Heel Pressure Ulcers: a study of wound healing

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Intellectual Property and Publication Statements

The candidate confirms that the work submitted is her own, except where work which has formed part of jointly-authored publications has been included. The contribution of the candidate and the other authors to this work has been explicitly indicated below. The candidate confirms that appropriate credit has been given within the thesis where reference has been made to the work of others.

The systematic review was co-authored by Nikki Stubbs, Lead Nurse, Tissue Viability, Leeds Community Healthcare. My own contributions, fully and explicitly indicated in the thesis, have been the writing of the protocol, the development of the search strategy, the selection of studies from the list of titles and abstracts, the assessment of each study for inclusion according to the selection criteria, the production of the data extraction sheet, data extraction, identification of the included study, the analysis including the assessment of bias and the writing of the review and is the guarantor of the review.

The co-authors contribution was to proof read and approve the protocol, collaborating on the development of the search strategy, the selection of studies from the list of titles and abstracts, the assessment of each study for inclusion according to the selection criteria, data extraction, contacting experts in the field and authors of retrieved studies for details of study data specific to heel pressure ulcers and missing data, identification of the included study, proof reading and approving the review.

A senior podiatrist (Linda Gregory) and Cochrane Wounds Group staff also contributed to the development of the search strategy. The strategy was run by a member of the Cochrane Wounds Group.

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Permissions

Permission to use images of body positions (figure 1.1) low air loss mattress (figure 3.2b), air fluidised bead bed (figure 3.2c) and the mechanism of an alternating mattress (figure 3.3) have been granted from Huntleigh Healthcare.

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Abstract

Background

Heels are a common location for pressure ulcers (PUs); they may be physiologically different to other PU sites and their healing is poorly understood.

Aim

To summarise the effects of support surfaces and identify prognostic factors in healing heel PUs.

Objectives

1. Review the effects of support surfaces for heel PU healing
2. Identify factors which independently impact on heel PU healing
3. Describe the characteristics of patients, current management practices and progress of heel PUs

Methods

Systematic review of the evidence of effectiveness for pressure relieving devices in the treatment of heel PUs.

Prospective cohort study of patients with heel PUs ≥ Grade 2 in an acute hospital and followed for 18 months or up till healed.

Results

Systematic review identified 467 potentially relevant articles, retrieved 70 for screening and included 1in a narrative synthesis. No recommendations for practice could be made.

Cohort study recruited 140 people with 183 heel ulcers. 77 (42%) ulcers healed, 88 (48%) did not heal due to death, 5 (3%) were on limbs subsequently amputated, 11 (6%) were unhealed at 18 months, 2 (1%) were lost to follow-up. Cox proportional hazards models identified 12 significant ($p \leq 0.2$) variables affecting time to healing in the univariate analysis. Eight entered the multivariate model: 2 reached significance ($p \leq 0.1$): severe (cf superficial) ulcers and the presence of (cf the absence) peripheral vascular disease (PVD) reduced the chance of healing.

Ulcer area did not change in a uniform manner. Treatments e.g. support surfaces and dressings were inconsistently used. Many patients experienced non-pressure ulcer related infections during the study.

Conclusion

It is not known if support surfaces aid heel PU healing. The severity of the PU and the presence of PVD are independent prognostic factors for healing. Further work is needed to explore prognostic factors which change over time.

Contents

Figures and Tables

Glossary and Abbreviations

Aetiology The cause or causes of a disease or abnormal condition

Collinearity When two exposure variables are highly correlated they are said to be collinear

Friction The resistance that one surface or object encounters when moving over another:

Imputation Estimation of missing values in a dataset based on prior knowledge, mean or median substitution, or regression techniques

Incidence The rate of occurrence of new cases of a particular disease or condition in a population being studied

Inception cohort A designated group of persons assembled at a common time early in the development of a specific clinical disorder (e.g., at first exposure to the putative cause or at initial diagnosis), who are followed thereafter

Likelihood The probability of the observed results given the parameter estimates

Logistic regression A technique designed to determine which variables affect the probability of an event

Neuropathy This is an abnormal and usually degenerative state of the nervous system or nerves in which motor, sensory or vasomotor nerve fibres may be affected. It is marked by muscle weakness and atrophy, pain and numbness

Pathology The study of the nature of diseases and especially of the structural and functional deviations from the normal that constitute or characterise a particular disease

Pressure Pressure is the force per unit area applied in a direction perpendicular to the surface of an object.

Prevalence This is the proportion of persons with a particular disease within a given population at a given time.

Prognostic factor Demographic, disease-specific, or co-morbid characteristics associated strongly enough with a condition's outcomes to predict accurately the eventual development of those outcomes

Prospective study Study design where one or more groups (cohorts) of individuals who have not yet had the outcome event in question are monitored for the number of such events which occur over time.

Retrospective study Study design in which cases where individuals who had an outcome event in question are collected and analyzed after the outcomes have occurred

Risk factor A risk factor is a variable associated with an increased risk of developing a condition or disease in the first place

Shear A strain, or change of shape, of an elastic body, consisting of an extension in one direction, an equal compression in a perpendicular direction, with an unchanged magnitude in the third direction.

Stepwise regression Variables are entered into the equation based on their measured relationship to the dependent variable. Methods include forward entry, backward removal, and a combination of forward and backward called stepwise

Abbreviations

AP	Alternating pressure support	**NCTV**	Nurse consultant – tissue viability
CI	Confidence interval	**NPUAP**	National pressure ulcer advisory panel
CCT	Controlled clinical trial	**PU**	Pressure ulcer
CLP	Constant low pressure support	**PVD**	Peripheral vascular disease
DFU	Diabetic foot ulcer	**SD**	Standard deviation
EPUAP	European pressure ulcer advisory panel	**SE**	Standard error
LU	Leg ulcer	**TVN**	Tissue viability nurse

Dissemination and publications

The following conference presentations have been given:

3rd Congress of the World Union of Wound Healing Societies. (2008) Toronto, Canada
Poster presentation: Is the current pathophysiology evidence relevant to heel pressure ulcers?
This paper reviewed the evidence base for the effects of pressure on skin and underlying tissues and described it's relevance to the development of PUs on different body sites. Differences between data collected at heels and other sites were highlighted.

12th Annual European Pressure Ulcer Advisory Panel (2009) Amsterdam, Holland
Oral presentation: Support surfaces for the healing of heel pressure ulcers: A Cochrane Systematic Review*
This paper presented the results of the systematic review The Preferred Reporting Items for Systematic reviews and Meta-analysis (PRISMA) statement was used to present the findings of the study.

13th Annual European Pressure Ulcer Advisory Panel (2010) Birmingham, England**
Oral presentation: A review of heel ulcers by comparing the anatomy of the heel to other body sites with photographic evidence of heel ulcers to illustrate the progress of wound healing
This paper presented a review of authoritative sources on anatomy and physiology of the skin and soft tissue which had identified differences between the heels and other pressure ulcer sites. The process of wound healing was discussed in context of the anatomy and physiology of the heel. This was illustrated with photographic evidence.

Post-graduate research student conference, University of Leeds and accepted for oral presentation at the 14th Annual European Pressure Ulcer Advisory Panel meeting (2011) Oporto, Portugal:
This paper will present the findings of the prognostic factor analysis.

The Cochrane Systematic Review has been approved for inclusion in the next submission to the Cochrane Library (issue 9, 2011, publication date 7th September 2011)

*This paper was also presented at the Post-graduate research student conference, University of Leeds (2010)
**This paper was also presented at the 2011 Annual Conference of the Tissue Viability Society. Kettering, England

Chapter 1 Background

1.1 Introduction

This chapter describes what pressure ulcers are, why they are important and the size of the problem. It then explains how they develop and finally puts forward the argument that pressure ulcers on the heels are different from other body sites. Many of the papers referenced here are several decades old, these are seminal papers. Searches for more recent work have revealed no repeats of the experiments or further studies that explore their findings with other methods of investigation.

The following chapter describes how pressure ulcers develop and heal and explores risk factors for development and potential prognostic factors for healing.

1.2 What are pressure ulcers?

Pressure ulcers have been the topic of at least two international organisations, the American National Pressure Ulcer Advisory Panel (NPUAP) and the European Pressure Ulcer Advisory Panel (EPUAP). These organisations recently collaborated and have agreed a common definition for pressure ulcers:

'A pressure ulcer is a localised injury to the skin and/or underlying tissue usually over a bony prominence, as a result of pressure, or pressure in combination with shear. A number of contributing or confounding factors are also associated with pressure ulcers; the significance of these factors is yet to be elucidated' (EPUAP, 2009).

Pressure ulcers usually occur over bony prominences such as the heel and sacrum (Dealey, 1991b) where there is little soft tissue, in particular subcutaneous fat, to provide padding. They can range in severity from intact skin with persistent redness to deep cavities extending down to the bone (see section 2.4 for more details). The diagrams in figure 1.1 identify with red dots the most common sites on the body where pressure ulcers occur based on the persons position.

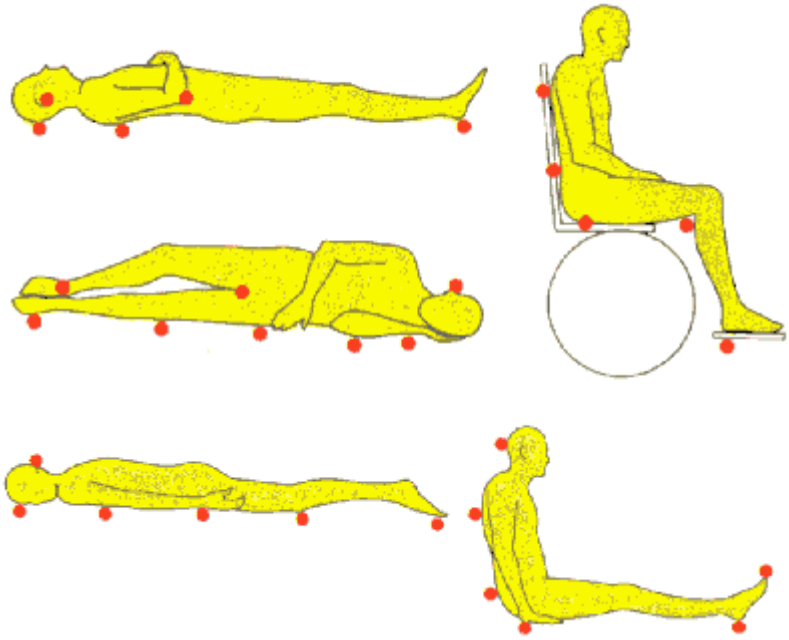

Figure 1.1 Body sites for pressure ulcers, adapted from Huntleigh Advanced Clinical Education presentation (2010)

1.2.1 What are heel pressure ulcers?

The heel is understood to be the back of the foot. The term usually refers to the lower, posterior aspect of the foot and extends around the plantar surface. It covers the apex of the calcaneum bone. Heel pressure ulcers are injuries caused by pressure and usually occur when a person is in the supine or semi-recumbent position as illustrated in figure 1.1.

1.3 Why are pressure ulcers important?

Pressure ulcers have a serious impact for the patient on their morbidity and quality of life. A systematic review by Gorecki *et al* (2009) identified the impact of pressure ulcers and pressure ulcer interventions on the health related quality of life (HRQOL) of adult patients. This review was produced by an international panel of experts; it was the first to use robust methods to synthesis the research on pressure ulcer related quality of life. The search strategy was not specifically stated but was assumed to be very broad, as the large number of studies initially identified. The systematic review identifies studies including acute, community and long term care populations. However no details are given in the review for where on the body the pressure ulcers were or the patients

underlying medical conditions. The systematic review identifies a number of themes and interventions which cause a substantial burden to patients but does not attempt to quantify them.

A study included in the Gorecki et al (2009) review, by Franks et al (2002) sets out to quantify the effects in a community population. This appeared to be a well executed study that identifies random samples of patients from District Nursing caseloads both with (cases) and without pressure ulceration (controls). The presence of pressure ulcers was confirmed by clinical examination. Patients were then assessed using the SF36 and the modified Barthel Scale. Although the study identified that patients with pressure ulcers had a significantly poorer physical and social function with a decrease in their mobility and ability to self care, than the control group, the overall findings show few demonstrable differences. A possible explanation for this could be the validity (sensitivity and specificity) of the assessment scales used with this population. It is also difficult to infer any causal relationship between the pressure ulcers and the decreased mobility as this type of study does not capture the pre-ulcer mobility. It is known that poor mobility is a risk factor for pressure ulcer development and hence it is expected that people with pressure ulcers have lower mobility than those without.

There is much debate amongst experts about whether pressure ulcers are a preventable complication (Fox, 2002). A survey of experts in the USA demonstrated divergent opinion on this issue (Brandeis, Berlowitz and Katz, 2001); personal experience of debates on this issue suggest that in an ideal world with optimal equipment and care then most pressure ulcers could be prevented. However in reality this is not achievable, therefore some pressure ulcers are inevitable. More recently in the UK the Department of Health has produced definitions of ‘avoidable’ and ‘unavoidable’ pressure ulcers based on a position paper by the Wound Ostomy and Continence Nurses Association in America (Patient-Safety-First, 2010). This suggests that if all the preventative measures that should have been done were not, then the pressure ulcer is avoidable. Likewise if the patients’ condition was evaluated, care planned and

implemented, with monitoring and evaluation, and revised plans if necessary, then the pressure ulcer is unavoidable.

Pressure ulcers are used as an indicator of quality of care, particularly in the care home setting both in the UK and the USA and as such are subject to litigation. Brandeis et al (2001) suggested that the spectrum of opinion over the appropriateness of pressure ulcers being a marker of quality supports the notion that pressure ulcer development is a complex process affected by a host of modifiable extrinsic factors, which makes prediction of risk an unreliable process.

The impact for the health care provider is also significant as there is an increased use of resources. In the UK one study carried out in 1993 the cost of preventing and treating pressure ulcers in a 600-bedded large general hospital was estimated at between £600 000 and £3 million per year (Department of Health, 1993). A more recent paper (Bennett, Dealey and Posnett, 2004) uses data from incidence and prevalence studies and trials to construct a model to estimate the cost of treating pressure ulcers. This is given as £1.4 - £2.1 billion annually (4% of total NHS expenditure). This paper has detailed explanations of the method used to derive costs. As all the data were taken from previous studies this presents several concerns over the reliability of costs which are partially acknowledged in the study:

- There is no search strategy given for the identification of studies used to calculate healing times and complication rates. It is not known if these are a reliable representation of normal healing rates.
- The data used have not fully taken into account the pressure ulcer healing rates i.e. while many ulcers heal within a few months, little is know about the duration and subsequent costs of those which take longer to heal Most studies of pressure ulcer healing use an endpoint of proportion of ulcers healed at a given point in time, there is no information on what happens to those which do not heal
- The relationship between grades; studies by Allman and Fowler (1995) and Nixon *et al.* (2007) have demonstrated a six fold increase in risk of subsequent skin breakdown of Grade 1 pressure ulcers.

- The use of trials data from intervention studies, where healing occurs in a controlled environment, may not be representative of usual care where there is greater variability.
- Despite agreed treatment regimes, the reality that compliance is difficult to achieve e.g. data collected during the PRESSURE trial (Nixon *et al.*, 2006) has indicated that not all pressure ulcers have dressings in place all the time. The implication of this would be reduced costs for dressings and nursing time, however the healing rates may be extended.

The costs calculated in this study were mostly attributed to nursing time, and increased significantly with the severity of the ulcer and the presence of complications such as infection. The costs in the study were based on institutional care. There is no information on the proportion of patients with a pressure ulcer which develops in hospital, then return to their own home and continue to receive care. Costs for domiciliary nursing visits are more per intervention than institutional costs. No account was taken of costs to the patients e.g. laundering costs, bedding, etc. It is likely that this study has underestimated the real costs of pressure ulcers.

1.4 The extent of the problem

The number of people affected by pressure ulceration can be measured through incidence and prevalence studies. Prevalence rates measure the number of people affected at a certain time or period and are given as a percentage of the population studied or at risk. Incidence rates measure the number of people who develop a new pressure ulcer during a given period of time and are also presented as a percentage of the population studied or at risk. The incidence rate gives an estimate of the probability or risk of developing a pressure ulcer, whereas the prevalence rate is dependent on the duration of ulceration and the incidence rate (adapted from Lilienfeld and Stolley (1994)). There are many prevalence and incidence studies published that show large variation in the reported rates. Some explanations for these discrepancies have been suggested via a systematic review by Kaltenthaler et al (2001):

- substitution of incidence for prevalence in analysis

- use of different classification (of the Grade or severity of the ulcer) systems
- under-reporting of pressure ulcers on transfer from different care facilities
- overestimation of prevalence data by not taking case-mix into account
- use of pressure ulcers as a measurement of quality, causing under reporting
- use of different study designs (prospective versus retrospective, observation versus chart reviews).

The inclusion or not of Grade 1 ulcers (description in section 2.4) affects the rates. Grade 1 ulcers are often excluded as they are often difficult to detect and this may lead to unreliability of their measurement (Kaltenthaler *et al.*, 2001).

It is important to know when different practitioners use a tool to assess an ulcer, that they reach a similar conclusion. Testing inter-rater reliability will identify this. Nixon *et al.* (2005) assessed the reliability of skin classification (all grades) and the presence of a pressure ulcer (defined as Grade 2 or above) between expert nurses and also between expert nurses and qualified ward-based nurses. Some of the methodological problems associated with using photographs was reduced by using a process of paired assessments of the patient's skin. They reported 100% agreement for the presence or absence of a pressure ulcer in paired assessments by experts, but noted some difficulties in the assessment of normal, blanching and non-blanching skin areas. Importantly, agreement between experts and qualified ward based nurses indicated clinically important differences in reporting the presence or absence of a pressure ulcer (ie Grade 2 and above) and high levels of under-reporting (39.7%) of Grade 1s by ward-based staff compared to experts.

DeFloor et al (2006) studied intra and inter-rater reliability between nurses assessing photographs of skin lesions and pressure ulcers and found intra-rater agreement was low (kappa = 0.38). Vanderwee et al (2006) studied nurses and researchers assessing patients and found a high level of agreement using a transparent disc (91.7%) and 'light finger pressure' (92.1%) to detect non-blanching erythema. Healey 1995, found that reliability was not good especially with the lower grades of ulcer (kappa = 0.29 for Torrance scale, kappa = 0.02

for Stirling 2 digit scale, kappa = 0.37 for Surrey. This was a small study with other limitations e.g. the use of photographs and the lack of training of observers,. Bates-Jenson *et al.* (1992) developed the Pressure Sore Status Tool, which was tested for validity and inter-rater reliability. Although this was claimed to be high initially only 2 specifically trained nurses were studied. In summary, if the tool used to assess the presence of a pressure ulcer or not and the grade of the ulcer is not reliable then the interpretation of the results from a prevalence or incidence study must be considered with caution.

Studies cited in the Kaltenthaler review have a range of prevalence in UK healthcare settings from 4.4% (Hallett, 1996) by a postal survey in a community setting to 37% by patient examination in a palliative care setting (Hatcliffe and Dawe, 1996). Incidence rates cited range from 2.2% (Bridel, Banks and Milton, 1996) in a year by medical record examination of a hospital population to 66% in 18 months by examination of elderly hip fracture patients (Versluysen, 1985).

These findings confirm as expected that prevalence and incidence are higher when the populations studied are more at risk e.g. in settings where patients are higher acuity and immobile, and where direct observation is used rather than record reviews or self reports. Case mix is suggested by Kaltenthaler *et al.* (2001) as a factor contributing to the variation; a study by Bours (2003) proposed a model for case mix adjustment for prevalence studies, taking into account factors such as age, sex, nutrition, incontinence. If modelling was used to standardise data then useful comparative measures could be obtained. A significant cause of variation in the data is due to information being collected using secondary sources rather than by patient examination (Kaltenthaler *et al.*, 2001).

If it is acknowledged that pressure ulcers are mostly a preventable complication with prevalence rates up to 18% in UK hospital populations (O'Dea, 1993) and costs estimated at up to £2.1 billion annually then it is useful to compare them alongside other hospital or health facility complications in terms of scale, importance and impact. These include drug errors, hospital acquired infections, deep vein thrombosis, pulmonary embolism, etc. If the case of hospital

acquired infection (HAI), which has been the subject of much media attention in recent years, is compared, prevalence rates for HAI are quoted in the second national prevalence survey as 9% (Emmerson et al 1996) with the preliminary results from the third national survey carried out in 2006 similar at 8.19% (HIS & ICNA, 2007) with an estimated cost of £1 billion per annum (The Patients Association, 2010). However this information is interpreted, there is a clear indication that pressure ulcers present a significant problem in most healthcare settings.

1.4.1 The extent of the heel pressure ulcer problem

Heel pressure ulcers are mentioned in incidence and prevalence surveys but precise numbers for given populations are not well recorded. Studies which have included separate data for heel pressure ulcer prevalence are given in table 1.1. The numbers given are 'number of patients with at least one pressure ulcer' of the 'total population surveyed'. The discrepancies described by Kaltenthaler (2001) also apply to this data.

Study	Population	Prevalence of all patients with PUs (%)	Prevalence of heel PUs (% of all PUs)
Pearson *et al.* (2000)	Acute care hospital patients in Australia	40/634 (6%)	38%
Garber & Rintala (2003)	Spinal cord injured US veterans living at home	215/553 (39%)*	26%**
Baumgarten *et al* (2003)	Newly admitted long term care facility residents in US	208/2015 (10.3%)	24.2%*
Vanderwee (2007)	Acute hospital patients in Italy, Belgium, Portugal, Sweden and UK	1078/5947 (18.1%)	26%

* Three year period prevalence

** Pressure ulcers on feet: includes malleolli and other sites

Table 1.1 Pressure ulcer prevalence surveys with proportion of pressure ulcers which are on the heel

Within the researcher's organisation the numbers are known for recent years as a point prevalence survey is carried out annually. The total number of pressure ulcers is given for one day in the year. These are given in table 1.2.

Year	Total number of patients with PUs (% of all in-patients at the time of the survey)	Total number of heel PUs (% of all PUs)
2006	274 (9.9%)	60 (22%)
2007	333 (12%)	85 (26%)
2008	336 (11.9%)	74 (22%)
2009	557 (12.9%)	107 (19%)
2010	372 (13.5%)	83 (22%)

Table 1.2 Prevalence of heel pressure ulcers in one acute NHS Trust

One study in the US suggests that prevalence of heel pressure ulcers is increasing (Barczak *et al.*, 1997). Two studies have been identified which specifically studied heel pressure ulcers. Monaghan *et al.* (2000) surveyed an acute hospital population in the UK and found a prevalence of heel pressure ulcers of 1.2% (28 of 2314 patients surveyed). This is low, however the population included paediatrics, maternity and a mental health hospital (these areas are usually excluded in acute hospital population based prevalence studies as the likelihood of pressure ulcers in these specialities is very low) and was based on staff report and record review. Campbell *et al* (2010) in a Canadian study of 150 elective orthopaedic and acute hip fracture surgical patients found and an incidence of heel pressure ulcers of 13.3%.

1.5 Duration of pressure ulcers

Information on healing times can be derived from trials of treatment interventions or epidemiological studies. There is a lack of precise information on time to healing, most studies (interventions or epidemiological) do not follow up to complete ulcer healing. There are several possible explanations for this:

- these wounds can take months/ years or never heal
- many patients die before their pressure ulcers heal

- trial follow-up is not long enough to capture healing of all ulcers

Bennett et al (2004) used the results from 15 trials of pressure ulcer treatments to calculate expected healing rates for the different grades of ulcers. They suggest mean time to heal for Grade 1 ulcers as 4.06 weeks, Grade 2 ulcers as 13.4 weeks, Grade 3 as 18.2 weeks and Grade 4 as 22.1 weeks. The studies cited vary in length from 4-52 weeks and none of the studies had 100% healing; no information is given regarding the study populations, the site of the ulcers e.g. sacrum or heel, or whether the remaining ulcers were unhealed or the patients died. It is unclear how the mean healing times were calculated; this information was not available in the original studies (and could not be calculated as healing times were not available for all the ulcers). These results may not be generalisable as clinical trials may not be pragmatic i.e. represent the 'normal' clinical situation: certain patients will be excluded (e.g. those with diabetes, those unable or unwilling to consent, patients who do not conform to treatment); patients are being monitored so are more likely to receive the planned treatment (dressings applied do not always conform to the care plan, dressings which 'fall off' are not always replaced immediately). The NICE guideline CG29 (RCN, 2005) summarises all intervention studies for pressure ulcer healing known at the time, none of which use time to healing as the primary endpoint.

There are very few prospective cohort studies which look at healing of pressure ulcers. This issue is acknowledged by Brown (2003) as the missing component of pressure ulcer quality assurance data. A prospective study has been identified whose primary aim was to validate a Pressure Ulcer Scale for Healing (PUSH) (Thomas *et al.*, 1997). The study population was 23 long term care home residents in the USA. Data were collected for 6 months and 21 (66%) of the ulcers healed in mean of 5.6 weeks to closure (SD +/- 4.08) with a range of 2 - 18 weeks.

Two studies have been identified which carried out a retrospective analysis of medical records:

- Garber and Rintala (2003) studied a cohort of inpatients at a Veterans Affairs Medical Centre but specifically looked at those on the Spinal Cord Registry. Outcomes were defined as the result of pressure ulcer treatment during that year. These were determined from the medical records from the time the ulcer first appeared in the first year of the study to either healing or the end of the study. Of the 102 patients studied 23 healed, 54 did not heal, 11 were surgically repaired and 14 were unknown. Duration was reported to be between one week and the entire 3 year duration of the study.
- Brown (2000) investigated the healing rates of 10 stage 4 pressure ulcers of the pelvic area on patients in a Veteran Affairs transitional care unit. They found healing times of 90-150 days. This study focused on healing trajectories and the relationship between wound area and healing rates and only selected patients whose ulcers had completely healed.

This suggests that data on healing times which only includes patients whose ulcers completely heal are likely to be an underestimate of the true average healing times.

1.5.1 Duration of heel pressure ulcers

A search for heel ulcer studies which state time to healing has revealed a single case study (Clarkson, 2003). This was a patient who had a necrotic heel pressure ulcer which, although the patient had an episode of infection, healed in six months.

1.6 Anatomy and physiology

An understanding of the structure and function of the tissues involved in pressure ulcer development will enhance an understanding of how they occur.

1.6.1 The skin

Structurally the skin consists of 2 layers: the epidermis and the dermis. Underneath the dermis is the subcutaneous layer, which in turn is attached to the underlying tissues and organs (depending on the body site).

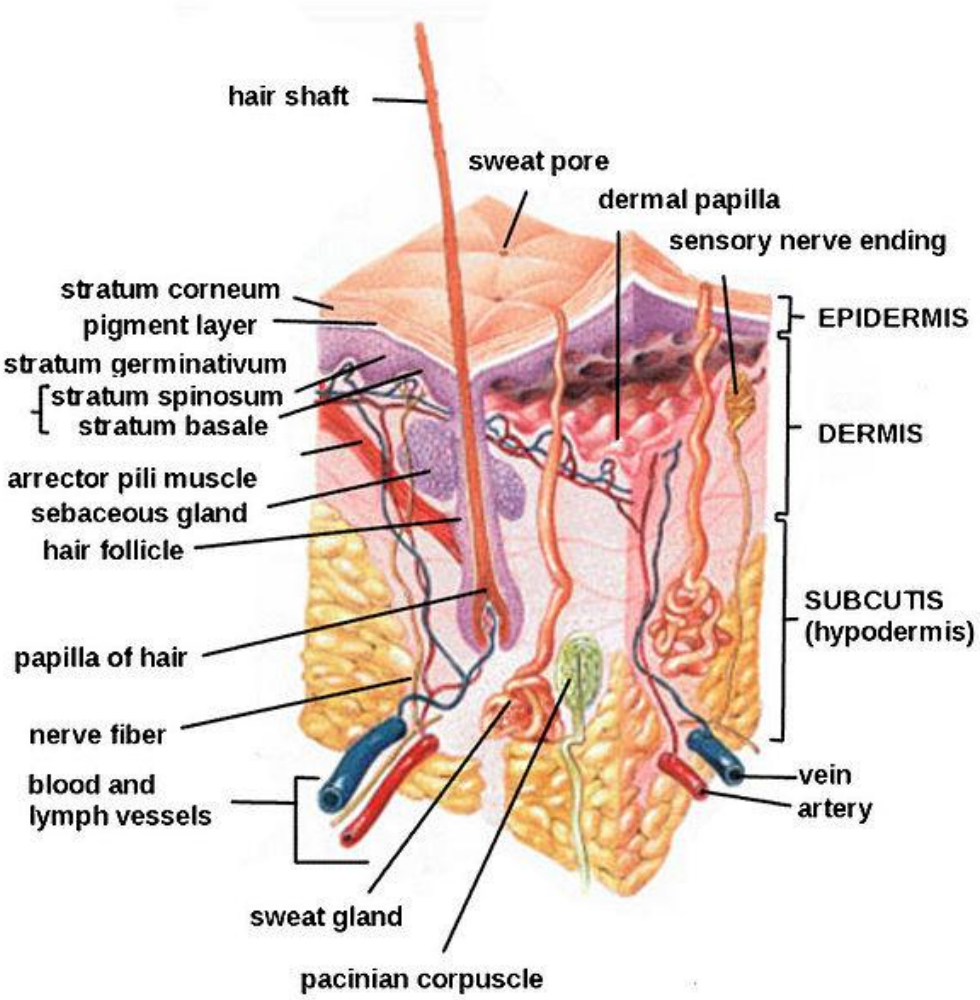

Figure 1.2 Structure of the skin

http://en.wikipedia.org/wiki/File:HumanSkinDiagram.jpg accessed 5.12.11

Epidermis

The epidermis is composed of 5 layers or strata, the outer layer being flat dead cells that are constantly shedding (stratum corneum). The next layer is the stratum lucidum, which is more apparent in thick hairless skin e.g. palms and soles. The next layer is the stratum granulosum, this is the layer where keratin is formed. This gives the skin its waterproof and bacterial resistant properties. Underneath this sits the stratum spinosum, which have layers of cells with prickly spines. The inner layer is the reproductive membrane (stratum germinativum) that generates the keratinocytes which then migrate through to the outer surface (Tortora and Grabowski, 1996).

Dermis

The dermis is composed of connective tissue containing cells, ground substance and fibres. The few cells in the dermis include fibroblasts, macrophages, plasma cells, adipocytes and mast cells (Tortora and Grabowski, 1996).

Collagen and elastic fibres contribute to the skins protection against mechanical damage. Within the deeper layers of the dermis, the collagen fibres are wrapped around with elastic fibres so that following extension, the elastic fibres are able to contract to return the tissue to normal. Studies have shown that tissue subject to initial high pressures has a good recovery rate, but periods of high pressure lead to realignment of the collagen and elastic fibres into parallel bundles (Edsberg *et al.*, 2001). However, as the tissue adapts to abnormal loading it is seen to have fewer but thicker collagen and elastic fibres (Edsberg *et al.*, 2000).

The varying thickness of the reticular region of the dermis accounts for the differences in the thickness of the skin. The reticular region is attached to the underlying tissue e.g. bone or muscle by the subcutaneous layer or hypodermis (Tortora and Grabowski, 1996).

1.6.2 Fascia

Two types of fascia are found: superficial and deep.

The superficial fascia lies immediately under the skin and contains varying degrees of areolar or fatty tissue depending on the site and the individual; it also connects the skin with the deep fascia (Tortora and Grabowski, 1996). Descriptions of the superficial fascia are sparse within general anatomy text books although some detail is provided in studies where the author's interests are in correction of deformities i.e. plastic surgeons. A study by Abu-Hijleh et al (2006) describes the superficial fascia containing the fatty tissue or panniculus adiposus. The nerves, blood vessels and lymphatics pass through this to the skin. In certain areas of the body it contains muscles e.g. facial and subareolar muscle of the nipple. It is also traversed by strong connective tissue bands

which bind the skin to the underlying aponeurosis of the scalp, palm and sole of the feet. Although this study confirmed the presence and thickness of a membranous fascia in areas of the body studied e.g. thigh, abdominal wall, leg, dorsum of foot and arm, these areas are not sites for pressure ulcer development.

The deep fascia covers or encloses either muscle layers or bone depending on the location. The strength of the fascia adds to the protection from damage of the underlying tissue. The deep fascia consists of predominantly collagen fibres to provide strength (Tortora and Grabowski, 1996).

1.6.3 Subcutaneous tissue

This is contained in the superficial fascia. It is made up of areolar connective and adipose tissue as well as some sensory nerve endings called lamellated or Pacinian corpuscles that are sensitive to pressure. In adults, adipose tissue contains relatively few blood vessels; its main function is insulation, energy reserve and protection. The depth and type of the subcutaneous tissue depends on body location, gender and body type. Soft adipose tissue forms an almost continuous layer under the skin. These fat cells are enmeshed in a loose fibrous tissue network with large amounts of tissue fluid and a rich network of blood vessels and lymphatics. The tissue can be distorted easily and slowly regains its shape through the pressure of the tissue fluid. Elastic adipose tissue however, is fibrous and firm and able to withstand sudden impacts or prolonged pressure. It is found in areas such as the heels, fingertips, and ischial tuberosities (Tortora and Grabowski, 1996).

1.6.4 Blood supply

The blood supply to the skin varies according to the region of the body and the age of the individual. The richness of the blood supply is usually attributed to its thermoregulatory function rather than the nutritional demands of the organ. Ryan, however points out that the blood supply also contributes to the swelling pressures of the ground substance, which promotes resilience, and turgor of the skin (Ryan, 1969). The arteries and veins are found in the subcutaneous layer and these produce capillary loops, which extend into the dermis.

1.6.5 Muscle

Of the common sites for pressure ulcer development, muscle is only found overlying the ischial tuberosities (Linder-Ganz *et al.*, 2008). Much work has been carried out studying the effects of pressure on muscle tissue both in animals and humans. It is important to note that these studies can only be generalised to pressure ulcers on this body site. See tables1.4-1.6 for a summary of studies.

1.6.6 Bone

The shape of the underlying bone predisposes certain weight bearing body sites to increased pressure. Most of these sites have several things in common: they are protruding parts of the body through which the weight of the body is transferred to the support surface (depending on the position and posture of the body), there is a generally a lack of soft tissue (e.g. muscle, adipose) between the bone and the skin, and the contour of the underlying bony structure has a small, curved surface area.

The most common body sites are presented here:

Sacrum (bottom of the spine)

The sacrum consists of a bony plate at the base of the spine with almost no muscle cover. The crista mediana (medial sacral crest) is a spur or prominence on the sacrum where the pressure ulcer usually starts. This section has a small surface area, and hence pressure may be high when moderate external forces are applied (see glossary for definition of pressure). It is the point at which the greatest force intensity is applied when a body is supported on an inclined surface (semi-recumbent position in bed or chair) (Bader, Barnhill and Ryan, 1986).

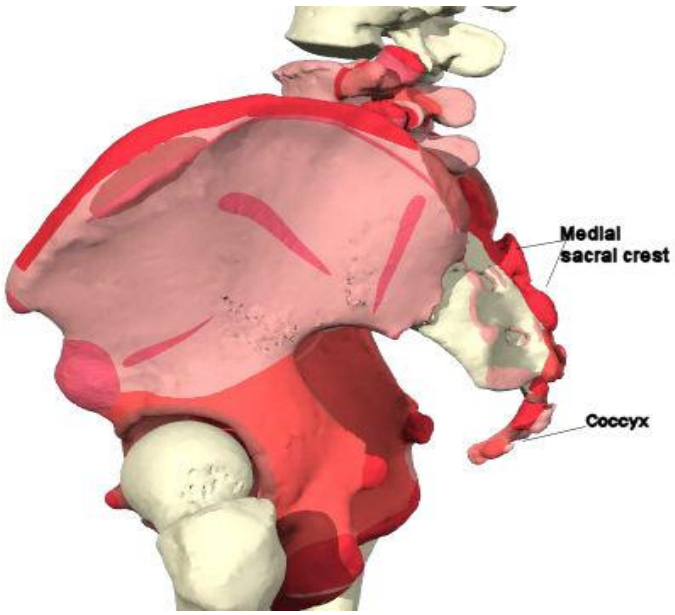

Figure 1.3 Bones of the sacrum illustrating the medial sacral crest

www.primalpictures.com accessed 5.12.11

Ischial tuberosities (buttocks)

Ischial tuberosities are the names given to two small bony triangular eminences at the lower edge of the pelvis, they are points of the skeleton at which the body weight is supported when seated. These points provide the attachment for several muscles including the Levator ani, the pelvic fascia and the sacrospinous ligament, which support the structures inside the pelvis. They are partially protected externally by the gluteus maximus muscle layers.

Figure 1.4 The hip bone illustrating the ischial tuberosity

www.primalpictures.com accessed 5.12.11

Greater trochanter (hip)

The greater trochanter is the bony prominence at the proximal end of the femur. It provides attachment for the muscles of the buttocks (gluteal muscles) and those of the thigh (vasti muscles) but is not itself protected by muscle (Tortora and Grabowski, 1996).

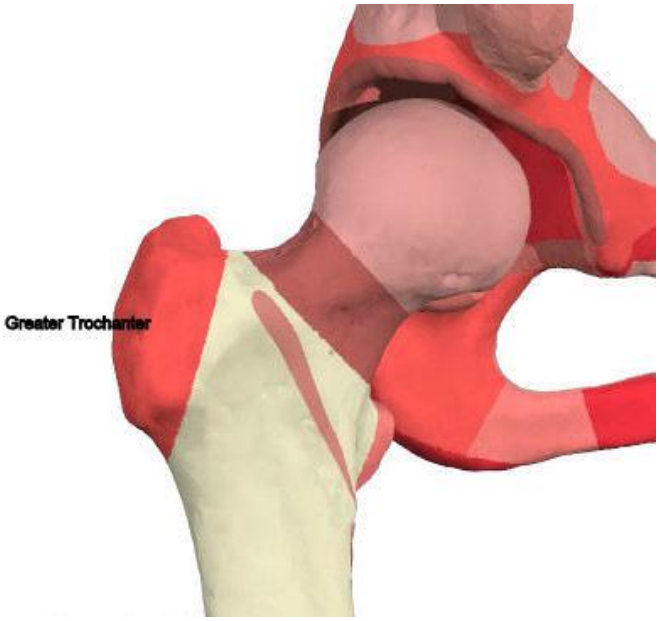

Figure 1.5 The greater trochanter

www.primalpictures.com accessed 5.12.11

Lateral malleolus (outer ankle)

The lateral malleolus or ankle is a bony prominence at the lower end of the fibula. It provides attachment for talofibular and calcaneofibular ligaments, but is not covered by muscles (Tortora and Grabowski, 1996).

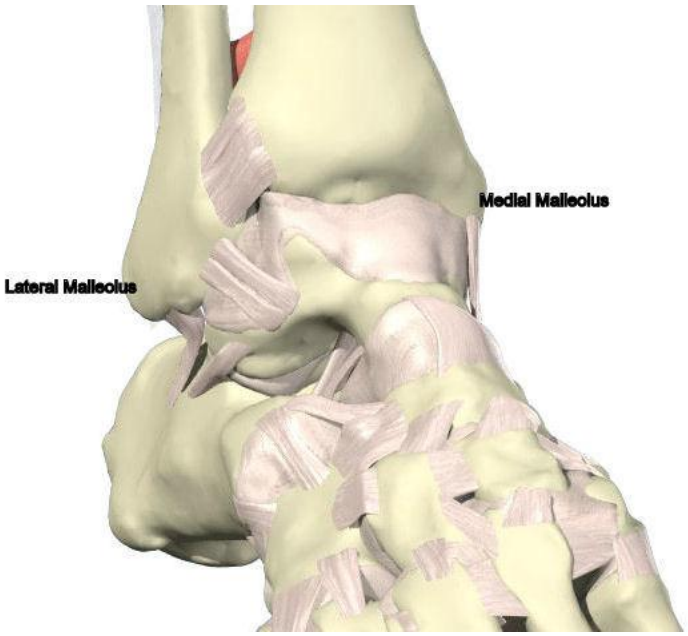

Figure 1.6 The lateral malleolus and associated bones and ligaments

www.primalpictures.com accessed 5.12.11

Calcaneum (heel)

The calcaneum is the bone of the heel. It has a tuberosity at its most prominent point where the plantar aponeurosis (thick fascia, along the sole of the foot) and the tendo calcaneous (Achilles tendon) are attached; this also has no muscle overlying (Tortora and Grabowski, 1996).

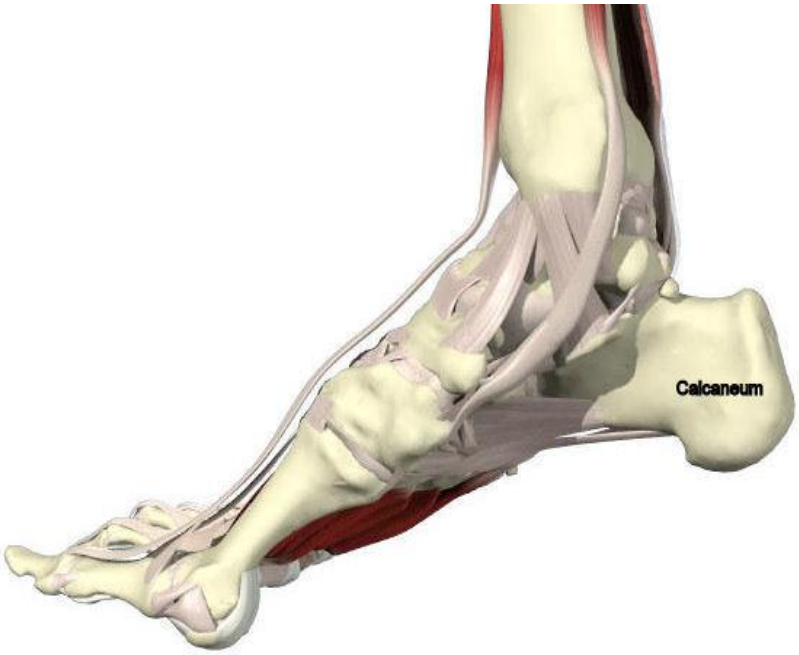

Figure 1.7 The calcaneum bone and the ligaments of the foot

www.primalpictures.com accessed 5.12.11

All these bony sites described act as anchor points for muscles via the tendons and aponeuroses. These are inelastic fibres that are composed of albuminoid collagen, which are sparingly supplied with blood vessels (Tortora and Grabowski, 1996).

1.6.7 Bursa

A bursa is small pad situated over a bony prominence. Bursae are sacs filled with synovial fluid and help with cushioning between bones, muscles, tendons. Of the pressure ulcer sites they are found on the ischial tuberosities, trochanter head and calcaneum (Tortora and Grabowski, 1996).

1.6.8 The anatomy and physiology of the heel

The above section has identified that variations exist with different body sites. Table 1.3 highlights some of the specific anatomic differences noted between the heel and other body sites.

Tissue type	Feet/ Heels	Other sites	Comment
Epidermis	Thicker stratum lucidum (1.4mm)	Average thickness of stratum lucidum is 0.1mm	Appears thicker but looks transparent over heel
Dermis Reticular region	Reticular region 3 mm or more thick	Varying thickness across body but much less than plantar surface of feet	High number of collagen and elastic fibres in heel reticular region allow extensibility and elasticity
Sebaceous glands	Absent	Present	No natural lubrication to keep skin supple
Eccrine sweat glands	Abundant	Reduced or absent	Sweat assists with temperature regulation
Hair follicles	Absent	Present, but depends on site	
Subcutaneous tissue	Elastic adipose tissue found under heels: fibrous and firm, able to withstand sudden impact or prolonged pressure	Soft adipose tissue is enmeshed in loose fibrous tissue, can be distorted easily and slowly regains shape	Elastic adipose tissue also found under ischeal tuberosities
	Abundance of Pacinian corpuscles to identify pressure	Sparse Pacinian corpuscles in most areas	

Blood supply	Rich blood supply	Varied depending on body site	Contributes to the swelling pressures of the ground substance which promotes resilience and turgor of skin
Nerve supply	Rich nerve supply	Varied depending on body site	
Muscle	No muscle over calcaneum	Muscle partially covers ischeal tuberosities when seated	Trochanter, sacrum and malleolli also have no muscle cover
Tendons and aponeuroses	Attached and partly covering the calcaneum	Also have some tendons and aponeuroses	Inelastic fibres composed of collagen, sparingly supplied with blood vessels
Superficial fascia	Dense over the heel and contains loculi of fat in the fascial pockets (makes skin firm and resilient)	Contains varying degrees of areolar tissue	Connects the skin with the deep fascia (the deep fascia generally encloses the muscles)
Deep fascia	Thickened over heel	Usually encloses muscles	Thickened fascia offers extra protection from pressure and shear

(adapted from Tortora and Grabowski (1996)

Table 1.3 Summary of differences between the anatomy and physiology of heel and other body sites

1.7 Aetiology: How do they develop?

Injuries due to pressure can affect any tissues of the body. However damage to soft tissue occurs more easily than to bone due to the relative resistance of the structures. Damage to internal organs due to external forces is also less likely as they are mostly protected by bony structures or muscle. The use of the term

‘pressure ulcer’ is usually restricted to injuries of the skin and subcutaneous tissue.

The external forces that are applied to the body which cause pressure ulceration are defined as pressure, shear and friction. In terms of the effects on the structure and function of soft tissues these will be considered separately although in a clinical situation shearing and friction cannot cause damage without pressure.

The incidence and prevalence of pressure ulcers have changed very little in recent years despite considerable advances in devices designed to offload the pressure. Some experts would justify this with the lack of knowledge of the aetiology of their development. A review of the evidence identifies many gaps in our understanding of the pathophysiology.

1.7.1 Pressure

Direct or localised pressure, occurring at the interface between the body and a support surface e.g. a bed or chair, due to the weight of the body and gravity will compress any skin and soft tissue found between the bone (hard resistant surface) and the external surface.

The effect of pressure on tissues has been studied extensively but not systematically. Tables 1.4 – 1.6 summarise some examples of some of the seminal studies, which are cited as evidence of our understanding of the effects of pressure.

