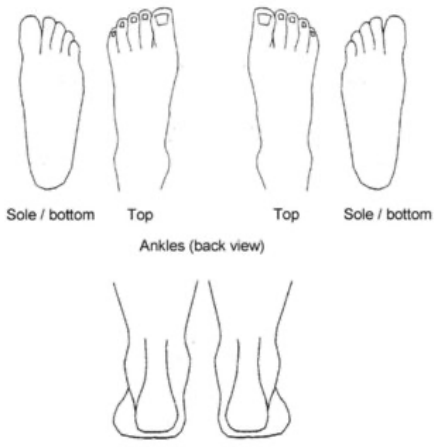
Transverse _____
Oblique _____

Description of Orthoses:

_____

_____

Location of Previous Ulceration:



Appendix 16 | Independent Sample t-Test Result to Confirm Matching based on Age and Duration of DM

Independent t-Test Results for Age:

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
Age	Control Group	44	67.77	10.120	1.526
	Experimental Group	44	68.05	9.233	1.392

Independent Samples Test

		Levene's Test for Equality of Variances			
				Significance	
		F	Sig.	One-Sided p	Two-Sided p
Age	Equal variances assumed	.514	.476	.448	.895

Independent t-Test Results for Age:

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
Duration of DM	Control Group	44	18.9091	9.72845	1.46662
	Experimental Group	44	18.6136	9.74373	1.46892

Independent Samples Test

		Levene's Test for Equality of Variances			
				Significance	
		F	Sig.	One-Sided p	Two-Sided p
Duration of DM	Equal variances assumed	.015	.902	.444	.887