Study	Type of cell/ tissue	Outcome measure	Method of testing	Findings
Compressive deformation and damage of muscle cell subpopulations in a model system (Bouten *et al.*, 2001)	Seeded mouse skeletal myoblasts cells grown in an agarose construct to grow myoblasts with multinucleated myotubes	Deformation index - Visual assessment and measurement of deformation using confocal microscopy	Cell damage assessed from evidence of membrane disruption or nuclear pyknosis or fragmentation calculated as % of damaged cells per total number of cells	Myoblasts and myotubes showed significant difference in deformation at 20% strain but less difference at 40% strain Cell damage was significantly higher in strained constructs than controls
The etiology of pressure ulcers: skin deep or muscle bound? (Bouten *et al.*, 2003)	Seeded skeletal muscle cells	Evidence of nuclear or membrane damage	Bespoke loading apparatus	Cell damage increases with the magnitude and duration of pressure
An *in vitro* model system to study the damaging effects of prolonged mechanical loading of the epidermis (Bronneberg *et al.*, 2006)	Engineered human epidermis equivalent	Histological examination, viability of cells (mitochondrial function) and the release of a pro-inflammatory mediator	Bespoke loading apparatus	2 hour loading increased inflammatory markers but no visible damage. 20 hours loading gave visible tissue damage and reduced cell viability

Table 1.4 *In vitro* studies of the effects of pressure

Study	Type of cell or tissue	Subject description	Outcome measure	Method of testing	Findings
Etiology and pathology of ischemic ulcers (Kosiak, 1959)	Soft tissue over the femoral trochanter or ischial tuberosity	Healthy dogs	Blood tests (haemoglobin, heamatocrit, sedimentation rate, serum proteins)	Air driven piston monitored with pressure adjustment mechanism	Time plotted against pressure produced a parabolic curve correlation showing an inverse relationship No correlation with nutritional status was found Microscopic examination suggests changes due to pressure occur in tissues at all depths to bone
Etiologic factors in pressure sores: an experimental model (Daniel, Priest and Wheatley, 1981)	Soft tissue over the femoral trochanter (skin, adipose, fascia lata, muscle)	Healthy pigs	Photo and visual assessment of incisional cross section of tissue. Visual histological analysis. 7 days post injury	Electromechanical pressure applicator on an immobile animal	Muscle damage: high pressure short duration or low pressure long duration (no damage visible externally) Muscle and deep dermis damage: high pressure long duration or low pressure prolonged duration (no damage visible externally) Muscle and skin damage: long duration (visible skin lesion)

Etiologic factors in pressure sores: an experimental model (Daniel, Priest and Wheatley, 1981)	Soft tissue over the femoral trochanter (skin, adipose, fascia lata, muscle)	Paraplegic pigs	Not stated	Not stated	'significant diminution of the pressure-duration threshold'
Ischemia-reperfusion injury in chronic pressure ulcer formation: a skin model in the rat (Peirce, Skalak and Rodeheaver, 2000)	Skin on the back	Healthy rats	Skin blood flow, % necrosis, trans-cutaneous oxygen tension, leucocyte extravasation	Implanted steel sheet under the skin, pressure applied via a magnet Laser Doppler flow meter, digital photographic analysis, Dual Channel Monitor, full thickness skin biopsies	Results suggest that extent of tissue damage was attributable to total number of ischaemia/ reperfusion cycles, duration of ischaemia, and the cycle frequency, not all results supported this but the authors explained it through the testing procedure. (blood flow was measured over the whole of the wound surface - reading of 0 when necrosed, $TcPO_2$ was taken part way along the surface)

Pressure sores - the problem (Brand, 2006)	Foot pad	Healthy rats	Histological examination upon autopsy	'Walking simulator' applying repeated pressures of 1.5kg/cm^2	Greater no. of repetitions led to greater temp. differential and longer to return to normal Stress (repeated daily applications of pressure) led to increase oedema, inflammation, cell separation in epidermis and then subcutis necrosis and adjacent hypertrophy Less 'stress' (lower pressures applied daily for 6 weeks with weekend breaks) led to hypertrophy with minimal inflammation and necrosis
A new MR-compatible loading devise to study *in vivo* muscle damage development in rats due to compressive loading (Stekelenburg *et al.*, 2006)	Tibialis anterior region	Healthy rats	Visual and MRI identified histological changes in muscle tissue during and after load application	MR compatible loading devise	Segmental necrosis was identified, loss of cross-striation Abnormal MR signal intensity associated with damaged muscle.

Table 1.5 *In vivo* animal studies of the effects of pressure

Study	Type of cell or tissue	Subject description	Outcome measure	Method of testing	Findings
Micro-injection studies of capillary blood pressure in human skin (Landis, 1930)	Capillaries in the skin of nail bed	Healthy humans	Closing pressures		Capillary closing pressure of 32mmHg
Experiences at Rancho los Amegos hospital with devices and techniques to prevent pressure sores (Reswick and Rogers, 1976)	Soft tissue over bony prominences (predominantly ischial tuberosities)	Spinally injured patients	Interface pressure measurements Supported by (subjective) clinical opinion and observations of potential and actual skin breakdown	Clinical measuring system (sensor element with sphygmo-manometer)	A ‘guideline’ pressure time curve with acceptable maximum pressures over bony prominences

The recovery characteristics of soft tissues following repeated loading (Bader, 1990)	Soft tissue over sacrum or ischial tuberosities	Healthy and debilitated humans	Surface oxygen and carbon dioxide levels	a)indentor applied to skin of sacrum b) dynamic sequential pressure relieving cushion	pO_2 at sacrum drops with pressure but recovery increases over time with healthy individuals. Recovering with relief of pressure but continues to drop with debilitated individuals. pO_2 of healthy seated individual recovering to normal after 25 mins. of sequential pressure pO_2 of debilitated individuals show varying responses
Sweat analysis following pressure ischaemia in a group of debilitated subjects (Polliack, Taylor and Bader, 1997)	Skin over the sacrum	Patients with severe and multiple physical disabilities	Sweat metabolite concentrations	Sweat pads applied to the patients sacrum	Median lactate and urea concentrations were 16 and 40% higher respectively. Wide variations in all metabolite concentrations were noted.

Blood perfusion hyperaemia in response to graded loading of human heels assessed by laser-Doppler imaging (Mayrovitz, Macdonald and Smith, 1999)	Heels	Healthy volunteers with no arterial disease or diabetes	Hyperaemic responses and tissue recovery times	Laser Doppler imaging following fixed load pressure	All heel loads and durations resulted in hyperaemic responses, largest response with loads between 60-120 mmHg. Recovery times increased with load duration and magnitude
The effects of pressure loading on the blood flow rate in human skin (Daly *et al.*, 2006)	Medial surface of the forearm	7 Healthy young subjects	Skin blood flow rates (derived form the Xe isotope clearance)	Pressure loading devise and gamma isotope counter	Flow rates dropped drastically between 0 and 15 mmHg then dropped again after 30mmHg
Strains and stresses in sub-dermal tissues of the buttocks are greater in paraplegics than in healthy people during sitting (Linder-Ganz *et al.*, 2008)	Gluteus muscle and fat tissue under the Ischial tuberosities	6 healthy and 6 paraplegic volunteers	Compression, tension and shear strains were measured	MRI imaging	All parameters were significantly higher in the paraplegic individuals than the healthy ones

Table 1.6 *In vivo* human studies of the effects of pressure

Tissue deformation has been studied at different levels:

- Cellular: different cell types can be cultured e.g. skin, muscle and subject to pressure e.g. (Bouten *et al.*, 2003)
- Functional cellular units: these can also be grown in a laboratory e.g. blood vessels, intracellular matrix e.g. (Bronneberg *et al.*, 2006)
- Composition of tissues: although each cell is subject to pressure, in the body there is likely to be interaction between tissue types, the effects of deformation will depend on the proportion and shape of the tissues over the bone. Deformation can be seen through Magnetic Resonance Imaging (MRI) and computerised modelling of tissues e.g. (Stekelenburg *et al.*, 2006; Gefen, 2007)

When animals are used to simulate pressure damage in humans they can be categorised into loose skin and fixed skin. Animals such as dogs, rabbits and mice have loose skin where as pigs have a fixed skin which is more like human skin. The density of hair growth through the skin is also different for loose skinned animals. Their skin is predominantly made up of hair follicles. The density of hair follicles in pigs is similar to humans. The clinical relevance of the study will be affected by the type of animal; the particular body site (whether skin or muscle is included); a healthy or debilitated individual; or a laboratory reconstruction of a body site is studied. Some examples of animal studies are summarised in Table 1.5.

To study the effects on *in vivo* human tissue would require histological examination; it is unethical to biopsy an area of damaged tissue and create a wound where a pressure ulcer is likely to occur. One study of cadavers has been identified, the aim of this study however was to identify osteoporosis in the underlying bone (Turk, Tsokos and Delling, 2003). A study by Smalls *et al.* (2006) looked at differences in skin thickness and its biomechanical properties (elasticity, deformation, laxity, energy absorption) in 30 women volunteers on 3 body sites (shoulders, calves and thighs). Significant differences were found between body sites for most properties tested. Although this study used a small number of mainly young healthy women the variations shown leads one to question the generalisability of results obtained from studies of a tissue on a

particular body site or individual to other pressure areas or individuals in different health states. Some examples of human studies are summarised in Table 1.6

Additional comments on the studies cited in tables 1.4-1.6 are given here:

In Bouten's study (2001), deformation measured was only 2 dimensional, it probably needed to be a 3 dimensional reconstruction to look at whole cell shape. Predictions of cell deformation are based on the assumption that the cell behaves like an incompressible solid but this proved not to be the case at higher strain levels. The authors postulated reasons for differences in response to high stresses of the two cell types e.g. different diameters, reorganisation of nuclei, lack of mechanical homogeneity of the cell membrane. Cell damage was recorded as membrane disruption or nucleus damage but did not distinguish between the two in the results. Cell strength is also thought to be based on the integrity of the cytoskeleton.

In Bader's study (1990) it was noted that sacral pressure testing was carried out on 14 individuals and ischial seating test on 28 individuals. Results quoted are for only 6 patients.

Tissue perfusion involves providing adequate nutrition and respiration at the cellular level. Pressure is thought to cause both collapse of the larger vessels and micro-vascular trauma which results in either haemorrhage or multiple micro-thrombi (Lowthian, 2005). The occlusion results in anoxia and cell death.

Sustained pressure on tissues is thought to result in a gradual sideways flow of the interstitial fluid and ground substance. This will reduce the interstitial pressures; this in turn will lead to a rupture of cells and capillaries (Witkowski and Parish, 1982).

The lack of venous and lymphatic drainage has been demonstrated by Miller and Seale (1981). The effect of this is assumed to be toxicity due to the build

up of metabolic wastes but no studies have documented this.

Reperfusion injury as a possible effect of pressure on tissues in the skin has been suggested based on the evidence in cardiovascular ischemic assault. The injury when the pressure is removed is thought to be mediated by oxygen free radicals, which exacerbate the tissue damage (Bouten *et al.*, 2003).

Despite the limitations of the *in vitro/in vivo* animal and human studies, they have led to theories of the mechanisms of pressure and its effects on tissues. Pressure is thought to affect the tissues in several different ways:

- Tissue deformation
- Lack of blood supply (ischaemia)
- Impaired interstitial flow
- Lack of venous and lymphatic drainage
- Possible reperfusion injury

Pressure causes deformation of the tissues, the intensity and duration of the pressure has been found to be inversely proportional to tissue breakdown i.e. high intensity or prolonged duration increase the risk of tissue breakdown (Reswick and Rogers, 1976). The precise magnitudes have not been defined as these vary between individuals.

1.7.1.6 Individual patient characteristics

It is acknowledged in some papers that the precise level at which damage occurs is not generalisable due to variation between patients (Bouten *et al.*, 2003; Bridel, 1993a).

Examples of factors which are reported, but not actually measured, in the studies to alter tissue's ability to resist damage include: atrophy of soft tissue coverage associated with paraplegia; destruction of deep muscle and subcutaneous tissue with scar replacement following repeated pressure loads; extension of tissue necrosis due to secondary infection (mentioned in Daniel

1981 but not referenced); oedema due to increased interstitial fluid resulting in increases distance from capillary to cell (rate of diffusion of oxygen and nutrients) (mentioned in Kosiak's (1959) theoretical paper); anaemia affecting the supply of oxygen which will be diminished with poor haemoglobin, also ischemia (Kosiak 1959) ; temperature and nutritional status (mentioned in Bouten (2003) but not referenced). Some of these are deductions from the anatomy and physiology; others are studied as risk factors and will be discussed in a later section.

In summary it appears from the research findings available that:

- there is no specific pressure at which tissue damage is certain to occur (Bridel, 1993a)
- extent of damage is increased with intensity and duration (Reswick and Rogers, 1976)
- repeated pressure can result in less damage if below a certain threshold (Bader, 1990)
- repeated pressure above a certain threshold will lead to more damage than a single period of sustained pressure (Bader, 1990)
- damage from repeated pressure may be due to inflammatory processes during reperfusion (Brand, 2006)
- damage to the tissues is from cell compression and rupture; vascular and lymphatic damage (Bader, Barnhill and Ryan, 1986)
- pressure affects skin and muscle tissue differently: different pressures are tolerated and damage occurs to the exoskeleton of muscle where the hemidesmosomes and tonofilaments between cells are affected (Stekelenburg *et al.*, 2006)
- the variables that affect this pressure include:
    - type of cells and tissues affected (Edsberg *et al.*, 2000)
    - the area over which the pressure is applied (Husain, 1953)
    - the individuals posture (Linder-Ganz *et al.*, 2008; Gefen, 2007)
    - underlying pathological processes which affect the tissues (Bridel, 1993a)

1.7.2 Shear

As pressure is defined as a force perpendicular to the skin surface, shear is the force parallel to the skin surface (Oomens, Loerakker and Bader, 2010). The clinical application of shearing occurs when soft tissue slides over bone. This is seen when a person is in a semi-recumbent position. The force of gravity tends to cause the person to slide down in the bed or chair. This force is opposed by the pressure and friction at the points of contact with the support surface resulting in the soft tissue resisting gravity and leading to shearing.

There have been several studies on the effects of shear. The same issues arise regarding the generalisability of their findings; the authors of *in vitro* studies would argue that these methods are necessary in order to examine the effects of shear in isolation from pressure because this cannot be performed *in vivo*. Most studies identified relating to shear within tissues used sheer caused during deformation from applied perpendicular pressure rather than sheer in isolation from pressure. Other studies identified are summarised in the table 1.7.

Study	***In vitro/ in vivo***	**Type of cell or tissue**	**Type of participant**	**Outcome measure**	**Method of testing**	**Findings**
Effects of externally applied skin surface forces on tissue vasculature (Bader, Barnhill and Ryan, 1986)	Probably *in vivo*		Healthy humans	Collapse of superficial micro-vasculature	Skin stretching device on forearm Tissue vasculature assessed by vital capillary microscopy	Occlusion of vessels occurred at a mean force of 1.33 N/mm and 10% strain Upon release of shear normal blood flow was restored even after 6 mins. strain
Stretch-mediated release of angiotensin II induces myocyte apoptosis etc (Leri *et al.*, 1998)	*In vitro*	Rat myocytes from heart muscle		Apoptosis as seen under confocal microscopy	Cell cultures adhered to a rubber substrate then stretched with equibiaxial stretch apparatus	Apoptosis occurred 4 - 12 hours after stretching, no effects seen at 10, 30 mins. or 2 hours. A proposed pathway for the role of angiotensin II in cell death

Influences of external forces (pressure and shear) on superficial layers and subcutis of porcine skin and effects of dressing material: are dressing materials beneficial for reducing pressure and shear forces in tissues (Ohura, Takahashi and Ohura, 2008)	*In vitro*	Porcine skin		Maximum shear force when different dressings were compared to control skin	1 Kilogram weight pulled across surface, measured with a strain gauge sensor under skin	Shear force in subcutaneous tissue less than in superficial layer Dressings reduced the shear forces

Table 1.7 Table of studies of shear forces

It is noted that the study by Bader & Barnhill & Ryan (1986) only looked at strain without pressure and only measured effects on blood vessels, no other cells were studied.

The initial effect of shearing is the rupture of the vascular and lymphatic vessels in the skin and subcutaneous tissue. In the subcutaneous tissue the vessels are mostly parallel to the skin, however in the planes of the deep fascia and intramuscular septa they follow ligaments and nerves (Tortora and Grabowski, 1996). This makes them vulnerable to distortion. Although the vessels in the dermis are more tortuous and less vulnerable in themselves, if deep vessels are damaged they will inevitably affect those in the dermis due to the lack of blood supply.

1.7.3 Friction

Friction forces occur when two surfaces rub together, this happens clinically for example when a person is slid up the bed during repositioning. The contact between the skin and the support surface can cause trauma to the epidermis and eventually the dermis. A study by Dinsdale (1974) demonstrated in pigs that a reduced pressure threshold is required for pressure ulcers to develop in the presence of friction. No human studies have been identified. The effects of friction are magnified by moisture (clinically this is due to incontinence or perspiration); this was demonstrated by Flam (1990) who found that moisture increased the abrasion of the skin when subject to friction.

It is suggested by Allman (1989) that friction and shear are most important in the development of superficial skin breakdown, whereas the effects of pressure and shearing begin in deeper tissues and spread up to the surface. He also suggests that friction and moisture produce their most harmful effects in the presence of excessive pressure.

1.7.4 The relationship between aetiology and severity of the pressure ulcer

For a detailed discussion of severity and grading see section 2.4. The

relationship between the nature of the damage and the severity of the ulcer has yet to be fully explored. From the studies identified, the damage to muscle tissue has been subject to the most scrutiny; however the pathophysiology of Grade 1 ulcers is probably still the most controversial. Histological changes were noted by Witkowski and Parish in 1982 when they compared biopsies of normal skin and non- blanching erythema. A study by Nixon *et al.* (2005) identified high blood flow of differing intensities between blanching and non-blanching erythema of the skin over sacrum and buttock regions following the removal of pressure. Studies of friction are pertinent to Grade 2 ulcers as these include blisters and superficial skin breakdown. Shearing forces will affect the skin and deep tissue although Bader and Barnhill's (1986) study of healthy humans suggest no sustained damage to skin.

1.7.5 Disease processes that specifically affect the heel

It has already been suggested in section 1.7.1.6 that systemic disease and homeostatic variations can affect tissue tolerance to pressure. There are particular clinical situations that affect the lower extremities more than other sites where pressure ulcers occur, which are likely to lead to change in duration of pressure or tissue tolerance.

1.7.5.1 Circulatory – Peripheral arterial disease

The circulation to the lower limbs can become compromised due to arterial diseases such as atherosclerosis. Although associated with increasing age poor circulation is seen in younger people particularly in association with factors such as smoking, diabetes and hypertension (Vogt, Wolfson and Kuller, 1992). The internal capillary pressures reduce and if subjected to external pressure are not able to respond appropriately to prevent occlusion. This was reported in the seminal work by Kannel and Shurtleff (1973).

1.7.5.2 Neurological

Neuropathy (reduced or altered sensation) has been identified as a risk factor for ulceration in the feet of people with diabetes (McNeely *et al.*, 1995). Neuropathy is also known to be associated with other diseases such as stroke, pernicious anaemia, spina bifida and multiple sclerosis although its precise prevalence is unknown (Neale *et al.*, 1981). Although no published papers have

been identified so far, data collected during a study of pain in leg ulcers (Briggs, 2003) has shown that many older people have some degree of neuropathy of the lower limbs. The presence of neuropathy may result in a person being unaware of pressure and, therefore, not responding to it (Raney, 1989).

1.7.5.3 Structural

Structural changes are seen in conditions such as Charcot foot in diabetic patients. The foot is often a site for trauma and fractures in all patients leading to changes in shape and potential pressure points. Gefen(2010) demonstrated through mathematical modelling that atypical anatomy such as a heavier foot with a sharp posterior calcaneum results in higher internal pressures on the tissues.

1.7.5.4 Oedema

Oedema is the presence of excess extra-cellular fluid which causes localised swelling. It is associated with peripheral vascular disease, especially venous incompetence (Cho and Atwood, 2002), the effects of gravity on a dependent limb and other physiological changes (Ciocon, Fernandez and Ciocon, 1993). The presence of oedema compromises tissue perfusion and removal of waste products (Ryan, 1969). Also, the weight of the extra fluid in the feet is likely to result in normal resting pressures being exceeded; which may have an impact on tissue tolerance of pressure (Gefen, 2010).

1.7.5.5 Diabetes

Although all the above clinical situations may apply in patients with diabetes, the additional feature of micro-vascular dysfunction is thought to be an important factor that affects the risk of ulceration to the foot. The processes involved are summarised and the evidence critiqued in a review by Chao and Cheing (2009). This review suggests hyperglycaemia is the central causative factor as it results in impaired vascular permeability, vascular tone and the auto-regulation of blood flow. Chronic hyperglycaemia results in structural and functional changes in nerve microvasculature with diabetic peripheral neuropathy and impaired inflammatory response.

1.8 Summary

Pressure ulcers are a major health problem causing distress to patients and costs to the health care provider. They occur predominantly on load bearing body sites where there is a bony prominence with the lower body and the heel being the most common sites. Information regarding how long they take to heal is sparse. This is most likely because of the long duration, high mortality rates in this affected population and studies of insufficient duration.

A review of the anatomy and physiology of the potential body sites affected has shown the similarities e.g. underlying bony prominences with small surface areas and differences e.g. only the ischial tuberosities have noticeable muscle present. However particular differences are noted for the tissue organisation at the heel.

The exact pathophysiology of pressure ulcers is unknown, probably because of the difficulties in researching this topic area: *in vitro* studies at a cellular level cannot capture the complex interactions of tissues. Animal models do not have similar enough skin structure and healthy human subjects do not present with the altered tissue ability to resist damage that is found in the potential pressure ulcer population; caution needs to be taken in generalising findings from these studies.

The differences between feet and other body sites in terms of anatomy, distribution and density of structures and blood supply, mechanical properties and potential for being affected by disease processes has been demonstrated. Pressure ulcers occur on the heel as it is a small surface area which can be subject to high pressures when the body is in a supine position or seated with the heels on a stool. Heel pressure ulcers are worthy of specific scrutiny in terms of prevention and healing. This will be presented in the next chapter.

Chapter 2 Pressure ulcer healing and prognostic factors

2.1 Introduction

In order to understand the healing process for heel ulcers and reveal what is already known about this topic some fundamental concepts need to be presented and the evidence to support them discussed. The order in which these are presented has been a difficult choice as there is no logical progression for understanding. Should the explanation of grading/ severity precede or follow the type of tissues found in the ulcer? The reader is advised to consider all sections of this chapter together to build a picture of heel pressure ulcer healing.

This chapter firstly clarifies some definitions that are used in the wound healing literature. It then describes the traditional model of wound healing in section 2.3. In section 2.4 it explains how pressure ulcers are classified in terms of their depth or severity. It explores what is specifically known about pressure ulcer healing in section 2.5. Section 2.6 relates the theory of healing to what is seen clinically as types of tissues in the pressure ulcers. There are many factors thought to influence pressure ulcer healing. These are discussed in section 2.7.

2.2 Definitions: healing intention, acute and chronic wounds, partial and full thickness wounds

Healing by primary (or first) intention was defined by Roper in 1987. It is said to occur when the edges of a clean wound are accurately held together, healing occurs with the minimum of scarring and deformity. Examples of wounds healing by primary intention are surgical incisions or clean traumatic wounds with minimal tissue loss. They are usually held together by sutures, staples, tape or glue.

Healing by secondary intention (Roper, 1987) is said to occur when the edges of the wound are not held together, the gap is filled by granulation tissue before

epithelium can grow over the wound. These are usually wounds which have large amounts of tissue loss or high bacterial levels e.g. abscess, leg ulcers or pressure ulcers.

Acute wounds are understood to be new wounds such as surgical incisions or traumatic injuries. They progress through stages of wound healing described in section 2.3.

Chronic wounds have various definitions; most of them refer to the time taken for a wound to heal regardless of the cause e.g. any wound which has failed to heal within three months (Mustoe, 2005). Alternative definitions describe chronicity in terms of wound type e.g. leg ulcers, pressure ulcers and diabetic foot ulcers (Brem *et al.*, 2003) as these wounds are associated with long healing even though they may heal in less than three months Difficulties arise when dealing with acute wounds e.g. surgical incisions or burn that take longer than 3 months to heal.

The terms ‘partial thickness’ and ‘full thickness’ wounds are often used when the process of wound healing is being discussed. Their origin is probably from texts on burns wounds where the terms are most commonly used but an original definition has not been identified. Alterescu and Alterescu (1992) note that a ‘partial thickness’ wound is one which only penetrates the epidermis, but not the entire dermis, whereas a ‘full thickness’ wound penetrates the epidermis and the dermis. The clinical implications of this differentiation are that because the dermis does not regenerate, full thickness wounds will need to contract, granulate and epithelialise which will result in a scar whereas partial thickness wounds only need to epithelialise to regenerate normal epidermis and there is no resultant scarring. The relevance of this to pressure ulcers is discussed in section 2.6.

2.3 Classic model of wound healing

Wounds are usually described as a break in the integrity of the skin. To understand what will affect the healing of pressure ulcers, knowledge of the

wound healing process is required. The stages of wound healing are described in similar ways in many text books. However the duration and significance of each stage is rarely discussed for different wound types e.g. pressure ulcers, surgical wounds, leg ulcers, etc. The knowledge about wound healing in humans was noted to be incomplete in 1975 (Lindstedt and Sandblom, 1975). A review of the evidence since this time suggests that gaps still exist. Many similarities exist between connective tissue healing in animals and humans, but it is not possible to completely transfer the information from animal experiments to humans.

The following summary is primarily adapted from a review paper by Broughton et al (2006), written by plastic surgeons. This is a well referenced and detailed account that includes details of chemical factors associated with impaired wound healing. Many of the studies cited in this review, or specifically referenced in this section, are based on the analysis of wound fluids taken during the various stages of wound healing and cultured *in vitro*. No studies have been identified which give precise details of the patient characteristics e.g. age, co-morbidities or the current wound management i.e. whether fluid was taken from under clot/ scab formation or occlusive wounds. Some animal studies e.g. mice are included, these have experimental incisional wounds. Very few studies are carried out on pressure ulcers *in vivo*. There are ethical concerns with this, e.g. taking biopsies from pressure ulcers may further compromise healing. No papers have been found which specifically describe the healing process for pressure ulcers. Details of what is known about pressure ulcer healing are given in section 2.4.

The wound healing process is usually described in 4 stages:

- Haemostasis
- Inflammation
- Proliferation
- Maturation

These phases are distinct in terms of the cellular and chemical activity but can

occur simultaneously, notably in chronic wound healing (Harding, Morris and Patel, 2002). The following sections describe each stage in more detail.

2.3.1 Haemostasis

This is the initial local reaction to tissue damage. Where damage to blood vessels has occurred there is extravasation of blood constituents into the interstitial space. Haemostasis is achieved through the vasoconstriction of the damaged vessels. Clot formation occurs; this is made up of collagen, platelets, thrombin and fibronectin. These factors release cytokines and growth factors that initiate the inflammatory response. This is a biochemical cascade, initiated by the release of platelets that results in the release of fibrinogen, which is converted to fibrin. This process is thought to be complete in less than one hour (Broughton, Janis and Attinger, 2006).

According to a review article by Singer and Clark (1999), in injuries where there is an absence of haemorrhage, platelets then are not essential to wound healing. No reference is provided for this statement.

2.3.2 Inflammation

During the clotting process, triggers are released, which activate other cascade processes. These result in a local vasodilatation, increased permeability of the blood vessels and attraction of neutrophils to the wound. The presence of kinins also enhances phagocytosis and stimulates the sensory nerve endings (Cooper *et al.*, 1994). As the blood vessels dilate there is an increase in the interstitial fluid, this carries plasma proteins, antibodies, erythrocytes, leucocytes and platelets. Platelets are responsible for the release of many growth factors e.g. tissue growth factor beta (TGF-β) and platelet derived growth factor (PDGF). Growth factors are cytokines, which in wound healing stimulate angiogenesis, fibroblast formation and epithelial cell migration (Mast and Schultz, 1996). Following the initial surge of neutrophils to the wound, other white blood cells, namely monocytes and T-lymphocytes migrate into the wound. Their role is the removal of nonviable tissue and bacteria (autolytic debridement) through phagocytic digestion and proteolytic enzyme (protease) activity (Broughton, Janis and Attinger, 2006). Proteases can have broad or

specific targets e.g. metalloproteinases specifically digest collagen. Undamaged collagen (intact extra-cellular matrix) is protected from destruction by protease inhibitors (Yager and Nwomeh, 1999) and the release of prostaglandin, which maintains the inflammatory response. It is suggested that this phase usually lasts 4-6 days depending on the extent of the damage and size of the wound.

The transition of the wound from inflammation to proliferation should occur as non-viable tissue is removed. Broughton et al (2006) stress the importance of the haemostatic and platelet derived factors in this transition. Reduced levels of these and other growth factors have been found in chronic wounds compared to acute wounds (Cooper *et al.*, 1994; Higley *et al.*, 1995). This has been suggested (Harding, Morris and Patel, 2002) as one of the reasons chronic wounds such as pressure ulcers are slow to heal. Other explanations for why some wounds are slow to heal include:

- reduced levels of protease inhibitors (this has been found in chronic leg ulcers) (Bullen *et al.*, 1995);
- impaired response to grow; fibroblasts found in venous leg ulcers had an impaired response to growth hormones attributed to senescence (Agren *et al.*, 1999).

Senescent cells are fibroblasts that have a (wound) age related decrease in proliferation potential.

2.3.3 Proliferation

This phase has a minimal role in wounds closing by primary intention e.g. sutured surgical wounds, as there is minimal tissue loss. Wounds healing by secondary intention may have a prolonged proliferative phase where there is extensive tissue loss. Proliferation can be subdivided into granulation and re-epithelialisation. It is suggested that this phase lasts from day 4 to day 14 according to Broughton *et al.* (2006).

<u>Granulation</u>

The reconstruction of the subcutaneous tissue consists of the formation of collagen, myofibroblasts, regrowth of blood vessels and capillary loops in an

extra-cellular matrix (Harding, Morris and Patel, 2002). This process is also stimulated by growth factors. Collagen is produced in this phase in order to give strength to the wound (Pierce *et al.*, 1991). The vascular regeneration is also prolific in order to maximize the supply of oxygen and nutrients. The myofibroblasts enable wound contraction. According to a study by Majno et al (1971) this is responsible for approximately 50% of wound closure. Although this was an *in vivo* study of wounds with extensive tissue loss on mice this figure is still quoted in many text books.

Epithelialisation

During this phase new epithelial cells are produced under the influence of other growth factor which are produced by the platelets and macrophages (Lawrence and Diegelmann, 1994). The cell proliferation takes place at the wound edges and hair follicles. The cells migrate laterally in a zipper like fashion, over the new granulation tissue till a continuous layer is formed. This was demonstrated by Clark *et al.* (1982) in guinea pigs. A moist environment is thought to be required for optimum growth: this theory was originally demonstrated in an animal model by Winter (1962). In 1991 faster healing rates were demonstrated with moist wound healing in human partial thickness biopsy wounds although not in full thickness wounds (Nemeth *et al.*, 1991). This study was criticised for the use of antiseptics under the occlusive dressings. In 2001 Agren *et al.* studied wounds on the lower legs of healthy volunteers, they found significantly better healing after 7 days of moist versus dry wound healing, but the difference was not significant after 14 days. Recently this notion of moist wound healing has been challenged in a study by Ubbink *et al.* (2008) who compared modern occlusive dressings with dry gauze and found no significant difference in healing rates in a variety of wounds (including dehisced surgical incisions, leg ulcer and pressure ulcers) on surgical patients. In wounds healing by primary intention, epithelialisation can occur within the first 48 hours (Broughton, Janis and Attinger, 2006). However in wounds healing by secondary intention, it may take days, weeks or months before there is a surface of viable granulation tissue for the epithelium to adhere.

2.3.4 Maturation

This phase occurs once the skin integrity has been re-established. During

maturation there is a reduction in vascularisation of the skin, realignment of the collagen and elastic fibres to increase the tensile strength of the wound. This phase can take 3 months to several years. The tensile strength immediately after wound closure is less than 50% of normal tissue. After 10-12 weeks a wound will regain 70-80% of its maximum strength (Kapan *et al.*, 2003). However this evidence is from rat models. A newly healed pressure ulcer would be at high risk of breakdown if subject to further pressure.

2.4 Pressure ulcer classification

The detail of the healing process, which takes place in pressure ulceration, depends on the severity and the associated phases of wound healing (see sections 2.5 and 2.6). Terminology used to define the severity of the ulcer, i.e. grade, stage or category is often used interchangeably. Briggs (2006) suggests this may lead to confusion among clinicians when attempting to describe pressure ulcers.

Many scales have slight variations in definitions, with most variance existing during the classification of the early stages of damage (Bethell, 2003). The relevance of this to pressure ulcer incidence and prevalence reporting has been discussed in section 1.4.

The purpose of grading as part of the assessment process is:

- To assess the extent of the damage
- To inform the management plan
- To monitor progress
- Improve outcomes
- Standardise record keeping

Many classification scales exist e.g. (AHCPR, 1992; Reid and Morison, 1994; EPUAP, 1998; NPUAP, 2009). Some classify Grade I as non-blanchable erythema (red skin which does not turn white with light finger pressure), although some (NPUAP, 2009) recognise that this is not practical to detect in highly pigmented skin. Henderson *et al.* (1997) extends the definition of Grade

1 to include pressure related alterations in skin colour, temperature, texture and sensation compared to adjacent or opposite skin. Scales that include blanching erythema e.g. Torrance (Torrance, 1983) are controversial as this thought to be is a transient state, which is not pathological (Harker, 2000; Nixon, Cranny and Bond, 2007; Bell, 2011). Some variation in the classifications relate to the description of the wound bed e.g. slough or granulating tissue, the presence or absence of necrotic tissue (preventing the depth of the wound to be accurately assessed) and the condition of the surrounding tissue. There are now two internationally recognised grading scales: EPUAP(2009) in Europe and NPUAP (2009) in the US. Their classifications are equivalent.

Disease assessment scales can be evaluated in a number of ways. These include assessment of validity (internal and external) and reliability (inter and intra-rater). Currently there is no objective test for diagnosing or measuring the severity of pressure ulceration, although some studies have attempted to develop the technology for clinical use one (Nixon *et al.*, 1999; Baldwin, 2001).This means that assessment of internal validity of a grading scale can not be formally tested. The reliability of an instrument will have implications for it's validity; a scale which is not reliable cannot have validity (Polit and Beck, 2004). Table 2.1 gives details of some of the more commonly used scales to highlight the differences between them. The term Grade is used (this includes grade or category) in this table and will be used throughout this thesis.

The importance of these variations in the way each Grade is defined becomes relevant when comparing incidence and prevalence data and has been discussed in section 1.4. A systematic review of inter-rater reliability of pressure ulcer classification systems has been performed by Kottner *et al.* (2009). This was a well executed review; details are given of the search strategy, the quality assessment and the numbers of studies identified, reviewed and included. It records that only studies published in English or German were included. The heterogeneity of studies resulted in a narrative review. Comments related to:

- the quality of studies (only 24 out of 339 potentially relevant studies met the inclusion criteria)

- the assessment methods (assessment of photographs rather than patients is thought not to be appropriate however the inter-rater reliability of both methods is both high and low in different studies)
- the qualification and training of raters (most studies did not provide sufficient detail of this)
- no study randomly identified raters (this suggests lack of generalisability of findings)
- classification systems used and the inclusion or not of intact skin (high inter-rater reliability is given in studies where high proportion of assessments were intact skin)
- testing in non-white skin was not mentioned.

This review did not discuss the fact that many studies do not give details or perform separate analysis for different body sites. It is unknown whether a pressure ulcer on the heel compared with another part of the body would affect the reliability of the assessment. Finally, Kottner et al's review was completed in 2008, it does not include any studies of the new NPUAP/ EPUAP grading launched in 2009

Author	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Additional** Grade	**Comment**
Torrance (1983)	Blanching erythema	**Non-blanching erythema**	Ulceration through dermis, distinct edges surrounded by erythema and induration	Ulceration into subcutaneous fat. Small-vessel thrombosis and infection compound. Muscle is swollen and inflamed, lateral extension results in undermining	Grade 5: Infective necrosis penetrates deep fascia, muscle destruction. Spreads along the fascial planes and bursae. Osteomyelitis can easily develop	First Grade of damage is = 2

National Pressure Ulcer Advisory Panel (NPUAP) (1989)	**Non-blanchable erythema of intact skin**	Partial-thickness skin loss involving epidermis and/or dermis	Full thickness skin loss involving damage or necrosis of subcutaneous tissue that may extend down to, but not through, underlying fascia	Full thickness skin loss with extensive destruction, tissue necrosis or damage to muscle, bone or supporting structures.		Adopted by the Agency for Health Care policy and Research (AHCPR) for use in the USA

Reid and Morison (1994) 2 digit Stirling scale	**1.1 non-blanching erythema** with localised heat 1.2 Blue/ purple/ black discolouration	2.1 Blister 2.2 Abrasion 2.3 Shallow ulcer without undermining 2.4 Any of these with underlying blue/ purple/ black discolouration	3.1 Crater without undermining 3.2 Crater with undermining 3.3 Sinus, the full extent is unknown 3.4 Full thickness skin loss with necrotic tissue (true extent of damage unknown)	4.1 Visible of bone, tendon or capsule 4.2 Sinus assessed as extending to bone, tendon or capsule	Grade 0: 0.1Normal appearance, intact skin 0.2Healed with scarring 0.3Tissue damage but not assessed as a pressure sore	A simplified version is known as the 1 digit scale Only scale to document ‘no damage’

European Pressure Ulcer Advisory Panel (EPUAP) (1998)	**Non-blanchable erythema** of intact skin	Partial-thickness skin loss involving epidermis and/or dermis	Full-thickness skin loss involving damage or necrosis of subcutaneous tissue that may extend down to, but not through, underlying fascia	Full thickness skin loss with extensive destruction, tissue necrosis or damage to muscle, bone or supporting structures.		Used extensively in Europe including the UK

National Pressure Ulcer Advisory Panel (2009)	**Intact skin with non-blanchable redness** of a localised area usually over a bony prominence. Darkly pigmented skin may not have visible blanching: its colour may differ from the surrounding skin	Partial thickness loss of dermis presenting as a shallow open ulcer with a red pink wound bed, without slough. Also may present as an intact or open/ruptured serum filled blister	Full thickness tissue loss. Subcutaneous fat may be visible but bone, tendon or muscle is not exposed. Slough may be present but does not obscure the depth of tissue loss. May include undermining or tunnelling.	Full thickness tissue loss with exposed bone, tendon or muscle. Often includes undermining or tunnelling.	Unstagable: Full thickness tissue loss in which the base of the ulcer is covered by slough(yellow, tan, grey, green or brown) and/or eschar (tan, brown or black) in the wound bed Deep tissue injury: Purple or maroon localised area of discoloured intact skin or blood filled blister due to damage of underlying soft tissue from pressure and/or shear. The area may be preceded by tissue that is painful, firm, mushy, boggy, warmer or cooler as compared to adjacent tissue. Deep tissue injury may be difficult to detect in individuals with dark skin tones. Evolution may include a thin blister over a dark wound bed. The wound may further evolve and become covered by thin eschar. Evolution may be rapid exposing additional layers of tissue even with optimal treatment.	Produced in collaboration with the EPUAP. The European version does not include the categories of Unstagable or Deep tissue injury

Table 2.1 Examples of pressure ulcer grading scales

Recent developments both in the US and Europe have led to new standardised definitions of pressure ulcer severity (NPUAP, 2009; EPUAP, 2009). This was included in table 2.1, however more detail is given in table 2.2. Classification systems use the term ‘stage’ or ‘grade’, although the recommendations of the combined European and US advisory panels is to use the word ‘category’ as this does not imply a hierarchy. In the US there was a need to separate ‘unstagable’ and ‘deep tissue injury’ as there are medico-legal aspects of attributing when or where the ulcer originated and reimbursement implications for these types of injuries. Although this was not fully supported in Europe, in practice in the UK many clinicians have found it beneficial to introduce these categories.

PU Grades	Definitions	Further description
Grade 1	Intact skin with non-blanchable redness of a localised area usually over a bony prominence. Darkly pigmented skin may not have visible blanching: its colour may differ from the surrounding skin	The area may be painful, firmer, soft, warmer or cooler as compared to adjacent tissue. Grade 1 may be difficult to detect in individuals with dark skin tones. May indicate ‘at risk’ persons (a heralding sign of risk)
Grade 2	Partial thickness loss of dermis presenting as a shallow open ulcer with a red pink wound bed, without slough. Also may present as an intact or open/ruptured serum filled blister	Presents as a shiny or dry shallow ulcer without slough or bruising. Bruising indicates suspected deep tissue injury
Grade 3	Full thickness tissue loss. Subcutaneous fat may be visible but bone, tendon or muscle is not exposed. Slough may be present but does not obscure the depth of tissue loss. May include undermining or tunnelling.	The depth of a Grade 3 pressure ulcer varies by anatomical location. The bridge of the nose, ear, occiput and malleolus do not have subcutaneous tissue, Grade 3 ulcers can be shallow. In contrast areas of extreme adiposity can develop extremely deep Grade 3 ulcers

Grade 4	Full thickness tissue loss with exposed bone, tendon or muscle. Often includes undermining or tunnelling.	The depth of a Grade 4 ulcer varies by anatomical location. Grade 4 ulcers can extend in to muscle and/or supporting structures e.g. fascia, tendon or joint capsule making osteomyelitis possible.
Unstagable (U)	Full thickness tissue loss in which the base of the ulcer is covered by slough(yellow, tan, grey, green or brown) and/or eschar (tan, brown or black) in the wound bed	Until enough slough and/or eschar are removed to expose the base of the wound, the true depth and therefore the Grade cannot be determined. Stable (dry, adherent, intact without erythema or fluctuance eschar on the heels serves as the 'body's natural (biological) cover' and should not be removed
Suspected deep tissue injury (sDTI)	Purple or maroon localised area of discoloured intact skin or blood filled blister due to damage of underlying soft tissue from pressure and/or shear. The area may be preceded by tissue that is painful, firm, mushy, boggy, warmer or cooler as compared to adjacent tissue. Deep tissue injury may be difficult to detect in individuals with dark skin tones. Evolution may include a thin blister over a dark wound bed. The wound may further evolve and become covered by thin eschar. Evolution may be rapid exposing additional layers of tissue even with optimal treatment.	

Adapted from (Black *et al.*, 2010)

Table 2.2 NPUAP/ EPUAP Pressure ulcer Grades based on the 2009 reclassification

The main difference in the new definitions is that any wound with slough present is now considered a Category 3 ulcer. The presence of slough is

discussed in more detail in section 2.5. By classifying sloughy wounds as category ‘3’ there is a working hypothesis that the wound has penetrated the full thickness of the dermis. The rationale is that epidermal or superficial dermal injuries do not produce enough inflammation to generate slough (Black *et al.*, 2010).

The new category of suspected deep tissue injury seems to be controversial: a paper by Gefen (2009) discusses the evidence base for each element of the statement e.g. changes in skin colour, pressure and/or shear and tissue firmness. Most of the evidence is from animal models or muscle tissue under ischial tuberosities in seated patients. He argues, for example, that changes in colour due to deep damage in muscle tissue are unlikely to be detected on the skin. In the researcher’s clinical experience the presentation of maroon or purple discolouration or blood filled blisters on heels definitely exists. What is lacking is the physiological explanation and healing pathway for these.

2.5 Healing of pressure ulcers

Section 2.3 has already described a model of wound healing which is generalised for all wound types. It was noted however that most of the evidence for the particular processes and presence of growth factors and hormones, etc was based on samples from acute wounds. Some references were made to particular evidence for healing in chronic wounds. The following section attempts to consolidate what is known specifically about healing of each Grade of pressure ulcer. The Grades described are based on EPUAP (1998).

2.5.1 Healing Grade 1 pressure ulcers

These ulcers do not present with broken skin, while the exact nature of the damage has yet to be established, in particular no detail of whether blood vessel rupture and the need for haemostasis and the ensuing chemical cascades occurs in every Grade 1 ulcer. It is assumed that the process of healing involves repair to the microcirculation and lymphatics and removal of toxins from the interstitial space. The progress of these ulcers is unclear, Halfens et al (2001) identified that following diagnosis of Grade 1 ulcers, re-assessment 4 hours later found that half had resolved but 21% subsequently

reoccurred. Furthermore 27.8% of patients in acute care settings, who had Grade 1 ulcers at the first and second (4 hours) assessment, went on to deteriorate to a higher Grade. The authors concluded that while Grade 1 ulcers are reversible, they provide a good indication of the patient being at risk as some patients went on to develop more severe ulcers. This study gives details of the body location of the pressure ulcer. It is noted that Grade 1 ulcers on the sacrum were less likely to change, however ulcers on the heel, particularly those in acute care were less stable and 17.6% went on to develop more severe ulcers. In a prospective inception cohort study by Allman *et al.* (1995), which aimed to identify risk factors for the incidence of Grade 2 and above pressure ulcers, they found that a non-blanching erythema (Grade 1 pressure ulcers) was an independent significant risk factor for development (Risk ratio = 7.52 Confidence interval 1.0 – 59.12). This study only mentions pressure ulcers in the sacrococcygeal area; of the 19 patients who had a Grade 1 pressure ulcer, 11 (57.9%) developed into a Grade 2 or greater. Bridel (1993b) reported the findings of her pilot study of patients undergoing major surgery. Thirty six patients had non-blanching erythema on either sacrum, buttocks or heels. Four out of the 36 patients remained either non-blanching or blanching up to day eight. These studies have demonstrated that the resolution or healing of Grade 1 pressure ulcers does not always occur, controversy still exits over whether these should be classified as pressure ulcers or predictors of pressure damage (Helberg *et al.*, 2006)

2.5.2 Healing Grade 2 pressure ulcers

Grade 2 ulcers require re-epithelialisation, if damage to the basal membrane (stratum germinativum) has not occurred, then re-epithelialisation will occur with restoration of full structure and function (Tortora and Grabowski, 1996). This is likely to be occurring with blisters and scuffing. Initially the reformed epidermis is only a few cells thick and appears translucent and light pink in colour. It takes several weeks for the layers to thicken and keratinize, allowing restoration of the previous integrity. In a study of intra-operative pressure ulcers (Nixon, 2001), of the five Grade 2 pressure ulcers on various body sites, two resolved within 24 hours to blanching erythema, one resolved to Grade 1 and two remained as Grade 2, all of which were still present after eight days.

If the damage is the full thickness of the dermis then granulation tissue will be required to support the re-epithelialisation (see section 2.2.3). This could occur in an ulcer without resulting in a cavity, but evidence has not been found which would reassure the researcher that slough would never be present. Although Black *et al.* (2010) state that Grade 2 ulcers do not have sufficient inflammation to generate slough it is unclear whether they have considered full thickness skin loss as Grade 2 or Grade 3 pressure ulcers.

2.5.3 Healing Grade 3 pressure ulcers

Grade 3 pressure ulcers have tissue loss that involves dermis and subcutaneous tissue. These ulcers may contain devitalised tissue (see section 2.3.2); a prolonged inflammatory phase during which autolysis of the devitalised tissue takes place and a prolonged proliferative phase to permit the replacement with new tissue has reasonable face validity however evidence to confirm this has not been found. Ryan *et al.* (1971) examined biopsy specimens from acute and chronic pressure ulcers, they found normal or increased fibrinolysis in acute ulcers and loss of fibrinolysis and heavy deposits of fibrin in chronic ulcers. Wound exudate in chronic ulcers has been found to be an excellent medium for fibroblast stimulation (Sporn, Roberts and Wakefield, 1986). It has also been suggested that wound fluid may sustain increased bacterial overgrowth, stimulating epidermal migration (Falanga, Zitelli and Eaglstein, 1988).

2.5.4 Healing Grade 4 pressure ulcers

Very little information is available about the healing of Grade 4 ulcers that involve underlying tissues such as muscle, tendon or bone. This may because they are relatively rare events. While the principles of healing of Grade 3 lesions apply, some texts report the association with osteomyelitis (Seiler and Stahelin, 1986).

Clinically, Grade 3 and 4 ulcers are likely to present initially with some non-viable tissue such as slough or necrosis. The resolution of this is the autolytic debridement process of inflammation described in section 2.3.2. The new category of unstagable (see table 2.2) is used to describe the non-viable tissue

of undetermined depth, in the EPUAP (1998) definitions these were included in the Grade 4 ulcers.

2.5.5 Healing of heel pressure ulcers

In terms of heel ulcers no studies have been identified which specifically describe all of the healing process. A study has been identified by Campbell et al (2010a) who looked at heel pressure ulcers in a population of patients following hip replacement. They found 12 pressure ulcers on admission to the rehabilitation unit (two Grade 1, five Grade 2, four suspected deep tissue injury and one unstagable (see table 2.2 for details of classification)). After one month both Grade 1 ulcers had resolved, two of the Grade 2 ulcers had not resolved and three of the sDTI and unstagable had not resolved. This was primarily an incidence study so no detail is given of treatments.

2.5.6 Bacteria and pressure ulcer healing

All wounds that do not heal by primary closure will be colonised with micro-organisms. Wounds such as pressure ulcers and leg ulcers, which contain non-viable tissue will have more micro-organisms (Smith *et al.*, 2010). The role of these micro-organisms in wound healing has not been defined, some studies indicate a positive association between higher bacterial counts and delayed wound healing, others show no association (O'Meara *et al.*, 2000).

Patients with pressure ulcers may be treated to reduce or eliminate the micro-organisms either by topical application directly to the wound or with systemic antibiotics.

The evidence for the effectiveness of systemic and topical anti-microbial agents in pressure ulcer healing has been reviewed as part of the NICE guideline CG29 (RCN, 2005). This review found very few studies of reasonable quality, none of the studies evaluated systemic antibiotics. Of the five small trials which evaluated topical antimicrobial treatments, only one showed a significant difference in healing rates (Gerding and Browning, 1992) (the others may have been too small to show any significant effect). This study found that Grade 1 or

2 pressure ulcers treated with oxyquinoline ointment had better healing rates than those treated with standard emollient.

A search for trials of topical anti-microbials carried out since the above review identified 3 further studies which included pressure ulcers (Meaume *et al.*, 2005; Beele *et al.*, 2010; Sibbald, Coutts and Woo, 2011). All 3 studies found better healing rates or reduction of bacterial burden in wounds treated with topical anti-microbial dressings. Unfortunately all studies had very small numbers, short follow up periods and the data for pressure ulcers was not presented separately from the other wounds studied, such that any conclusions drawn from the findings need to be viewed with caution.

2.6 Tissues described in pressure ulcer classification systems

The anatomical tissues related to pressure ulcers have been described in section 1.6. Additional tissue types may be also be present in the wound bed depending on the time since the injury and the stage of the healing process. Individual pressure ulcers progress to their maximum severity before healing commences. Once healing commences, the severity classification is not applicable as the new tissue does not restore previous structure and function (National Pressure Ulcer Advisory Panel (NPUAP), 1995). Although a healing Grade 3 or 4 pressure ulcer will reduce in depth, the new granulation tissue does not have the same structure and function as the previous tissue e.g. muscle, adipose (see section 2.2). It is important to identify the tissue type as these can be used to describe ulcer healing. These are described below. Individual studies use various classification systems or provide a description of the wound, in order to make comparisons and for ease of interpretation all references to grading have been converted to those given in the EPUAP/NPAUP (2009) scales. This also applies to the studies cited in section 2.7 and throughout this thesis unless otherwise stated:

2.6.1 Blister

Although blisters are initially not open wounds, they are included here as they result from pressure damage to the skin. Blisters or sub-epidermal bullae are formed when the epidermis and dermis separate; they become filled with

serous fluid. Detached epidermis shows no visible damage at first, but becomes necrotic hours later (Seiler and Stahelin, 1986). Blisters caused by friction appear within the epidermis beneath the stratum granulosum and not in the sub-epidermal tissue (Sulzberger *et al.*, 1966).

If the loose epidermis of a blister becomes detached then the fragile dermis is exposed, which is then at risk of further damage from pressure, shear, friction and trans-dermal water loss. These are categorised as Grade 2 pressure ulcers (both when the blisters are covered or open).

2.6.2 Granulation tissue

Granulation tissue is new tissue produced during the proliferative phase (described in section 2.3.3). This tissue remains undifferentiated, soft and fragile. It can however, support the re-epithelialisation of the dermis as it migrates from the ulcer edges. Granulation tissue is seen in healing Grade 3 and 4 pressure ulcers.

2.6.3 Slough

Slough is described by Black *et al.* (2010) p.37 as:

'a coagulum of serum and matrix proteins produced by inflamed wounds. Slough is usually described as a type of necrotic tissue. However, slough is a mixture of serum proteins (fibrin, albumin, immunoglobulin) and denatured matrix proteins (collagen). These extracellular fluids form during inflammation and leak into interstitial spaces due to capillary dilation.'

Slough occurs during the inflammatory phase of wound healing and will be naturally removed through autolysis or 'passive debridement'. While it's removal by debridement is recommended as this is thought to speed up the healing process (see section 2.3.2), there is no evidence that this has any beneficial effect on pressure ulcer healing. Slough can be seen in Grade 3 and 4 pressure ulcers.

2.6.4 Necrosis

Non-viable tissue is described as necrotic. This may be any anatomical tissue e.g. skin, muscle or granulation tissue or slough. It is recognized by its dark

colour and leathery appearance. This is due to desiccation and the presence of haemoglobin. In its desiccated state it is known as eschar (Black *et al.*, 2010). In previous categories of severity, necrotic tissue was included as Grade 4, mainly because the depth of damaged tissue was unknown. This is now categorized separately as 'Unstagable'(NPUAP, 2009).

2.7 Factors which affect the healing of pressure ulcers

Potential factors were identified from a review of the epidemiological data on wound healing and through extrapolation of the theory of wound healing. Epidemiological studies identified, which include an analysis of factors associated with healing, have been compiled into table 2.3 and table 2.4 gives details of other studies of prognostic factors for healing for other similar types of wounds such as diabetic foot ulcers. These studies are cited in the subsequent sections.

Consideration was also given to factors that affect pressure ulcer development as these may also affect healing. It is thought that prevention of pressure ulcers is a good marker for healing (Margolis, Knauss and Bilker, 2002). A systematic review of the evidence for risk factors for pressure ulcer development has been conducted as part of a programme of research on pressure ulcers funded by the National Institute for Health Research (NIHR). Findings of this review have been personally communicated to the researcher and are soon to be published (Nixon *et al.*, 2010) Table 2.5 gives details of epidemiological studies of pressure ulcer development that specifically include heel ulcers.

Study	Types of study and setting	Type of wound	No of wounds/ patients	Analysis type	Significant Independent prognostic factors*	Prognostic factors: significant in univariate but non sig. in multi-variate analysis	Findings
Van Rijswijk & Polansky (1994)	Secondary analysis of prospective cohort study data Acute, extended care or rehabilitation facility	Grade 3 and 4 pressure ulcers (mean ulcer area used for multiple ulcers) body site not stated	48 patients with 56 wounds	Cox proportional hazards (PH) at baseline then at 2 weeks (time to healing)	Nutrition at baseline Age, nutrition, % reduction in ulcer area after 2 weeks	Coherent/ confused Immobility Age, gender Incontinence Diabetes General health Skin condition Number of ulcers Weight and body build Tissue type Surrounding skin Odour Exudate Pain	21 (37.5%) ulcers healed. Mean time to healing 70.3 days (SD=52.9)

Berlowitz *et al.* (1997)	Retrospective cohort Long term care institution	PU (largest ulcer, no details of body site)	819 patients	Logistic regression (healed at 6/12)	Age ≥75 years Rehabilitation services Immobility (-ve) Incontinence (-ve) Grade 2 (comp Grade 4) Grade 3 (comp Grade 4)	Bedridden Unable to feed self MS Quadriplegia Oxygen therapy No rehab. services	Grade 2=72% healed Grade 3=45% healed Grade 4=31% healed
Bergstrom *et al.* (2008)	Retrospective cohort Long term care institution	PU - all Grade 2 ulcers (excl. Grade 1,3,4)	1241 PUs on 774 people	Cox PH with frailty model for clustering of patients Max 96 days follow up	Smaller ulcer size Agitation Eating problems Needing physical assistance (-ve) A&E attendance (-ve) Ulcer on extremity (-ve)	High blood nitrogen levels Low albumin High or low BMI High temperature Dehydration Incontinence Peripheral oedema Heart failure Death	45% healed

Takahashi *et al.* (2009)	Retrospective cohort Patient's home consultations by the Mayo clinic wound specialist	PU or other chronic – ischaemic, venous, neuropathic, mixed	397 patients	Logistic regression 6/12 follow up	Multiple ulcers (-ve) High haemoglobin	Ulcer area Age Gender Stroke PVD Diabetes Depression Dementia Arthritis Falls Neuropathy*	34% healed in 6/12

Bergstrom (2005) (Same data set as (2008)	Retrospective cohort Long term care institutions	PU Grade 2 (partial thickness) or Grade 3 and 4 together (full thickness) on coccyx, back, buttock, feet, trochanter or ischial tuberosities	1589 ulcers on 882 patients	Bivariate analysis Grade 2 v Grade 3and 4 Multivariate ordinary least squares regression 12/52 follow up	Grade 2: Dementia with agitation Episode duration PU size Moist or dry dressing Incontinent of urine Soap/ saline cleanser Grade 3 or 4: Debridement Dementia and depression Sufficient enteral feeding PU size Moist (as opposed to dry) dressing	Same as independent factors for both Grade 2 and Grade 3 or 4	Analysis was for change in ulcer area, no time to healing information given

*All factors a positive influence on wound healing unless otherwise stated

Table 2.3 Prognostic factor studies of pressure ulcer healing

Study	Types of study and setting	Type of wound	No of wounds/ patients	Analysis type	Significant Independent prognostic factors	Prognostic factors: significant in univariate but non sig. in multi-variate analysis	Findings
Winkley *et al.* (2007)	Prospective cohort Community chiropody and hospital foot clinics	First diabetic foot ulcer	253 patients	Cox PH with robust standard errors Modelled for outcomes of mortality, amputation and recurrence 18/12 follow up	Mortality: Age, Better glycaemic control Moderate ischaemia Depression Amputation: Severity Recurrent ulceration: Microvascular complications	Neuropathy Type of diabetes Diabetic treatment Smoker Alcohol	84% survival rate 15% amputation 43% recurrence

Margolis *et al.* (2000)	Retrospective cohort study Meta-analysis of control arm data from RCTs -Settings not stated	Diabetic Neuropathic foot ulcer (reference ulcer)	27 630 patients	Multivariable logistic regression (data set split into modelling and validation sets 70:30) Healed wound by 20/52	Wound size, duration and Grade	Age Gender Treatment centre	47% healed, 6% amputated, 0.2% died in modelling set
Nather *et al.* (2008)	Prospective cohort study Patients treated by the multi- disciplinary foot team	Diabetic foot problems	202 patients	Stepwise logistic regression 17/12 data collection	PVD Infection	Age Gender Race Smoking Alcohol Obesity Hyperlipidaemia Stroke Hypertension IHD Duration of diabetes Neuropathy	Minor surgery on 75% patients Major amputations in 27%

Table 2.4 Prognostic factor studies of other similar chronic wound healing studies

Study	Types of study and setting	Type of wound	No of wounds/ patients	Analysis type	Significant Independent prognostic factors	Prognostic factors: significant in univariate but non sig. in multi-variate analysis	Findings
Tourtual (1997)	Prospective cohort study Nursing units within acute hospitals	Heel PUs	209 in first study 291in second study	Forward stepwise logistic regression	Braden subscale of friction and shear and moisture	Race Conscious level Pain Oedema Previous PU Topical treatment Support surface Compression devices Smoking Diseases: endocrine, metabolic, nutritional, immune, diabetes, circulatory, respiratory , renal	26% developed heel ulcer in first study 21.7% developed heel ulcer in second study

Okuwa *et al.* (2006)	Prospective cohort study Long term care facility	Lower extremity pressure ulcers (toe, heel, malleoli, tibia, fibula)	259 patients	Backwards stepwise Cox regression model	ABPI Length of bedfast period Male gender	Contractures Haemoglobin Sodium levels Chlorine levels	37 PU developed on 33 patients

Table 2.5 Risk factor studies of pressure ulcer incidence which specifically include heel ulcers

2.7.1 Patient related factors

Age

Age is often associated with delayed healing (Jaul, 2010). Wywialowski (1999) attributes this to reduced body fat, collagen and elastin. Age was not associated with healing in the Bergstrom study (2005). In the Berlowitz *et al.* study (1997) older age was associated with better healing. Age has also found to be a risk factor for development of pressure ulcers in 12 out of 32 studies that included it as a variable in their model (Nixon *et al.*, 2010). Whether age is a confounder due to the probability of other disease processes increasing with increase in age is unknown.

Gender

It is thought that wound healing can be delayed in women who are post menopause, due to lack oestrogen (Campbell *et al.*, 2010b). In one study, being male was associated with better healing rates than female (van Rijswijk and Polansky, 1994). However in the study by Takahashi *et al.* (2009) better healing was achieved in the females, the authors attributed this to higher burden of co-morbidities in men. In several studies gender was identified as a prognostic factor but did not emerge as independent from a multi-variate model. A case-cohort study (comparing information from a cohort of individuals with all patients with the disorder of interest in the population) by Margolis *et al.* (2002) identified an association between women over 65 years being treated with hormone replacement therapy (HRT) and a reduced risk of developing pressure ulcers. Nixon *et al*.(2010) found limited evidence that gender was associated with pressure ulcer development (4 out of 15 studies that included it as a variable in their model however the studies had serious limitations).

Nutrition

The argument that adequate nutrition is required for wound healing has good face validity; however evidence to support this is limited. Bergstrom *et al.* (2005) found that sufficient enteral feeding was positively associated with healing. Van Rijswijk and Polansky (1994) found longer healing times in patients who had satisfactory or poor (rather than good) nutritional status. A Cochrane systematic review of nutritional support for prevention and treatment of pressure ulcers (Langer *et al.*, 2003) found insufficient evidence such that it is unclear whether nutritional support is beneficial for healing. In the Nixon *et al*.

(2010) review, although 34 studies included nutrition and in 13 of these it emerged as an important risk factor, the quality of the studies resulted in uncertainty. Consideration needs to be given to how this factor is measured (i.e. proxy markers such as food intake, 'body mass index', haemoglobin and albumin levels) and whether malnutrition increases the risks or whether more than adequate nutrition reduces the risks compared to adequate nutrition.

Co-morbidities

The effect of co-morbidities needs to be considered in terms of their influence on mobility or perfusion. Diabetes and cardiovascular disease were not associated with healing in the Bergstrom *et al.* (2005) study; functionally debilitating conditions such as multiple sclerosis and quadriplegia were independently associated with reduced healing in the Berlowitz *et al.* study (1997). Takahashi *et al.* (2009) found several co-morbid conditions emerging as significant in the univariate analysis but non remained significant after adjustment in the multi-variate model. In the Nixon *et al.* (2010) review, most co-morbidities were not considered as individual risk factor but they were included in the 'general health status' factors, diabetes however, did emerge as an independent predictor of pressure ulcer development in 5 out of 12 studies.

Activity and mobility

Immobility is considered to be one of the main contributing factors in pressure ulcer development (Bergstrom *et al.*, 1987). It also emerged strongly in the Nixon *et al.* (2010) review. In the study by Berlowitz *et al.* (1997) immobility emerged as a significant independent predictor of non-healing. In the Bergstrom *et al.* (2008) study 'needing assistance with activities of daily living' was a factor entered in the model but was not significantly associated with improved healing. However in their explanation for the patients with dementia and agitation having improved healing they suggest the increased mobility of the agitation could increase tissue perfusion. They noted they had not included mobility or tissue perfusion in their study.

Mental state

Although dementia with agitation was associated with a greater reduction in ulcer area in the Bergstrom et al study (2005), the authors attributed this to increased mobility and perfusion. Patients in the van Rijswijk (1994) study, who were coherent had significantly better healing rates than those who were

confused, independent of other factors. Mental status was considered in the Nixon *et al*. (2010) review, very few studies included this and it did not emerge as a key risk factor for pressure ulcer development. Consideration of mental status in the literature mostly focuses on cognitive ability rather than mood; it is possible that low mood or depression will affect a patient's motivation to move.

Incontinence

The study by Berlowitz *et al.* (1997) found patients with incontinence to be significantly less likely to heal (independent of other factors). They attributed this to the bacterial colonisation and infection inhibiting wound healing. Incontinence was included in the Bergstrom *et al.* (2008) study but did not emerge as significant. Nixon *et al.* (2010) considered skin moisture, which included incontinence, as a risk factor. This emerged as statistically significant in 14 out of 28 of the studies that included it in their model.

Haemoglobin

A higher haemoglobin was found to be significantly associated with better chronic ulcer healing in the study by Takahashi *et al.* (2009). Haemoglobin is sometimes considered as a marker for nutritional deficits. In the Nixon *et al.* (2010) review, haemoglobin emerged as a significant factor in 5 out of 11 studies which included it, although the studies had major limitations.

Smoking

Smoking was identified in studies of diabetic foot ulcers (Margolis *et al.*, 2000; Nather *et al.*, 2008; Winkley *et al.*, 2007) and in the incidence of heel pressure ulcers (Tourtual *et al.*, 1997) as a prognostic factor but did not emerge as independent of other factors in any of these studies. It has not been identified as a potential factor affecting the healing of pressure ulcers, however it is not clear whether it was considered as a potential factor in some of the studies. The evidence of delayed wound healing and risk of complications such as infection is reported in surgical wounds (Salcido, 2007). Smoking is considered as an element of perfusion in Nixon *et al.*'s review (2010), although the studies identified had serious limitations smoking emerged as a significant risk factor in 2 out of 4 studies, which included it in their model.

Medications

Medications have not been considered in the pressure ulcer healing literature; this is probably because they may not be independent prognostic factors. They

may however be considered markers for the diseases they are treating and their effects on perfusion or mobility. Particular medications such as steroids and antibiotics may have a direct effect in terms of suppressing inflammation and reducing the toxicity from bacteria respectively. However no robust evidence has been found to support or refute these notions.

2.7.2 Wound related factors

Ulcer size

Most references to ulcer size are interpreted as the surface area of the wound. Graumlich *et al.* (2003) include ulcer depth as a variable, both small ulcer area and small ulcer depth were associated with better healing in the univariate analysis. Ulcer depth may be more relevant to ulcer Grade or severity (considered in the next paragraph), Berlowitz *et al.*(1997) refers to the variable of ulcer size but reports this as Stage 2, 3 or 4. Work by van Rijswijk and Polansky (1994) has demonstrated that changes in ulcer area can predict healing in full thickness pressure ulcers. They found that ulcers which did not achieve either 45% reduction in wound area after 2 weeks or 77% reduction in wound area after 4 weeks were significantly less likely to heal during the study (maximum 4 months). However ulcer area at baseline was not a predictor of healing. This may be because this was not an inception cohort (a study recruited patients with pressure ulcers, which were new events or had been present for varying lengths of time and would be at different stages in the healing process). Larger ulcer size was associated with delayed healing in the univariate analysis in the study by Graumlich *et al.* (2003). Data for the adjusted analysis is not given independently of the intervention. In the study by Takahashi *et al.* (2009) ulcer area was also significantly associated in univariate analysis, but did not emerge in the multivariate analysis. Ulcer size was found to be an independent predictor of healing in both the Grade 2 and the Grade 3 or 4 ulcers in the Bergstrom *et al.* (2005) study.

Ulcer Grade/ severity

The record review by Berlowitz *et al.* (1997) found that pressure ulcer Grade was an important predictor of healing: Grade 2 ulcers were most likely to heal and Grade 4 ulcers were least likely. Bergstrom *et al.* (2005) analysed Grade 2 and Grade 3/4 ulcers in separate models. Takahashi *et al.* (2009) did not

consider Grade, probably because they included several types of chronic wounds such as leg ulcers and foot ulcers.

Location

In the Bergstrom *et al.*(2008) analysis of time to healing of the Grade 2 ulcers, pressure ulcers on the extremities (head, arms, thighs, lower legs or heel) were significantly and independently less likely to heal than other body locations. None of the other studies identified consider location of as a predictor of healing.

Tissue type

Based on the knowledge of the wound healing process, the type of tissue in a wound will be related to the progress of healing i.e. necrotic tissue will be present following the initial damage, granulation tissue will be found later following the removal of non-viable tissue. Analysis of the data from the van Rijswijk (van Rijswijk, 1993) study found that the presence of necrotic tissue at baseline was significantly associated with reduced healing and granulation tissue was significantly associated with improvement in healing of Grade 3 and 4 pressure ulcers, however these were not subject to multi-variate analysis. In their later study van Rijswijk and Polansky (1994) did not find tissue type a predictor of healing, however there were small numbers of ulcers in this study. Xakellis and Chrischilles (1992) did find that the presence of necrotic tissue in Grade 2 and 3 pressure ulcers was associated with slower healing in a univariate analysis (but not when adjusted for the presence of exudate). Bergstrom et al (2005) and Graumlich *et al.* (2003) did not record tissue type.

Exudate

Exudate (volume or consistency) is not recorded in many studies; this is probably because it is most likely to be a subjective assessment. Higher levels of exudate are associated with the inflammatory phase of healing especially when autolytic debridement is taking place (see section 2.3.2), it may also be associated with increased interstitial fluid e.g. in the presence of oedema. Xakellis and Chrischilles (1992) found that exudate present at baseline was an independent prognostic factor for reduced healing rates in Grade 2 and 3 pressure ulcers. Only 3 out of these 39 ulcers were on the calcaneum, there was not mention of local oedema but the authors suggest that the high exudate may be associated with infection.

Wound pain

Although wound pain is acknowledged as a common feature of wounds and is strongly associated with the presence of infection (Woo *et al.*, 2008) it has only occasionally been considered as a prognostic factor for healing. Van Rijswijk and Polansky (1994) did include it in their baseline covariates but it was not found to influence healing time, although this was a small study.

Surrounding skin

The condition of the surrounding skin may be associated with adverse conditions in the wound e.g. erythema is associated with wound infection (Santy, 2008), maceration is associated with increased exudate, oedema is associated with increased interstitial fluid. All these factors may have an adverse effect on wound healing. Van Rijswijk and Polansky (1994) did not find the condition of the surrounding skin to be a predictor of wound healing. Surrounding skin condition was not considered in other studies.

Duration prior to recruitment

None of the studies cited in this section were inception cohorts. Van Rijswijk and Polansky (1994) noted and grouped the number of days prior to recruitment with 14% of pressure ulcers being present for > 9 months but did not report this as a potential predictor of healing; Bergstrom *et al.* (2005) recruited existing long term care facility residents who developed a pressure ulcer but also newly admitted residents with a pressure ulcer (previous duration of the ulcer was not recorded); Berlowitz *et al.* (1997) recruited patients who had pressure ulcers on a given date but there is no mention of ulcer duration prior to recruitment; ulcer duration was included in the Graumlich *et al.*(2003) study which found the better healing with shorter duration; in the Takahashi *et al.* study (2009) patients were recruited from their first contact with the wound clinic but prior duration is not mentioned. Wound duration has been identified as a predictor of healing in other wound healing studies (Margolis, Berlin and Strom, 1999; Margolis *et al.*, 2003).

2.7.3 Interventions

Wound cleansing and dressings

The controversy over the benefits of moist wound healing has been discussed in section 2.3.3. In the study by Bergstrom et al (2005) Grade 2 pressure ulcer

healing was positively associated with moist wound dressing as was the use of antiseptic, antibiotic or commercial cleansers compared with soap and water. A Cochrane systematic review of evidence for cleansing of pressure ulcers found a statistically significant improvement in healing with an antiseptic cleanser when compared with sodium chloride 0.9% (Moore and Cowman, 2008).

Relief of pressure

A Cochrane systematic review (Moore and Cowman, 2009) of repositioning has identified that this intervention has not been studied for healing of pressure ulcers. Pressure relieving devices such as mattresses were considered in the review of evidence for the NICE guideline (RCN, 2005), although many studies were identified the quality of studies was such that no firm conclusions could be drawn. There was some evidence to suggest that air flotation support surfaces when compared to alternating pressure supports or standard care did improve healing. There was no evidence of differences in healing of pressure ulcers with the use of low air loss (when compared with foam mattresses), alternating pressure therapy (when compared with each other or static fluid overlays) or continuous low pressure therapy (when compared with foam replacements).

2.7.4 Factors specific to healing heel pressure ulcers

In order to identify appropriate prognostic factors to include in a study of pressure ulcer healing specific to heels, consideration was given to all the factors mentioned in sections 2.7.1-2.7.3. As the types of wounds included in these studies were not specifically heels, consideration was given to factors which may be more pertinent to the pathophysiology of heel pressure ulcers (see sections 1.6.8 and 1.7.5).

Prognostic factor studies of diabetic foot ulcers (Margolis *et al.*, 2000; Winkley *et al.*, 2007; Nather *et al.*, 2008) were reviewed and two studies of risk factors for incidence of heel or lower extremity pressure ulcers (Tourtual *et al.*, 1997; Okuwa *et al.*, 2006), these studies were summarised in tables 2.4 and 2.5 respectively.

Braden subscale of friction and shear

This was identified in the Tourtual *et al.* (1997) study along with skin moisture as being independent risk factors for heel pressure ulcer development.

Ankle Brachial Pressure Index (ABPI) or peripheral arterial supply

The study by Okuwa *et al.* (2006) found several factors that were positively associated with development of lower extremity pressure ulcers but only ABPI, male gender and prolonged bed rest were independent predictors. Peripheral arterial disease was identified in the Winkley *et al.* (2007) study along with being older, low haemoglobin and depression were associated with mortality for patients with diabetic foot ulcers. ABPI was identified in the Nather *et al.*(2008) study along with infection as a significant independent predictor of major amputation.

Other factors

Margolis *et al.* (2000) in their study of predictors of healing of neuropathic diabetic foot ulcers found that wound size, duration and Grade were independent predictors of healing.

2.8 Summary

This chapter sets out what is known about the wound healing process in acute wounds then considers what happens specifically in pressure ulcers and heel pressure ulcers. It has highlighted how incomplete our knowledge of wound healing is generally and emphasises a greater lack of knowledge of pressure ulcer healing.

The specific areas where there are gaps in knowledge of pressure ulcer healing are:

- whether the evidence from acute wound healing and animal models can be translated to pressure ulcer healing in humans
- whether vascular rupture always occurs with injury
- whether the presence of platelets are an essential part of any wound healing process
- the duration (and range) of each phase of wound healing in chronic wounds i.e. inflammatory phase, proliferative phase
- whether the transition from the inflammatory to the proliferative phase can take place with little or no haemorrhage (reduced platelet derived growth factors)

- what levels of protease inhibitors are present in pressure ulcers
- the role of myofibroblasts and wound tensile strength of healed pressure ulcers

Classification systems and descriptors for the severity of pressure ulcers, the different tissue types and what is known about their relationship have been presented. Additionally no studies of inter-rater reliability of wound classification have been found specifically for heel pressure ulcers.

No tests have been identified with the purpose of diagnosing or measuring the severity of pressure ulcers therefore the internal validity of any classification scale can not as such be measured. The classification of sloughy wounds as Grade 3 as full dermal loss has not been tested.

It may be that more work has been dedicated to factors which influence the development rather than healing of pressure ulcers, however these factors are accepted as potentially influencing healing and so have been considered here. In order to identify potential prognostic factors for healing heel pressure ulcers a review of the evidence for healing all pressure ulcers and incidence in related wounds has been performed. No specific prognostic factors for heel pressure ulcers have been identified. As heel pressure ulcers have been noted to differ in terms of anatomy, mechanical properties and potential for disease from other body sites the need to identify specific prognostic factors is apparent.

The gaps in knowledge for healing of heel pressure ulcers has led to the following research questions:

What are the prognostic factors for healing of heel pressure ulcers?

What are the characteristics of patients who have heel pressure ulcers?

What are the characteristics of current practice i.e. the dressings and topical treatments including debridement, support surfaces used, specialist advice?

What is the progress of heel pressure ulcers through the stages of wound healing?

What are the adverse sequelae of this patient population e.g. death, septicaemia, amputation, infection, length of stay, destination post discharge?

Chapter 3 Pressure relieving devices for treating heel pressure ulcers: a systematic review

3.1 Introduction

This chapter reports a systematic review of the evidence of effectiveness of support surfaces or other medical devices for reducing pressure as part of the treatment of heel pressure ulcers. It describes the rationale for carrying out a systematic review, the research design, the process for identifying, appraising the quality and the risk of bias in the studies identified. It then comments on the findings of the studies and the risk of bias within and across studies. It summarises the recommendations for clinical practice and future research based on the findings of the review.

The Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) www.prisma-statement.org standard is now offered as a quality standard for reporting systematic reviews, this chapter utilises the statement in the review of the evidence.

3.2 Research question

What are the relative effects of pressure-relieving interventions used to treat heel ulcers?

3.3 Research design

It has already been suggested in the previous chapter that there are three elements, which are thought to contribute to the healing of heel pressure ulcers, namely:

- Local wound management e.g. dressings and other therapies
- Management of the patients' internal risk factors such as co-morbidities
- Relieving the pressure on the wound

It is acknowledged that a study of the healing of heel ulcers should consider all aspects of treatment including devices used to relieve the pressure on the wound. While it is beyond the scope of this thesis to carry out a primary investigation into the use or effectiveness of pressure relieving devices, it was

thought to be important to identify any evidence base for their use. The findings of this investigation may identify effective pressure relieving interventions which will be used to inform the analysis of the epidemiological study of prognostic factors for healing of heel pressure ulcers.

The most comprehensive way to review the evidence is to carry out a systematic review to a recognised quality standard. A systematic review is a method of secondary research which has the potential to assimilate all the available evidence; critically evaluate the quality and risk of bias in the studies; where appropriate combine results to produce a precise estimate of overall treatment effect (meta-analysis); provide a narrative result of the findings; generate new research questions and possibly demonstrate particular areas where there is a lack of evidence (Egger, Smith and Altman, 2001).

When carrying out a search for information it is important to have the assurance that all the available information is identified, the quality of the information is scrutinised and results assimilated appropriately.

It has been demonstrated by Antman *et al.* (1992) that evidence derived from narrative reviews or single studies may reach certain conclusions about the relative effectiveness of an intervention which are not supported by a systematic review of the evidence. These may mislead the user whereas a systematic review process provides the reader with the assurance of the findings based on the explicit nature of the quality assessment process.

The process used in this review follows the guidance from the Cochrane Collaboration (Higgins and Green, 2008). The reporting of findings is in accordance with the statement of Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) (Liberati *et al.*, 2009). PRISMA is a 27 item checklist of items which are essential for transparent reporting a systematic review and a four phase flow diagram which identifies the number of identified records, excluded articles and included studies.

The purpose of the PRISMA statement (Moher *et al.*, 2009) is to guide readers of systematic reviews as to the quality of a review, enabling them to assess the strengths and weaknesses. The PRISMA statement was developed by an international group of review authors, methodologists, clinicians, medical editors and a consumer. It followed the previously devised statement, checklist and flow diagram which gave a preferred method for presenting the report of a meta-analysis. The objective was to revise and expand this Quality of Reporting of Meta-analysis (QUOROM) checklist (Moher *et al.*, 2009). It had been recognised that the development of the science of reviews had progressed in recent years. However there were a few particular concerns that needed to be addressed:

- The requirement to have a protocol, which is registered, (also the scope to amend the protocol in light of the studies identified)
- More attention needed to be given to the assessment and reporting of bias, both within the individual studies and across studies e.g. publication bias
- The recognition that not every systematic review will identify studies where results can be assimilated statistically (meta-analysis)
- Declaration of funding

The PRISMA statement checklist can be found at www.prisma-statement.org. This chapter uses the PRISMA statement checklist from Items 3-26 to present the review and then provides a critique of the process.

3.4 Introduction

Heel pressure ulcers, their development and management in terms of risk factors and topical treatments have been described in detail in the previous chapters. Very little is known about the contribution of the reduction or relief of pressure to the wound healing process. The rationale for this review is based on the assumption that the reduction of external pressure on the pressure ulcer will have a positive effect on the wound healing process.

3.4.1 Ways of reducing pressure

Reduction of pressure can be achieved through various actions:

1. Pressure can be removed by repositioning the body such that it is supported by areas of healthy tissue e.g. if the pressure ulcer is on the sacrum, the patient is placed in a lateral position (see figure 3.1).

Right lateral position.

Figure 3.1 Patient shown in right lateral position

While relief of pressure on the ulcer may be beneficial in the short term, if pressure is sustained on healthy tissue this may result in further ulceration at a different body site. Normal practice would be regular repositioning that aims to prevent pressure being sustained for long enough to cause damage. This may include a period of time with pressure on the ulcer, when the patient has several ulcers or a certain position is essential e.g. sitting up for eating. The physiological dose of this therapy is often difficult to determine as patients tend to roll back into the supine position.

A systematic review of the evidence for repositioning to treat pressure ulcers has been conducted in December 2008 by Moore and Cowman (2009). This aimed to identify and synthesise the findings from all randomised controlled trials concerned with different repositioning regimes with the primary outcome being a measure of healing of any pressure ulcer. This review found no RCT or Controlled Clinical Trials (CCT) which met the inclusion criteria. The authors concluded that the practice of repositioning patients has good face validity. However there is no available RCT evidence to provide specific guidance with respect to how frequently the patient should be moved, or what positions to use and which, if any, particular patients would benefit.

A support surface can be used, which reduces the overall pressure on the ulcer. In the laws of physics it is known that the pressure on an object is equal to the force exerted by the object divided by the area over which the force is applied. Any devices that increases contact with the body area by conforming to the shape of the body generally or the heel specifically will reduce the magnitude of the applied pressure. The devices which work in this way are known as constant low pressure devices (CLP). They vary in their construction, for example foam, gel, sheepskin, air filled or water filled devices (see figure 3.2). They also vary in complexity and price from simple homogonous foam or gel product through air filled cells e.g. low air loss mattress to highly technical and expensive air fluidised bead beds.

Figure 3.2 Examples of CLP suppor surfaces

(from top left clockwise) Foam mattress; low air-loss mattress replacement; air fluidized bead bed

A support surface can be used which mechanically varies the pressure on the ulcer, usually by alternating between periods of none and high pressure. These are known as alternating pressure (AP) surfaces (see figure 3.3). They are mostly found as beds, mattresses or seating cushions and are constructed of a series of air filled sacs which inflate and deflate in sequence.

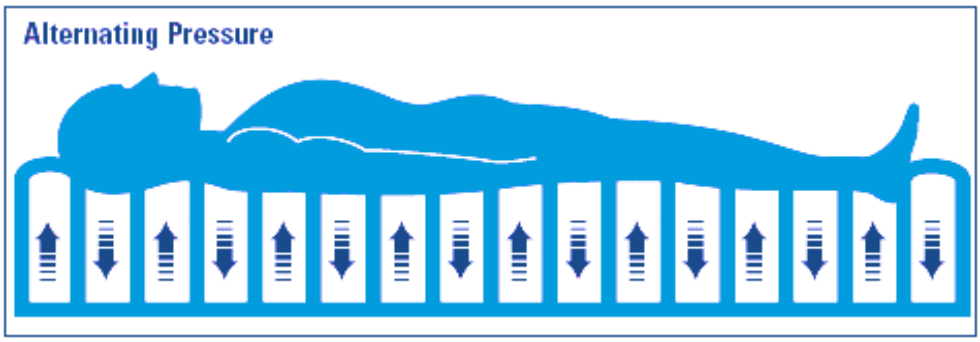

Figure 3.3 Diagram of mechanism of alternating pressure support surface

A device may be used which constantly offloads the pressure from an ulcer e.g. Repose™ heel protectors. This results in other areas of the body giving support. There is therefore a potential risk of damage to these other body tissues, these devices are generally limited to use for a short period of time or in mobile patients e.g. a device which offloads the pressure from a heel ulcer when walking (see figure 3.4). Such devices may be used in the short term during a surgical operation e.g. devices which relieve pressure from the face when patients are in the prone position.

Figure 3.4 Examples of offloading devices: Repose™ heel boot (left); PRAFO™ boot (right)

3.4.2 Types of support surfaces

When investigating the effectiveness of a support surface, a decision about a suitable control intervention will need to be made. The usual practice for the care of a patient with a pressure ulcer is to provide additional pressure relief to the standard hospital mattress or chair. In most cases it is deemed unethical to not provide additional relief for the control group. The multitudes of devices on the market vary considerably in terms of cost e.g. foam mattresses range from approximately £80 - £500 each and AP mattress replacements range from £2000 - £6000, depending on mechanical robustness, ease of use and patient

comfort. The choice of control intervention should take into account both primary outcomes (the healing of the pressure ulcer) and also the secondary outcomes such as unit costs, overall costs (including power supplies, service maintenance and depreciation), nursing time and patient quality of life. When considering the quality of a study of support surfaces, consideration will need to be given to the appropriateness of the control and the secondary outcomes. Categorisation of support surfaces would be helpful to trialists and reviewers as this would promote the use of a clinically meaningful comparator.

The previous section described broad categorisations of pressure reducing devices. Using the CLP and AP supports categories there has been further detailed categorisation of CLP devices provided by NICE in their guideline CG29 (RCN, 2005) which are based on those defined in a previous Cochrane systematic review by Cullum et al (2004):

'CLP support surfaces can be grouped according to their construction:

- *Standard foam*

The conformability and resilience of foam products may vary considerably between manufacturers. Foam may be shaped, convoluted ("egg crate foam"), of various densities or of a combination of densities.

- *Visco-elastic foam*

This is specialised foam, available in varying densities, that moulds to body shape in response to body temperature.

- *Air flotation*

This is an inflated mattress replacement/overlay that manually or automatically adjusts airflow allowing immersion and redistribution of pressure. It is adjustable to individual reposition to maintain immersion and redistribution of pressures.

- *Air fluidised*

A constant flow of air is passed into a deep tank containing minute silicone beads retained by a permeable membrane. The agitated beads take on the properties of a fluid. Lying on the surface allows significant immersion and therefore redistribution of pressure.

- *Low air loss*

A constant flow of air inflates a row of permeable fabric cells. Manual or automatic adjustment of airflow allows significant immersion and therefore redistribution of pressure.

- *Gel/fluid*

Fluid surfaces – e.g. water-filled mattresses – which allow significant immersion and therefore redistribution of pressure. The density/viscosity of the gel/fluid will govern the degree of immersion and how stable the support surface is in terms of posture.

• Combination products

Many CLP surfaces, particularly cushions, use a variety of materials to provide optimum pressure relief and postural stability.

N.B. The type and construction of cover material may have a significant impact on the conformability of the surface.'

(RCN, 2005) p.79

However, a recent Cochrane systematic review (McInnes *et al.*, 2008) of support surfaces for prevention of pressure ulcers, suggests a division of the support surfaces into 'high tech' and 'low tech'.

High tech includes all AP devices, air fluidised bead beds and low air loss mattress CLP. All other CLP devices are considered 'low tech' and other support surfaces such as limb protectors are considered in a separate category.

In reality the paucity of evidence for any type of support surface makes it difficult to guide clinical practice. Studies such as Price *et al.* (1999) have attempted to challenge the assumption that 'high tech is better than low tech'.

3.4.3 Pressure relieving devices for prevention or treatment

A study of the papers investigating the clinical effectiveness of pressure relieving devices in pressure ulcer prevention and treatment in 2002/3 found more studies focused on prevention than treatment (Zanca *et al.*, 2003). The pathophysiology of the effects of pressure on body tissues leading to ulceration led to the notion of relieving the pressure as the key preventative intervention. Similar assumptions are made when identifying the relief of pressure as the key intervention for treating pressure ulcers.

It is tempting to assume that interventions which are effective in prevention would also be effective in the treatment of pressure ulcers. While this proposition has face validity, there is insufficient evidence to suggest that the presence and magnitude of effectiveness would be the same.

McInnes at al. (2008) performed a systematic review of support surfaces for prevention concluding that foam mattress replacements were more effective than standard hospital mattresses at preventing pressure ulcers in patients at high risk. They were unable to draw any firm conclusions about the relative effectiveness of AP or CLP support surfaces but suggest that AP mattress replacements may be more cost effective than AP overlays. They did find that medical grade sheepskin overlays are more effective at reducing the incidence of pressure ulcers than standard care alone. However no details are given for the site of the pressure ulcer. The review did include some studies of heel pressure relieving devices, but no significant differences were found between the intervention and control groups. The McInnes review was conducted in 2008, this reviewer is aware of one recently published RCT of a heel pressure relieving device (Donnelly *et al.*, 2011), which was not included. Further studies may have been undertaken since this time.

The RCN (2005) reviewed support surfaces for treatment and concluded that: ‘There is some evidence to show that air flotation supports reduce the size of more established pressure ulcers compared to a modified alternating pressure support, or standard care (standard bed with CLP supports, medical grade sheepskin, gel pads, air-filled supports, water-filled mattresses and high-density foam pads).There is no conclusive evidence to support the superiority of either alternating pressure support surfaces or continuous low pressure supports in the treatment of existing pressure ulcers’. There is no detail given in the review to identify sites of the pressure ulcers on the body.

A search of the Cochrane Central Register of Controlled Trials for any trials of support surfaces for treatment has not revealed any new studies although other studies may have been carried out.

3.4.4 Heel pressure ulcers

The previous chapter has already described the difference in the anatomy of the heel and the pathophysiology of pressure ulcer development relative to other body sites at risk of pressure ulcer development. It has also discussed what is known about the healing process and suggested potential physiological

differences found in the feet, which may specifically influence the healing process in the heel.

The systematic reviews discussed in section 3.4.3 were carried out over a year ago and do not give any details of healing heel ulcers. It is for these reasons that this systematic review has focused specifically on the healing of heel pressure ulcers.

3.4.5 Objectives

To examine whether any pressure relieving devices improve the healing of heel pressure ulcers this study reviews all randomised controlled trials (RCTs) that assess efficacy of devices for treating heel pressure ulcers compared to other devices or standard care in participants of any age in any care

While several related reviews use the term 'support surface' to describe the intervention of interest, it was felt that this term was too limiting as it suggests a bed, mattress or cushion. It was felt that the term 'pressure relieving device' is a broader, more inclusive term which would be more appropriate for heel ulcers. It was expected that this would identify studies of specific devices for off loading the pressure from the heel as well as support surfaces.

3.5 Methods

3.5.1 Protocol and registration

The protocol is published on the Cochrane data base, address:
http://mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD005485/frame.html
It is registered as - McGinnis E, Stubbs N. Pressure relieving devices for treating heel pressure ulcers (Protocol). Cochrane Database of Systematic Reviews 2005, Issue 4. Art. No.: CD005485. DOI: 10.1002/14651858.CD005485.
The full review will be published on 7th September 2011 (Issue 9).

This protocol was written by the researcher and approved by the co-author.

According to Liberati *et al.* (2009), having a review protocol which is available for scrutiny reduces risk of bias occurring when carrying out the review.

Predetermined outcomes, methods of data extraction and analysis will reduce the likelihood of post hoc decisions such as selective outcomes reporting which may lead to bias.

A study by Silagy *et al.* (2002) examined 47 Cochrane systematic reviews and found that 43 had a major change such as the addition or deletion of an outcome measure, between the protocol and full publication. While some of these changes may be due to the exclusion of outcomes which were not reported in any of the studies, it is well known that bias from selective outcome reporting in RCTs exists (Chan *et al.*, 2004) and therefore the potential for this to be extrapolated to a review is high. This may lead to over estimates of the benefits of the intervention.

3.5.2 Eligibility criteria

3.5.2.1 Types of participants

All patients with existing heel pressure ulcers in any care setting were eligible. For the purposes of this study, a heel pressure ulcer was defined as localized damage to the skin and underlying tissue (EPUAP, 1998) Grades 1-4, believed to be caused by pressure, shear or friction, found on all or part of the external aspect of the calcaneum (the bone at the back of the foot) extending from the plantar surface to below the Achilles tendon.

Consideration has been given to the inclusion of patients with diabetic foot ulcers (DFUs) on the heel. DFUs are wounds in people with diabetes, which occur anywhere on the foot, including the heel and can be pressure related. There are two Cochrane systematic reviews on preventing and treating DFUs, but these do not define foot ulcer so may include heel pressure ulcers (Spencer, 2000; Valk Gerlof, Kriegsman Didi and Assendelft Willem, 2001) Neither of these reviews looked at heel ulcers as a subgroup. Patients with DFUs of the heel will therefore be included.

3.5.2.2 Types of interventions

Pressure relieving or reducing aids are usually used in combination with wound care to improve healing of a pressure ulcer. Pressure-relieving aids include the following devices listed below.

Mattresses:

foam overlays

foam mattress replacements

alternating air-filled overlays

alternating air-filled mattress replacements

air overlays

air-fluidised bead beds

Heel-specific aids:

air-filled booties

foam foot protectors

gel foot protectors

pillows and other aids positioned under the legs to relieve pressure

splints or other medical devices

sheepskin

It was intended that eligible studies would be those that compared any of the interventions listed above either with each other, no intervention or standard care as defined by the trial. Where records were identified, which did not specify on which body sites the pressure ulcers were, it was intended to retrieve full articles and, if appropriate, write to authors to establish whether heel ulcers were included and if data was available to carry out separate analysis.

3.5.2.3 Types of outcome measures

Primary outcomes

1. Proportion of heel ulcers healed within a defined time period
2. Time to complete healing of heel ulcer

Secondary outcomes

1. Costs of pressure relieving devices
2. Total costs of interventions (including servicing and maintenance) where given
3. Any measure of patient comfort
4. Any measure of ease of use
5. Any measure of health-related quality of life
6. Adverse events associated with the intervention.

While the main outcome of interest is related to the healing of the ulcers, evidence from other studies (RCN, 2005) suggest that it is unlikely that a large body of evidence in this field will be found. In order to provide guidance for clinical staff where there is little evidence of effectiveness for interventions it is important to consider all the related outcomes which will be of relevance to both clinical staff and patients as these may inform decisions.

3.5.2.4 Types of studies

All randomised controlled trials (RCTs) which compared the effectiveness of pressure-relieving devices on heel pressure ulcer healing were included. RCTs which compared effects of pressure relieving devices for diabetic foot ulcers specifically were to be included if heel ulcers were separately identified. Controlled clinical trials (CCTs) were to be included only in the absence of RCTs. There was no restriction on publication status, year or language of publication. This is discussed in further detail in section 3.6.6.

3.5.3 Information sources

Trials to be considered for this review were sought from the Cochrane Wounds Group Specialised Register and the Cochrane Central Register of Controlled Trials (CENTRAL) which considers years from 1966 to present (searched 25.3.11). Searches were also performed on Ovid MEDLINE – (1948 to November Week 3 2011), Ovid MEDLINE - In-Process & Other Non-indexed Citations (Searched 29.3.11) Ovid EMBASE - (1980 to 2009 Week 12), EBSCO CINAHL – (1982 to 25.3.11).

The Cochrane Wounds Group Specialised Register has been compiled through searching the major databases including MEDLINE, CINAHL and EMBASE and is regularly updated through searching the Cochrane Central Register of Controlled Trials, hand searching of wound care journals and relevant conference proceedings.

The search strategy was developed from strategies used in similar reviews of pressure relieving devices. It included additional terms used by current

manufacturers to describe their products, also terms used by podiatrists to describe heel specific devices. Terms used to identify RCTs and CCTs were those used by the Cochrane Wounds Group. The strategy was developed by the lead reviewer in collaboration with the co-reviewer, a senior podiatrist and the Cochrane Wounds Group. It was run by a member of the Cochrane Wounds Group. The strategy was approved as part of the protocol by the reviewers.

3.5.4 Search

The following search strategy was used:

#1. BEDS single term (MeSH)
#2. (bed or beds or bedding)
#3. mattress*
#4. (cushion* and (foot or feet))
#5. (foam or foams or cutfoam)
#6. overlay*
#7. (pad or pads or padding)
#8. (gel near pressure)
#9. (gels near pressure)
#10. (pressure near relie*)
#11. (pressure near device*)
#12. (pressure near reduction)
#13. (pressure near reducing)
#14. (pressure near redistribution*)
#15. silicore
#16. ((low next pressure) and support*)
#17. ((low next pressure) and device*)
#18. (constant near pressure)
#19. (alternat* near pressure)
#20. (air near suspension*)
#21. (water near suspension*)
#22. (heel near protector*)
#23. sheepskin*
#24. (foot next waffle)
#25. (air next bag*)

#26. (elevation near device*)
#27. (static next air)
#28. shoe*
#29. footwear*
#30. (callus near remov*)
#31. hosiery
#32. orthoses
#33. orthosis
#34. (orthotic near device*)
#35. (orthotic near therap*)
#36. (foot near pressure)
#37. (foot near protect*)
#38. (feet near pressure)
#39. (feet near protect*)
#40. (heel near pressure)
#41. (heel near protect*)
#42. (contact and cast*)
#43. (walking near cast*)
#44. (boot near pressure)
#45. (boots near pressure)
#46. (booties near pressure)
#47. (glove* near water)
#48. (heel near lift)
#49. (heel near float*)
#50. (heel near suspension*)
#51. (heel near elevat*)
#52. (splint* near heel)
#53. (trough near leg*)
#54. (trough near foot)
#55. (trough near feet)
#56. (trough near heel)
#57. (glove* and heel)
#58. (foot near device*)
#59. (feet near device*)
#60. (heel near device*)

#61. pillow*

#62. (#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #56 or #57 or #58 or #59 or #60 or #61)

#63. DECUBITUS ULCER explode all trees (MeSH)

#64. (decubitus near ulcer*)

#65. (bed near ulcer*)

#66. (pressure near ulcer*)

#67. (pressure near sore*)

#68. (bed near sore*)

#69. (#63 or #64 or #65 or #66 or #67 or #68)

#70. (#62 and #69)

#71. (heel or foot or feet)

#72. (#70 and #71)

The search strategy was last run on 30th March 2011.

There was no restriction on date of publication, language of publication, or publication status (published or unpublished work). Studies and articles cited in articles identified were checked for eligibility.

3.5.4.1 Searching other resources

Experts in the field were contacted and asked if they had been involved in any further studies or were aware of recent or ongoing studies on the treatment of heel pressure ulcers. Manufacturers of pressure-relieving equipment were contacted for studies which included heel pressure ulcers. In the original published protocol (McGinnis and Stubbs, 2005) it was planned to hand search two journals: Phlebology and Diabetic Foot for the ten most recent years. At the time these journals were not indexed in any electronic data base and the reviewer thought that they may be a potential source of publication of relevant studies. These two journals are now indexed in Medline and the most recent year hand searched at the Cochrane Wounds Group editorial base.

3.5.5 Study selection

Two reviewers separately examined the titles and abstracts of trials generated by the search to identify those with potential relevance. Disagreements were resolved by consensus. Full texts of potentially relevant articles were retrieved. With the full text of these articles, the two reviewers independently assessed each study for inclusion according to the selection criteria.

3.5.6 Data collection process

Details of eligible trials were extracted and summarised using a data extraction sheet. The data extraction sheet was devised by the lead reviewer, who identified the key information required from the study and had examined similar sheets used by other reviewers, it was piloted by each reviewer using it to data extract from the same publication and comparing the extractions

Attempts were made to obtain any missing data by contacting the study authors. Data from studies that had been published more than once were included only once. However, where trials were published more than once, the data extraction process utilised all available sources to facilitate the retrieval of the maximum amount of trial data possible. Data extraction was undertaken by the two reviewers independently. Disagreements were resolved by consensus.

3.5.7 Data items

The following data was extracted:

- author, title, date of study and publication
- source of reference
- sample size
- patient inclusion and exclusion criteria;
- country and study setting;
- baseline variables, for example age, sex, diagnosis, co-morbidity, baseline risk, details of existing ulcers;
- description of interventions;
- numbers of patients - both randomised and analysed;
- description of any co-interventions;
- follow-up period;

- results;
- outcome measures;
- adverse events;
- use of intention-to-treat analysis;
- trialists' conclusions.

3.5.8 Risk of bias in individual studies

The validity of the studies was assessed to detect potential sources of bias from the study design. Assessment included:

- use of clear inclusion and exclusion criteria;
- extent of allocation concealment at the point of randomisation;
- method of generation of the randomisation sequence;
- baseline comparability of treatment groups for important variables;
- use of intention-to-treat analysis - whether participants were analysed in the groups to which they were originally randomised;
- length of follow up and extent of loss to follow up;
- evidence of blinded outcome assessment.

The information was recorded on the data extraction sheet. Data was extracted by each reviewer separately for each trial, which definitely met the inclusion criteria. Those where there was uncertainty (usually due to lack of information), clarification was sought from the trial authors.

Following attempts to contact authors the two reviewers then considered the included studies together with all additional information provided. This enabled agreement to be reached on what should be used in the data synthesis.

3.5.9 Summary measures

Summary measures were not pre-specified. The primary outcome measures were the number of ulcers healed in a given time or time to complete healing. The results of ulcers healed or not healed (dichotomous variable) were presented as Relative Risk (RR) with confidence intervals (CI). Relative risk is the pressure ulcer healing rate in the intervention group divided by the healing rate in the control group and indicates the likelihood of pressure ulcer healing

on an intervention device compared with a comparison device. RR will be used rather than odd ratio as event rates are high and odds ratio is likely to give an exaggerated impression of the size of the effect (Deeks, 1998). If studies had been identified with primary outcomes as time to complete healing (a continuous measure using the same scale) then results would have been presented as Mean Difference, This would be a calculation of the difference in means using the number of participants, the mean response and its standard deviation to weight each study.

3.5.10 Planned method of analysis

A narrative summary and if appropriate, a meta-analysis, of results was planned. The method of synthesising the studies depends upon the quality, design and heterogeneity of studies identified. If the clinical characteristics, methodology, outcome measures or statistical tests are too variable it would be inappropriate to perform a meta-analysis. It was planned to estimate the extent of heterogeneity between study results using the I^2 statistic (Higgins *et al.*, 2003). This examines the percentage of total variation across studies due to heterogeneity rather than to chance. Values of I^2 over 75% indicate a high level of heterogeneity. In the presence of statistical heterogeneity we planned to use a random-effects model for pooling. If there was no statistical heterogeneity or where I^2 is less than 75%, we planned to apply a fixed-effect model. Results would be presented with 95% confidence intervals. Estimates for dichotomous outcomes would be reported as relative risks and mean difference for continuous outcomes.

3.5.11 Risk of bias across studies

This inclusion of this item is a relatively new consideration for systematic reviews and it was not anticipated at the protocol stage of this review. It is however discussed in more detail in the results section.

3.5.12 Additional analysis

It was planned to carry out two subgroup analyses, to identify whether the summary effects would vary in relation to specific characteristics of study participants:

- Specific conditions e.g. diabetes or peripheral vascular disease are known to affect healing rates (Fahey *et al.*, 1990)
- Grade of ulcer. It is known that the reliability of pressure ulcer diagnosis and classification is particularly poor with Grade 1 pressure ulcers (Nixon *et al.*, 2005). A comparative analysis of outcomes for groups which include or exclude Grade 1 ulcers was planned.

3.6 Results

3.6.1 Study selection

A flow diagram is given for the study selection process in figure 3.5 using the PRISMA template.

PRISMA 2009 Flow Diagram

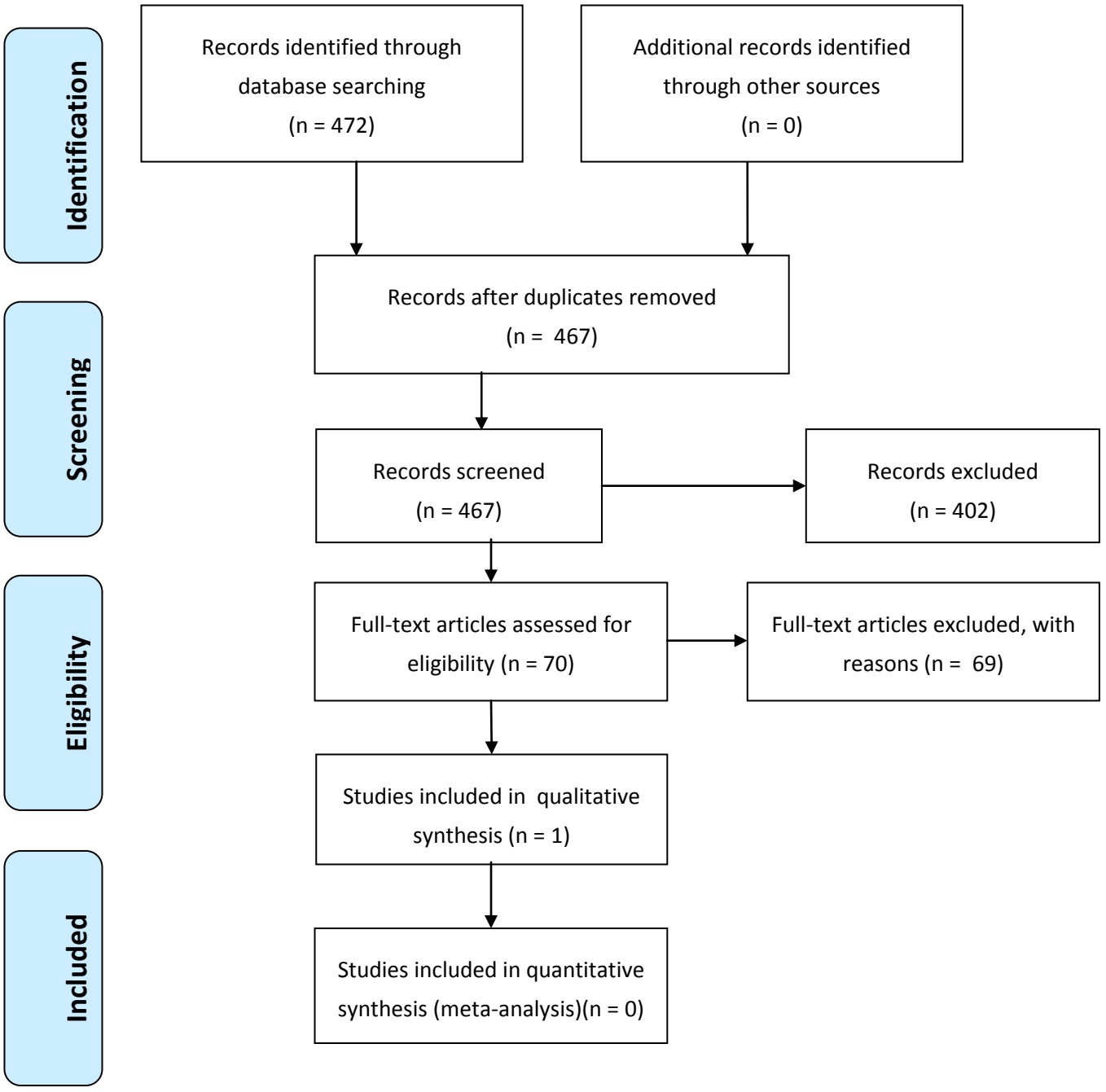

Figure 3.5 PRISMA flow diagram (adapted from Moher *et al.* (2009))

The initial search identified 472 records of studies. Letters or emails were sent to ten wound care experts, three replies were received. Fifteen letters were sent to manufacturers of pressure redistributing devices, two responses were received. No further trials were identified.

Following independent review of the abstracts by the two reviewers, 70 were thought to potentially meet the inclusion criteria or contain useful references and were retrieved. The two reviewers independently assessed the studies for inclusion according to the selection criteria. Several studies were thought to be potentially eligible if the original data was available and heel outcomes could be analysed separately. 20 authors were written to or contacted, three responses were received: one stating no heels were included, one stating no separate data was available and one providing the original thesis with full method and results.

Fifteen studies were conference presentations. Searches for further publications by each of the listed authors were made but only two full publications with useful data were obtained.

Sixty nine studies were excluded: ten were reviews, 18 studies were not RCTs, 18 studies were concerned with prevention (rather than treatment of the ulcer), nine considered treatment of pressure ulcers on body sites other than the heels, 12 considered treatment of ulcers on various body sites including heels but data could not be analysed separately and two were reviews in another language.

3.6.2 Study characteristics: Russell (2000) Published and unpublished data

One study met the inclusion criteria:

Russell L, Reynolds TM. Randomised controlled trial of two pressure-relieving systems. Journal of Wound Care 2000;9,2:p52-55.

Characteristic	Description
Sample size	141 patients (113 patients with heel ulcers)
Inclusion and exclusion criteria	Inclusion criteria - patients with a pressure sore Grade 2 (Torrance, 1983) i.e. non blanching erythema with and without epidermal loss, and above; able to give informed consent. Exclusion criteria - patients who were unwilling to participate; randomised equipment was not available; patient who had previously been in the study; patients who weighed > 25 stones.
Care setting	Healthcare of the elderly unit in the UK

Baseline variables	The following baseline variables were given and appeared to the reviewers to be similar - age, Waterlow score (risk of developing pressure ulcers (Waterlow, 1998), Burton score (nutrition indicator (Russell *et al.*, 1998)), average Grade of sore, worst Grade of sore. Gender and duration or size of pressure ulcer was not recorded
Study group A	70 patients (55 with heel ulcers): average severity of pressure ulcers (Torrance (1983)) = 2.46
Study group B	71 patients (58 with heel ulcers): average severity of pressure ulcers (Torrance (1983))= 2.57
Description of interventions	Both groups had two interventions: AP mattresses and cushion systems Group A: Nimbus 3 mattress and Aura seat cushion Group B: Cairwave mattress and Proactive seat cushion
Number of patients (randomised and analysed)	In total this study recruited 186 patients, 141 were analysed. This included both heel and sacral pressure ulcers. As a result of further communication with the author, heel data were provided and could therefore be analysed separately. See figure 3.6 below.
Description of co-interventions	Pressure ulcers were treated according to the Trust Wound Care Formulary, the Tissue Viability (TV) nurse's recommendations and the TV link nurses protocol. Patients were turned according to manufacturer's recommendations: four hourly for those assigned to the Nimbus system and eight hourly for those assigned to the Cairwave system, or more often if requested by the patient or considered necessary by the nursing team.
Follow up period	Patients were followed up till they healed, were discharged or died. Data was collected weekly. No time to healing was given.
Allocation method	Randomisation was by computerised random number generation and treatment allocation was by consecutively numbered sealed opaque envelopes. Personnel and patients were not blinded to treatment.
Results - both group	113 patients with heel ulcers were randomised to either Nimbus + Aura or Cairwave + Proactive. See figure 3.6 for details.

Outcome measures	Completed study (healed, discharged or died), also patient comfort. Patient comfort was measured using a visual analogue scale taken from Gray and Campbell (1994) An economic evaluation was planned but no details are given in the available documents. Data collectors for healing outcomes were not blinded to the intervention but those who collected patient comfort data were.
Adverse events	No adverse patient events were reported. Two Nimbus mattresses, 10 Aura seat cushions, 7 Cairwave therapy systems and 6 Proactive cushions required repair.
Use of intention to treat analysis	Although the author says an intention to treat protocol was used. The analysis is given for those who 'completed study' and those who 'completed study' and died. Those who were discharged were assumed not to have healed. There is no analysis which takes full account of all those lost to follow up
Trialists conclusions	Nimbus mattress + Aura cushion is more effective for treating heel ulcers than the Cairwave mattress + Proactive cushion.

Table 3.1 Russell (2000b) Study characteristics

The data in Russell's publication and personal communication included sacral pressure ulcers. This heel ulcer information has now been extracted and has been compiled into a flow diagram shown in figure 3.6.

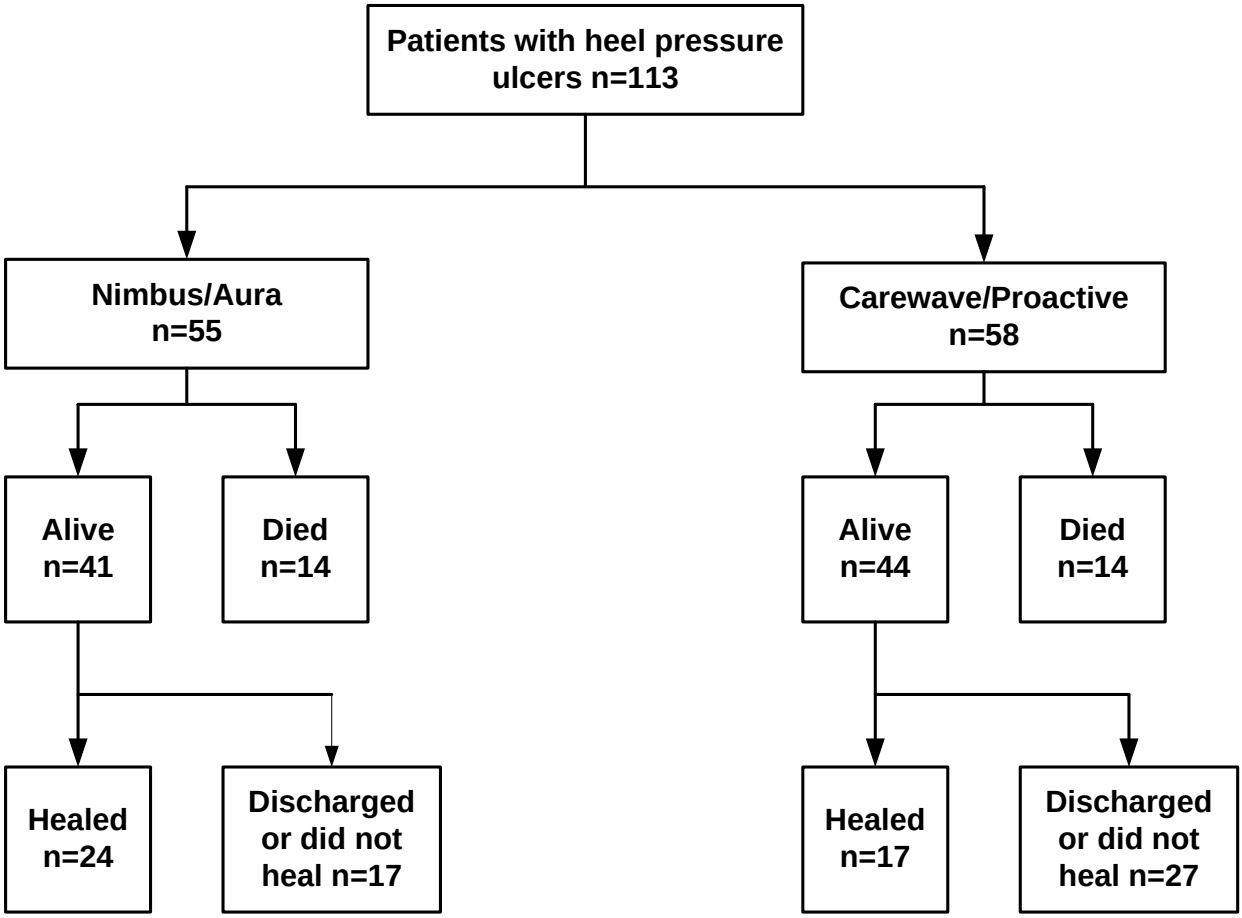

Figure 3.6 Flow chart of data heel ulcer data, extracted from publication and personal communication

3.6.3 Risk of bias within the study

When carrying out a review of research studies it is important to consider bias at both the study level and the review level. Bias at review level is considered in section 3.6.6.

A bias in a research trial is ‘a systematic error or a deviation from the truth in results or inferences’ (Higgins and Green, 2008). Biases can occur when either the design, conduct, analysis or reporting of a trial have insufficient rigour. The effect of a bias may lead to an over or under-estimation of treatment effect depending on the type of bias. It is important to consider bias in each reviewed study as the process of meta-analysis carries a risk of overestimating effect size if the pooling of results are taken from poor studies, whose results are in favour of the intervention. It is important to recognise that the results of a study

may not be biased even though it may not have been carried out in a rigorous manner or it may have been inadequately reported (due to word limits in publications). In order not to assume ‘error’ the term ‘risk of bias’ is preferred by reviewers. The main types of bias can be classified as follows:

- Sequence generation - was the sequence for allocation of the intervention adequately generated (truly random)?
- Allocation concealment - was the treatment allocation adequately hidden from those who were recruiting subjects and the participants themselves?
- Blinding of participants, personnel and outcomes assessors - was knowledge of the allocated intervention adequately prevented in the study such that any results could not be affected by individuals preconceived ideas or expectations?
- Incomplete outcome data - where all outcome data was not available, has the analysis taken this into account and considered how this affected the results?
- Selective outcome reporting - do reports of the study include all planned outcomes, omissions may suggest only favourable outcomes reported or not address important qualitative outcomes?
- Other sources of bias - any other important concerns about the quality or validity of the study such as inclusion bias (selection of subjects from an unrepresentative group), performance bias (systematic differences in the care given apart from the intervention of interest), attrition bias (loss of participants to follow up, particularly when unequal across groups)?

(Higgins and Green, 2008)

3.6.3.1 Risk of bias in Russell (2000)

In the Russell study, adequate sequence generation to allocate the intervention was achieved by using a series of computer generated random numbers to allocate intervention, which were placed in sealed opaque consecutively numbered envelopes to achieve allocation concealment.

The risks of biases present include:

- Performance bias
    - blinding of participants and care providers did not take place. In a trial of a medical device it is usually impossible to blind the patient to the treatment. While both groups had a specific intervention, patients previous experience of particular equipment may influence their comfort reporting. It is not possible to blind the staff caring for the participants.
    - detection bias It is very difficult to blind the data collectors. An option would be to take photographs of the wounds and have them analysed by someone blinded to the intervention. In this study the data collection was carried out by one of 3 designated nurses. There was no stated test of inter-rater reliability. However, the nurses 'regularly work together', suggesting some degree of agreement. A study by Nixon *et al.* (2006) included an assessment of inter-relater reliability for the grading of pressure ulcers. This study found good levels of agreement between research nurses although where agreement did not occur this was for intact skin, blanching and non-blanching erythema. The Russell study only recruited those with Grade 2 and above using the Torrance scale (1983). However, Grade 2 on this scale includes non-blanching erythema with and without epidermal loss. It is probable that their assessment of this Grade of pressure ulcer would not have good agreement. Reliability of the skin assessment cannot be assured. Data collection for the patient's comfort rating was carried out by an auditor, who was unfamiliar with the treatments. The data collection tool was based on a non-validated scale used by Gray and Campbell(1994).
- Attrition bias
    - Protocol deviations occurred with two patients being unable to sleep on the mattresses (no detail of which allocated treatment group these were). Loss to follow up has resulted in a high risk of bias. One aim of the study was to compare the efficacy of the two mattresses and cushion systems in the treatment of pressure ulcers. The results are given for numbers of patients who

completed the study (healed, discharged or died). Intention to treat (ITT) analysis is reported to have been carried out, however the author only includes those who had died not those who were discharged from hospital. The loss to follow up was up to 56% in one group and 71% in the other. Even if a full ITT analysis had been carried out these significant losses can bias the study (Bowers, House and Owens, 2005). Details of loss to follow up are given and are summarised in figure 3.6 of this review.

The length of follow up is not given; data were collected at weekly intervals many patients were discharged after only the baseline data collection. The average length of stay (21.5 days for both groups) gives an indication of follow up time although there is no suggestion of a relationship between hospital stay and healing.

Both treatment groups were comparable at baseline for most of the relevant variables however the gender mix is not given or the size and duration of the ulcer prior to recruitment. It is known that healing in post menopausal women is longer than in men due to the influence of hormones (Gilliver and Ashcroft, 2007), (Gniadecki *et al.*, 1996) and studies of leg ulceration and diabetic foot ulceration have suggested that the size and duration of a wound is likely to influence its likelihood of healing (Margolis, Berlin and Strom, 2000; Margolis *et al.*, 2000). If a treatment group had more older women or pressure ulcers of greater size and duration it is likely that the results would favour the other group.

Although this was a well designed and executed study, the non-reporting of baseline comparability for gender and duration and size of ulcers and the significant loss to follow up through patients either dying or being discharged has a major impact on the confidence which can be placed on the findings of the study.

3.6.4 Individual results of the Russell (2000) study

The primary outcomes of interest to this review were proportion of heel ulcers healed within a defined time period or time to complete healing of heel pressure ulcers. Russell (2000) used the outcome of 'completed study'. Results are reported for the number of heel ulcer patients who completed the study and an ITT for those who completed and died. (Two patients healed in the Cairwave group and 6 patients in the Nimbus group).The following figures (figure 3.7 and 3.8) show the risk ratios and forest plots for both these sets of data.

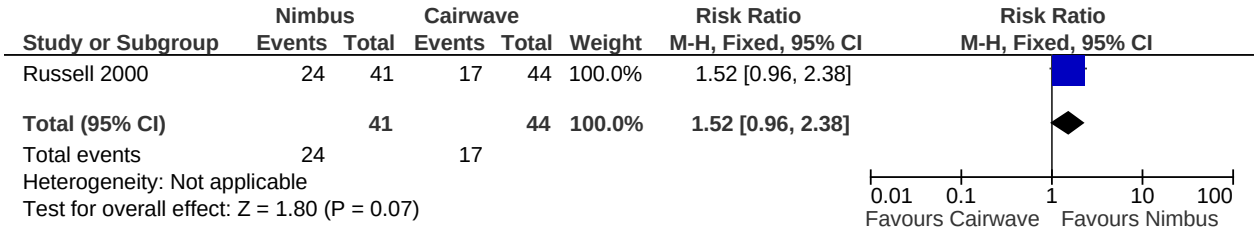

Figure 3.7 Data from Russell study including Forest Plot where event is healed and denominator is 'completed study alive'

This gives a risk ratio of 1.52 with a confidence interval of 0.96 - 2.38. Although this shows a trend towards the effectiveness of the Nimbus and Aura system, the confidence interval crosses the line of no effect so the difference in effect is not statistically significant (p = 0.07)

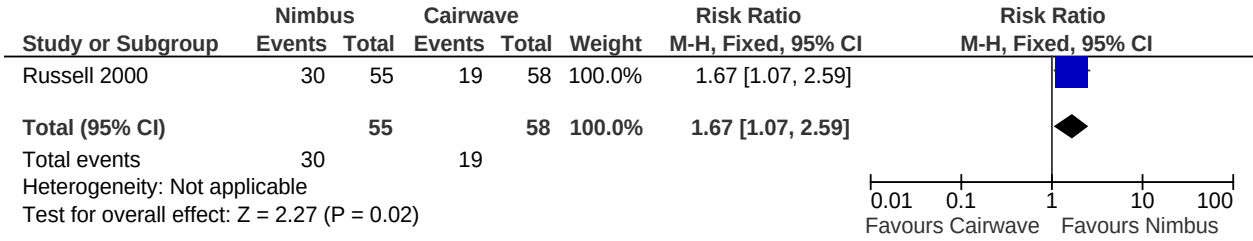

Figure 3.8 Data from Russell study including Forest Plot where event healed and denominator is 'completed study alive + died'

Figure 3.8 represents an analysis carried out by Russell et al (2000) which includes the patients who died. It gives a risk ratio of 1.67 with a confidence interval of 1.07 - 2.59). As this does not now cross the line it is statistically significant (p = 0.02) in favour of the Nimbus and Aura mattress system.

Further sensitivity analyses are performed taking into consideration patients who were either discharged prior to healing or did not heal is given in section 3.6.7.

Secondary outcomes:

- Cost of pressure relieving device - costs of the mattresses and cushions are not given
- Total cost of interventions - total costs of interventions are not given (an economic analysis was planned but not reported in the documents available)
- Patient comfort - Patient comfort was measured using a non-validated visual analogue scale taken from Gray and Campbell (1994). Data were collected by members of the audit department. It contained questions which assessed mattress comfort, sleep and cushion comfort. The information available is not presented separately for sacral and heel pressure ulcers. Statistical comparisons were only carried out on data from patients who completed the trial. Mean comfort scores were calculated for each question and did not show any statistical significant difference between the 2 groups. Full details are given in table 3 of the publication (Russell *et al.*, 2000)
- Ease of use - Ease of use was not specifically considered although reference is made to training on both mattress systems and a 'run in' period to ensure staff were familiar with both systems. No specific differences were reported.
- Health related quality of life - this is not reported.
- Adverse events - No patient adverse events were reported. 2 Nimbus mattresses, 10 Aura seat cushions, 7 Cairwave mattresses and 6 Proactive cushions required repair
- Subgroup analysis - not enough detail is available to perform subgroup analysis for either co-morbidity or Grade of ulcer.

3.6.5 Synthesis of results

As only one study was included, no synthesis could be undertaken.

3.6.6 Risk of bias across studies

When carrying out a systematic review it is important to consider both the risk of bias within each study and the risk of bias across all the identified studies. It is well known that studies which show a statistically significant treatment effect are more likely to be published, more likely to be published in English, more likely to be cited by other authors and more likely to produce multiple publications and therefore more likely to be identified for systematic reviews (Sterne et al Chapter 11 p 189 in (Egger, Smith and Altman, 2001). It is with this in mind that the rigorousness of the method for finding studies is vital. A systematic review may show evidence of treatment effect from a number of studies when the reality is either no evidence of effect or a result which favours the control when unpublished studies are included. Even when searches for studies have been rigorous it is advisable to check for publication and other biases across the retrieved studies. It is also apparent that trial quality influences the size of estimated treatment effects and smaller trials are more likely to be of poorer quality (Egger, Smith and Altman, 2001)This information can be used to produce a funnel plot (a scatter diagram of treatment effect against study size) which will show asymmetry when either publication bias or exaggerated treatment effects are present in small studies of poor quality.

While the main concern regarding bias across studies relates to whether studies are published or not, there are other potential sources of bias e.g.:

- Duplicate publications (where the reviewers are unable to identify multiple publications of the same study). In 1989 Gotzsche demonstrated through a review of trials of non-steroidal anti-inflammatory drugs for the treatment of osteoarthritis, the difficulties in identifying multiple publications and the discrepancies such as differences in outcomes reported and treatment effects, between different publications of the same study (Gotzsche, 1989). He recommended the adherence to editors' guidelines to reduce these occurrences. While it could be argued that this problem is likely to have reduced in recent times a more recent review by Tramer *et al.* (1997) of trials of an anti-emetic to reduce post operative vomiting, also

demonstrated that the results of nine trials had been published 25 times, similar difficulties were found in identifying duplicates and the effect of a meta- analysis of all the studies led to a 23% over estimate of the drugs efficacy.

- Time lag bias (where trialists have delayed submitting studies for publication with a view that non significant findings will not be of interest) A review by Hopewell *et al.* (2007) identified two studies which looked at time to publication. Trials were classified by whether they showed a positive effect or a non-significant or null. It was found that those which showed a positive effect were published several years sooner than those with a null effect.
- Location bias (where studies have been published in non indexed journals and are difficult to identify or the study has been carried out in a third world country). A review by Pittler *et al.* (2000) demonstrated that trials of complementary therapies with a positive result were more likely to be published in low impact journals and were more likely to be of poorer quality whereas trials published in high impact journals showed equal positive and null or negative results.
- Language bias (non significant findings are more likely to be published in a local rather than international journal). Egger *et al.* (1997) compared publications of studies in German and English and found that more studies with positive results were published in English. Although this study was carried out some time ago and it is thought that more studies are published in English now, it remains important for a review to consider all languages to reduce the possibility of bias in the results.

In order to minimise any publication bias manufacturers of pressure relieving devices were contacted for unpublished data and leading experts at research centres were contacted for any unpublished studies. Attempts were made to reduce duplicate publication bias by checking trialists' names and similarities in study settings, populations or interventions. As there was only one study identified, duplicate publication was not an issue. Language bias was hoped to be reduced by considering studies in any language however, although no original studies were identified in non English language, 2 reviews were

identified which were not translated. The search strategy identified several other treatment studies which included heel ulcers but attempts to contact the authors for separate heel data proved fruitless.

3.6.7 Additional analysis

It had been planned to look at subgroups such as those with diabetes, and those with Grade 1 (EPUAP) - non blanching erythema. In the Russell *et al.* (2000) study no detail was given for Grades of ulcer or co-morbidities to enable subgroup analysis.

The issue of missing data in the Russell *et al.* (2000) is worthy of further investigation. Sensitivity analysis have been performed below, firstly looking at heel ulcers which healed in each group (figure 3.9)

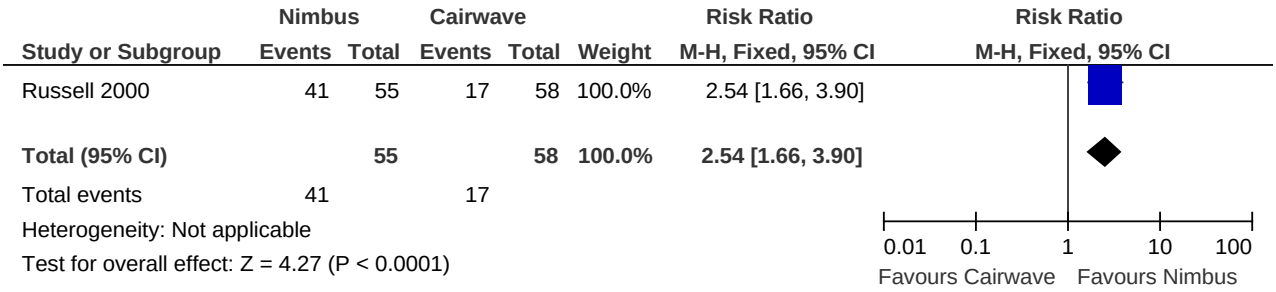

Figure 3.9 Data for Russell study showing risk ratio and forest plot for heel ulcers healed

However, given that there were greater numbers of patients lost to follow up in the Cairwave group two alternatives were also considered: if all the patients lost to follow up in the Cairwave group had healed (figure 3.10) and if all the patients lost to follow up in the Nimbus group had healed (figure 3.11).

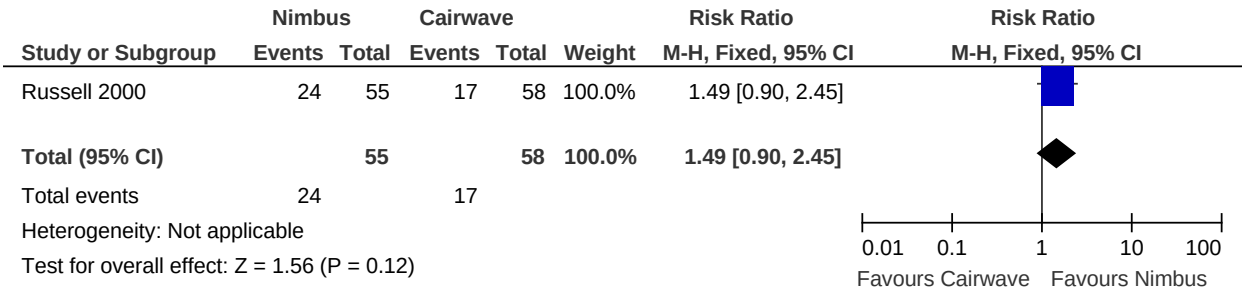

Figure 3.10 Data from Russell study showing risk ratio and forest plot: all patients lost to follow up in Cairwave group assumed to have healed and those in the Nimbus group assumed to have not healed

Figure 3.11 Data from Russell study showing risk ratio and forest plot: all patients lost to follow up in Nimbus group assumed to have healed and those in the Cairwave group assumed to have not healed

Figures 3.10 and 3.11 represent best case scenarios for each intervention. It is clear that the study findings are dependent on what happened to the patients 'lost to follow up'. The study is therefore subject to attrition bias.

3.7 Discussion

3.7.1 Summary of evidence

Overall, the evidence is not sufficiently robust to determine the relative effectiveness of pressure relieving devices for healing heel pressure ulcers. Only one randomised controlled trials was found, while having a robust design, randomisation and baseline comparability had so many lost to follow up that findings need to be viewed with extreme caution. The use of the outcome 'completed study' made interpretation of data difficult. According to the trialists

there was no reported difference in outcome of comfort between the two groups.

The biases within the study would prevent it from being used as evidence to inform policy makers and care service providers. However it is recognised that using pressure relieving devices is standard practice for patients with heel pressure ulcers. This review does not recommend discontinuation of this practice.

3.7.2 Limitations

3.7.2.1 Identified studies

The main limitation of this review is the lack of available studies which met the inclusion criteria.

Although large numbers of papers were retrieved the lack of detail to enable subgroup analysis of heel patients or the lack of progress from conference presentation to full publication limited the findings. Earnest attempts were made to find full studies from authors, citations, internet searches, experts and manufacturers.

One review was identified which was written in Chinese but no translator was found to assist with interpretation of this information, one review was identified which was written in Danish and published in the journal ‘Vard I Norden’, attempts to obtain this paper were unsuccessful. As reviews are not primary studies and were only being retrieved to explore citations these studies were excluded. One further title ‘Clinical trial of the Freedom Bed’ which, although written in English, was published in the journal ‘Prairie Rose’ but again the journal was not available, however advice from the Cochrane Wounds Group suggested that this journal would be unlikely to have trials published in it and was therefore excluded.

The included study was carried out in a ‘Care of the Elderly’ setting. While many people who have heel pressure ulcers are elderly and are in care of the

elderly settings, there are also patients with heel ulcers in other settings such as orthopaedic wards, vascular wards and the community. While it is possible that any findings could be transferable, not enough is known about the wound healing process in different patient populations to be confident about the generalisability.

3.7.2.2 Data collection form

The data collection form, whilst capturing all the data required, from a practical perspective did not seem to be totally user friendly. In hindsight the reordering of the information and changing the size of some of the cells on the table would make data extraction and the visibility and explicitness of the information easier. When additional information was sought from original authors, the data extraction sheet was not comprehensive enough to capture this appropriately e.g. with the Russell paper it was not always clear which facts related to the whole study population (patients with sacral and heel ulcers) or which was heel specific. Also when a study was published more than once, the form should have the ability to record information from all publications.

3.7.2.3 Search strategy

The search strategy was developed to include studies of patients with diabetic foot ulcers. There was a possibility that such studies may have included heel pressure ulcers. The list of titles generated did not include any diabetic foot ulcer papers. On reflection this may have been related to the fact that the strategy did not include the free text term '(heel or foot or feet) near ulcer', If this had been included as #69 in the search strategy before the heel pressure ulcer descriptors were merged it would have identified more studies. Discussion took place with a member of the Cochrane Wounds Group and citations of treatment studies for diabetic foot ulcers which were identified in other systematic reviews were informally examined. Most of these were found to include only ulcers on the plantar surface of the foot or forefoot and some specifically excluded ulcers on the heels. The potential benefit of re-writing and running the strategy for all the years, in all the databases at this moment was not thought to justify the work entailed. This would however be a consideration for the future.

3.7.2.4 Study selection process

The large number of records identified through the original database search was intentional; there was awareness of lack of potential studies which specifically looked at healing of heel ulcers. It was felt that it was more likely that heel data could be extracted from other studies which included all pressure ulcers sites or studies which looked at prevention and treatment. As the separate data was not identified in the full publications, many authors were written to. Unfortunately the response rate was disappointing: either people had moved on or just did not respond. Where records retrieved were conference presentations (15 records), Medline searches were also carried out for authors names in the hope that full publication had later taken place. This did not reveal any further studies.

A paper by Dumville *et al.* (2008) looked at the publication rates of abstracts from wound care conferences (European Wound Management Association Conferences in 2001 and 2002). Of the abstracts identified (467) only 29 (6%) presented results of RCTs and only 57 (12%) of all abstracts were found to have an associated publication. Dumville et al (2008) compared publication rates with previous studies and found that between 32-53% abstracts were subsequently published in full. These previous studies related to medical rather than nursing conferences and did not specify whether they included all types of studies. However Timmer *et al.*(2002) reviewed only publications of RCTs from gastroenterological conference abstracts and found a 51% publication rate. Dumville et al (2008) discuss the possible reasons for low publication rates and suggest that weaker study design, lack of 'positive' results (results significantly in favour of intervention) and motivation for conference presentation (conference attendance rather than increasing the knowledge in wound care) are contributing factors. While these suggestions are valid it is important to bear in mind the relative development of nursing as an academic profession (a study by Hale and Hill (2006) also found lack of clinical research in the field of rheumatology nursing), how amenable nursing care is to RCTs (Lindsay, 2004) and necessity for expensive RCTs given that medical devices such as support

surfaces and wound dressings can be marketed without robust evidence from a clinical trial.

Seven other reviews were included in the retrieval of papers as it was thought they may identify further studies not retrieved through the original search strategy. This was not the case however and probably resulted in unnecessary work. Other ways could be considered in the future for increasing the likelihood of finding studies e.g. searches of doctoral theses.

3.7.2.5 Risk of bias in included studies

With trials of medical devices such as mattresses it is virtually impossible to, 'blind' the staff or patients to treatment allocation. It is important, therefore to discuss and include information about staff or patient preferences prior to the study and which treatment, if any was familiar to the staff as this could be seen as leading to significant bias in the study. This issue was not dealt with in the study. The importance of minimising other biases such as allocation concealment, masked outcomes assessment and good study follow up and reporting has already been discussed.

3.8 Summary and Conclusions

3.8.1 Implications for practice

The findings of this review do not lead to any recommended changes in practice. Current guidelines for practice (RCN, 2005) based on a review of support surfaces for all pressure ulcers, recommend the use of pressure relieving devices for all patients with pressure ulcers. Clinical staff, policy makers and users should be mindful that there is no evidence to support one support surface over another for heel pressure ulcers and consideration should be given to patients quality of life (pain, discomfort, activity and mobility, intrusiveness (noise, size of device)) as a priority as well as ease of use, reliability, direct and indirect costs (purchase price, lifespan, maintenance).

3.8.2 Implications for research

Clearly further well designed trials of support surfaces (and in particular devices specifically for heel pressure relief) for treating heel pressure ulcers are needed. These should include:

- Clear inclusion and exclusion criteria, ensuring sample is representative of an appropriate population
- A sample size calculation to ensure the studies are adequately powered, taking into consideration the available evidence for death rates and other loss to follow up
- Robust randomisation process and allocation concealment
- Blinding of personnel and outcomes assessment as far as practically possible e.g. using photographs of the wounds which can be assessed by persons blind to the intervention
- Appropriate outcome measures for healing such as time to complete healing
- Clear secondary outcome measures using validated scales to capture patient related issues such as pain, discomfort, ease of mobilisation and cost effectiveness
- Reporting baseline comparability to include important details such as ulcer size and duration

Consideration needs to be given to populations to be studied, these need to include elderly, vascular, diabetic, orthopaedic patients in both hospital and community settings.

Recruiting sufficient patients in pressure ulcer studies is often difficult as many patients appear incapacitous (lack capacity to consent). Recent changes due to the Mental Capacity Act (Great Britain, 2005) have led to better recruitment as the focus has been on an improved assessment of capacity specifically to research studies and for those who do not have capacity - identifying what would have been the patients intentions with regard to research studies rather than carers responding on behalf of the patients.

The high death rate in the pressure ulcer population (Thomas *et al.*, 1996a) is a major challenge when planning a trial. To ensure enough patients are followed up to healing will always be difficult. Possible alternative strategies could be considered e.g.:

- identify risk factors for death and exclude these patients

- look at healing rates/ improvement in ulcers rather than a single end point of healing
- more frequent data collection points to capture all changes in pressure ulcer status
- look at alternative research methods other than RCTs (e.g. pre-post comparison, intervention-control comparison, adopters versus non-adopters comparison (Kirkwood and Sterne, 2003))

In modern 'in patient' settings the movement of patients between wards and early discharge to alternative care risks compromising data collection. Robust patient follow up with the continuation of the trial intervention needs to take place.

Given that many patients with pressure ulcers may have a very poor prognosis then healing may not be the most important outcome of interest. More consideration should be given to what are traditionally considered to be secondary outcomes such as patient quality of life (Gorecki *et al.*, 2009) and cost effectiveness (RCN, 2005) of the interventions.

The need to distinguish between the populations of patients with sacral, ischial and heel pressure ulcers remains: no studies were identified which looked specifically at pressure relieving devices for heel ulcers despite many different devices for heel pressure relief being on the market e.g. Repose heel boots, Heelift, Pressure Relief Ankle Foot Orthosis (PRAFO). The risk factors for healing are likely to be different (see previous chapter). The effects on the patients' quality of life both of the ulcer and of the device used to treat it are also likely to be different from pressure ulcers on other body sites.

3.8.3 Summary

While this review is unlikely to lead to a significant change in clinical practice, it has clearly identified the lack of evidence base for pressure relieving devices for treating heel pressure ulcers. It will alert clinical staff and policy makers to the lack of robust evidence upon which to base decisions on the use of devices to support healing of ulcers on the heels. It may prompt one to being more

mindful of the effects of devices on patients' quality of life and also to consider the cost effectiveness and utility of the devices available.

It has also identified some key issues to inform future research design in this important field of pressure ulcer management.

Chapter 4 Methods

4.1 Introduction

The previous chapters of this thesis have identified the gaps in knowledge of pressure ulcer healing and in particular of heel pressure ulcers, and what influences the process. In order to increase the knowledge a cohort study was been identified that looked at the prognostic factors for healing. This chapter describes the rationale for this study method and the process of the study. This is summarised in the flow chart in figure 4.1.

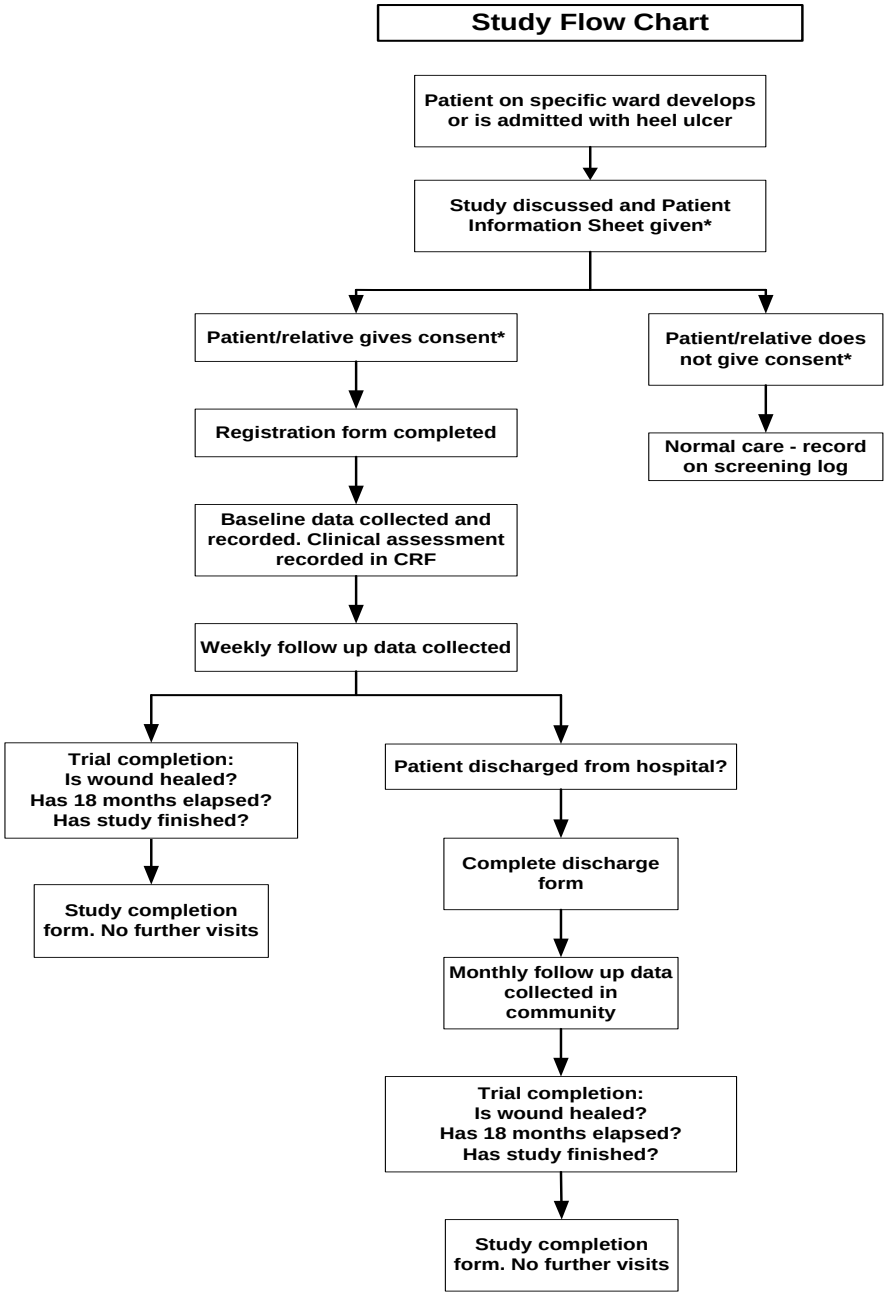

Figure 4.1 Study summary flow chart

4.2 Aims and Objectives

The main aim of this study was to identify prognostic factors for healing of heel pressure ulcers.

The secondary objectives are to:

1. describe the characteristics of patients who have heel pressure ulcers
2. describe the characteristics of current practice i.e. the dressings and topical treatments including debridement, support surfaces used, specialist advice
3. describe the progress of heel pressure ulcers through the stages of wound healing
4. determine the adverse sequelae of this patient population e.g. death, septicaemia, amputation, infection, length of stay, destination post discharge

4.3 Research Design

4.3.1 Choice of design

This was a single centre prospective cohort study of the prognostic factors for wound healing in patients with pressure ulcers on their heels. Following informed consent, eligible patients with heel ulcers Grade 2 or greater of any duration had baseline assessments, then weekly follow-up during their stay in hospital and at monthly intervals following discharge for a period of 18 months or until healed.

A cohort study design was chosen as it can identify exposures or characteristics of interest, which are thought to influence an outcome; in this case wound healing. It enables the exploration of possible causal relationships. A prospective cohort study is the preferred method for an observational study as the quality and nature of the data collected can be controlled (Altman, 1991).

While a retrospective study may have been quicker and easier to perform, an informal review of clinical records of this population identified that there would not be the quality of information required due to missing data. Simon & Altman (1994) in their editorial on statistical issues caution against retrospective studies due to problems with missing data and the fact that data on potential prognostic

factors may not be available. Retrospective studies are subject to many biases including selection bias, detection bias, recall bias and inaccuracy of retrospective data (Altman, 1991).

The main disadvantages of a cohort study are that if the outcome of interest is rare, then there is a need to recruit and follow up a lot of patients to provide enough data for analysis. The study can be expensive, especially if the time to the event of interest is long. There may also be difficulty maintaining contact with participants.

4.3.2 Quality issues and potential for bias

In experimental studies there are widely accepted standards for the design and conduct, analysis and reporting (Simon and Altman, 1994). A search for similar standards in observational studies has identified the STROBE statement (Vandenbroucke *et al.*, 2007), which is intended to improve study reporting. Although no recommendation is made for the design of the study, this is implicit in how it is reported. The STROBE statement consists of a checklist of twenty two items of which eighteen are common to the cohort, case-control and cross sectional studies, and four are specific to each of the 3 study designs. The statement (the 18 generic items and the four specific cohort items) has been used in this chapter to guide the design and reporting of this study.

4.3.2.1 Loss to follow-up

Study participants can be lost to follow-up for several reasons. These include:

- People who do not wish to continue with data collection for what ever reason and ask to be withdrawn from the study
- People who leave the study site to an unknown location and contact is lost
- People who move to a location outside the study site where follow-up cannot take place

It is important to keep loss to follow-up to a minimum as it will reduce numbers for analysis and potentially introduce bias (if loss has occurred selectively). The potential for loss to follow-up was considered during the study design; in particular the burden of the study for the patients was kept to a minimum; patients were only recruited who lived in Leeds and approval was sought to

follow up patients within the Leeds community. The reasons for loss may be related to outcome and become a source of bias. To investigate this bias, those lost to follow-up were compared for baseline socio-demographic and clinical characteristics with those who continued in the study to identify any systematic differences.

Loss to follow-up may not always lead to biased estimates. A study by Osler *et al.* (2008) which investigated bias due to loss to follow-up of a cohort of Danish men found the associations between the prognostic factor and outcome were nearly the same in the sample as in the full population. They drew this conclusion by calculating a relative odds ratio (OR) as the ratio of the OR of responders to the OR of the whole population, this being close to one. This methodology had been used in a previous study of low participation bias in cohort studies (Nohr *et al.*, 2006) although both studies have concerns over the calculation and size of the confidence intervals and the generalisability of the findings.

A review by Hudak et al (Hudak, Cole and Haines, 1996) set out criteria for clinical epidemiological validity assessment of prognosis, which assessed studies as providing strong evidence if follow-up was ≥ 80%. These criteria have been used by subsequent authors to gauge the strength of evidence of studies, it would seem reasonable to expect no more than 20% loss to follow-up.

4.3.2.2 Selection of participants

The particular population from which the sample is selected may affect the probability of an outcome occurring. This may mean the findings of the study have limited external validity and are only relevant to this particular population. In this study the likelihood of healing may be affected by:

- Being an inpatient with underlying medical problems of patients in a particular speciality
- Being treated within a tertiary centre where patients may have more complex health needs

- Being cared for in a setting where there is a Tissue Viability (TV) Nurse Consultant
- Being in a research study with regular contact with a Tissue Viability Specialist

The characteristics of this study population will limit generalisability of the findings (Goldberg *et al.*, 1985). This is considered further in the discussion in section 8.2.3.2.

4.3.2.3 Changes over time

Prior to the start of the study, consideration was given to the possibility that due to the study there would be an increased awareness of heel pressure ulcers in the staff looking after these patients and practices could change. The literature review reassured the researcher that there was little evidence of effectiveness for any treatment interventions that were not already part of standard clinical practice in the participating research centre. If any new evidence had come to light during the study, then this would have been considered in the analysis. However, it was still possible that staff caring for the study patients would be more aware of their heel pressure ulcer due to the regular visits from the TV Nurse Consultant and practice would have developed above the normal standard. This is considered further in chapter 8.

4.3.3 Point of recruitment

This study is a prospective cohort study with patients having the exposure of interest i.e. a heel pressure ulcer. This type of cohort study is particularly useful as:

- the researcher can determine the effects of changes in prognostic factors on outcomes
- investigate several potential prognostic factors when the specific influencing factors are not known
- maintain follow up

adapted from Lilienfeld and Stolley (1994).

Ideally the duration of the ulcer should be calculated from the start date of the ulcer to healing. However some of the patients had a heel pressure ulcer that had been present for several months or years prior to recruitment. To have used the start date of the ulcer to calculate duration of healing would have presented several difficulties:

- The time of onset was mostly established by patient report and as such may not have been accurate
- The baseline characteristics were not known at the start of the ulcer
- The presence or changes in potential prognostic factors is not known up to the point of recruitment

To have only utilised data from new heel pressure ulcers i.e. the inception cohort, would have markedly reduced the number of patients recruited. As the potential heel ulcer population is already small the study has included patients with new and established pressure ulcer at recruitment. The concerns regarding the precision and lack of information will be addressed by sensitivity analysis. This is discussed in section 8.3.1.

Figure 4.2 illustrates the different time points at which pressure ulcers occurred in relation to the recruitment and follow-up times in the study. The arrow heads may represent either the event (ulcer healing occurs) or censoring (patient lost to follow-up, death, amputation of affected limb, end of study or eighteen months of follow-up). The start of the arrow represents the point at which the pressure ulcer occurred, the ones which start to the left of the ‘start of study’ are known as left censored. For further details of endpoints and censoring see sections 4.12.2 and 4.12.3.

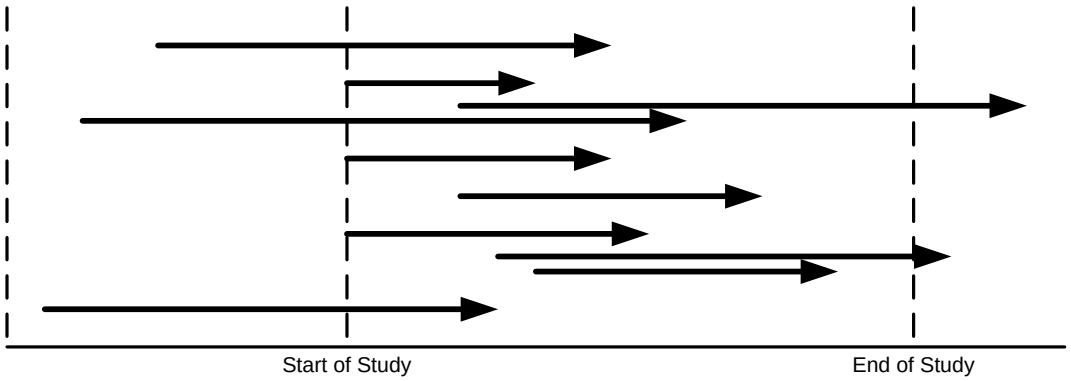

Figure 4.2 Diagrammatic representation of ulcer episodes in relation to patient recruitment over time

While the majority of data are subject to right censoring, it can be seen that some patients are left censored. This was taken into account in the survival analysis when the model was fitted.

4.4 Population and Sampling

The patient population was defined as all those who were admitted to Leeds Teaching Hospitals NHS Trust with a heel pressure ulcer (≥ Grade 2) (EPUAP, 2009) or developed one during their stay on one of the following wards:

- Orthopaedics and Trauma
- Vascular
- Care of the Elderly
- Neurosciences
- Surgical
- Diabetology

These areas consistently demonstrate comparatively high prevalence of heel ulcers in the annual pressure ulcer prevalence audits in the Trust and will therefore be more likely to generate the most subjects for the study. It was impractical for the researcher to visit all wards within the Trust. The possibility of this affecting the external validity or generalisability of the findings is discussed in chapter 8.

4.4.1 Inclusion criteria

- Patients who were aged 18 or over
- Patients who were admitted with or developed a Grade 2 or greater heel pressure ulcer
- Patients were on the wards of one of the above specialities

If patients had or developed more than one heel ulcer they were still eligible. Patients able to consider the risks and benefits of being involved in the study were approached to ask for written informed consent. Where this could not be obtained from the patient their representative was approached to ask for 'relative assent'.

The classification of severity of pressure ulcers has been discussed in Chapter 2. As this study started prior to the new EPUAP(2009) pressure ulcer categories being introduced, the adaptation of the EPUAP (1998) classification has been used throughout, as described in Box 2.1.

4.4.2 Exclusion criteria

- Patients who were unable or unwilling to give informed consent or those who had no appropriate representative to approach for 'relative assent'
- Patients who it was ethically inappropriate to approach e.g. those where death was imminent. Any patients meeting the criteria of the Liverpool Care Pathway (Marie Curie, 2010) for the dying were not approached.

Liverpool Care Pathway eligibility criteria:
The patient has a known irreversible life-threatening illness of any aetiology
Reversible causes for the patient's current deterioration have been considered and appropriately managed
Intensive care and resuscitation have been discussed by the team and have been deemed to be inappropriate for the patient.

Box 4.1 Criteria for the Liverpool Care Pathway

Patients were eligible regardless of whether or not they were under the care of a Tissue Viability Specialist/ Consultant (in the hospital or community) or a Medical Practitioner specifically advising on the wound management. This is because there is currently insufficient evidence to suggest that this affects healing rates.

4.5 Recruitment and registration

Patients were identified and recruited through two methods:

- Clinical staff working in the study areas listed above, who were informed (verbally and in writing) of the study, were asked to refer any patients with a heel ulcer.
- The researcher visited all relevant clinical areas weekly and identified any potentially eligible patients through questioning the nursing staff

A full verbal explanation of the study and a Patient Information Leaflet were provided by the researcher for the patient to consider. This included detailed information about the rationale, design and personal implications of the study. Following information provision, patients had at least 24 hours to consider participation and were given the opportunity to discuss the study with their family and healthcare professionals before they were formally asked whether they were willing to take part.

When consent had been obtained, the patient was registered and allocated a registration number. The patient was then only identified with this number.

Details taken from the patients medical records and confirmed with the patients at registration were:

Patient name
Ward and hospital
Address
Telephone number
GP name and address
Date of birth
Hospital number
Name of Consultant
Date of written informed consent/ assent

Ethnic origin

The registration sheet was the only record of identifiable patient information; this was kept in a locked filing cabinet in a locked office at the hospital.

4.6 Consent process

4.6.1 Informed Consent

Assenting patients were formally assessed for eligibility and invited to provide informed, written consent. Formal assessment of eligibility and informed consent were undertaken by the researcher or latterly by a research nurse. The right of the patient to refuse consent without giving reasons was respected. Furthermore, the patient remained free to withdraw from the study at any time without giving reasons and without prejudicing any further treatment. A copy of the consent was given to the patient, one filed in the hospital notes and the original retained by the researcher.

4.6.2 Relative Assent

Within the study population there is known to be a high proportion of elderly confused patients, who are unlikely to be able to give informed consent. This was demonstrated in a study by Mason *et al.* (2006) who found that 40% of people eligible to take part in their study were confused or lacked capacity to consent . To try and ensure that this group of patients were represented in the study, a process of relative assent was used. The current study based the Ethics Committee application on the Mason *et al.* (2006) study. Relative assent was requested from the patient's named next of kin, defined as 'those who were both a relative of the patient and the named next of kin (as recorded in the hospital or nursing notes). This included: spouse or common law partner, sibling, son or daughter, grandson or grand-daughter, daughter or son-in-law. Relatives were approached if they were visiting the patient but were not contacted by the researcher for the purposes of arranging to meet to discuss the study. Figure 4.3 represents the consent process used from August 2007 to August 2008.

The Mental Capacity Act (MCA)(DoH, 2008) changed the basis on which assent could be obtained and hence a substantial amendment to the protocol was needed in September 2008 to ensure compliance with the Act. This resulted in a change from the concept of relative assent to consultee agreement. The personal consultee is ‘someone who has a role in caring for the person who lacks capacity or is interested in that person’s welfare, but is not doing so for remuneration or acting in a professional capacity’(DoH, 2008). A nominated consultee is ‘someone who is appointed by the researcher to advise the researcher about the person who lacks capacity, wishes and feelings in relation to the project, and whether they should join the research’(DoH, 2008). Figure 4.4 represents the consent process used from September 2008 to August 2009.

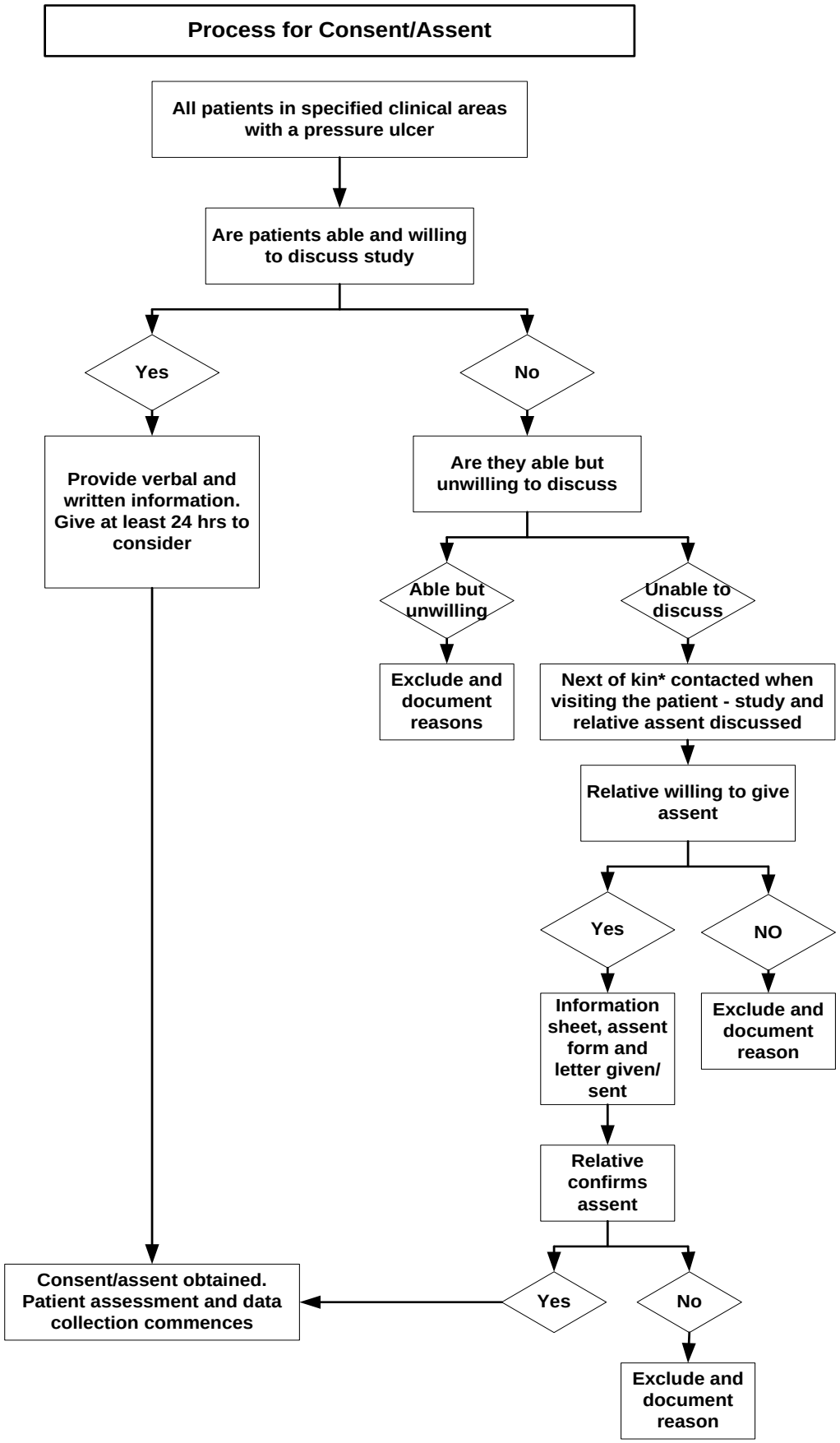

Figure 4.3 Assent/ consent process prior to substantial amendment in Aug 2008

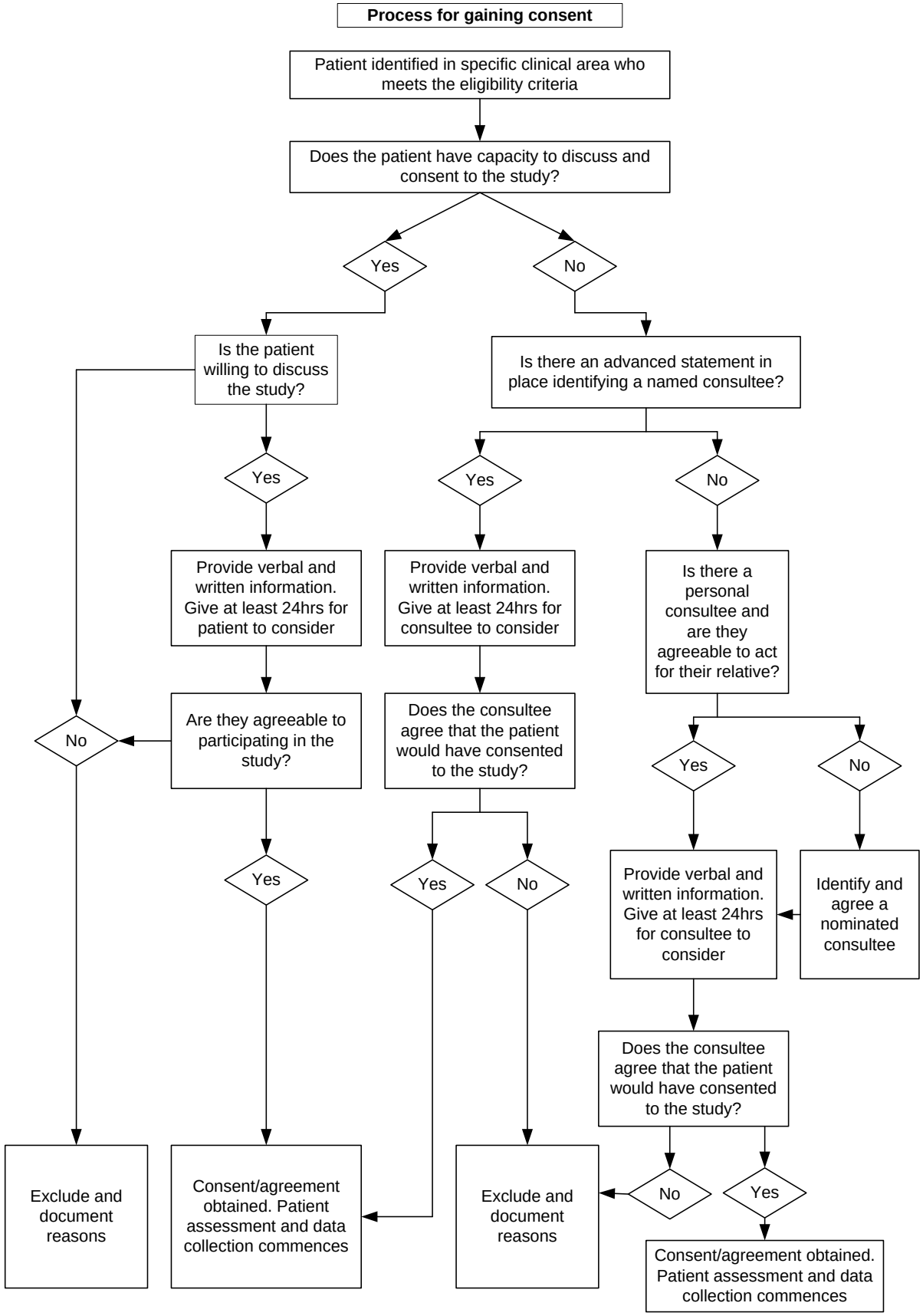

Figure 4.4 Consent process used after Aug 2008 to comply with the Mental Capacity Act (2008)

4.6.3 Non-recruitment

If there were systematic differences between those who took part in the study and those who did not, this would lead to bias and affect the external validity of the study.

A log was completed for all patients screened for eligibility who were not enrolled. This stated their age, gender, ethnicity and the reason for non-recruitment. This information was then compared with the baseline data for recruited patients.

4.7 Measures

The derivation of the variables is presented in the table 4.2. box 4.2 gives the mattress classification, box 4.3 gives the neuropathic assessment protocol, table 4.3 gives the classification of wound infection and box 4.4 gives the description of the Grades/ severity used in the study.

In a study in which the researcher has no control over the exposure variables, any findings which suggest associations may be as a result of confounding effects of a variable e.g. age or interactions between two variables e.g. smoking and peripheral arterial disease. How these are dealt with in this study is explained in section 4.12.5.6.

4.7.1 Patient related variables

The variables collected are given in table 4.1, these included patients' demographic details, potential prognostic factors and factors which would inform the secondary descriptive analysis:

Variable	Demographic detail	Potential prognostic factor	Descriptive analysis/ wound healing process
Age	X	X	
Gender	X	X	
Ethnicity	X		
Speciality	X	X	
Co-morbidity		X	
Smoking		X	
Medication		X	
Pain*		X	X
Nutritional status		X	X
Braden* Nutrition Activity Mobility Moisture Friction/sheer Sensation		X	
Neuropathy*		X	
Arterial disease*		X	
Support surface*			X
Severity of ulcer*		X	
Size of the ulcer (area)*		X	X
Ulcer duration prior to recruitment		X	
Tissue type*		X	X
Surrounding skin*		X	X
Dressings*			X
Debridement*			X
Bandages*			X
Specialist involvement*			X
Significant events*			X
Photographs*			X

*These elements were also collected on an ongoing basis.

Table 4.1 Variables collected and how they were used

The choice of candidate variables for the prognostic factor analysis was derived from the review of other prognostic factor studies in section 2.7. Incontinence was included as the 'moisture' element of the Braden scale. Neuropathy was included in the current study, it is uncertain which of the studies cited included it as a candidate factor, however it was found to be a significant factor in the univariate analysis in the Winkley et al (2007) and Nather et al (2008) diabetic studies even though this did not emerge as independent in the multi-variate analysis. Pressure relief, wound exudate, wound cleansing and dressing type were all omitted as candidate factors, based on the researchers clinical experience, they were expected to vary so much during the study that a baseline exposure would not be representative.

While it is recognised that several of the above factors may not be independent of each other e.g. speciality and co-morbidity, it was felt that the study being the first of it's kind coupled with the lack of evidence particularly in this patient population and a concern for overlooking important factors led to the broader inclusion criteria.

4.7.2 Patient logistics

The following details were collected, which relate to the patient's pathway through the study period:

- Accommodation prior to admission and on discharge
- Length of stay
- Ward moves and readmissions

4.8 Piloting

When the data collection forms and data collection protocol had been devised these were piloted with the first three patients during August 2007.

This internal pilot included a review of the following:

- the data collection forms for ease of use and clarity of information recorded
- the patient information leaflet and consent process (discussed with the patients)
- the wound mapping

- the wound photograph procedure
- the total burden of research for the patients
- any impact of ward activity

No problems were identified for the patients or ward staff, however the wound mapping and photographs presented practical problems for the researcher. As the ulcers were on the back of the foot they were difficult to access as patients were either sat in a chair or laid in bed and unable to lay prone. For details of how these variables were collected see table 4.2.

Mapping the wounds was thought to be inaccurate due to the curved plane of the surface. Following discussion with the study supervisors it was agreed that precise wound area measurements were not required for the endpoints, but that trends in changes in size were useful. Mapping was therefore continued.

The use of a colour target card with the photographs was initially proposed as it would give a centimetre scale, a colour reference, the date and the patient registration number for each photograph taken. This was discontinued after the pilot as there was no where to mount the target card.

4.9 Data Monitoring and Validation

Data collection during the first year (August 2007 – August 2008) was carried out by the researcher as chief investigator. Completeness of data for each patient was checked at each visit by examining the entry for the previous visit in the CRF. Where possible, missing data was sought and retrieved. During the subsequent data collection period (September 2008 – April 2010) the researcher was assisted by an experienced research nurse, whom she personally trained and supervised. Particular attention was paid to recording of skin/ulcer classification as previous research has demonstrated the need to address inter-rater reliability issues of classification scales (Nixon *et al.*, 2005). At frequent intervals during the data collection period, ulcers assessed by the research nurse were also assessed and classified by the researcher (either by patient assessment or photographic review).

4.10 Data quality

4.10.1 Missing data

All data was entered into an Excel spreadsheet by the researcher. When routine data were absent in the research record, which had been taken from the medical records(e.g. Haemoglobin level and medication), these were retrieved and data entry completed. For non-routine data that was absent and could not be retrieved, this was recorded as 'missing' in the database.

Reasons for missing data included:

- the patient was too tired for data collection
- they were due to attend X-ray or physiotherapy and data collection was cut short
- conditional consent to the study which excluded taking part in the Doppler assessment
- ABPI assessments placed more of a burden on the patient and were not appropriate to carry out
- The patient's cognitive ability prevented them giving appropriate responses to questions about pain or sensation.

Hence complete data was not obtained for all patients prior to exiting the study.

4.10.2 Range and consistency checks

For all categorical variables, all observations were checked to ensure they belonged to one of the allowed categories. For continuous data, histograms were plotted to identify any 'outliers' and these were then checked with the original CRFs. All ulcer descriptors (severity, tissue type, surrounding skin condition) were validated with the photographic records, where these existed.

As the Excel spreadsheet was continually revisited when variables were recoded for further analysis, completeness and accuracy of data was checked at each revisit. Data lock occurred on the 31st December 2010.

4.11 Statistical considerations

A sample size of approximately 200 patients was planned. This was based on:

- Lack of definitive evidence regarding event rate to aid calculation of sample size (Berlowitz *et al.*, 1997) reported a healing rate of 50% at 6 months
- The throughput of patients from the Nurse Consultant caseload
- The practicalities of time taken to recruit and collect data for 20 patients/ month
- Death rate of 25% over two months (Bridel, Banks and Milton, 1996)

Originally statistical guidance (Altman, 1991) p 349 was sought which suggested that 'there is no rule.. but a guideline might be to look at no more than *n*/10 variables where *n* is the sample size'. This should allow the study of up to 20 variables or risk factors. Subsequent discussion with supervisors identified an error in the above text which would lead to an over estimate in the number of variables which may be considered. It is now recommended that at least 10 patients *with the event of interest* (ulcer healing) are required for each factor in the model (Harrell *et al.*, 1985).

As there was uncertainty over the number of ulcers that would reach the primary endpoint, the exact number of variables considered in the model was not pre-specified but were reconsidered at the analysis stage. With a 50% healing rate and 25% death rate between 75 and 100 patients might heal, allowing between 7 and 10 variables to be studied.

4.12 Data Analysis

Data were entered into an Excel spreadsheet and then subsets of data were copied into statistical data analysis package, Stata version 11.1 (2009). This was used for all data analysis.

4.12.1 Analysis population

The analysis population for the primary analysis was all heel ulcers identified at the start of the study with at least baseline data recorded. Where patients had more than one ulcer the healing of each heel ulcer was considered as a separate event. The analysis population included all heel ulcers on patients who: healed, died, had their limb amputated, or withdrew and hence were lost

to follow-up having completed at least one follow-up data collection. Any heel ulcers on patients that had not healed after 18 months or at the end of the study were censored at that point. Any patients who were lost to follow up with only baseline data collected were excluded.

4.12.2 Endpoints (time to event)

The primary endpoint was time to complete healing of the ulcer from the point of recruitment to the study. This is defined as the number of days between the day of baseline data collection until complete re-epithelialisation of the skin at the ulcer site. This was visually assessed and photographed by the researcher.

4.12.3 Censoring

Data are described as censored when either the event does not occur during the study period or the time at which the event occurs is unknown. Data were censored in this study when the following occurred:

Loss to follow-up

Moving away from the area in which data collection was possible: some patients who had been resident in Leeds prior to their admission to hospital were discharged to areas outside Leeds e.g. moved to Nursing Homes nearer families. Patients were also lost to follow-up if they withdrew from the study for other reasons.

Amputation

Pressure ulcers of the heel are often found on patients with very poor arterial supply. Where ulcers are not healing or deteriorating then amputation may be an option.

Death

High death rates are noted in pressure ulcer populations; Thomas *et al.* (1996a) found a death rate of 59.5% a year after acquiring a pressure ulcer in hospital compared to 38.2% for those without a pressure ulcer. When death occurs (and if possible the cause of death) this was recorded.

Withdrawal from study

Patients may withdraw themselves from the study for other reasons.

Data collection suspended

Data were collected for each patient for a maximum of 18 months. Data was still being collected for some patients at the end of the study. This was also recorded.

4.12.4 Baseline patient and ulcer characteristics

Patient characteristics at baseline(age, gender, ethnicity, clinical speciality, co-morbidities, smoking history, Braden score, medication, haemoglobin level) and ulcer characteristics (duration, duration prior to recruitment, ulcer area, severity, tissue type, surrounding skin, pain, neuropathic and arterial status and dressings) were described, including frequencies, percentages, means (standard deviations), medians (and ranges) were calculated.

4.12.5 Primary analysis

This was performed using Cox proportional hazards (PH) model (Cox, 1972) with robust standard errors (SE) to allow for clustering, to identify possible prognostic factors for healing.

4.12.5.1 Choice of model

The Cox PH model was chosen as there was a lot of censored data, and survival times were available. If a logistic model had been chosen for the primary analysis then much of this data would be un-usable. The Cox PH model has several benefits, including:

- Performing as a semi-parametric model but also giving similar results to a parametric model e.g. Weibull, especially as the distribution (of the healing times?) was unknown with this data.
- It is possible to calculate the hazards ratio (HR) without knowing the baseline hazards function.
- Although the Cox model likelihood function only considers probabilities for those ulcers that heal, survival information from ulcers which are censored is used.
- It is easier to use and makes fewer assumptions than other models Adapted from Kleinbaum (1996)

4.12.5.2 Analysing clustered (correlated) data

If a patient has heel pressure ulcers on both legs then these cannot be seen as independent as certain variables e.g. diabetes will affect both ulcers and the effect size is likely to be magnified. SE estimates are usually based on the assumption of independence and would not be reliable. In this study the ulcers are clustered at the patient level; there are lots of clusters, each with a small number of variables. The intraclass correlation describes the relationship of the observations within a cluster.

There were several possible alternatives for dealing with the intraclass correlations including multilevel modelling, robust SE (also know as Huber White or sandwich SE) or a frailty model. All these methods use the principle of an additional unmeasured/randomly distributed covariate, which will elevate the SE. Robust SE method was chosen because it did not require a model (was a straightforward implementation) and was available in standard statistical software packages

4.12.5.3 Sensitivity analysis without clustering?

A sensitivity analysis utilising the population of patients rather than ulcers was considered given the routine use of this approach. The issue of regression SE in clustered samples is discussed by Rogers (1993) and Williams (2000); they confirm that the use of robust SE is appropriate by supporting the view that if the largest cluster is 5% or less of the sample the bias should be negligible. Dupont (2009) p. 472 also comments that with large sample sizes the robust SE estimates converge to the true estimate. He does however note that the estimates may not apply if there are many missing values, particularly if these are not randomly distributed.

In order to assess the reliability of the findings of this study it is important that the analysis methods used are comparable with other studies in the same field. A review of the analysis methods in published studies of prognostic factors for wound healing (or risk factors for non-healing) found a study that used robust SE (Winkley *et al.*, 2007), and also two studies which analysed both the

clustered and un-clustered data, and found that both gave similar results (Margolis, Berlin and Strom, 1999) and (Bergstrom *et al.*, 2005).

Given the above information, small cluster size and the small number of missing values and the expectation that a sensitivity analysis would lead to similar results with and without clustering a decision was made not to include this analysis.

4.12.5.4 Modelling process

The Cox regression analysis was first performed with each variable separately; this gave a HR, a confidence interval (CI) and the statistical significance (p value). Each variable was then entered into a model and rerun with the addition of one other variable at a time. The model was then subject to an automated selection procedure (backwards stepwise selection) to fit each significant variable into the model. The accepted level of significance was $p \leq 0.2$ for entry in to the stepwise model and $p \leq 0.1$ for the final model.

Automated model selection is a process whereby the computer program will allow the multiple testing of a number of variables by either entering each variable into the model (forwards) or withdrawing (backwards) them, one at a time and testing for significance at the specified level. If this is done in a stepwise fashion it allows for variables, which were originally discarded as non significant, to be re-entered into the model and potentially become significant given the presence of other variables. While this is a convenient process, caution is required as there is a risk of finding variables with false significance due to multiple testing. Backwards stepwise selection was chosen as this is less likely to miss a significant variable and it provides a fuller model that predicts better than other selection processes.

The Cox regression analysis is based on the assumption that the hazards are proportional. In order to test the proportional hazards assumption i.e. that the ratio of the hazard rate to the baseline hazard is constant, survival curves were

plotted for each variable in the model. The hazards were proportional for all parallel straight lines on the plots.

4.12.5.5 Data reduction and recoding

The original Excel spreadsheet contains all the information collected unprocessed. Different analysis requires different numbers and format of variables, appropriate coding collapse was not clear before the start of the study. Where possible full information was used rather than reduced by recoding to prevent loss of information.

For the Cox proportional hazards model, all variables were entered into the univariate analysis with their original coding. Data reduction was performed for two of the variables that reached significance at the specified level for the purposes of the multi-variate analysis. The intention was to reduce the number of variables which were entered into the final model and increased the number of observations in each category. This results in more chance of finding a significant estimate with smaller confidence intervals:

- Severity. This was recorded in the CRF under 7 different categories (see box 4.4); these were reduced to two categories of superficial and severe. ‘Superficial’ included dry scab, blisters with clear fluid or blood, and full thickness skin loss. ‘Severe’ included cavities, cavities with underlying structures and necrosis. The rationale for this split was clinically meaningful and has been used in other studies (Bergstrom *et al.*, 2005).
- ABPI. This was recorded as actual readings in the CRF and was included in the univariate analysis as a continuous variable. Following review of the high numbers of missing observations it was realised that several ABPI readings had not been taken due to inappropriateness (see section 4.10.1). The re-categorised readings were entered into the univariate model, but the proportion of missing observations remained greater than a third, so ABPI was excluded from the multi-variate model.

4.12.5.6 Collinearity

Collinearity occurs when two variables are highly correlated. If two variables are used in models which are strongly collinear then there is a chance that the output will suggest that neither is associated with outcome, when the one or both actually have a strong association (Kirkwood and Sterne, 2003).

The variables that were significant at the $p \leq 0.2$ following the univariate analysis, were examined for correlation. Where collinearity existed, the variables were examined for statistical and clinical quality e.g. absence of missing data, numbers of categories within variable, numbers of observations, clinical relevance of the variable and the most appropriate variable used in the multi-variate model.

4.12.6 Descriptive analysis

Ulcer characteristics were described during follow-up including:

- ulcer tissue type
- size and severity of the ulcers
- surrounding skin descriptions
- dressings used
- debridement
- bandages used
- pain profiles

Characteristics of current practice during follow-up were described including:

- support surfaces used
- specialist involvement
- significant events

Details of the patient's journey were described including:

- length of stay
- change of accommodation
- readmission rates and ward moves

4.13 Photographs

Photographs of the ulcers were visually assessed for each patient and used to verify details of tissue type and ulcer classification.

4.14 Study Approval

The study protocol was completed March 2006. This was submitted to Leeds West Research Ethics Committee and received a favourable opinion in June 2006. It was also submitted for research governance approval from the R&D department of Leeds Teaching Hospitals Trust, which was received in April 2006 and Bradford South and West Primary Care Trust (PCT) Research & Development Unit (for approval of patient follow-up in Leeds PCT), which was received in June 2006. An application for an honorary contract with Leeds PCT was approved in August 2007.

A substantial amendment request was made in December 2007 for changes to the frequency of collection of the Braden Score and ulcer photographs and patient withdrawal options (request to continue collecting data from patient records should the patient wish to withdraw from the study). The committee did not approve the patient withdrawal options. The Ethics committee also requested an application for Section 30 approval under the Mental Capacity Act for the inclusion of patients who do not have the capacity to consent for themselves.

Subsequently two substantial amendments were approved in September 2008 which included the approval under Section 30 and 34 of the Mental Capacity Act and an amendment to the pain assessment scale. The pain assessment scale was changed from a single question asking for the severity of current pain in a ‘likert’ type scale to include three further questions asking about pain triggers, pain relievers and a description of the pain.

4.15 Detail of variables

The derivation of the variables, the rationale for their collection and which analysis they were used for presented in table 4.1

Variable	Derivation
Age	Age on admission to the study was taken from the date of birth in the medical records
Gender	This was taken from the medical records
Ethnicity	This was taken from the medical records
Speciality	This was recorded at each visit. It is the speciality of the patient's current medical consultant practice
Co-morbidities	These were taken as described in the admission clerking in the medical records. They include: diabetes if known; neurological deficit to include CVA whether new or old, MS, etc; heart disease to include ischaemia and failure; respiratory disease to include COAD, bronchitis, emphysema; malignancy- progressive disease especially cachexia but not if resolved e.g. previous breast lump; fracture – related to this episode of care of below waist or spine; surgery > 2 hours this episode of care
Smoking	Smoking history was recorded. If the patient had been smoking up to the point of current admission (may not actually have smoked since admission) or within last 3 weeks, this was recorded as current. Previously smoked was recorded if the patient stopped more than 3 weeks ago.
Medication	Details of the name of any prescribed medication were taken from the patients drug chart. These were then coded according to the body group they affected according to BNF (Martin, 2007) classifications
Pain	Patients were asked to rate the pain in each affected heel ulcer as none, mild, moderate or severe. Patients were asked to verbally describe their pain: whether it was present at time of assessment, what triggers the pain, what relieved it and how it felt at its worst. This information was recorded as free text at each visit and subsequently coded

Nutrition	Measurement of blood haemoglobin levels were taken as a proxy measure for nutrition (Harris *et al.*, 2007). The haemoglobin level was taken from the medical records, the most recent recorded level on admission to the study during the patient's current episode of care
Braden scores	The Braden ((Bergstrom *et al.*, 1987) scale is a risk assessment instrument for pressure ulcers. It has been proven to have a high reliability and validity. It constitutes six elements which are individually assessed then combined to give a score. It was used in this study for its individual elements. Each is considered to be a risk factor for the development of a pressure ulcer and may therefore be a prognostic factor for healing. Information for each factor was derived from patient assessment and details from the nursing records
Neuropathy	Neuropathic assessment was carried out in accordance with Leeds Community Podiatry service Protocol (see Box 3)
Arterial disease	Assessment of arterial disease was carried out using a Doppler ultrasound to measure brachial and foot (dorsalis paedis and posterior tibial) systolic blood pressures and calculating the ratio (Ankle Brachial Pressure Index). The procedure was performed in accordance with published guidance (Vowden, Goulding and Vowden, 1996) This was then coded as Arterial disease absent if ABPI is ≥ 0.8; some arterial disease if ABPI was ≥0.6 and <0.8 or severe arterial disease if ABPI was <0.6 or if the ABPI had been inappropriate due to the obvious arterial disease (the procedure would be too painful)
Support surface	These were recorded at each visit. The classification used is found in the NICE guidelines (RCN, 2005), reproduced in Box 2. If specific heel pressure relieving devices were used these were also recorded

Severity of ulcer	This was recorded at each data collection. The cohort study commenced prior to the new EPUAP/ NPUAP (2009) classification. The researcher chose to use the previous EPUAP (1998) definitions which are defined in table 2.1. However these were felt to be inadequate for the type of damage seen on the heel in the researchers' clinical practice. They were therefore adapted and the classifications used in the study are given in Box 4.4.
Size of ulcer	Wounds were mapped at each visit using a standard grid and a fine tip permanent marker pen, where possible with the foot at a 90° angle to the leg. Maps are marked with patient registration number, date, left or right heel, and arrow indicating direction of leg. The maps were used to calculate the ulcer area using 'Mouseyes' software program
Duration of ulcer prior to recruitment	If the ulcer was present prior to admission then an estimate of date of onset was established based on patients report and any record of ulcer on previous admission. Duration of ulcer during the study was also recorded
Tissue type	The tissue type was visually assessed and coded according to the stage in the wound healing process (adapted from (Black *et al.*, 2010)). It was described as follows: Blister – either fluid or blood filled or drained Necrotic – desiccated eschar, non-viable tissue, black/ brown in colour Slough – non-viable tissue and bacteria, grey/ yellow/ white in colour Granulation – new capillary beds and intracellular matrix, red in colour Epithelialisation – new epithelial growth, pink/ white in colour Other – this is predominately dry scab, thought to be excess epithelialisation If more than one tissue type was present, the predominant type was recorded

Surrounding skin	The condition of the skin around the pressure ulcer was visually assessed and described as follows: Callous – excessive thickening of the epidermis on the heel around the ulcer Fissure- a crack in the epidermis on the heel, which may or may not penetrate dermis Oedema – light finger pressure applied anywhere on the foot (below malleoli) which leaves an indentation when removed Erythema – the area of skin around ulcer is either bright red, dark red or darker than normal skin tone Macerated – saturation of epidermis with fluid, appears white and soggy Other – may include epidermal separation subsequent to blister formation
Dressings	A record was made of the actual dressings in situ on the ulcer at each visit. A judgement was made as to whether the intention was to keep the ulcer dry or moist: dry wound healing would include no dressing at all, gauze (including Release, Melolin type pads) with paper type adhesive e.g. Hypafix, Micropore, may include dressings such as Kaltostat or Inadine on a dry wound; moist wound healing would include any dressing with occlusive backing such as Allevyn, Tielle, films, may or may not have additional creams to assist hydration such as Aquaform gel. N.B. Foams such as Allevyn may be used for protection on dry eschar where debridement is not being attempted; these are classed as dry wound healing Where antiseptics were used as a dressing, these were also recorded.
Debridement	A record was made if active debridement had taken place since the previous visit. Sharp debridement is nursing, medical or podiatry staff either using a blade or scissors on the ward or surgically in an operating theatre. Other debridement includes larvae therapy, enzymatic (Varidase) or chemical (Eusol)

Bandages	A record was made if bandages were in place at each visit: retention bandages would be crepe, K-band or K-lite or equivalent, stockinette (does not include tubigrip); compression bandages includes K-plus, Setopress, Tensopress, 4 layer bandages, short stretch bandages, Tubigrip, compression hosiery and anti-embolytic stockings
Specialist involvement	If the ulcer management of the pressure ulcer had been specifically prescribed by a specialist e.g. Tissue Viability, Podiatry, Vascular or Plastic surgeon, this was recorded at each visit
Significant events	A field diary was kept of any significant events including incidents of infection (both infection in the pressure ulcer site and unrelated infections), physical and psychological events which appeared to have an impact on the patients wellbeing. Occurrence of infection of the pressure ulcer Wounds may exhibit acute or chronic infections or a patient may become systemically unwell due to the bacteria in the ulcer. Definitions of infection are difficult to find. Table 4.3 has been compiled from a review of the literature and is based on expert opinion
Photographs	Photographs were taken at each visit with a digital camera. This was set on 'close up' setting, positioned approx 40-50 cm away from ulcer, all dressings removed and the ulcer cleaned if necessary. All photographs are stored on a memory card then transferred to main computer (see section 4.8 for changes following piloting)
Change of accommodation	Details of accommodation prior to admission, any transfers to other wards within the hospital, accommodation on discharge and any subsequent changes in accommodation are taken from the patient, nursing staff or medical notes
Length of stay	The date of admission and the date of discharge are taken from the medical records and the duration calculated in days

Table 4.2 Variables collected, their derivation and application

*The management of pressure ulcers in primary and secondary care (June 2005) Royal College of Nursing and National Institute for Health and Clinical Excellence p*80 of 245

'Pressure-relieving surfaces can be divided into two main categories: continuous low pressure (CLP) and alternating pressure (AP).

Continuous low pressure surfaces aim to mould around the shape of the individual to redistribute pressure over a greater surface area. Alternating pressure surfaces mechanically vary the pressure beneath the individual, so reducing the duration of the applied pressure.

CLP support surfaces can be grouped according to their construction:

• Standard foam

The conformability and resilience of foam products may vary considerably between manufacturers. Foam may be shaped, convoluted ("egg crate foam"), of various densities or of a combination of densities.

• Visco-elastic foam

This is specialised foam, available in varying densities, that moulds to body shape in response to body temperature.

• Air flotation

This is an inflated mattress replacement/overlay that manually or automatically adjusts airflow allowing immersion and redistribution of pressure. It is adjustable to individual reposition to maintain immersion and redistribution of pressures.

• Air fluidised

A constant flow of air is passed into a deep tank containing minute silicone beads retained by a permeable membrane. The agitated beads take on the properties of a fluid. Lying on the surface allows significant immersion and therefore redistribution of pressure.

• Low air loss

A constant flow of air inflates a row of permeable fabric cells. Manual or automatic adjustment of airflow allows significant immersion and therefore redistribution of pressure.

• Gel/fluid

Fluid surfaces – e.g. water-filled mattresses – which allow significant immersion and therefore redistribution of pressure. The density/viscosity of the gel/fluid will govern the degree of immersion and how stable the support surface is in terms of posture.

• Combination products

Many CLP surfaces, particularly cushions, use a variety of materials to provide optimum pressure relief and postural stability.

N.B. The type and construction of cover material may have a significant impact on the conformability of the surface'.

Box 4.2 Classification of support surfaces

1. Use 10 gram monofilament
2. Sites to be tested are 1st, 3rd 5th toe, plantar surface at base of each of previous toes and middle of heel pad. Mark with a tick if present and cross if absent
3. Demonstrate monofilament test on patient's hand (ask patient to close eyes)
4. The approach, skin contact and departure of the filament should be approximately 1.5 seconds duration
5. Apply sufficient force to cause the filament to bend
6. Do not allow the filament to slide across the skin or make repetitive contact at the test site
7. Randomize the selection of test sites and time between successive tests to reduce the potential for patient guessing
8. Ask the patient to respond 'yes' whenever the filament is felt and record response
9. Apply the filament along the perimeter of and not on ulcer site, callus, scar or necrotic tissue
10. Monofilaments should not be used to test more than 10 patients in one session and should be left for 24 hours to recover.

Neuropathy was considered present if there was a negative response in 2 or more test sites.

Box 4.3 Leeds Community Podiatry Service Neuropathy testing Protocol

Acute/local infection	**Chronic infection/critical colonisation**	**Acute systemic infection**
• Abscess/pus • Cellulitis/ excessive inflammation • erythema • oedema • heat • pain • Unexpected pain /tenderness • Abnormal smell • Dehiscence	• Delayed Healing • Discoloration of ulcer bed or reformation of sloughy/necrotic tissue • Friable bleeding of granulation tissue • Pocketing/bridging at the base of the ulcer • Increased exudate • Wound breakdown	• Raised CRP • Raised white cell count • Pyrexia/fever • Flu like symptoms e.g. aching/ malaise

Adapted from (Cutting *et al.*, 2005; Wysocki, 2002)

Table 4.3 Signs and symptoms associated with different types of infection

0 = No ulcer

1 = Non-blanching erythema (discolouration, warmth, oedema, induration)

2a = Blister with/without clear fluid

2b = Blister with blood

2c = Abrasion/friction damage (epidermis only)

2d = Full thickness skin loss, no cavity

3 = Full thickness skin loss with subcutaneous tissue involvement (cavity)

4 = Extensive destruction including damage to muscle, bone or underlying structures

5 = Tissue necrosis of undetermined depth

Box 4.4 Grades of severity of pressure ulcers used in cohort study

4.16 Summary

In order to meet the aim and objectives of this project a prospective cohort study design was used. The method was designed to minimise bias, particularly loss to follow-up and recruitment of the representative population. The study recruited patients from specialities known to have greater numbers of heel pressure ulcers. Data were collected from medical and nursing records, patient observations and interviews. The sample size estimates were based on limited data and a pragmatic approach to time constraints. The primary data analysis utilised a Cox proportional hazards regression model based on time to event with robust standard errors to allow for clustering. Descriptive analysis of ulcer characteristics, current practice and the patients' journey over the course of the study achieved the secondary objectives of the study.

Chapter 5 Primary analysis

5.1 Introduction

This chapter follows the first section of the analysis plan described in Chapter four, meeting the primary aim of this study. It gives the patient recruitment rates and the baseline characteristics of the patients and ulcers. It then reports the results of the prognostic factor analysis using the Cox proportional hazard model with robust standard errors. The descriptive analysis of the findings of the secondary study objectives are described in chapter six.

5.2 Patient recruitment

The study took place during 33 months between Aug 2007 and April 2010. Patients were actively recruited during a 2 year period (24.8.07 - 6.8.09) and followed up for a period of 18 months or until their ulcer healed, the patient died or left the study for other reasons or the study ended.

During the study 336 patients were screened for inclusion of which 148 were recruited. Figure 5.2 includes the reasons for non-recruitment. Figure 5.1 show the cumulative frequency of patients recruited. The troughs were mainly associated with the researcher's holidays. The target was 20 per month.

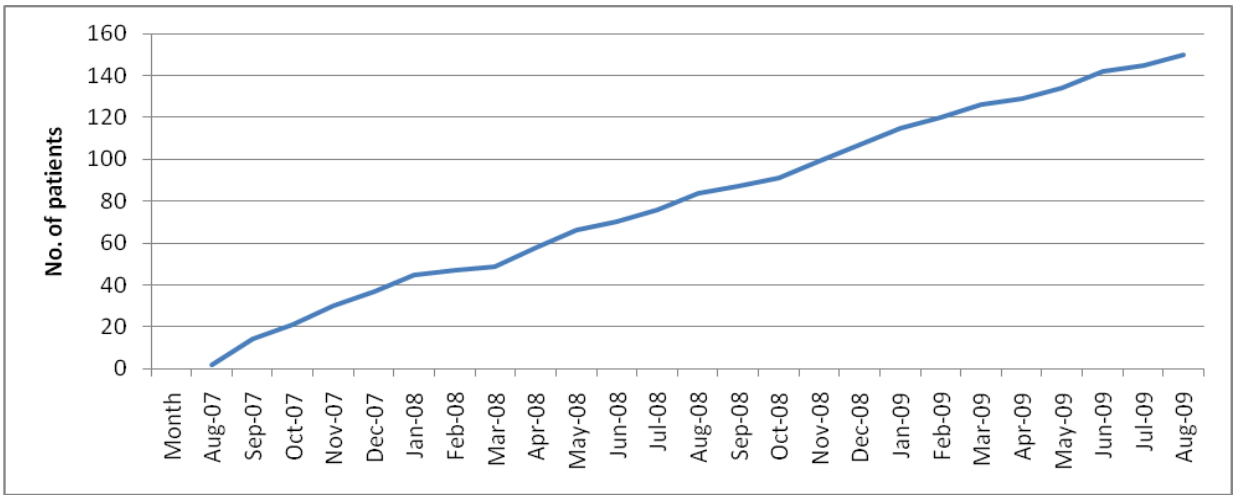

Figure 5.1 Cumulative total of patients recruited during study

Figure 5.1 includes all 148 patients who consented. Following consent, eight patients were withdrawn and no follow-up data were collected. These patients

were excluded from the analysis population and any data which had been collected was discarded:

- One was withdrawn by her son
- Two were withdrawn at the patient's request
- One patient was reported to have a Grade 2 pressure ulcer but this was revealed to be a Grade 1 ulcer which did not deteriorate
- One was found to have a wound that was not a pressure ulcer
- One discharged himself with no known address
- One patient was found to live outside the Leeds area
- One patient was too ill for full data collection and subsequently died

Figure 5.2 shows the flow of patients through the study.

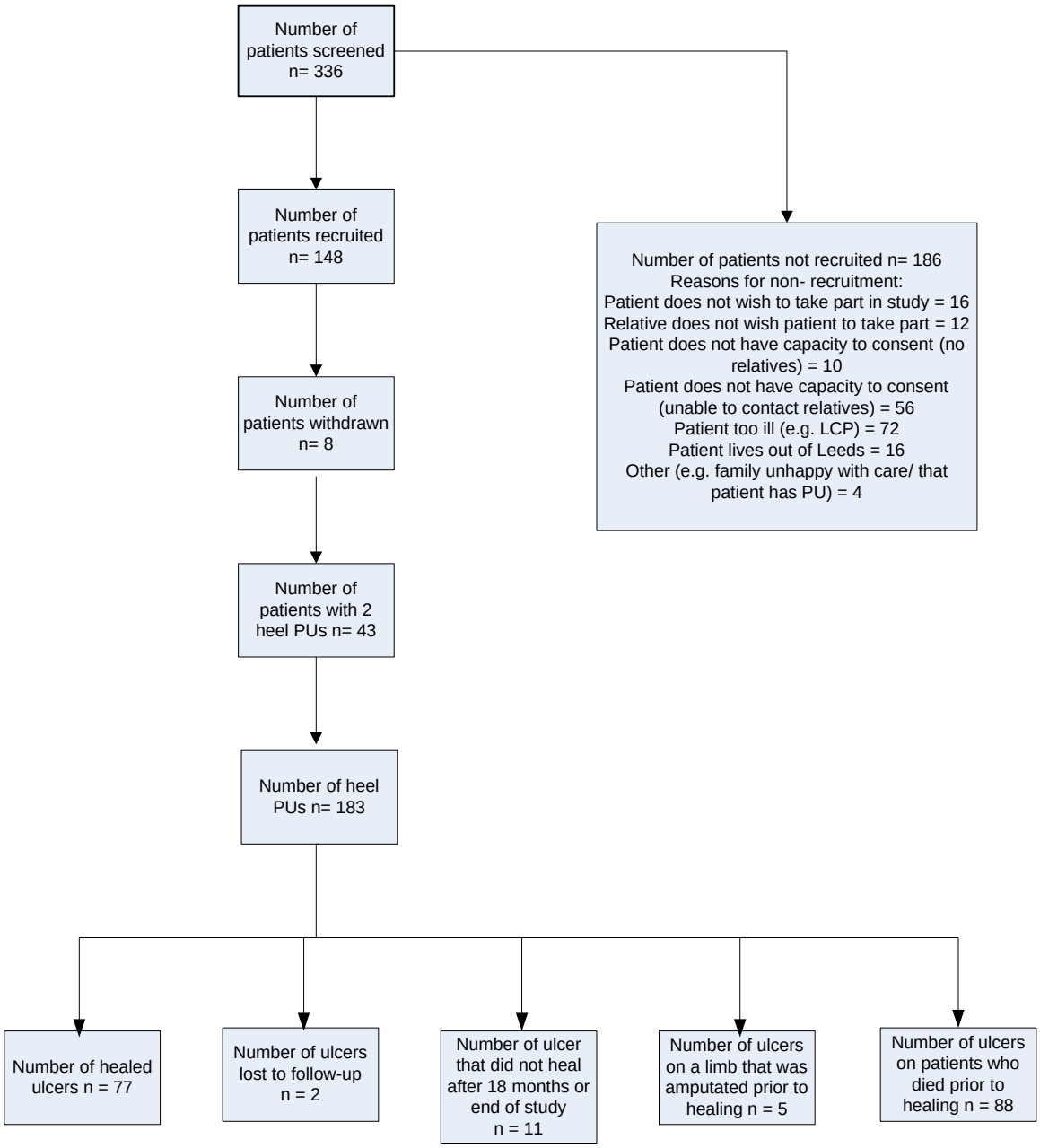

Figure 5.2 Recruitment and outcomes for all heel pressure ulcers

The reasons included in the 'other' section of 'reasons for non-recruitment' were due to the patient or their relative having major concerns over the development of the pressure ulcer and were in the process of considering legal action against a care organisation. It was felt that the research study may aggravate circumstances and the researcher was advised not to approach these patients or their families.

The two ulcers on patients who were subsequently lost to follow-up were included in the analysis: one discharged himself from hospital with no home address, the other left hospital to a location outside the Leeds area.

5.3 Data analysis

5.3.1 Baseline characteristics

Table 5.1 gives details of the patient characteristics; table 5.2 gives details of the ulcer characteristics at baseline. The percentages given in the total column are based on the categories within the variable; the percentages given in the outcome groups are based on the outcomes within the category e.g. within the variable gender of the 66 males: 26% had one ulcer that healed, 41% had one ulcer which did not heal, 7.5% had two ulcers that both healed, 18% had two ulcers of which one healed and 7.5% had two ulcers of which neither healed. For gender variable 47% of the patients were male and 53% were female.

		Value / frequency (% for each variable, unless otherwise stated)					
Variable/ attribute		**Patients with 1 ulcer**		**Patients with 2 ulcers**			**Total number of patients**
		Ulcer healed	**Ulcer not healed**	**Both ulcers healed**	**Both ulcers not healed**	**One not healed**	
		N = 43	**N = 53**	**N = 12**	**N = 22**	**N = 10**	**N = 140**
Age	Mean (SD)	77(13.5)	80 (14.5)	78 (14.9)	88 (7.0)	76 (20.0)	80 (14.1)
	Median (range)	81 (32-102)	85 (27-95)	81 (39-94)	89 (72-99)	81 (20-89)	84 (20-102)
	Missing	0	0	0	0	0	0
Gender	Male	17 (26%)	27 (41%)	5 (7.5%)	12 (18%)	5 (7.5%)	66 (47%)
	Female	26 (35%)	26 (35%)	7 (10%)	10 (13%)	5 (7%)	74 (53%)
	Missing	0	0	0	0	0	0
Ethnicity	White British	39 (29%)	52 (39%)	12 (9%)	22 (16%)	10 (7%)	135 (96%)
	Asian	1 (50%)	1(50%)	0	0	0	2 (1.5%)
	Afro-Caribbean	2 (100%)	0	0	0	0	2 (1.5%)
	Eastern European	1 (100%)	0	0	0	0	1 (1%)
	Missing	0	0	0	0	0	0

Speciality	Care of the Elderly	26 (28%)	34 (37%)	8 (9%)	17 (19%)	6 (7%)	91 (65%)
	Vascular	1 (6%)	10 (59%)	2 (12%)	3 (17%)	1 (6%)	17 (12%)
	Orthopaedics	5 (46%)	3 (27%)	0	2 (18%)	1 (9%)	11 (8%)
	Neurosciences	5 (62.5%)	2 (25%)	0	0	1 (12.5%)	8 (6%)
	General surgery	4 (45%)	2 (22%)	2 (22%)	0	1 (11%)	9 (6%)
	Diabetology	2 (50%)	2 (50%)	0	0	0	4 (3%)
	Missing	0	0	0	0	0	0
Haemoglobin	Mean (SD)	10.8 (1.5)	10.7 (1.9)	10.8 (2.0)	10.7 (1.2)	11.8 (1.8)	10.9 (1.7)
	Median (range)	11(7.6-14.5)	10.9 (6.7-15.9)	10.3 (8.2-15.4)	11.1 (7.8-12.4)	11.8 (8.8-15.6)	11(6.7-15.9)
	Missing	1	0	0	0	0	1
Smoking	Current	3 (22%)	8 (57%)	1 (7%)	2 (14%)	0	14 (10%)
	Previous	22 (33%)	22 (33%)	5 (7%)	13 (20%)	5 (7%)	67 (48%)
	Never	18 (31%)	23 (39%)	6 (10%)	7 (12%)	5 (8%)	59 (42%)
	Missing	0	0	0	0	0	0

Medication*	Anticoagulants	35 (31%)	45(40%)	7(6%)	17(16%)	8(7%)	112 (80%)
	Cardiovascular	29(31%)	39(42%)	4(4%)	14(15%)	7(8%)	93 (66%)
	Endocrine	15(28%)	25(47%)	2(4%)	6(12%)	5(9%)	53 (38%)
	Nutrition	20(26%)	32(42%)	5(6%)	17(22%)	3(4%)	77 (55%)
	Steroids	6(50%)	3(25%)	1(8.3%)	1(8.3%)	1(8.3%)	12 (9%)
	Analgesics	31(30%)	37(37%)	11(11%)	14(14%)	8(8%)	101 (72%)
	Antibiotics	12(37%)	12(37%)	2(6%)	6(20%)	0	32 (23%)
	Gastrointestinal	33(34%)	36(37%)	7(7%)	15(15%)	7(7%)	98 (70%)
	Central nervous system	25(33%)	28(37%)	5(7%)	11(15%)	6(8%)	75 (54%)
	Respiratory	8(35%)	7(31%)	1(4%)	6(26%)	1(4%)	23 (16%)
	Obstetrics, gynaecology and urinary tract	4(40%)	3(30%)	1(10%)	2(20%)	0	10 (7%)
	Other	5(42%)	5(42%)	1(8%)	1(8%)	0	12 (9%)
	Missing	0	0	0	0	0	0

Braden score factor							
Sensory	Completely limited	0	1(100%)	0	0	0	1(1%)
	Very limited	2(11%)	9(47%)	5 (26%)	2(11%)	1(5%)	19(13%)
	Slightly limited	25(34%)	31(42%)	4(5%)	7(9.5%)	7(9.5%)	74(53%)
	No impairment	16(35%)	12(26%)	3(7%)	13(28%)	2(4%)	46(33%)
Moisture	Completely moist	0	2(100%)	0	0	0	2(2%)
	Very moist	5(29%)	11(65%)	0	1(6%)	0	17(12%)
	Occasionally moist	16(38%)	18(43%)	2(5%)	1(2%)	5(12%)	42(30%)
	Rarely moist	22(28%)	22(28%)	10(13%)	20(25%)	5(6%)	79(56%)
Activity	Bedfast	5(21%)	13(54%)	2(8%)	3(13%)	1(4%)	24(17%)
	Chairfast	17(26%)	23(36%)	7(11%)	12(19%)	5(8%)	64(46%)
	Walks occasionally	13(34%)	13(34%)	2(5%)	7(19%)	3(8%)	38(27%)
	Walks frequently	8(58%)	4(28%)	1(7%)	0	1(7%)	14(10%)

Mobility	Completely immobile	3(18%)	10(59%)	1(6%)	2(11%)	1(6%)	17(12%)
	Very limited	15(23%)	21(32%)	7(10%)	17(26%)	6(9%)	66(47%)
	Slightly limited	13(36%)	15(42%)	3(8%)	3(8%)	2(6%)	36(26%)
	No limitation	12(57%)	7(33%)	1(5%)	0	1(5%)	21(15%)
Nutrition	Very poor	4(20%)	9(45%)	0	6(30%)	1(5%)	20(14%)
	Probably inadequate	8(19%)	20(48%)	3(7%)	8(19%)	3(7%)	42(30%)
	Adequate	11(37%)	11(37%)	4(13%)	4(13%)	0	30(21%)
	Excellent	20(42%)	13(27%)	5(10%)	4(8%)	6(13%)	48(34%)
Friction and shear	Problem	11(30%)	16(43%)	1(3%)	7(19%)	2(5%)	37(26%)
	Potential problems	19(25%)	25(33%)	10(13%)	14(19%)	7(10%)	75(54%)
	No apparent problems	13(45%)	12(43%)	1(4%)	1(4%)	1(4%)	28(20%)
	Missing	0	0	0	0	0	0

Co-morbidity*	Diabetes	15(31%)	24(50%)	2(4%)	2(4%)	5(11%)	48 (34%)
	Neurological deficit	24(35%)	25(36%)	6(9%)	11(16%)	3(4%)	69 (49%)
	Heart disease	14(27%)	22(43%)	3(6%)	9(18%)	3(6%)	51(36%)
	Respiratory disease	7(28%)	10(40%)	0	7(28%)	1(4%)	25 (18%)
	Malignancy	9(47%)	7(37%)	2(11%)	1(5%)	0	19 (14%)
	PVD	3(10%)	16(55%)	1(4%)	5(17%)	4(14%)	29 (20%)
	Fracture	8(36.5%)	8(36.5%)	2(9%)	2(9%)	2(9%)	22 (16%)
	Surgery > 2 hours	2(18%)	3(27.5%)	2(18%)	3(27.5%)	1(9%)	11 (8%)
	Missing	0	0	0	0	0	0
SD=Standard Deviation *Patients may have more than one co-morbidity or group of medication							

Table 5.1 Patient level information

It can be seen from table 5.1 that more patients had one ulcer than two; there was approximately equal numbers of male and female patients; most patients were recruited from Care of the Elderly speciality; approximately half the patients had previously been smokers; the most frequently prescribed medications included anticoagulants, cardiovascular medication, analgesics and gastrointestinal medication; most patients had reduced mobility and activity; diabetes and neurological deficit were the most common co-morbidities.

Variable		**Healed n = 77**	**Did not heal n = 106**	**Total n = 183**
Duration prior to recruitment (days)	Mean (SD) Median (range) Missing	105.39 (223.18) 21 (0-1475) 3	61.49 (136.83) 24 (0-1091) 17	80.93(181.48) 23 (0-1475) 20
Neuropathy	Present Absent Missing	23 (30%) 31(40%) 23(30%)	24(23%) 25(23%) 57(54%)	47(26%) 56(30%) 80(44%)
ABPI	ABPI≥0.8 ABPI,0.8 but ≥0.6 ABPI,0.6 or inappropriate Missing	40(52%) 4(5%) 12(16%) 21(27%)	30(28%) 7(6%) 26(25%) 43(41%)	70(38%) 11(6%) 38(21%) 64(35%)
Severity	Superficial Severe Missing	45(58%) 32(42%) 0	38(36%) 65(61%) 3(3%)	83(45%) 97(53%) 3(2%)
Area	Mean (SD) Median (range) Missing	7.9 (7.61) 5.33 (0 .34 - 43.14) 2	10.11(8.08) 7.9 (0.24-35.99) 13	9.09 (7.9) 6.48 (0.24-43.14) 15
Tissue type	Blister Granulating Sloughy Necrotic Other (dry scab) Missing	19(25%) 12(16%) 15(19%) 26(34%) 4(5%) 1(1%)	21(20%) 14(13%) 17(16%) 50(47%) 1(1%) 3(3%)	40(22%) 26(14%) 32(18%) 76(42%) 5(3%) 4(1%)

Surrounding skin	Healthy	23(30%)	28(26%)	51(28%)
	Erythema	3(4%)	7(7%)	10(5%)
	Macerated	5(6%)	7(7%)	12(7%)
	Dry/ flaky	12(16%)	18(17%)	30(16%)
	Oedema	26(34%)	30(28%)	56(31%)
	Other	5(6%)	9(8%)	14(8%)
	Missing	3(4%)	7(7%)	10(5%)
Pain	None	34(44%)	32(30%)	66(36%)
	Mild	8(11%)	7(7%)	15(8%)
	Moderate	5(6%)	16(15%)	21(11%)
	Severe	5(6%)	10(9%)	15(8%)
	Missing	25(33%)	41(39%)	66(36%)
	SD = Standard Deviation ABPI = Ankle Brachial Pressure Index			

Table 5.2 Ulcer level information

There was a wide range in the number of the days prior to recruitment; the median number of days is slightly shorter for those which healed. There was a larger proportion of ulcers without neuropathy, a good arterial supply (ABPI), less severe ulcers, less sloughy and necrotic tissue that healed. Although the mean and median ulcer areas were smaller for those ulcers that healed, the range was very similar for both healed and unhealed. There is very little difference in the baseline tissue type or surrounding skin for those ulcers which did or did not heal, however there appears to be less in the ulcers that progressed to healing.

5.3.2 Cox proportional hazard regression analysis

Results are available for 183 heel pressure ulcers; 77 of these ulcers healed.

5.3.2.1 Univariate analysis

Table 5.3 shows the results of the univariate analysis for each variable considered a potential prognostic factor for healing.

	Variable	Hazard ratio	95% confidence interval	Significance (p value)	
Age		1.002	0.983 - 1.021	0.812	
Gender	**Male (cf female)**	1.340	0.841 - 2.133	0.2189	
Speciality	Care of the Elderly	1.509	0.930 - 2.446	**0.095***	
	Vascular	0.468	0.231 - 0.951	**0.036***	
	Orthopaedic	0.594	0.251 - 1.405	0.235	
	Neurosciences	1.771	0.629 - 4.990	0.279	
	Surgery	1.051	0.595 - 1.856	0.864	
	Diabetology	0.658	0.184 - 2.354	0.520	
Smoking	Non-smoker	*Referenc*			0.526
	Previous	*e*	0.479 - 1.258	0.305	*(trend)***
	Current	0.777	0.363 - 3.510	0.832	
		1.130			
Haemoglobin		1.004	0.872 - 1.157	0.953	
Co-morbidites	Diabetes	0.818	0.505 - 1.324	0.415	
	Neurological deficit	0.912	0.582 - 1.427	0.687	
	Heart disease	0.772	0.489 - 1.282	0.343	
	Respiratory	0.700	0.342 - 1.434	0.330	
	disease	1.351	0.810 - 2.256	0.249	
	Malignancy	0.417	0.210 - 0 .825	**0.012***	
	PVD	1.049	0.531 - 2.074	0.890	
	Fracture	1.071	0.408 - 2.810	0.889	
	Surgery > 2 hours				

Medication	Anticoagulants	0.943	0.535 - 1.661	0.838	
	Cardiovascular	0.862	0.545 - 1.365	0.527	
	Endocrine	1.013	0.632 - 1.628	0.954	
	Nutrition	0.524	0.323 - 0.847	**0.008***	
	Steroids	1.570	0.680 - 3.628	0.291	
	Analgesics	1.477	0.820 - 2.663	**0.194***	
	Antibiotics	0.887	0.479 - 1.643	0.703	
	Gastrointestinal	0.869	0.510 - 1.481	0.606	
	Central nervous system	1.105	0.697 - 1.754	0.670	
	Respiratory	0.549	0.314 - 1.959	**0.035***	
	Obstetrics, gynaecology and urinary tract	0.907	0.456 - 1.800	0.780	
	Other	0.794	0.346 - 1.819	0.585	
Braden	Sensory	1.121	0.743 - 1.694	0.585	
	Moisture	0.976	0.672 - 1.417	0.897	
	Activity	0.968	0.726 - 1.290	0.823	
	Mobility	1.119	0.876 - 1.430	0.367	
	Nutrition	1.104	0.877 - 1.389	0.400	
	Friction & sheer	1.041	0.754 - 1.438	0.804	
Duration prior to recruitment		0.999	0.999 - 1.000	0.357	
Neuropathy (present cf. absent)		0.738	0.432 - 1.260	0.265	
ABPI	No arterial disease (ABPI≥0.8)	*reference*			**0.149*** *(trend)***
	Some arterial disease (ABPI,0.8 but ≥0.6)	0.478	0.181 - 1.262	0.136	
	Severe arterial disease (ABPI,0.6 or inappropriate)	0.611	0.326 - 1.146	0.125	
Ulcer severity (servere cf. superficial)		0.498	0.319 – 0.777	**0.002***	
Area		0.967	0.929 - 1.005	**0.090***	

Tissue type	Dry scab	*reference*			**0.088***
	Blister	0.207	0.049 - 0.886	0.034	*(trend)***
	Granulating	0.163	0.040 - 0.663	0.011	
	Sloughy	0.149	0.036 - 0.608	0.008	
	Necrotic	0.153	0.038 - 0.612	0.008	
Surrounding skin	Healthy	1.26	0.789 - 2.016	0.333	
	Erythema	0.510	0.204 - 1.277	**0.151***	
	Macerated	0.560	0.280 - 1.118	**0.100***	
	Dry/ flaky	0.839	0.436 - 1.614	0.599	
	Other	1.228	0.588 - 2.566	0.585	
	Oedema	1.124	0.713 - 1.771	0.614	
Pain	None	*reference*			0.700
	Mild	0.856	0.463 - 1.580	0.619	*(trend)*
	Moderate	0.837	0.415 - 1.686	0.618	
	Severe	0.530	0.184 - 1.528	0.241	
	* Indicates p≤0.2 ** Where the variable is an ordered categorical the significance of each category relative to the reference category (first/smallest) is given but also the level joint significance or trend for the whole parameter				

Table 5.3 Univariate analysis of potential prognostic factors

From table 5.3, the following variables reached significance at the p≤0.2 level:

- Speciality of Care of the Elderly
- Speciality of Vascular
- PVD as a co-morbidity
- Prescribed nutritional medication
- Prescribed analgesics
- Prescribed respiratory medication
- Presence of PVD (ABPI)
- Severity
- Area
- Tissue type
- Presence of erythema on surrounding skin
- Presence of maceration of surrounding skin

The hazard ratios for Care of the Elderly speciality and prescribed analgesics were both greater than one, suggesting that the probability of healing was greater in the presence of these two variables. The hazard ratio for ulcer area was almost one, suggesting that this had very little effect on healing. All other variables suggested the probability of non-healing was greater in the presence of the variable (for the categorical variables) – or the value increased (for the continuous variables).

It is also noted from table 5.3 that steroid medication and neurosciences speciality also have hazards ratios greater than 1.5, suggesting that the probability of healing was greater in the presence of these two variables, but these did not reach significance at the p≤0.2 level.

The ABPI variable had 64 (35%) of the observations missing, so a decision was made not to include this in the multi-variate model. The number of observations for the presence of erythema and maceration of the surrounding skin was also very small. These were therefore also excluded from the multi-variate model.

5.3.2.2 Test of collinearity

All the variables in table 5.3 were examined for collinearity. A cut off point for the correlation coefficient was taken as ± 0.5. This identified several clinically meaningful correlations e.g. diabetes (an endocrine disease) and endocrine medication, Braden factors for activity and mobility, pain and neuropathy, vascular speciality and PVD, severity of the ulcer and tissue type.

From the variables that reached significance at the p≤0.2 level, two correlations were considered further:

- Vascular speciality and having PVD. The clinical setting is likely be related to the patient's co-morbidity e.g. vascular speciality, having PVD and a low ABPI.

	PVD	ABPI	Vascular
PVD	1.0		
ABPI	0.46	1.0	
Vascular	0.62	0.30	1.0

Table 5.4 Correlation coefficients for arterial disease related variables

PVD and Vascular speciality had a correlation of 0.6, so a decision was made not to include both in the multi-variate model. As there was a stronger correlation between ABPI and PVD than Vascular speciality and ABPI then it was decided to use the PVD variable in the final model. Vascular speciality was the least preferred variable as this would include all patients who were on the vascular ward, who may not have PVD and also patients with PVD who were admitted for other conditions.

- Severity of the ulcer and the tissue type in the ulcer bed. Both these variables included some of the same clinical descriptions.

	Tissue type	Severity
Tissue type	1.0	
Severity	0.61	1.0

Table 5.5 Correlation coefficients for ulcer categories

Severity and tissue type had a correlation of 0.6, so a decision was made not to include both in the multi-variate model. As severity had only 2 categories (therefore had greater numbers for each category) this was used in the multi-variate model.

5.3.2.3 Multi-variate model

The following variables were entered in the multi-variate model:

- Speciality of Care of the Elderly
- PVD as a co-morbidity
- Prescribed nutritional medication

- Prescribed analgesics
- Prescribed respiratory medication
- Severity
- Area
- Gender

Gender was included in the model as this is a known factor that influences wound healing (see section 2.7.1) even though the level of significance in the univariate analysis was outside the cut off point of ≤0.2.

In the final model two variables emerged that reached significance at the p≤0.1 level. Details are given in table 5.6.

Variable	**Hazards ratio**	**95% confidence interval**	**Significance (p value)**
Severity	0.476	0.303 - 0.748	0.001
PVD	0.404	0.202 - 0.808	0.010

Table 5.6 Results of multi-variate modelling using a stepwise automated process

This suggests that with this heel ulcer population:

- the estimated effect of ulcer severity at baseline (having a severe rather than a superficial ulcer), after controlling for the confounding effects of the presence of all other variables in the model, will give approximately half the chance of healing (95%CI 0.3-0.8).
- the estimated effect of the presence of Peripheral Vascular disease at baseline, after controlling for the confounding effects of the presence of all other variables in the model, will give approximately a 0.4 times the chance (i.e. 60% less chance) of healing (95%CI 0.2-0.8).

5.3.2.4 Sensitivity analysis

In order to ascertain whether the choice of variable (where collinearity existed) to be included in the multi-variate model had affected the findings. The modelling was repeated with each of the excluded variables in turn.

Variable	Hazards ratio	95% confidence interval	Significance (p value)
Severity	0.481	0.303 - 0.761	0.002

Table 5.7 Results of multi-variate modelling substituting vascular speciality for PVD

Variable	Hazards ratio	95% confidence interval	Significance (p value)
PVD	0.413	0.206 - 0.830	0.013

Table 5.8 Results of multi-variate modelling substituting tissue type for severity

While the same variables reached significance, this did not occur in the same model. This suggests that the choice of variable (where collinearity existed) was appropriate.

5.3.2.5 Testing the proportional hazards assumption

To check whether the hazards were proportional, charts were plotted of the log of the cumulative hazard function in the groups with and without each variable entered into the multi-variate model. They show that the proportional hazards assumption is correct as the lines were almost parallel for all variables. The charts for the two variables which were found to be significant at the $p \leq 0.1$ are shown in figures 5.3 and 5.4.

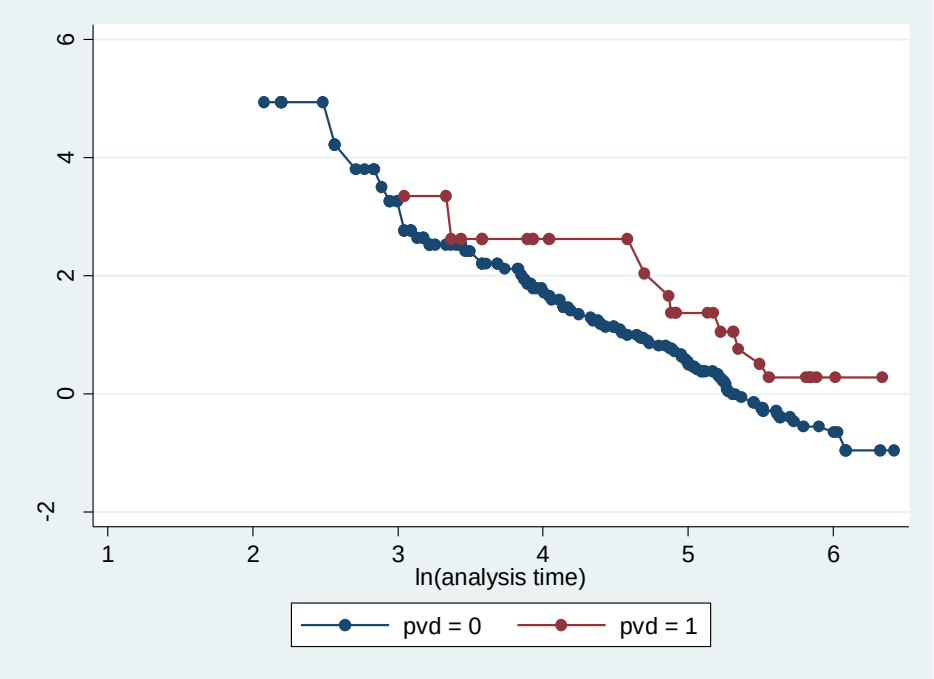

Figure 5.3 Cumulative hazard (log scale) against analysis time (log scale) for PVD variable

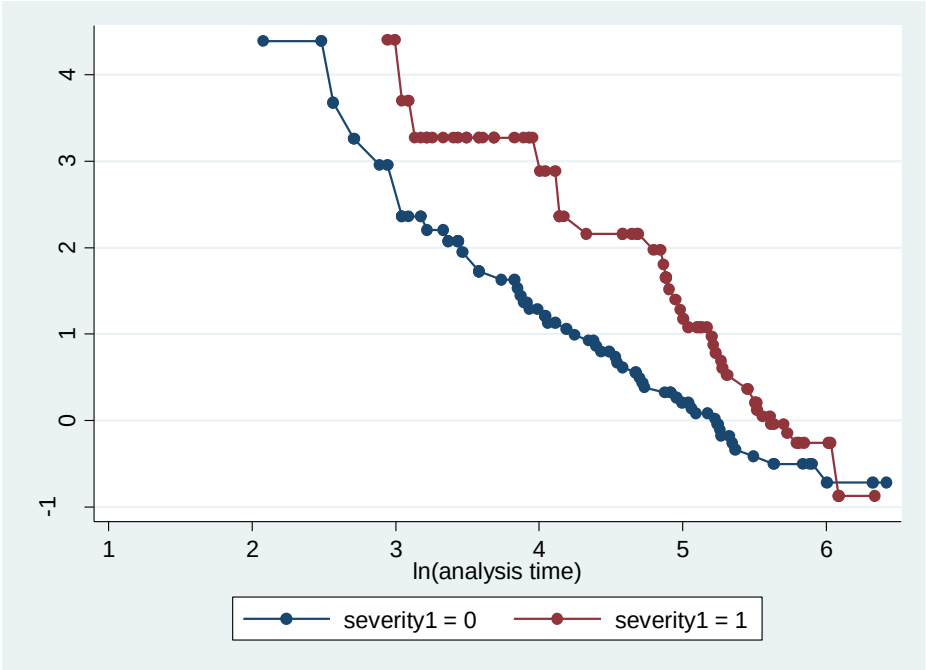

Figure 5.4 Cumulative hazard (log scale) against analysis time (log scale) for severity variable

5.4 Summary

This prospective cohort study of 140 patients with 183 heel pressure ulcers recruited participants from the specialities of Care of the Elderly, Vascular, Diabetology, Orthopaedics and Surgery.

Seventy seven of the 183 ulcers healed, 87 did not heal because the patient died, 5 were on limbs which were amputated, 11 had not healed after 18 months or by the end of the study and 2 ulcers were on patients lost to follow-up.

From the data collected on baseline variables thought to be prognostic factors for healing, 12 factors were found to be significantly associated with healing at the $p \leq 0.2$ level in a univariate Cox regression model. Five variables were excluded from the multivariate model: two of these factors due to collinearity and three due to the very small number of observations. Eight factors (including gender) were included in the final model. Severity of the ulcer and the presence of PVD were found to be significant prognostic factors for healing at the $p \leq 0.1$ level.

Chapter 6 Secondary descriptive results

6.1 Introduction

The previous chapter presented the results of the analysis of the prognostic factors which met the primary aim of the study. The secondary objectives were to:

1 describe the characteristics of patients who have heel pressure ulcers
2 describe the characteristics of current practice i.e. the dressings and topical treatments including debridement, support surfaces used, specialist advice
3 describe the progress of heel pressure ulcers through the stages of wound healing
4 determine the adverse sequelae of this patient population e.g. death, septicaemia, amputation, infection, length of stay and destination post discharge

This chapter describes the findings of these secondary objectives. A full and detailed discussion of these findings is presented in chapter seven.

Some of the data used in this chapter was captured at baseline, however, most of the data were captured at the follow-up visits, some of the characteristics are described based on the actual number of times the observation was recorded, some are then described in terms of an episode e.g. an ‘episode’ of erythema was deemed to have occurred when it was recorded on one or more sequential occasions. There were potentially 929 observations; where observations are quantified missing numbers are given in each section.

6.2 Characteristics of patients

Patient characteristics have already been described in section 5.3.1.

6.3 Characteristics of current practice

6.3.1 Dressings

The dressings in situ on the ulcer at the time of assessment were recorded at baseline and at each subsequent visit. Details are given in Table 6.1. The dressing at baseline is given in the top row. There were 928 dressing observations in total (one missing), the second row of the table gives details of the total number of dressing observations See Table 4.2 for details of how these were captured and coded.

Dressings					
	Moist wound healing	**Dry wound healing**	**Moist wound healing + antiseptic**	**Dry wound healing + antiseptic**	**No dressing**
Baseline	55 (30%)	72 (39%)	27 (15%)	19 (10%)	10 (6%)
Total observations	297 (32%)	234 (25%)	213 (23%)	51 (6%)	133 (14%)

Table 6.1 Frequency of dressing type

The most frequently occurring dressing type was moist wound healing. Only 20 ulcers had one dressing type throughout their full episode of care. For nine of the ulcers this was moist wound healing. If no dressings were in place this was seen on ulcers which were either dry black eschar (n=15) or dry scabbed (n=30) or blister (n=16). No ‘open’ or exudating ulcers were found without a dressing.

6.3.2 Bandages

There were 927 observations of ‘bandage’ variable (2 missing): 253 (27%) recorded no bandages, 648 (70%) recorded retention bandages and there were 26 (3%) records of compression bandage on 11 ulcers. More than half the ulcers had both retention bandages and no bandages at different times during the study. No one ulcer had compression for the whole data collection period.

6.3.3 Debridement

The process of passive (autolytic) debridement has been described in section 2.3.2 and the reputed need for active debridement discussed in section 2.6.3. There were 929 observations for the 'debridement' variable of which 860 (92.5%) recorded none/passive debridement, 66 (7%) occasions of sharp debridement on 45 ulcers and 3 (0.5%) episodes of larvae therapy on 3 different ulcers were recorded.

6.3.4 Support surfaces

Table 6.2 shows the type of support surface in use at baseline. For details of the classifications see Box 4.2 in section 4.15.

Pressure relieving support surface	**No of patients**
Standard foam	18 (13%)
Visco-elastic foam	36 (26%)
Low air loss	26 (18%)
Alternating pressure	45 (32%)
Air flotation	3 (2%)
Heel specific support	1 (1%)
Standard foam + heel specific	4 (3%)
Visco-elastic foam + heel specific	6 (4%)
Missing	1 (1%)

Table 6.2 Support surfaces including specific heel devices in use at baseline

The majority of patients had a low air loss or alternating pressure mattress on their bed at some point during the study. Of the 18 patients who had 'standard foam' at baseline only 6 had a low air loss or alternating pressure mattress at the next visit. Seven patients had 'standard foam' throughout the study with a low air loss or alternating pressure support surface for a maximum of one week only.

Thirty patients who had a low air loss or alternating pressure mattress for most of the study period had at least one week with a standard foam mattress. Twenty four patients had a heel specific device such as a Repose© heel trough at some time in addition to the mattress but only one patient had a specific heel device for the whole study period.

6.3.5 Specialist involvement

Details of how this was recorded were given in section 4.15 table 4.1.There were 749 observations pertaining to whether specialists were involved in the care of the heel ulcer, of these 215 (29%) noted that specialists were involved. Of the 77 ulcers that healed, 40 (52%) had been seen by a specialist at some point; of the ulcers that did not heal, 36 (34%) had been seen by a specialist. If the specialists were Tissue Viability, their involvement was intermittent. Some patients with diabetes were regularly seen by the diabetic podiatry team. Some patients were in hospital because of their heel ulcer and were seen by the vascular surgeons or diabetologists, these would be recorded as having specialist involvement.

6.4 Progress of heel ulcers

6.4.1 Duration and outcome

Patients recruited to the study were followed up for a maximum duration of 18 months. For patients still in the study at this point, data collection was censored and the outcome classified as non-healed. Data were also censored for patients who were lost to follow-up, died, had their limb amputated or end of study.

	Healed	**Non-healed (censored)**	**Total**
Mean number of days(SD)	135 (102)	102 (130)	116 (120)
Median number of days(range)	121 (8-440)	43 (4-614)	63 (4-614*)

*Two patients had a final data collection at 20 rather than 18 months.

Table 6.3 Summary of time to healing or censoring

A total of 140 patients with 183 ulcers were included in the analysis. Sixty patients died with 88 heel pressure ulcers. Details of the outcome for all ulcers are given in table 6.4.

Endpoint	Censored				Total
Healed n = 77(42%)	Ulcer on patient who died n = 88 (48%)	Ulcer on a leg which was amputated n = 5 (3%)	Non-healed* n = 11(6%)	Lost to follow-up n = 2 (1%)	Total number of ulcers n=183

* Non healing was defined as ‘at end of study’ or ‘at end of 18 months’

Table 6.4 Details of ulcer outcome

6.4.2 Tissue type

Tissue type was recorded as one of five categories at each visit. Photographic examples are given for each category in figures 6.1 – 6.5.

The tissue type at baseline is described in table 5.2. This stated that 42% of the ulcers presented as necrotic tissue, 22% were blisters, 18% were sloughy, 14% were granulation tissue, 3% were a dry scab and one observation was missing. It was related to stage of the pressure ulcer when the patient was recruited. If the ulcer was a new event then it would most likely be a blister. However, if the ulcer had been present for some time then the ulcer may be in the inflammatory or proliferative phase (or the transition between the two) seen as necrotic/ sloughy tissue moving to granulation. Details of tissue type collected at each time point illustrated progression of the ulcer through wound healing or not.

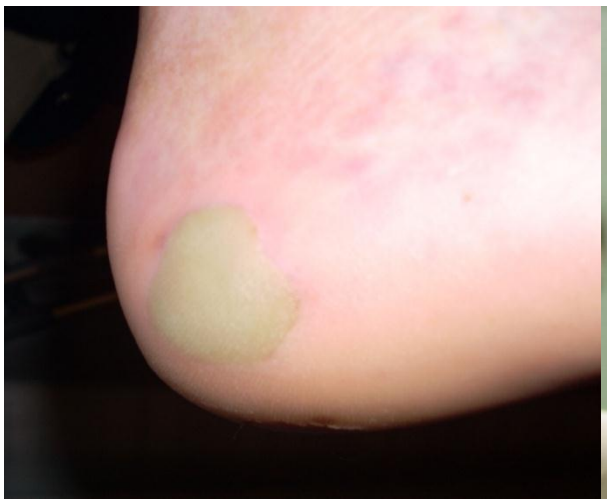

Figure 6.1 Blister

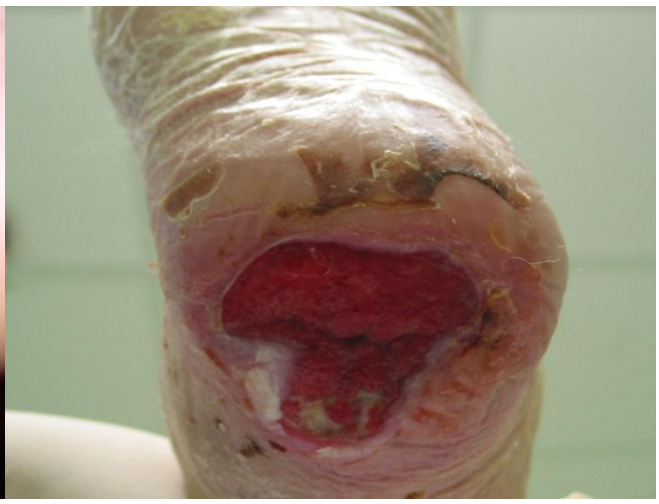

Figure 6.2 Granulating

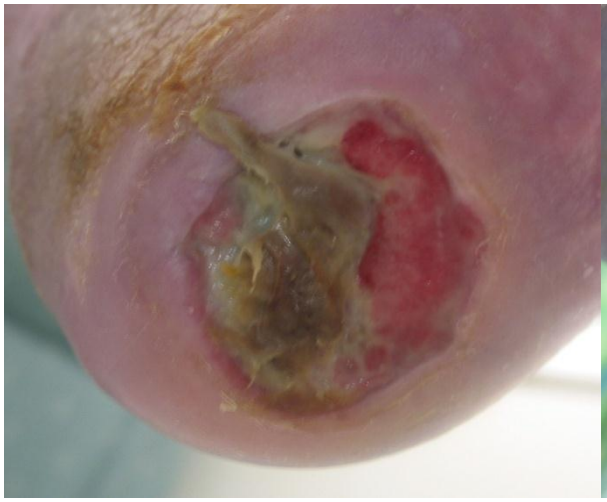

Figure 6.3 Sloughy

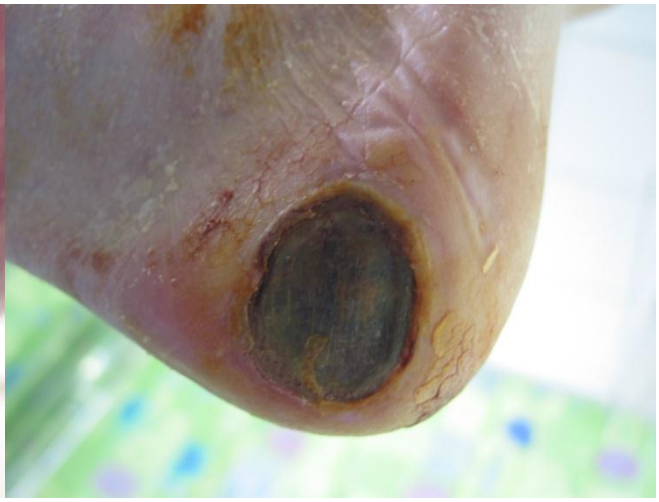

Figure 6.4 Necrotic

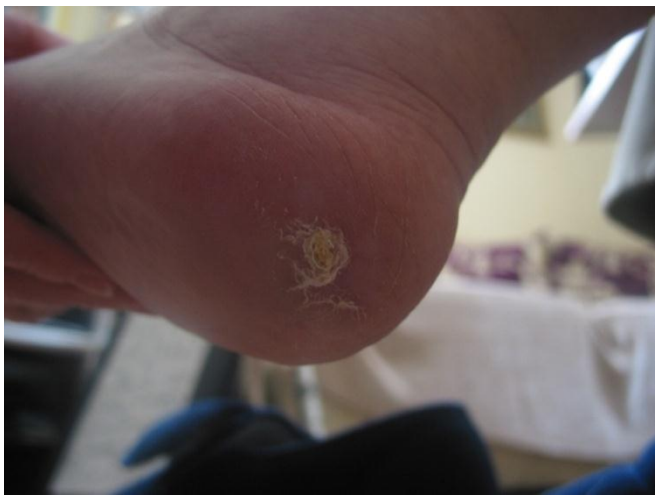

Figure 6.5 Other – dry scab

Of the 77 pressure ulcers that healed, 75% were seen to have progressed through the phases of wound healing to a ‘dry scab’ then intact skin, except 19 (25%) ulcers. Table 6.5 gives a breakdown of the tissue type prior to healing.

Dry scab	Granulation	Necrosis	Blister	Total healed ulcers
58 (75%)	12 (16%)	5 (6%)	2 (3%)	77 (100%)

Table 6.5 Tissue type prior to healing

6.4.3 Ulcer size

Ulcer size is recorded as surface area (calculated from the tracing of the perimeter of the ulcer, see table 4.2) at baseline in given in table 5.2. This gives the mean area as 9.09 (S.D. 7.9) cm^2. Data for changes in ulcer area were visually examined. The following trends were noticed in many of the ulcers:

- Area can increase before it decreases
- The rate of area reduction is greater during the early stages of wound healing
- Final ulcer closure can be prolonged

Ulcers which did not heal also showed similar trends. Some examples of wound healing trends in indicative ulcers are given in figures 6.6 – 6.9. Data were collected initially at weekly intervals but then monthly following discharge from hospital (hence the time points are not evenly distributed).

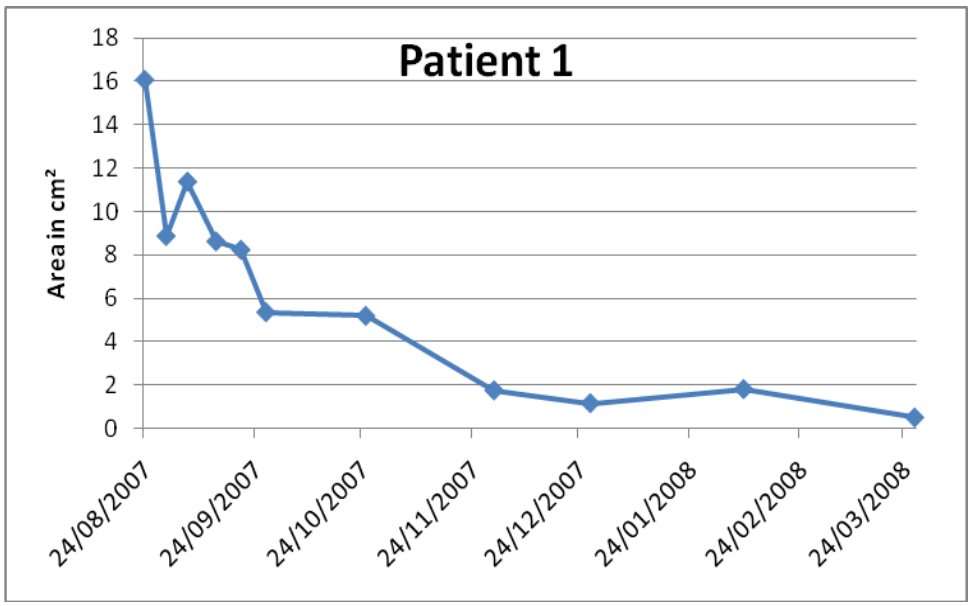

Figure 6.6 Wound healing trend, Patient 1

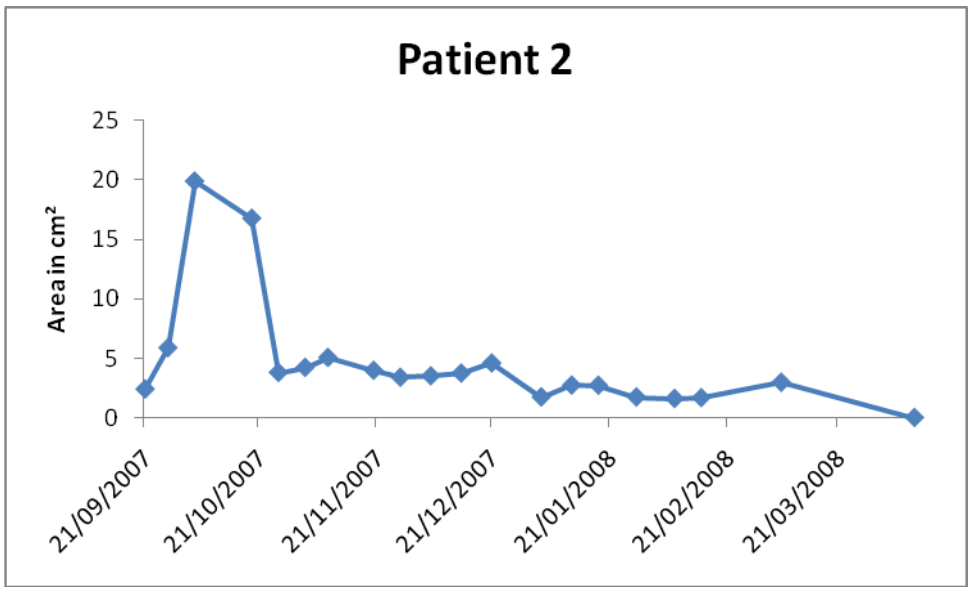

Figure 6.7 Wound healing trend, Patient 2

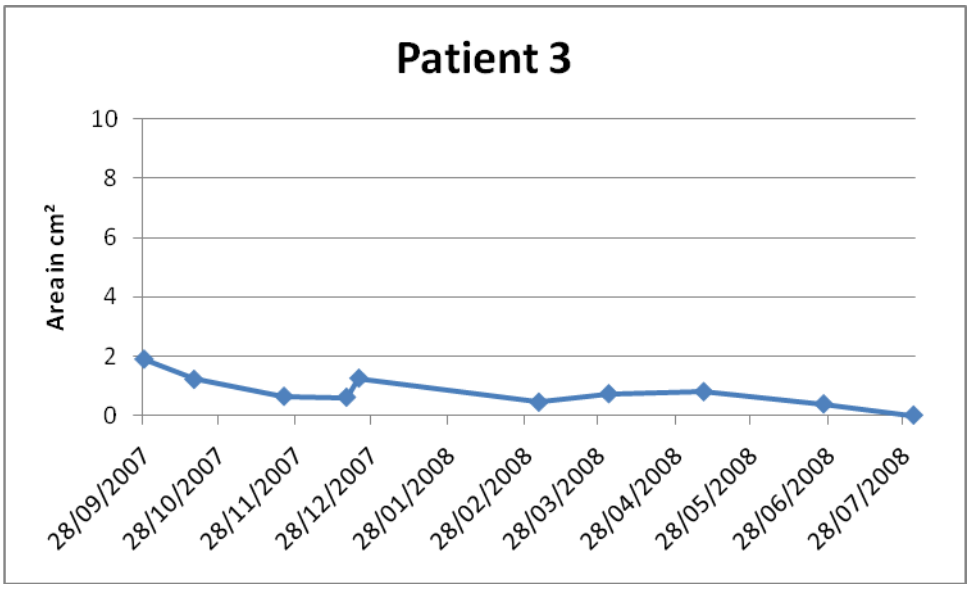

Figure 6.8 Wound healing trend, Patient 3

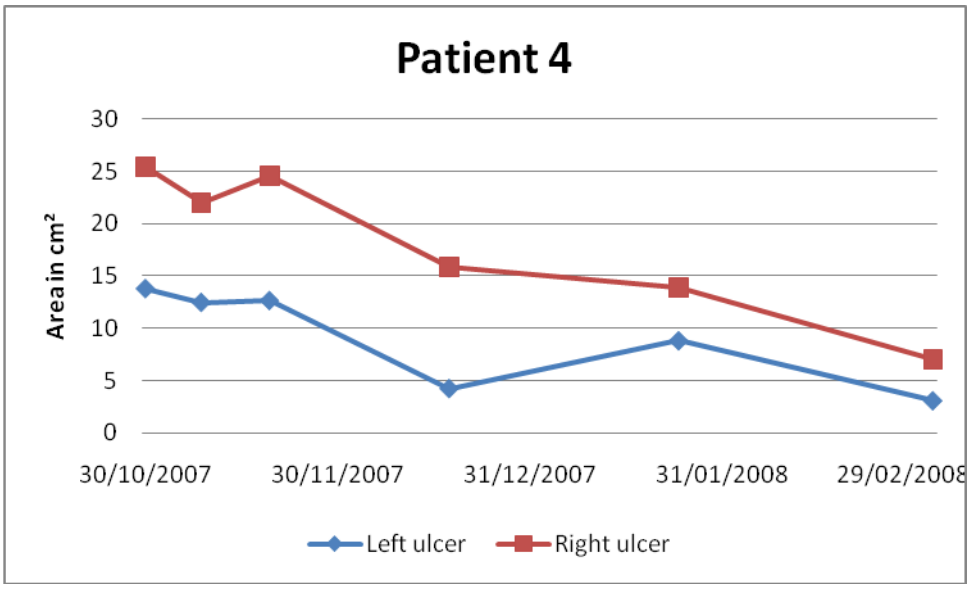

Figure 6.9 Wound healing trends, Patient 4: both ulcers unhealed

6.4.4 Ulcer severity

The original coding recorded for ulcer severity is described in table 6.6. The classification used in the prognostic factor analysis is shown in brackets: superficial and severe, following recoding as described in section 4.12.5.5. Details of the ulcer severity at baseline are described in table 5.2, this showed that 45% of ulcers were superficial 53% were severe and 2% of data was missing.

Code	Description (recoded)
3	Blister/ clear fluid (superficial)
4	Blister with blood (superficial)
6	Full thickness skin loss (superficial)
7	Cavity (severe)
8	Cavity with underlying structures (severe)
9	Necrosis (severe)
10	Dry scab (superficial)

Table 6.6 Descriptions of original coding for ulcer severity

The relationship between severity and tissue type from the literature has been discussed in section 2.6.

Twenty four ulcers were identified as clear fluid filled blisters at baseline. Six (25%) of the blisters dried out with the epidermis still intact, this eventually ‘fell off’ to reveal intact skin. Other blisters became more severe wounds with 7 (29%) progressing to necrotic ulcers.

Thirty four ulcers were identified as blood filled blisters at baseline. Nineteen (56%) of the blood blisters progressed to become necrotic ulcers and 8 (23%) developed into open wounds; either full skin loss or a cavity.

Twenty five ulcers were full thickness skin loss at baseline. Seven (28%) became necrotic, six (24%) were dry scabs at next visit, seven (28%) were unchanged when the patient died and five (20%) were healed

Twenty nine ulcers were cavities at baseline. Fifteen (51%) progressed towards healing and granulated up to skin level, 8 (28%) remained unchanged, four (14%) became necrotic and two (7%) deteriorated to expose bone. Of these two, one had been debrided by the surgeons in the operating theatre and one had been debrided with larval therapy

Seventy six ulcers were necrotic at baseline; however 87 ulcers became necrotic at some point. Nearly half of these ulcers did not progress i.e. either the patient died, the limb was amputated with the necrosis or the necrotic ulcer was still present after 18 months or the end of the study. Eleven of the ulcers which were necrotic, this tissue subsequently ‘dropped off’ to reveal intact skin.

One ulcer was a cavity with exposed bone at baseline, this subsequently became necrotic.

No time frames have been given for the above descriptions as there was so much variation for ulcers within each category.

Figure 6.10 illustrates some of the tissue types which were found in one ulcer. This was a clear fluid filled blister at baseline, One week later; the blister has 'de-roofed' revealing:

1. Edges of the old epidermis crusted with dried serous fluid
2. Raw dermis (full epidermal loss)
3. Full thickness skin loss (full dermal and epidermal loss)
4. Ischaemic tissue which is mostly covered by a
5. Layer of slough (dead tissue)

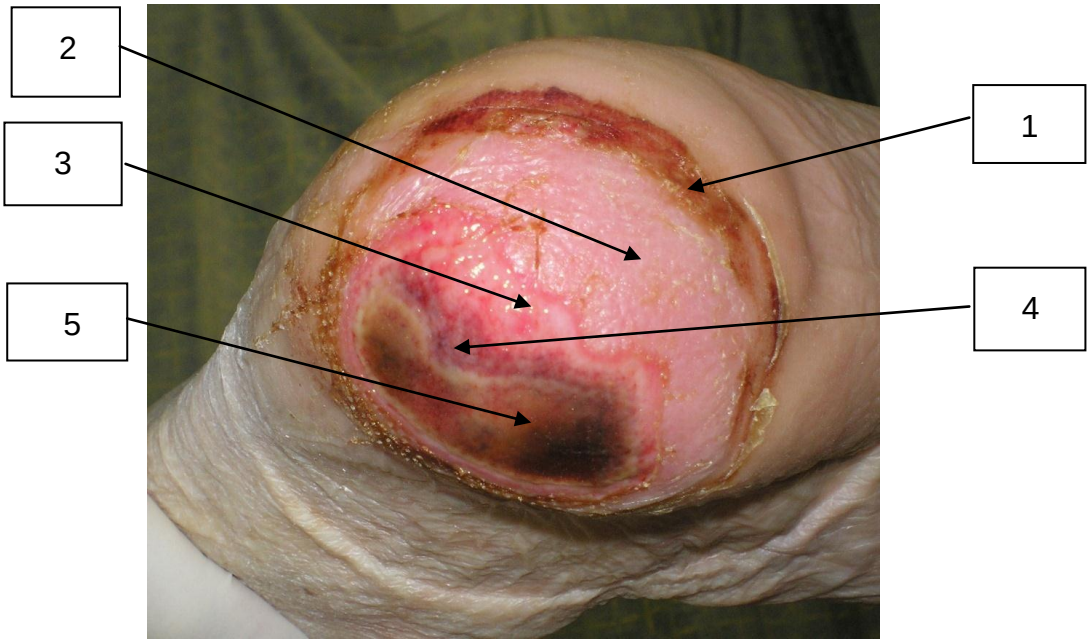

Figure 6.10 Blister which has 'de-roofed'

The two blisters in figure 6.11 occurred on the same patient (left and right heel), figure 6.11a developed full thickness skin loss, figure 6.11b 'fell off' to reveal intact skin.

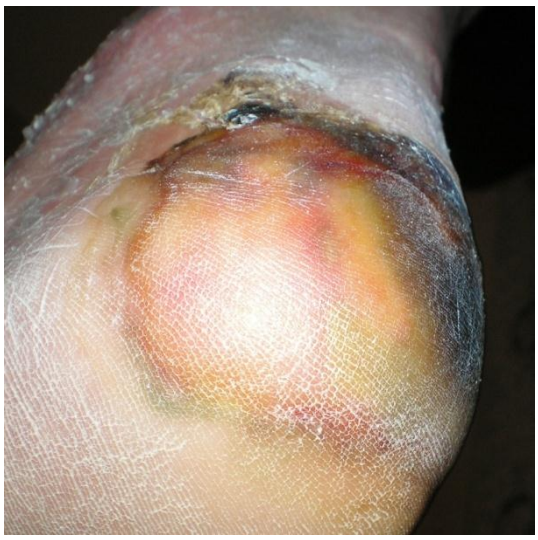

Figure 6.11a Blister to full thickness skin loss

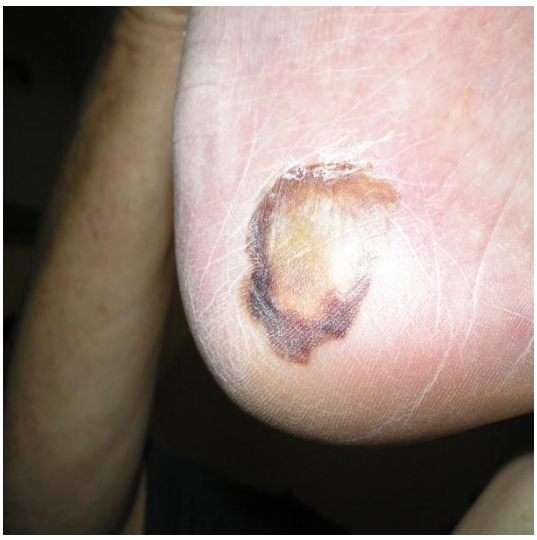

Figure 6.11b Blister to intact skin

6.4.5 Surrounding skin

The condition of the surrounding skin at baseline is given in table 5.2, this showed 31% had oedema, 28% was healthy, 16% were dry/flaky, 7% were macerated, 5% had erythema 8% other and 5% missing. From the follow-up data, the most commonly occurring skin condition (mode) was ‘normal or healthy’. This was recorded on 329 (36%) out of 921 occasions. The next most frequently recorded surrounding skin condition was ‘dry and/or flaky’; this was recorded on 157 (17%) occasions.

6.4.5.1 Erythema

The presence of erythema (redness) was observed on 34 occasions (including 14 episodes where erythema was recorded on two or more consecutive occasions). Erythema is considered to be associated with local inflammation, infection or pressure. As most of the ulcers were being assessed after the initial injury and had pressure relief it was felt that the erythema was more likely to be due to inflammation/ infection rather than pressure.

6.4.5.2 Oedema

The presence of oedema in the surrounding skin was observed on 263 occasions, either on its own or in association with maceration and/or erythema. Oedema in the foot and lower limb can be associated with co-morbidities such vascular disease, albumin deficiencies and gravitational effects e.g. after sitting for long periods.

6.4.6 Pain

Not all patients were able to report pain in their ulcers at each visit (usually due to cognitive impairment); no pain data is available at all for ulcers on 18 patients. Severity of pain at baseline for each ulcer is given in table 5.2. This showed that 36% of patients reported no pain, 27% reported some pain and data for 66 ulcers (36%) are missing.

Patients reported current pain levels at each visit, from the potential 929 observations 114 (12%) were missing, 548 (59%) has no pain, 62 (7%) had mild pain, 108 (12%) had moderate and 97 (10%) had severe pain. Most of the patients who reported no pain in their ulcer at baseline did report pain at other times.

In addition worst pain severity was recorded; 55 ulcers showed a trend that suggested pain was reducing with reducing severity of the ulcer. Pain levels in 13 of the ulcers fluctuated in association with fluctuations in ulcer severity i.e. if the ulcer deteriorated, the pain got worse and then as it improved the pain reduced. When patients were asked if anything triggered the pain, it was reported for 89 of the ulcers that pressure or contact with a support surface triggered the pain e.g. if the patient was laid in bed, the pressure of the mattress was causing the pain or if they were able to walk, it was the contact with the floor. Some other pain triggers were having the dressing removed or changed.

6.5 Adverse sequelae

Any events during the study period which were considered to potentially have an effect on the wound healing but not part of the data being collected were recorded in field notes. It is likely that other events occurred that the researcher was not aware of due to the intermittent data collection. These were then coded for data entry. Most patients did not experience any notable events, some patients experienced several e.g. recurrent infections. Most readmissions to hospital were not due to the heel pressure ulcer. Table 6.7 gives the results of this.

Number of events (percentage of all events)				
Infection (or antibiotics given) for study ulcer	**Other infection (or antibiotics given)**	**Change in social circumstances e.g. bereavement**	**Rapid deterioration of patient**	**Readmission to hospital**
18 (13%)	74 (53%)	2 (1.5%)	6 (4%)	27 (19%)

Table 6.7 Frequency of adverse events per patient

Details of infection (or courses of antibiotics) episodes are given in table 6.7. Most other infections were due to *Clostridium difficile* bowel infections, some others were chest or urinary tract.

Episodes of other infection	**Wound infection episodes**			
	0	**1**	**2**	**3**
0	76 (54%)	6 (4%)	0	0
1	42 (30%)	7 (5%)	0	0
2	4 (3%)	0	0	0
≥3	3 (2%)	1 (1%)	0	1 (1%)

Table 6.8 Details of infections per patient

More than half the patients were not known to have any infections during the study, however 11% were known to have experienced at least one wound infection and 42% were known to have experience at least one other infection.

6.6 Length of stay

The mean length of stay in hospital of each patient from the time of recruitment was 25.2 days (S.D. = 42.5), the minimum was 0 (patient discharged on the day of recruitment) and the maximum was 313 (one patient). The median was 23 days (inter-quartile range 13-44).

6.7 Change of accommodation

The patients' type of accommodation was recorded prior to admission and following discharge. The category other was the home of a patient's relative. The findings are presented in table 6.9.

Accommodation prior to admission	**Accommodation following discharge**	**Number of patients (percentage)**
Home n=100 (71%)	Home Residential home Intermediate care bed Nursing home Died Other Missing	45 (45%) 2 (2%) 12 (12%) 20 (20%) 16 (16%) 2 (2%) 3 (3%)
Nursing home n=14 (10%)	Nursing home Died Missing	12 (86%) 1 (7%) 1 (7%)
Residential home n=15 (11%)	Nursing home Residential home Intermediate care bed Died Missing	4 (27%) 5 (33%) 1 (7%) 2 (13%) 3 (20%)
Intermediate care bed n=4 (3%)	Home Intermediate care bed Died Missing	2 (50%) 1 (25%) 1 (25%) 0

Other n=5 (4%)	Home Other Missing	1 (20%) 3 (60%) 1 (20%)
Missing n=2 (1%)	Missing	2(100%)

Table 6.9 Type of accommodation for each patient prior to admission and following discharge

Nearly half of the patients admitted from their own home returned there, some who went to an intermediate care bed would have gone home later after the follow-up period was completed. Of the patients who died, these were from all types of accommodation although a smaller proportion died who were admitted from nursing homes than other accommodation: however this may have occurred by chance as the numbers in this group were very small.

6.8 Readmission rates and ward moves

Information was collected regarding how many times the patient moved wards and whether they were readmitted during the study. Table 6.10 summarises these.

Frequency	**0**	**1**	**2**	**3**	**4**	**5**
No. of ward moves/ person	113 (81%)	16 (11%)	6 (4%)	3 (2%)	1 (1%)	1(1%)
No. of readmission	106 (76%)	23 (16%)	9 (6%)	1 (1%)	1 (1%)	0

Table 6.10 Number of ward moves and readmissions

The information on ward moves was taken from the point of recruitment. Many of the elderly patients who were admitted via A&E would have been on the medical admissions unit prior to speciality where they were recruited from. Some patients may have been on several wards prior to recruitment. Although over 80% of patients never moved wards, a number of patients did move several times, many of these were transfers to and from the infectious diseases ward when they had a bowel infection, some were moves within the speciality to accommodate operational requirements of the wards, a few were between specialities when patients required different interventions.

Three quarters of the patients were not readmitted during the study, the reason for readmission for most patients who were readmitted one or two times was not related to the heel pressure ulcer. The patient who was readmitted three times was a lady with uncontrolled epilepsy who fell several times requiring hospital admission. The patient who was readmitted four times had diabetes and other co-morbidities; three readmissions were due to his heel pressure ulcer and one was due to a urinary tract infection.

6.9 Additional analysis

6.9.1 Changes over time

The study spanned a period of more than five years including preparation, data collection and analysis Changes in patients, the researcher, the organisation or political and economic issues may have been influential. Changes in the researcher are discussed in chapter 7. In chapter 4 there was a concern that practice may change over time with regard to the management of heel pressure ulcers, for example different dressings or support surfaces may have improved healing rates. Figure 6.12 shows the length of time patients were in the study for each consecutively recruited patient. No trend is noticed.

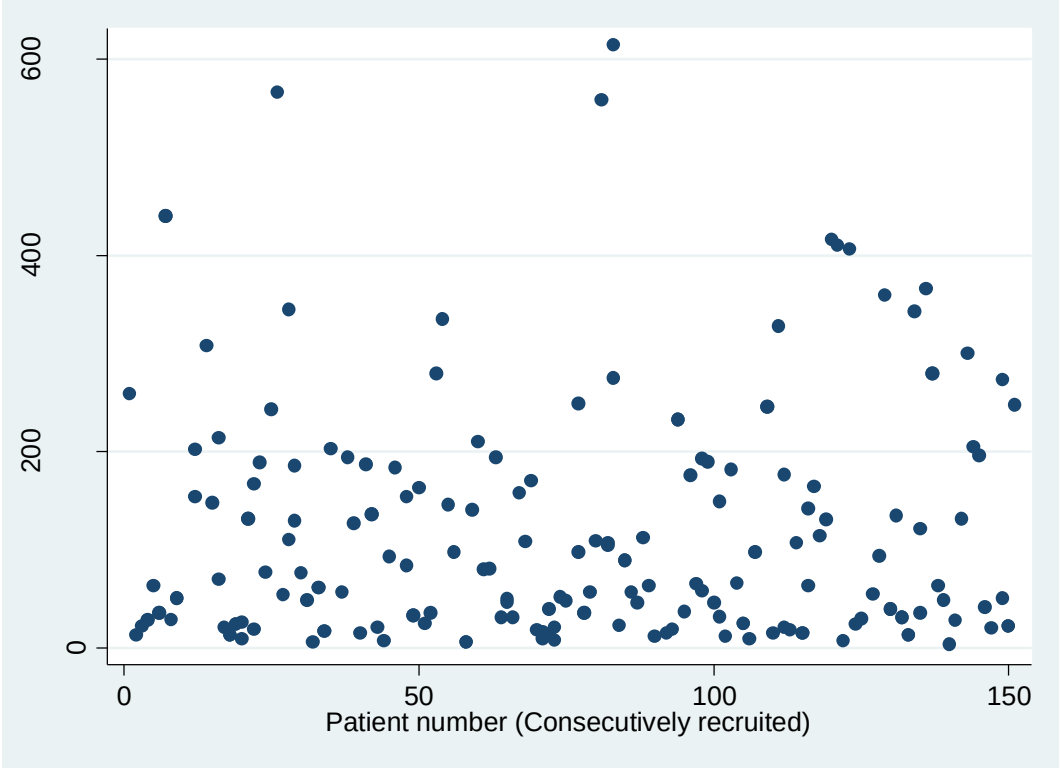

Figure 6.12 Relationship between duration in study and time of recruitment

No new national guidelines were published during the study. Local guidelines were updated and staff training on pressure ulcer prevention and management continued throughout the study. Figure 6.13 shows the type of dressings used at baseline for each patient, this suggests that fewer antiseptic dressings were used later in the study, less ulcers had no dressings but there is no noticeable difference between the number of ulcers with 'moist' as opposed to 'dry' wound healing. Coding for the dressings is given in table 6.11, details of how these were collected and coded is given in table 4.2. Similar coding was used in the Bergstrom *et al.*(2005) study.

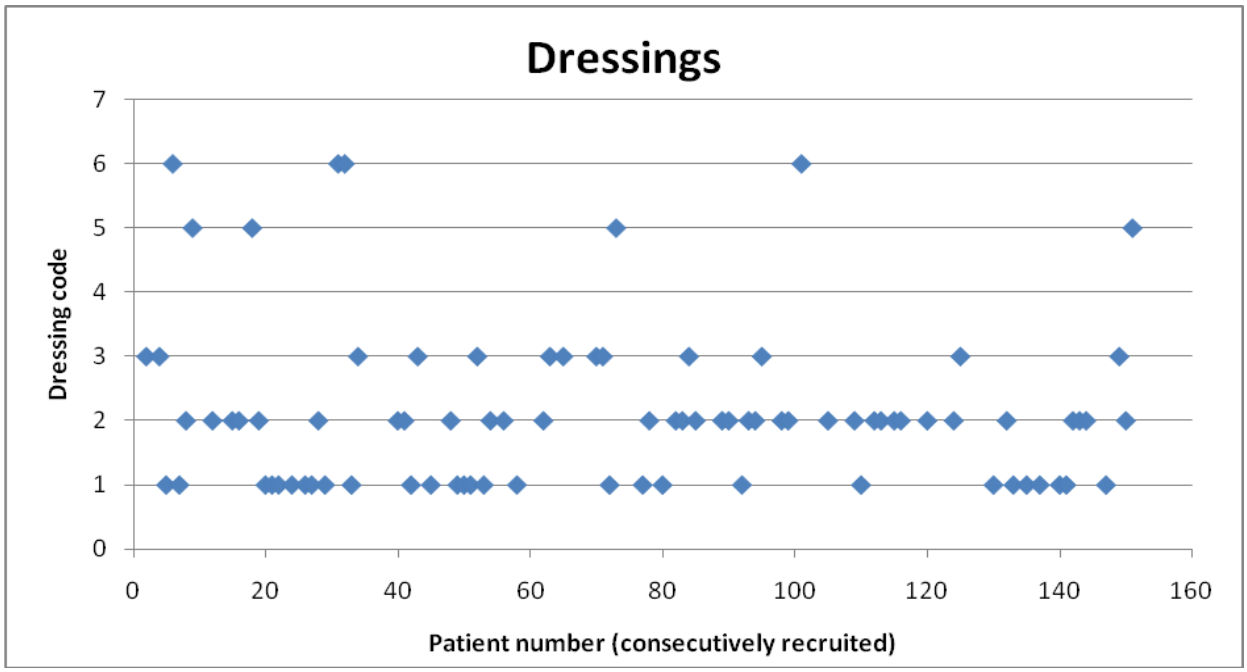

Figure 6.13 Relationship between dressing type and patients consecutively recruited

Code	Dressing
1	Moist wound healing
2	Dry wound healing
3	No dressing
4	Antiseptics
5	Moist wound healing with antiseptics
6	Dry wound healing with antiseptics

Table 6.11 Coding for dressings

Figure 6.14 shows the type of support surface used at baseline for each patient, although no trend is noticed, there does appear to be less code 1 (standard foam mattress with no pressure relief used later in the study)

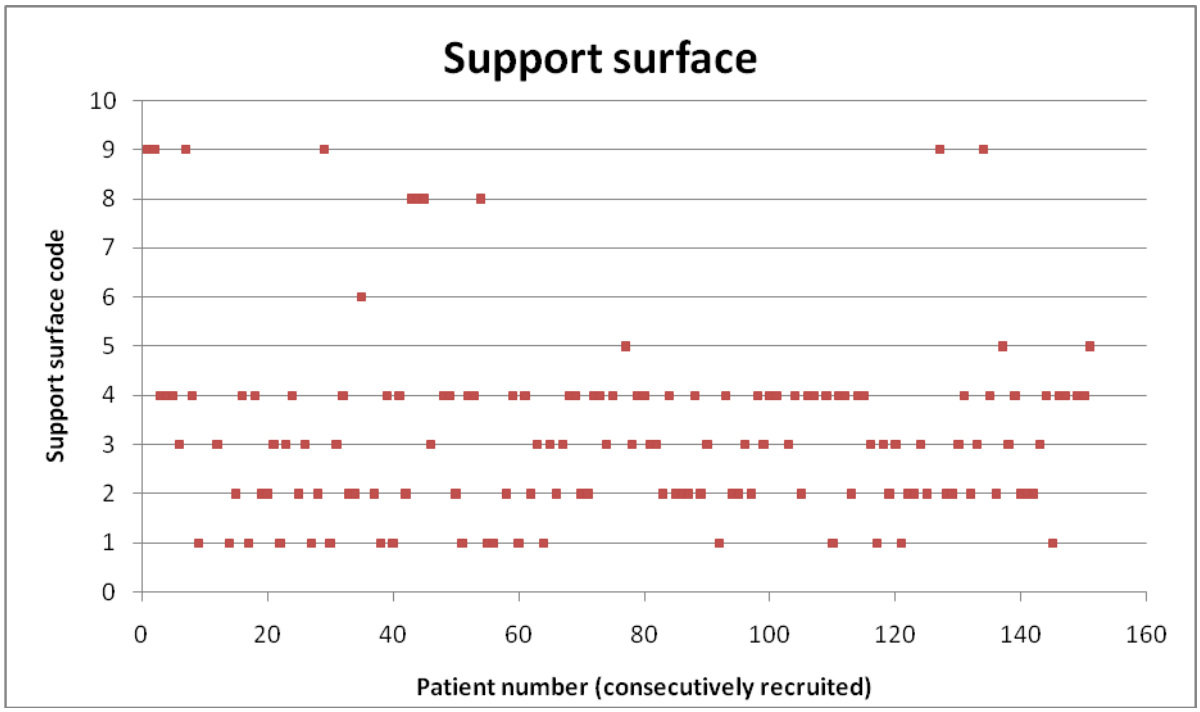

Figure 6.14 Relationship between support surface and patients consecutively recruited

The coding for figures 6.14 is given in table 6.12, this has been adapted from the RCN guidelines (RCN, 2005) and details are given in Box 4.2.

Code	Support surface
1	Standard foam
2	Visco- elastic foam
3	Low air loss
4	Alternating pressure
5	Air flotation
6	Heel specific support
7	Other
8	Standard foam + heel specific
9	Visco- elastic + heel specific

Table 6.12 Coding for support surfaces

The patients were all cared for by particular specialities, the researcher is not aware of any changes in admission criteria for these specialities such as changes from inpatient to day case surgery. It is possible that the dependency of the population may have changed. A review of the annual pressure ulcer prevalence for the Trust for the last 5 years showed very little change in the proportion of patients at risk high of pressure ulcers although the overall proportion of patients at risk has apparently decreased. See table 6.13 for details.

Year	% of patients at risk	% of patients at high risk
2010	49	18
2009	49	18
2007	71	19
2006	75	17
2005	75	21

Table 6.13 Proportion of inpatients at risk of pressure ulceration during annual prevalence audits

This is the collective data for the whole organisation and not specifically the specialities from which the patients were recruited. It is suggested that this is representative, however no work has been identified which confirm this.

6.10 Summary of findings for the secondary objectives

This study identified on 140 patients who were included in the study with 183 heel pressure ulcers. Fewer than half the ulcers healed, Eighty eight of the ulcers were on 60 patients who died during the study. Most of the ulcers that healed had a ‘dry scab’ prior to full re-epithelialisation. Ulcer area did not change in a uniform manner, some ulcers got bigger before they got smaller. Treatments such as support surfaces and dressing were notably inconsistent over the period of the study. Details were given of the patients’ journey, most patients were admitted from their own homes but fewer than 50% returned home following discharge. Approximately a third of patients experienced a significant event during the study; these were mostly non-pressure ulcer related infections. Further discussion of these issues can be found in chapter 8.

Chapter 7 Being a practitioner researcher

7.1 Introduction

Throughout this report I have acknowledged that I am also a clinical practitioner. The reflections and potential implications of this have been considered worthy of a separate chapter of this thesis. The aim of this chapter is to fully inform the reader of my clinical and research background; what demands, constraints and opportunities were available to me and the likely effects of these on the research project.

7.2 Context

Over recent years there has been an increased awareness of the benefits of clinical research in healthcare in the UK. The Department of Health has produced several reports which will enable the recommendations set out in the 'Research for Patient Benefit Working Party' report (Research for Patient Benefit Working Party, 2004) to be implemented. In 2005 a report was produced in response to concerns about 'the perilous state of academic medicine and dentistry in the UK' (UKCRC, 2005). This highlighted the lack of career structure, lack of flexibility and balance between clinical and academic training and the shortage of posts following completion of training for doctors and dentists. The report made recommendations about training for all staff from undergraduates to Specialists to Consultants and the further development of clinical academic careers. A similar report was produced for nursing (UKCRC, 2007). This set out the principles for improving the clinical academic workforce in nursing; however the contribution to this report from senior NHS staff as stakeholders was small. This is reflected in the report as its perspective appears to be that of the academic institutions and there is no acknowledgement of the barriers within the nursing management structure that the researcher has experienced. Without clear incentives for the NHS, this report is unlikely to have much impact.

A review of the available literature on clinical practitioners who are researchers provided some additional comment. Some documented discourse on the lack of medical practitioners who pursue a research career alongside their clinical practice has been identified. A survey (Pfeiffer, Burd and Wright, 1992) carried out in a mental health care setting in the USA asked psychiatrists,

psychologists and social workers for their views on scientist-researchers. Most respondents in this study reportedly approved of the scientist-researcher model however they did not participate in research due to time, lack of funding and thought not to be part of their job.

The notion of the researcher, who is also a clinical practitioner, has been presented and debated in detail by Reed and Proctor(1995). While their work primarily considers qualitative research by non-medical practitioners, their comments can be considered and evaluated for all research studies and healthcare professions.

A publication by Miller *et al.* (1998) on professional integrity in clinical research was produced in response to allegations of ethical abuse in clinical research which had been reported in the media. This paper focused on physicians conducting drug trials, particularly in cancer and schizophrenia. They describe two models: one of the physician investigator as a clinician, the other the investigator as a scientist. The risks presented include; the financial incentives to recruit, the misconception existing in the patients, and to a certain extent the clinicians, that the research is therapeutic and not exclusively ‘for the sake of science and the benefit of future patients and present researchers’. They do however conclude that the solution is not to remove the clinical role from the investigators, but cultivate a concept of ‘moral identity’ of the physician investigator with equal elements of the scientist and clinician.

7.3 Background of the researcher, a personal perspective

My career has been mainly in clinical nursing practice within the NHS except for two years in management. The last 20 years has been in the field of Tissue Viability, a specialist area focusing on the prevention and management of wounds. I have always had an interest in the evidence base supporting practice and frequently experienced frustration with the fundamental lack of good quality research into the development of the treatments used and the lack of analytical and reflective skills of nurses. In this speciality, some practitioners have a strong partnership with treatment manufacturers. It is sometimes difficult to separate the benefits of a contribution to development, research, provision and

use of products and a marketing strategy. I have been particularly conscious of this and have always strived to maintain an objective approach to dealing with commercial representatives. I have always had a desire to understand any research data presented as evidence; to interpret the relevance and value of any investigation in this field and its applicability to practice and ultimately to investigate and therefore contribute to the evidence particularly in areas where controversy exists or patient outcomes are significantly affected.

An influential text in my early career (Walsh and Ford, 1989) proposed that nursing needed to change from its ritualistic practices which were continued even in the light of research evidence e.g. evidence for improved healing rates with a moist wound healing environment was known yet porous dressings which promoted a dry wound environment were used. It suggested that nursing could not call itself a profession, until this change happened, it could only be considered a caring craft. I think it is likely that a review of practice would raise similar concerns today.

Jarvis (2000) suggests that the theory practice/gap, which still existed 11 years ago in nursing, is being addressed to some degree by practitioner-researchers, although they are experiencing feelings of inadequacy in their research findings as these have been produced only from their own work environment. He states that nurse consultants are probably in a better position than others who work within tight organisational constraints, to reduce the theory practice gap by making pragmatic changes in practice. I support this view and feel I am in a privileged position as a nurse consultant to bring about change.

My future career plans are to stay in clinical practice, while developing my research skills. I value highly the role of the practitioner researcher and feels this role makes an important contribution to both research and clinical practice. I am concerned that researchers who do not engage with clinical staff and patients are at risk of investigating irrelevant topics, and clinicians who do not engage with researchers are at risk of carrying out ritualistic rather than patient focused care. The potential for bias, if I felt dependent on a positive outcome of the research study to support my career has been considered, but is thought not to be present.

I am a Nurse Consultant in Tissue Viability (NCTV) at the study site. I had been in this role for 14 years, of which the last seven have been at the study site. Plans to conduct the study were discussed prior to my appointment to the current post. The NCTV role consisted of approximately 50% clinical consultation for the prevention and management of wounds including pressure ulcers. Other elements of the role included teaching, research and strategic development. Since as I had instigated the new service within the organisation I had worked hard to establish relationships with clinical staff, primarily nurses, but also medical staff and allied health professionals. Referrals for clinical consultation arose predominantly from the specialities included in this research study.

I was responsible for setting standards of care for patients with and at risk of developing pressure ulcers, through written guidelines, education, clinical education and as a role model in delivering care to patients.

I had some experience of clinical research having undertaken a small study to inform my MSc dissertation while with a previous employer. Although this previous organisation had been very supportive of the research, there were very few nurses undertaking research. Fortunately a nursing research development unit had recently been established and I was attached to this unit. When I was appointed to my current role, no other nurse researchers were identified within the organisation and managerial support and understanding was limited. Although research is a core element of the Nurse Consultant role, the performance measures of the post did not include research and there was an expectation that I would deliver a new clinical service and improve organisational performance on key indicators such as pressure ulcer incidence and prevalence.

A limited research training had been undertaken as part of my MSc programme. Certain courses were available through the University during the preparation of this thesis; however competing demands for time were frequently an obstacle to accessing this support. Research ethics and governance approval process can be a challenge for seasoned academic researchers, to

proceed with these as a novice clinical researcher was challenging. Although support networks existed in the University, to access these meant time out of either research or clinical time and travelling to the different venue.

I had acted as local Principal Investigator on a Health Technologies Assessment research study (Iglesias *et al.*, 2004) that had given me valuable experience of research project management, designing, implementing and evaluation data collection tools and working with a research nurse.

Access to library and Information Technology facilities was a mix of both University and NHS Trust. Overall this worked well to allow me to work remotely.

7.4 Implication for the study

7.4.1 Constructing the research question and the design of the study

In my role as NCTV, during clinical consultations there is a need to advise on the management of pressure ulcers. While international guidelines existed (EPUAP, 1998), these were explicit about the uncertainty of relevance to heel pressure ulcers, in particular, the role of debridement. My preference would have been to have undertaken an intervention study of debridement, however full cognisance was taken of the lack of information on healing times, death rates, types of interventions currently used, such that sample size and power calculations would be difficult if not impossible. The current study was primarily exploratory with the aim of informing a potential future intervention study. The variables collected in this study were numerous. I was advised against ‘data greed’ and consequently some were removed. The choice of variables was mostly based on my clinical experience given the lack of available valid evidence. Particular examples include:

- I felt that some patients, who were on Inotropic drugs to improve cardiac function in critical care, were experiencing poor blood supply to their feet which would affect wound healing.
- I felt that some patients, who were on anti-coagulant therapy, were being over medicated and the excessive bleeding may affect wound healing

This resulted in details of all medication being collected. In hindsight most of these were actually proxy measures for a disease or co-morbidity. The presence of the actual disease was also a variable collected. It was probably un-necessary to collect both sets of variables. With regard to the two specific examples, only 2 patients had received Inotropes (numbers too small to be significant) and the data collected on the use of anti-coagulants did not include information on whether this was being over prescribed.

I was aware of variability of treatments e.g. dressings and pressure relieving aids, both between patients and within individual patients over time. In order to identify any potential effects of treatments it was considered important to capture these changes over time. The primary analysis was undertaken with baseline data, excluding those factors which varied over time. While data is available on the time dependent variables, it was beyond the scope of this study to include a time dependent analysis. However my intention is to analyse and publish at a future date.

My knowledge of the research population was influential. It was known that they would be aged and thus challenge the researcher in regard to their cognitive abilities and in particular their understanding and resultant capacity to consent. This perspective therefore resulted in modification and adaptation to the research design, with particular regards to the process of relative assent and latterly consultee agreements (in response to changes in the research guidance around capacity and consent contained in the Mental Capacity Act (2005)). It aimed to minimise the burden of data collection from the patients and gave an option for ‘opt out’ for the ABPI diagnostic assessment as this could potentially cause discomfort or inconvenience. This was particularly helpful when relatives were consulted on the decision to participate, but did result in a large amount missing data for this variable.

7.4.2 Conducting the research

I was aware of the potential conflict of interest of my clinical role during data collection, this included identification of patients, recruitment, objectivity of data collection and ethical dilemmas over nursing practice.

An essay written by a group of complementary therapists discusses some of the problems of being practitioner researchers (Lewith *et al.*, 2009). This paper included a series of vignettes in which practical examples of practitioner research are given. One example presents the individual's concerns over giving a 'sham' (placebo) treatment and feeling nervous about being 'found out'. Some of the problems of randomised trials such as recruitment and administering the control arm as a practitioner did not occur in the current study as it was observational. A practitioner researcher will be well aware of the differences in patients included in a study and those not recruited. In Lewith *et al.* (2009) a herbalists describes his concerns that the patients in the trial did not have all the co-morbidities of his usual patient group and felt uncomfortable over how useful the findings would be. I felt that the patients included in my study were representative of the population based on both the screening data and intuitive knowledge and therefore the potential for selection bias was low.

Patients were identified by visiting wards and asking staff whether they had anyone who met the inclusion criteria. This could potentially have been an emotive question as it required nurses to admit to the NCTV to having patients with pressure ulcers which could have been perceived as a measure of their standards of care. I tried to ensure a non-judgemental attitude when recruiting.

Occasionally I would carry out the dressing change on the ulcer in order to collect the data; this would assist the nursing staff by relieving them of the task that day. It is likely that this action could be seen to encourage reciprocation by staff identifying other patients for the study. The number of occasions when this occurred was small, I carried out the dressing change according to the plan of care; it is unlikely that my participation would influence the outcomes.

Some of the patients who were recruited had already been referred to me for clinical advice. I was very careful to provide impartial advice about the study in order to ensure there was no coercion to take part. Reassurance was given such that the patients would continue to receive the same level of care from me and other staff, even if they chose not to take part.

The possibility of selective recruitment was considered. I was aware of the probability of patients dying in this population; it would have been tempting to selectively recruit patients who were considered more likely to survive. As mortality rates were higher than other similar studies (42% in the current study compared with 26% in the Berlowitz (1997) study), this suggests that no selective recruitment occurred.

All data collected were in accordance with a predetermined protocol. Most of the data collected were objective information from nursing and medical records. Subjective assessments were made of the ulcer severity, tissue type and condition of the surrounding skin with the assistance of agreed tools to aid decision making. It is difficult to provide full assurance of the reliability of these assessments; however data for a wound selected at random was compared with the photographic evidence at a later date when the researcher was less likely to be influenced by the presence of the patient or a desire for the wound to be improving. During the later part of the study a research nurse assisted with data collection. This nurse was trained by the researcher in assessment. No formal inter-rater reliability tests were undertaken although the research nurse was supervised and again data were checked against the photographic evidence. It may have been helpful to test out the inter-rater reliability of the assessments by requesting another wound care expert to examine some of the data alongside the photographic evidence, especially as severity of the ulcer was found to be a prognostic factor.

It was possible that I may have encountered some ethical dilemmas while observing clinical practice during data collection. Consideration would have to be given with regard to how and what was acceptable and unacceptable practice. Every attempt was made to keep the two roles separate, if clinical consultation was requested during data collection the staff were asked to make a formal referral to the TV service. Occasionally I came across a safety issue such as an electrical mattress which was alarming and not functioning properly. In these cases I did intervene to rectify the problem. Where clinical consultation regarding dressings or pressure relieving devices was not sought I relied on my knowledge of the scarcity of evidence of effectiveness of any of these interventions to restrain myself from intervening in practice. If I was particularly

concerned when a ulcer was deteriorating I would suggest a clinical consultation request would be appropriate. I was aware of a few occasions, where medical staff assumed, that because they had seen the NCTV with a particular patient, that clinical consultation was being provided. These assumptions were corrected where possible, however the full extent of this problem may not have been known.

Changes in me did occur. As thesis preparation is an ongoing process, I became more knowledgeable in the subject matter, developed and refined my critical appraisal skills and continually challenged my beliefs about clinical practice. My clinical role continued alongside the research and practice development took place based on increasing knowledge, reflective practice and networking with other experts.

7.4.3 Data analysis

It is important that my values were known and the study design was such to reduce their influence. I had insight into my desire to improve outcomes for patients and to be able to give good evidence based advice on the management of heel pressure ulcers. This was considered in the analysis and caution was taken with interpretation.

The analysis plan was predetermined. When potential risk factors were identified through the univariate model, careful consideration was given to the clinical significance and relationship with other variables prior to entry into the multivariate model. While potential prognostic factors were identified, this was a small exploratory study and the evidence was suggestive of association not conclusive of causation. Generated theories can be tested in larger studies.

7.4.4 Dissemination of findings

The findings of any study of pressure ulcers have the potential to be contentious as the association between pressure ulceration and practice falling below an agreed standard can be strong. This particular study included:

- Patients who developed pressure ulcers while in the care of my employers
- Identified variability in nursing practice (e.g. dressings, support surfaces) including practice outside Trust guidelines

- Is explicit about the number of patients who died with a pressure ulcer.

It is important that this information is firstly communicated appropriately within the organisation; particularly to staff that were caring for these patients.

Findings will be presented both internally and externally to the academic, professional and public within the context of reasonableness and sufficiency of clinical practice. I must ensure that I do not compromise my future role as a clinician and a researcher within the organisation.

7.5 Review of potential bias and validity due to the researcher practitioner

The above sections have considered many aspects of being a researcher practitioner and they have been structured following the format introduced in Reed and Proctor (1995). Detection bias may have been present if patients with heel pressure ulcers were not identified e.g. if particular ward staff were reluctant to disclose patients to the researcher, or if I was more aware of patients particularly with severe pressure ulcers because of my clinical specialist role; every effort was made to overcome this.

Recruitment bias may have been present if there had been difference in those who were recruited and those who declined participation. Although reliable records of patients with heel pressure ulcers do not exist, I was particularly careful not to coerce patients who were already know to me, or avoid recruiting those who were near death; screening and recruitment rates were similar.

Internal validity of the study was felt to be enhanced due to my knowledge of the patients (co-morbidities, duration of healing, potential changes of location to ensure minimum loss to follow-up), study site (patients were representative) and variables (could be fully defined and precisely measured and available for most patients).

When the characteristics of the patients recruited were examined, external validity was not thought to be compromised by me being in the post of a NCTV in study organisation.

7.6 Summary

I have been explicit and transparent throughout this report in describing my dual role as clinician and researcher. I have been cognisant of potential biases due to competing loyalties. Hopefully the study has benefited from my detailed knowledge of clinical patient pathways to elicit useful research information which may have been overlooked by a non-clinical researcher. Sufficient detail has been given such that the research could be repeated by a non-clinician and the same results obtained.

Chapter 8 Discussion

8.1 Introduction

This chapter starts with a summary of the strengths and weaknesses of the study. It then provides a critical appraisal of the study methods and results; it follows the order of the Methods, Primary then Descriptive analysis chapters. includes comparisons with other relevant studies, setting the results in the context of the body of knowledge, including other studies about prognostic factors for wound healing. The key findings and new knowledge are highlighted and implications for clinical practice are considered. The systematic review chapter included a critical appraisal of its own study methods, its findings are noted in section 8.7. Potential areas for future research are suggested in the following chapter.

8.2 Summary of strengths and weaknesses

This is the first study to identify prognostic factors for healing of heel pressure ulcers. Three studies have looked at prognostic factors for healing pressure ulcers not confined to the heel; two of these have used retrospective data from case note reviews (Berlowitz *et al.*, 1997; Bergstrom *et al.*, 2005) and one performed a secondary analysis of prospective cohort study data (van Rijswijk and Polansky, 1994). The prospective cohort methodology in this study has ensured minimal missing data and only two patients were lost to follow-up. The study inclusion criteria were very broad and very few patients were screened and then not recruited; this ensured that the study population was representative of the heel pressure ulcer population. The use of relative assent and latterly the use of personal or nominated consultees ensured that those patients who lacked capacity to consent were represented in the study.

The study used the endpoint of complete healing, this was achieved with a long duration of follow-up (18 months) and the ability to continue data collection in the community when patients were discharged from hospital. Most other studies choose an outcome of healed or not healed by a given time which means that time to complete healing in unknown for a number of patients (van Rijswijk and Polansky, 1994; Berlowitz *et al.*, 1997; Bergstrom *et al.*, 2005; Takahashi *et al.*, 2009). Although the majority of pressure ulcers not confined to the heel will heal within six months very little is known about those that continue beyond this

point. This study has provided valuable information about ulcers that take a long time to heal. This will assist healthcare professionals (and enable them to inform patients) to have realistic expectations about difficult to heal wounds. It will help inform resource needs and enable patients and their carers to make choices about treatments which will affect their quality of life. It will also help inform future research studies, in particular trial planning.

This study thus identified new information regarding the prolonged final stage of ulcer healing and the presence of scab formation during this time. However, the relevance of this information has yet to be established.

This study identified two prognostic factors that were independently associated with healing; the severity of the pressure ulcer (as determined by ulcer Grade) and the presence of peripheral vascular disease. The severity of the ulcer has also been identified in a study of pressure ulcers on residents in a long term care institution (Berlowitz *et al.*, 1997) and has good clinical validity. The presence of PVD has been identified in two prospective cohort studies of patients with diabetic foot ulcers (Winkley *et al.*, 2007; Nather *et al.*, 2008) which also has good clinical validity.

Although the study population was chosen from specialities which were considered to have a higher proportion of heel pressure ulcers and the setting was a large tertiary hospital with Nurse Consultant level of Tissue Viability expertise, these factors were thought to have minimal influence on the outcomes. The sample represents normal patients with heel pressure ulcers, seen in practice with a range of ulcer durations. The findings are therefore likely to be generalisable to most acute care institutions in the UK.

More than half of the heel pressure ulcers did not heal, but most of these were on patients who died. The Cox proportional hazard model was chosen to enable maximum use of the data available; nevertheless, the lack of data would still have had some influence of the power of the variables to be prognostic. When patients had ulcers on both heels, data was collected for both ulcers and robust standard errors were used in the analysis to overcome the effects of clustering (Williams, 2000).

Patients were recruited who already had pressure ulcers. While an estimation of the start date of the ulcer was made; no information was collected for variables which may have affected the healing prior to recruitment. Although time to healing was calculated, this was only from the time of recruitment. An inception cohort would have been preferable, but this would have required additional resources.

Data were missing for important variables such as neuropathy, ABPI and pain. The reasons for this were discussed and the main reason was cognitive impairment. Some of the data therefore were missing at random and so with more information, imputation methods could have been used, which would have improved the generalisability of the findings.

The reliability of some variables e.g. wound area measurements, co-morbidity, has been questioned. These have been considered and the variance is thought to be random and therefore will have limited influence on the findings. There was however a concern over how the smoking variable was defined and coded as this was expected to be prognostic; this should be reconsidered for future studies. The data on co-morbidity may have been insufficient to be prognostic, a better measure of severity and impact of a disease needs to be considered for future studies.

The time intervals for follow-up data collection when patients were discharged were longer, this was based on the assumption that there would be less change in variables e.g. less rapid wound healing, changes in dressings, tissue types. Changes in treatments and tissue types had more variability than expected, what happened in between data collections was unknown, however this did not affect the key findings (prognostic factors) of the study.

Two factors which may have been prognostic (based on evidence from other studies) were not collected: the presence of multiple wounds and mental state. In hindsight these should have been included.

This study has followed the reporting recommendations suggested in the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) (Vandenbroucke *et al.*, 2007) statement. This has assisted in promoting the quality of the study and its report.

8.3 Research design

8.3.1 Choice of method

A prospective cohort study was chosen as this was considered to be the preferred method for an observational study to identify prognostic factors (Altman, 1991). It can identify exposures or characteristics of interest which are thought to influence outcome. It was acknowledged that potential difficulties may occur if the outcome of interest was rare or the time to event was long. This would result in the need to recruit a high number of patients and become costly in terms of follow-up time. It has already been acknowledged in section 4.3.1 that data from a record review would risk large amounts of missing data and retrospective data collection is at risk of many biases. This study proved to have a long time to event (median time to healing was 121 (range 8-440) days) given the available time for data collection; however the lack of missing data confirms that this was the most appropriate method.

8.3.2 Sample size

The sample size calculation for the current study took into account healing and death rates from other studies (see section 4.11). The target recruitment rate was 20 patients per month; unfortunately the actual rate of 6 per month was lower than expected. This was mainly due to the time needed to screen and recruit patients. If further studies were being considered recruitment rates could be improved with more researcher time. The sample size calculation was based upon a patient level analysis i.e. 1 ulcer per patient, this was expected to give 75-100 events (of ulcers healed). This would allow for between 7 and 10 variables in the model based on the assumption that 10 events per variable are needed for the analysis (Harrell *et al.*, 1985). During the development of the statistical analysis plan, other papers were identified that analysed data at the ulcer level. Further discussions with the statistician confirmed that this would have the benefit of being able to use all the data when a patient had 2 heel ulcers. The impact of this was a higher number of events which allowed more variables to be considered in the model. The implications of including 2 ulcers

per patient are considered in section 4.12.5.2. By limiting the number of variables considered and in particular excluding those with small numbers of events gives more confidence in the findings (narrower confidence intervals).

8.3.3 Overcoming bias

8.3.3.1 Loss to follow-up

While only two ulcers (on two patients) were lost to follow-up during the study there were more ulcers (106 of 183 ulcers) which were censored than healed e.g. due to the death of the patient. Although there were no systematic reasons for censoring that the researcher was aware of and no patients were known to have died due to their heel ulcer, the effects of the variables can only be included up to the point of censoring. This had a major impact on the amount of data included for analysis. When compared to other studies, the proportion of patients who were lost to follow-up (e.g. 21% were lost to follow-up during the 6 months follow-up period in the study by Berlowitz *et al.* (1997)) was much less, although the proportion who died was more (25.7%). This is probably due to the study methodology and the population. Berlowitz et al (1997) studied patients in a long term care facility and did not follow-up patients who were discharged; their method was a retrospective cohort study, data were obtained from an administrative database. The overall impact of the high number of patients who did not reach the endpoint of healed was to limit the number of variables which could be considered in the final analysis.

8.3.3.2 Selection of participants

Although the study site was chosen for convenience, not only was it the place of work for the researcher, it was also a large city centre teaching hospital providing both local and tertiary services. Whilst it is possible that patients who were admitted for tertiary care due to their complex needs, may not be representative of the heel pressure ulcer population, the majority of these patients were excluded as they did not live in the city (could not be followed up) and most patients were recruited from Care of the Elderly, which is a non tertiary service. This suggests that the findings are generalisable to non-tertiary care.

The choice of clinical specialities that the patients were recruited from was intended to optimise potential recruitment in the time available. The specialities

were chosen as they had consistently high levels of heel pressure ulcer prevalence in the annual internal audits. By restricting the sample population in this way it may have affected the generalisability of the findings. For example, if patients had been recruited from other specialities e.g. respiratory or cardiac medicine, other prognostic factors may have been more prevalent, such as respiratory disease, which would have produced different results in the modelling. If other specialities had been included this would have increased the screening time and reduced recruitment rates.

Patients were followed up after discharge from hospital, and approximately two thirds of the data of the patients' episode collection time was following discharge, all but 13 of the ulcers that healed did so following discharge. Most patients were recruited from Care of the Elderly; this speciality provides a close affiliation with long term care such as Nursing Homes and Community nursing care for patients in their own homes. If future analysis of time dependent co-variates was performed, where the data was collected could be important as this could be influenced by the care environment e.g. treatments could depend the local formulary of products available, skill mix of nursing staff, etc.

During data collection a record was made when the patient was being seen by a specialist specifically for the management of the heel pressure ulcer. The specialist could have been the researcher herself as a Tissue Viability Nurse Consultant (TVNC), a Diabetologist, a diabetic Podiatrist or a Vascular surgeon. However no distinction was made between which one. In section 6.3.4 the involvement of the specialist is discussed and it is noted that 52% of the patients who healed were seen by a specialist. However 34% of the patients who did not heal were also seen by a specialist. It is likely that patients referred to a specialist will differ systematically from those who are not e.g. they are likely to have worse ulcers but as no data is available for this it is difficult to comment further on any association between specialist involvement and healing.

It could be suggested that an organisation supported by a TVNC should have an above average standard of care for pressure ulcers with the result of better outcomes for these patients, but no literature has been found to support this. A

survey carried out by the Patients Association (The Patients Association, 2010) compared acute Trust activity levels (based on finished consultant episode bed days) against the number of TVNs in post. While the researcher's Trust is not quoted in this table (Patients Association (2010) Figure 1.1) it has one of the highest activity levels compared to all the Trusts and a lower than average Whole Time Equivalent (WTE) Tissue Viability Nurses. There are fewer Tissue Viability resources available compared to other Trusts. It unlikely that one person could have an extraneous impact and therefore limit the generalisability of the findings.

The issue created by having a researcher who is also a clinical practitioner was considered worthy of further detailed discussion as presented in Chapter 7.

8.3.3.3 Changes over time

Changes in patients, the researcher or the organisation over time are considered in section 6.9.1. Slight changes such as progressively less antiseptic dressings and less wounds without dressings and less 'standard foam' mattresses, have been demonstrated but these were unlikely to influence findings.

8.3.4 Recruitment

It has been discussed in section 4.3.3 that an inception cohort study of new incident pressure ulcers would have been a preferred method as the duration of the ulcer prior to recruitment is thought to be unreliable and the factors influencing healing prior to recruitment are unknown. However, this would have markedly reduced the number of patients recruited. This is a shortcoming of the study and were it to be repeated with an inception cohort design then more recruiting centres would be needed. However a lot more resources would be required.

The inclusion and exclusion criteria were comparable with other studies. From the screening data and the researcher's experience it would seem that most patients with heel ulcers were considered for the study and nearly half (72 out of 186) of those not included were near death, see figure 5.2.

When a ward was visited, screening data were captured to enable comparisons of the recruited and non-recruited populations. Recruitment rates were lower than expected; this was attributed to the time taken for data collection. It is likely that there were patients with heel pressure ulcers who were not screened or recruited, as there were sometimes periods of several weeks in between visits to a particular ward. This may have led to the possibility of selection bias. However the range of age, gender, co-morbidities, ulcer duration and severity, etc suggest that any that were missed were likely to be at random (no systematic differences) and therefore reduce the potential for selection bias.

8.3.5 Consent process

Patient recruitment commenced before the introduction of the Mental Capacity Act (DoH, 2008). A protocol amendment (September 2008) led to the researcher being able to be clearer with relatives with regard to their role as personal consultee for the patient as well as utilising healthcare professionals as nominated consultees (see section 4.6). With this amendment, the rate of non-recruitment due to patients lacking capacity, reduced for those who did not have a relative. A nominated consultee (in all cases the medical consultant) was used for three patients. The overall recruitment rate was not noticeably affected.

Mason *et al.* (2006) describe the consent process utilised in a large randomised control trial of pressure relieving mattresses. Their process included relative assent but found that 45% of relatives approached refused to provide assent for their incapacitated relative compared to 17.7% of patients with capacity that were approached. As their study pre-dates the MCA, there was no facility to approach a professional legal representative of the patients who lacked capacity. A large proportion (93%) did not have a relative; the authors felt that proxy consent did not really help with recruitment.

There is very little written about the effects of the MCA on recruitment to research studies. Most of the literature relates to the concern for the inappropriate recruitment to intervention studies. However a comment in the British Medical Journal does suggest that the MCA is supportive of those who wish to study people with diminished capacity (Ludman, 2008). A paper by

Warner *et al.*(2008) based on their RCT of a dementia treatment discusses the issue of assessing capacity to consent. They used the Mini Mental State Examination (MMSE), which is a measure of cognitive function as a criterion for capacity, but found it not to be a reliable proxy measure (as an independent predictor of capacity in a regression analysis). The patients' capacity was assessed by the researcher, but there were no details of the training or experience of assessing capacity. They did clearly present some of the arguments for demonstrating capacity in terms of the patient's ability to understand and retain information, whilst balancing their ability to choose and be able to communicate that choice. They acknowledge that patients may have lucid intervals and capacity can vary depending on the complexity of the issue. In the current study whenever a patient's capacity was of concern, the researcher endeavoured to establish capacity with respect to study participation only and was mindful of the ability to retain information and changes in lucidity: capacity and consent were re-established or confirmed at each visit.

8.4 Data collection

8.4.1 Variables collected

The variables collected were derived from the potential prognostic factors for healing presented in chapter 2, including demographic details and attributes that would inform the secondary objectives. Some factors are worthy of further discussion in terms of their reliability, validity and the precision with which they can be measured:

Speciality

Speciality was taken from the patient's current medical consultants practice (rather than the ward as patients could be 'outliers' from their consultant's regular ward). While this was not a physiological attribute of the patient it was included as it informed the baseline characteristics. It was used in the regression analysis, partly as a marker for the dominant disease processes but also as a proxy measure of the care environment. It is possible that ward organisation, nursing, medical and allied health professionals' skills and knowledge have influenced the healing outcomes. It is difficult to study all these variables as predictors of patient outcomes. Some studies have attempted to look at length of stay based on nursing hours, skill mix and expertise. These are reviewed in the background to one study (Tschannen and Kalisch, 2009) which

then investigates the same issues. This finds that nurse 'hours per patient day' reduced length of stay, but level of 'nursing expertise' (level of understanding and grasp of the clinical situation) increased length of stay, and skill mix had no impact. The authors acknowledge that there are many other factors which influence length of stay and theirs was a small study with length of stay being as little as one day, so differences would be difficult to detect. A comprehensive study of the effects of nurse staffing levels on patient outcomes was carried out by Aitkin *et al.* (2002). They found that in surgical patients, for each additional patient per nurse there was an associated 7% increase in likelihood of the patient dying within 30 days of admission and a 7% increase in the likelihood of failure-to-rescue.

Co-morbidities

Co-morbidities were extracted from the medical records. This information has several limitations: it was only as accurate as the recorded history taking of the medical staff, no checking of this information took place; no measure of the severity of the disease was recorded; several co-morbidities were grouped together based on body systems e.g. patients who had Multiple Sclerosis were grouped together with those who had a CVA, while both have experienced damage to the nervous system, the type and extent of damage could be very different as could the possible effect on wound healing.

Smoking

Smoking history was established through asking the patient. This was recoded into very broad categories: previous smoker could be anything from a life long smoker stopping 40 cigarettes a day three weeks previously to 10 cigarettes a day from someone who only smoked for a couple of years as a teenager. This has two potential shortcomings:

- Patient self report could be unreliable; the patients may not wish to disclose their 'bad habits'. A letter by (Hajek and Snuggs, 2011) questions the validity of the self report of smoking in the 2001-2008 National Health and Nutrition Survey. The authors' (Yeager and Krosnick, 2011) response critiques the studies that challenge the assumption that self report is valid and reaffirms the assumption. The debate seems to be whether participants are aware of their blood being tested for cotinine (a marker for cigarette consumption). There appears to still be uncertainty over the reliability of self report. Although the

studies quoted are all based on maternity populations (Ford *et al.*, 1997; Parna *et al.*, 2005) rather than the predominantly elderly population of this current study, the drivers to mislead may differ across populations.

- The category of previous smoker is very wide (nearly 50% of patients). It may have been more appropriate to record this variable differently e.g. as number of 'pack years smoked'. A 'pack year' is 20 cigarettes smoked/day for one year (Prignot, 1987). While there is little work published on the affects of smoking on the healing of chronic wounds such as PUs, some studies have looked at surgical wounds and dental wound healing. Dental wound healing is not considered here as the direct effect of smoking on the mouth is know to be a confounder. Sorensen *et al.*(2002) looked at wound healing complications in breast cancer surgery and found that both light and heavy smoking to be significantly and independently associated with post operative wound infection (Odds ratio 2.05 (CI 1.07-8.16) and 3.46 (CI 1.52-7.85) respectively). An earlier study of wound healing complications following surgical repair of calcaneous fractures (Folk, Starr and Early, 1999) based on retrospective data also identified current smoking as a risk factor but also a history of smoking more than 10 pack years was significant risk factor for complications such as dehiscence or infection.

<u>Medications</u>

Details of medications were taken from the patients drug chart. This was recorded for two reasons: both as a marker for a disease process or for the direct effects of the medication on the PU healing. The potential limitation was the grouping of the coding of the medications. These were coded according to the British National Formulary (Martin, 2007) based on body system on which they act e.g. insulin (for diabetes) and thyroxine (for thyroid disease) were both coded as endocrine treatments. Each group of drugs was used as a variable in the univariate analysis. If endocrine treatments had emerged as significant it would have been difficult to comment on the association. However the three which emerged as significant were nutrition, analgesics and respiratory, all of which are reasonably homogenous groups. It may have been more appropriate to record the actual drug and use this in the analysis rather than the generic category.

<u>Braden scores</u>

The data for the Braden score was taken mainly from the nursing records (unless this was clearly out of date, in which case the patient was reassessed). Studies of sensitivity and specificity or validity and reliability of the Braden scale found the summary score as a predictor of risk (Pancorbo-Hidalgo *et al.*, 2006). The Braden scale was utilised in the current study for its individual components. Kottner *et al.* (2009) studied the inter-rater reliability of its constituent items and found the reliability of 'moisture', 'sensory perception' and 'nutrition' were low. It is perhaps therefore, not surprising that these items did not emerge as significant in the univariate analysis. The researcher had recently become aware of some lack of reliability (both in her practice and that of the ward nursing staff) between the Braden sensory perception score and the neuropathic status of the foot. When data from both these characteristics were tested for collinearity (see section 5.3.2.2) there was no association between these factors. This could be due to the lack of awareness of neuropathy when assessing using the Braden score or inaccurate reporting of sensation (particularly with patients with poor cognition) for the neuropathy test.

Sensory Neuropathy

Many patients (44%) did not have their neuropathic status established with the monofilament. The test was not performed on some patients either because it was inappropriate at the time of data collection (the patient was about to go for an investigation or was waiting to have a meal), or they did not appear to understand the test and how to respond appropriately when asked whether they could feel the monofilament. The impact of missing data is discussed in section 7.3.2.

Arterial status

Similarly, many patients (35%) did not have their arterial status established by measuring their ankle brachial pressure index (ABPI). This was either not done due to the inappropriate time of data collection as above or the patient had not consented to the test or the limb was considered too ischaemic or the procedure was too painful to obtain a reading. The impact of missing data is mentioned in section 5.3.2.3 and discussed further below in section 8.4.2.

Support surfaces

The data with respect to the support surface was based on equipment seen under or with the patients. No record was made when a mattress was not working properly or the proportion of time the patient spent in bed with the

pressure relief. When patients were sat out of bed they mostly had their feet on the floor, although occasionally a foot stool was used. No record of pressure relief for the heel was made for patients if and when they walked. Although most heel specific devices were Repose© heel troughs, these are not suitable to wear when walking. Occasionally a PRAFO© boot was used which could also provide pressure relief when walking, although the details of this was not recorded. The unknown efficacy of support surfaces has already been discussed in the systematic review in chapter 3.

Size of the ulcer and photographs

Area was measured using a clear acetate mapping grid to trace the perimeter of the wound. Difficulties with mapping and photographing ulcers have already been discussed in section 4.8. Much has been written about the reliability and validity of various techniques to measure wound size (Gethin and Cowman, 2006; Shaw *et al.*, 2007; Bowling *et al.*, 2009; Mayrovitz and Soontupe, 2009). These studies generally compare different wound techniques and overall the findings suggest that with larger wounds acetate tracings are reasonably reliable. However the study by Shaw et al (2007) looked at diabetic foot ulcers and found the measurements were less accurate than digital photography image processing or the additional use of a formula to calculate the area of an eclipse. Although a variety of wounds were studied, only one study has been identified which considers the problems of measuring wounds over a curved surface (Liu *et al.*, 2006). They acknowledge a number of devices already exist e.g. stereophotogrammetry and laser scanners, but these are complex and expensive. They propose a combination of laser scanners and photographs, while their study reports that lasers are becoming cheaper, this method would have been beyond the scope of this project. The main outcome in this study was time to complete healing; data for ulcer area was used in the descriptive analysis and not subject to any statistical testing. Changes in ulcer area may be clinically important in terms of type of dressing used, associated levels of exudate and feedback on ulcer progress to the patients.

Wound treatments

Treatments such as dressings, debridement or bandages were recorded at each visit; the inconsistencies of treatments have already been identified in chapter 6. It is likely that further inconsistency occurred in between visits especially when patients were out of hospital and data collection was at

monthly intervals. No formal record was made of treatments between visits although the researcher was aware from talking to patients and informal reviews of the nursing notes that variation did occur. From the data collected it was not clear whether changes in treatments were in response to a change in the condition of the wound or for some other reason.

8.4.2 Missing data

Data was missing at baseline for the following variables used in the prognostic factor analysis: one entry for haemoglobin, 20 observations for duration prior to recruitment, 80 (44%) observations for neuropathy, 64 (35%) observations for ABPI, three observations for severity, 15 observations for area, 4 observations for tissue type, 10 observations for surrounding skin and 66 (36%) observations for pain. The haemoglobin observation was missing as this test had never been performed on this patient; the duration prior to recruitment was due to lack of the patients' ability to recall this information and insufficient detail in the records to provide a reliable estimate. It is uncertain why the other data were missing. A more timely data checking system may have prevented this.

If these patients had been omitted totally from the analysis it would have reduced the power of the analysis, variances would be over estimated, confidence intervals would be too wide and it would have resulted in an un-representative subset of patients (Burton and Altman, 2004).

The missing variables of neuropathy and pain were mainly due to the patient's lack of cognitive ability to respond to the questions. It is possible that this may reduce the generalisability of the findings to populations with cognitive impairment. Data were collected for the variable of 'sensory perception' on the Braden scale which should include patients with sensory neuropathy. However no correlation between these two variables was seen. The reliability and validity of each measure may be worthy of further investigation, particularly in populations with cognitive impairment. In terms of healing there was more of missing neuropathy data (71%) in the ulcers that did not heal compared to those that did.

Reasons for missing ABPI data has been discussed previously. Data not collected due to ischaemia had PVD; vascular speciality, PVD and ABPI were correlated (see section 5.3.2.2) so PVD was used in the final model. A sensitivity analysis using vascular speciality resulted in the same variable emerging as significant which gave some level of assurance of the findings; however the lack of reliability of these measures is acknowledged. Some patients did not have ABPI performed due to pain; given that a high amount of data were also missing for pain it possible that this may have affected the generalisability of the findings to the population of patients with painful heel pressure ulcers. There were more ulcers (67%) with missing ABPI data that did not heal compared to those that did.

Reasons for missing pain data were mainly due to the patient's inability to report this due to cognitive impairment. There were also more ulcers (62%) without baseline pain data in the non-healing group than in the healed group.

There are several methods for dealing with missing data including substituting values from surrogate variables, with median values calculated from the non-missing data or with multiple imputation methods(Burton and Altman, 2004). For imputation methods to produce unbiased hazard ratios, a multiple imputation method is preferred providing less than 50% of cases have missing data and the data is missing at random (Marshall *et al.*, 2010). Data can be 'missing completely at random' (the missingness is an entirely random process that doesn't depend on anything), 'missing at random' (the missingness depends on some measurable variable, this could be cognitive function in this study) or 'missing not at random' (where there is a systematic reason which has the potential for bias). As suggested above, some of the data are 'missing at random' so it would be possible to impute, however the percentage missing was so small this was not considered to be necessary. This study has followed the guidelines suggested by Burton & Altman (2004) (table 2) for reporting prognostic studies with missing data. The overall amount of missing data was low (7.6%), no imputation methods were used and full explanations are given of how these variables were dealt with and known reasons for missing data are discussed. This has reduced the potential for bias and allows the reader to make informed judgements about impact of the missing data.

8.5 Primary analysis

8.5.1 Baseline characteristics

The baseline characteristics have been split into patient and ulcer level. Demographic characteristics were compared to the two similar studies that have looked at predictors of pressure ulcer healing in long term care residents(Berlowitz *et al.*, 1997; Bergstrom *et al.*, 2005). The average age of this study population was greater (above 80 years in the current study compared to around 75 in the 2 cited studies); the ratio of males to females was 47:73 in the current study, 36: 64 in the Bergstrom *et al.* study and 96:4 in the Berlowitz *et al.* study (this was carried out in a facility for military service veterans); ethnicity was not reported in the other studies; mental status in terms of dementia and depression were reported in the Bergstrom *et al.* study in 72% of the population; terminal illness (6.6%), incontinence (81%), immobility (90%) and confined to bed (15%) were reported at baseline in the Berlowitz *et al.* study. In the current study skin moisture was 14%, immobility was 12% and confined to bed was 17%. This shows that the current study had a slightly older population who had low levels of incontinence, were generally less active but more mobile. This is in keeping with the fact that the current study recruited from acute care setting rather than long term care facility.

8.5.2 Prognostic factors

The 12 candidate variables identified (see table 5.3) as significant at the $p \leq 0.2$ level and the final model are consistent with the findings in other studies (see tables 2.3 – 2.5) and reflect the aetiological factors that are commonly described as associated with pressure ulcer healing. Care of the Elderly and prescribed analgesics were positively associated with healing. It is possible that being an elderly person (as most of the population were) cared for in this speciality would provide care that was more sensitive to the patients overall needs. As such more health deficits would be identified and addressed, giving better patient outcomes. However it may be that being in another speciality that the other co-morbidities e.g. having PVD or a hip fracture, were more important than being elderly. Further work would be needed to explore this. Being ‘prescribed analgesics’ can be considered either a marker for pain (which may not be related to the heel pressure ulcer) or for having an opportunity for pain to

be controlled. No data were collected to inform this; therefore no assumptions can be made.

The hazard ratio for ulcer area suggested this variable had very little effect on healing. This is consistent with the van Rijswijk and Polansky (1994) study. A particular feature of pressure ulcers is that superficial ulcers (such as blisters) can be larger in area than severe ulcers. A large blister is more likely to heal than a small necrotic wound due to the processes involved (see section 2.6.1). When Bergstrom et al (2005) separated out Grade 2 ulcers (which may have included blisters) from Grade 3 and 4 ulcers and analysed them separately, they found that ulcer area was independently associated with healing. The study of diabetic neuropathic foot ulcers by Margolis *et al.*(2000) did find area an independent predictor of healing, although not enough detail was provided to know whether blisters were included in this study. It would appear that pressure ulcer size is not necessarily related to severity.

8.5.3 Significant independent variables

Two variables were found to be independently associated with heel pressure ulcer healing.

Severity/Grade

The impact of ulcer severity on prognosis for healing has some consistency with the other literature in pressure ulcer and foot ulcer healing. Severity of the pressure ulcer as a prognostic factor for healing has clinical validity. There are more processes involved in healing a severe rather than a superficial ulcer. There are a few studies that include severity as a variable. It was found to be an independent predictor by Berlowitz *et al.* (1997). Bergstrom et al (2005) analysed superficial and severe ulcers separately and van Rijswijk and Polansky (1994) only included severe pressure ulcers so severity could not be included as a variable. In the study by Margolis *et al.*(2000) of diabetic neuropathic foot ulcers severity was an independent risk factor and in Winkley *et al.* (2007) increased severity was a predictor for amputation.

Peripheral vascular disease

This variable is also consistent with the other literature in foot ulcer healing literature. It also has clinical validity. Perfusion to the foot is reduced as this disease compromises the patency of the blood vessels. The supply of oxygen

and nutrients to the ulcer will therefore be compromised and delay healing. PVD is a crude measure of perfusion. This factor was not reported in all the studies of pressure ulcers, as most studies do not list the candidate factors it is impossible to know whether it was not considered or did not emerge as significant. It is only likely to be considered as a candidate factor for peripheral pressure ulcer rather than pressure ulcers of the trunk (sacrum, buttocks, hips, etc) and no studies of healing of these wounds have been identified. This appears to be the first study to identify this prognostic factor. It was found not to be an independent predictor in the Takahashi *et al.* (2009) study which included all chronic wounds including pressure ulcers (52.4%), venous leg ulcers (5.8%), ischaemic ulcers (28%) neuropathic ulcers (3.3%) and mixed ulcers (10.4%). However, PVD was an independent predictor in the diabetic foot ulcer study by Nather *et al.* (2008). Unfortunately the authors did not define how they measured PVD.

8.5.4 Non-significant variables

The following variables were expected to be prognostic given the review of the evidence and previous studies.

Nutrition

It has already been suggested in section 2.7.1 that some of the reason why nutrition does not show as a prognostic factor is due to how it is measured. The current study captured nutrition as part of the Braden score, haemoglobin as a proxy measure and nutrition associated medication (included prescribed supplements and vitamins). Only the nutritional medication (as a prognostic factor for delayed healing) emerged from the univariate analysis as reaching the appropriate significance level. It may be that nutritional support was a marker for poor nutrition. A review (not reported to be systematic) by Thomas (2001) considered the evidence for nutrition in the treatment of pressure ulcers and concluded that the impact of nutrition on healing remains uncertain. This is probably due to lack of studies of reasonable size and heterogeneity of populations, interventions or measures used.

Co-morbidities

It was surprising that particular co-morbidities such as diabetes and cardiovascular disease did not emerge as significant factors as they may have a particular impact on perfusion and wound healing. In other studies they were

associated with poor healing but not independent of other variables (Berlowitz *et al.*, 1997; Bergstrom *et al.*, 2008; Takahashi *et al.*, 2009). They may have been well controlled in this patient population and were therefore less important than other variables such as PVD. Further research is required that considers the severity and impact of a disease process.

Wound duration

This is known to be a predictor of long healing in other wound healing studies (see section 2.7.2) such as leg ulcers (Margolis, Berlin and Strom, 1999). It was noted in section 2.7.2 that duration prior to recruitment was not considered in other studies even though van Rijswijk and Polansky (1994) recorded that 14% of the pressure ulcers had been present for > 9 months. While prolonged duration of the wound is well known in leg ulcer research, it is possible that researchers have overlooked that it is also an issue in pressure ulcer healing. Although duration prior to recruitment was included as a variable it did not appear to have any influence on outcome. This may have been due to the inaccuracy of this information.

8.5.5 Other factors not considered as candidate variables in the cohort study

Multiple wounds

The presence of multiple chronic wounds has been identified in the univariate analysis in one study (van Rijswijk and Polansky, 1994) and in the multi-variate analysis in another study (Takahashi *et al.*, 2009). It had been intended to include this variable in the current study but during piloting it was found difficult to elicit this information accurately from either the patients or their records so it was excluded. In hindsight more effort could have been made e.g. full skin assessments, to enable inclusion. This may have affected the ability to recruit patients.

Mental condition

There is some evidence that mental state (confusion cognitive ability) is a predictor of non-healing, as described in section 2.7.1. In the Bergstrom *et al.* (2005) study dementia, agitation, and depression were defined from the ‘Comprehensive Severity index’, ‘International Classification of Disease’ and ‘Minimum Data Set’. The researcher was uncertain whether these classifications would be as explicit in medical records in the UK. Mental

condition (both cognitive state and mood) is a relatively unexplored area in wound healing research, there is some face validity in the association between both of these and movement (confusion and agitation or lack of motivation to move respectively) but the physiological pathways e.g. the effects of serotonin, etc on healing have not been considered. Some exploratory work with medical records would be worthy if mental condition was considered for a future study.

8.6 Descriptive analysis

In this section the data used to inform the characteristics of current practice and the progress of the heel ulcers included information from follow-up visits. No statistical analysis was performed on these data.

8.6.1 Characteristics of patients

8.6.1.1 Mortality rates

The mortality rate of patients in this study was higher than expected; this may have been due to the longer follow-up time, compared to other studies. Pressure ulcers are known to be associated with increased mortality rates (Berlowitz and Wilking, 1990; Thomas *et al.*, 1996b; Brown, 2003; Takahashi *et al.*, 2008) in hospital, community and long term care settings. Most authors acknowledge that pressure ulcers are not the cause of death; when mortality rates are adjusted for age, co-morbidity, etc then pressure ulcers are no longer a predictor of death(Berlowitz and Wilking, 1990; Thomas *et al.*, 1996b). The proportion of patients who died was 42.8% in the current study with 18 month follow-up. Twenty six percent of patients died in the Berlowitz *et al.* (1997) study and 27% in a previous study by Takahashi *et al.* (2008) of patients with pressure ulcers in long term care institutions both with a 6 month follow-up.

Donini *et al.* (2005) in their retrospective review of long term care patients found the mortality of patients whose pressure ulcers were healing was significantly lower (10.3 vs. 61.1%) than the remaining sample. Berlowitz and Wilking (1990) calculated the relative risk (RR) for mortality of patients admitted with pressure ulcers compared to those admitted without pressure ulcers. This was 1.9, those who developed pressure ulcers after admission (RR= 3.1), those whose pressure ulcers failed to improve (RR= 3.3) in long term care hospital for six week follow-up.

Brown (2003) examined the relationship between healing and mortality in a cohort of 74 inpatients at a Veterans Affairs Medical Centre with a median age of 75 years. He found a 180 day mortality rate of 68.9% with an average of 47 days from ulcer onset to death. Patients with spinal cord injury and foot lesions were excluded from this cohort.

Langemo and Brown (2006) reviewed the evidence for 'skin failure' as a constituent of multi-organ failure. They differentiated between 'acute skin failure', which is an event associated with an acute illness or an extreme medical condition. 'Chronic skin failure' is described as being associated with a steady decline in chronic illness and occurs near the end of life and, as such, may be inevitable. The findings of their review do not provide much evidence to support this hypothesis although it has clinical validity. Insufficient detail was collected on severity and progress of co-morbidities to comment on whether the above proposition applied in the current study.

8.6.2 Characteristics of current practice

All the variables in this section were collected at baseline and follow-up. The baseline observations were not considered as potential prognostic, as they were known to vary during the data collection period, such that the baseline observation would not be representative of the whole episode.

8.6.2.1 Dressings

Type of dressings was presented in the follow-up data. The most frequently occurring dressing type was 'moist wound healing' on 32% of observations. The objectives of the study by Bergstrom *et al.* (2005) included identifying treatment characteristics associated with pressure ulcer healing. Their coding of dressings included moist, dry, none or multiple dressings and found that moist wound healing was a significant predictor of healing in both the Grade 2 and the Grade 3 and 4 pressure ulcers. This supports national and local guidance for moist wound healing for pressure ulcers. It needs to be acknowledged however that cohort studies cannot attribute cause and effect. Systematic reviews of randomised controlled trials of treatments would have the potential to demonstrate effectiveness; unfortunately a search of the Cochrane library (http://www.thecochranelibrary.com/view/0/index.html) revealed only a small

number of systematic reviews that have looked at specific types of treatments in pressure ulcers and have found very little evidence of effectiveness (Kranke *et al.*, 2004; Baba-Akbari Sari *et al.*, 2006; Jull, Rodgers and Walker, 2008; Aziz *et al.*, 2010).

Bergstrom *et al.* (2005) were surprised at the large variation of treatment practices. These changes in treatments did not appear to be consistent or related to the reassessment or changes in the condition of the ulcer. They expressed concern at the lack of adherence to treatment protocols and guidelines and suggest an impact on outcomes and costs. In the current study similar variations were noticed. Dressings at baseline were not included in the prognostic factor analysis as the subsequent inconsistencies would have made this unreliable. It is possible that a time dependent co-variate analysis could be undertaken at a future date see section 9.2.

8.6.2.2 Bandages

Bandage use was presented in the follow-up data. Retention bandages were in place at 70% of the observations. This is related to the use of non-adherent dressings (the bandage holds the dressing in place). It is uncertain whether the use of non-adherent dressings is an active decision based on the concern for the condition of the skin surrounding the ulcer being unable to tolerate adhesives or a decision based on the lack of availability of adhesive dressings in the organisation. Further work would be needed to explore this.

Eleven ulcers had compression bandaging applied for some of the time. A search for evidence on the compatibility of compression bandaging for venous incompetence and the presence of heel pressure ulcers has found a lack of studies or guidelines. One study does report the risk of amputation subsequent to pressure damage in a cohort of patients with compression bandaging (Callam *et al.*, 1987). An audit by Cock (2006) considers the safe and effective use of anti-embolism stockings and suggests that there is a strong link between development of pressure ulcers on the heels and stockings such that they should be contra-indicated. More research is needed in this area.

8.6.2.3 Debridement

The majority of ulcers were not actively debrided (see table 4.1). However on 7% of observations sharp debridement had been performed and 3 ulcers had larval therapy for debridement. It has been acknowledged in section 2.3.2 that the evidence base for active debridement is sparse. The active debridement was generally carried out by specialists. The researcher was particularly interested in whether heel pressure ulcers would heal quicker with active debridement. It was surprising that sharp debridement occurred on so few occasions; this may be due to concerns over the competency of nurses in carrying out sharp debridement procedures (O'Brien, 2003). Enzymatic debridement was not available on the formulary in the acute Trust so was unlikely to be used in the study. Larva therapy is expensive and requires skills in application so its use is predominantly in areas where staff are competent e.g. Diabetology so limited use is not surprising.

8.6.2.4 Support surfaces

The lack of good evidence (see chapter 3) to underpin guidelines on treatment of heel pressure ulcers (McGinnis & Stubbs 2011) is reflected in the variation of pressure relief found in the study.

8.6.3 Progress of heel ulcers

8.6.3.1 Duration and outcome

The time taken for the ulcers to heal from the point of recruitment was variable. The median time to healing from recruitment was 121 days with a range of 8 to 440 days. The original sample size calculation was based on a study by (Berlowitz *et al.*, 1997) which gave a healing rate of 50% at 6 months. In this study patients were recruited from a long term care institution and the mean age was 70.4 years. No details were given of body site affected, 22% had Grade 4 ulcers. The follow up time was 6 months, during which time 25.7% of the patients died. The reasons for the differences in healing rates (current study 42% healed after 18 month follow-up) could be that heel pressure ulcers take longer to heal than pressure ulcers on other body sites and are not representative of all pressure ulcers and superficial ulcers take less time to heal than severe. The latter reason was confirmed in the current study with the analysis of prognostic factors.

No other prospective cohort studies of pressure ulcer with an endpoint of healed ulcer have been identified. However van Rijswijk and Polansky (1994) carried out a secondary analysis of data (for Grade 3 and 4 pressure ulcers) collected prospectively with the original intention of comparing the characteristics of patients with partial thickness or full thickness pressure ulcers. They found a median time to healing of 69 days with 25% healing after 50 days and 75% healing after 243 days with an overall 37.5% of patients whose ulcers healed. Time to healing (using Cox proportional hazard model) was used in the van Rijswijk and Polansky (1994) and the Bergstrom *et al.*(2005) study. However the duration of follow up was limited to 4 months (healing time given above is assumed to include duration prior to recruitment as times given exceed data collection time) and 12 weeks respectively. The proportion healed after 6 months in the Bergstrom *et al.* (2008) study was given as 45%. Details of these studies can be found in tables 2.3-2.5. Differences in the time to healing could be due to:

- Case mix: although van Rijswijk and Polansky (1994) recruited in-patients in acute care they also recruited from extended care and rehabilitation facilities. The other two studies (Berlowitz *et al.*, 1997; Bergstrom *et al.*, 2005) recruited from long term care facilities. Overall the patient population in the current study was more likely to be more ill.
- The definition of time to healing: for the current study this was calculated from time of recruitment (although duration prior to recruitment was included as a variable this was not thought to be very precise). Van Rijswijk and Polansky (1994) is assumed to include duration prior to recruitment.
- Types and severity of pressure ulcers: all of the studies included pressure ulcers on all body sites, no specific information has been found on healing times for heel pressure ulcers. Not all studies included Grade 4 (Bergstrom *et al.*, 2008) and Unstagable ulcers which were included in the current study.

One of the explanations suggested by van Rijswijk and Polansky (1994) as to why prognostic factors for wound healing have not been clearly defined for patients with chronic wounds with long duration, (such as pressure ulcers) is because of the loss to follow-up for reasons unrelated to the study . Many studies report proportion of pressure ulcers healed by given points in time and

healing trajectories are calculated; these are unlikely to be reliable for ulcers that take longer than 6 months to heal as there are no pressure ulcer studies that follow patients beyond this time. The importance of 'complete healing' as an outcome measure is discussed by Bradley *et al.* (1999) in their systematic review. Changes in wound area and proportion of wounds healed are dependent on baseline comparability of wound size. They are also not meaningful to patients, who may still be experiencing a detrimental effect on their quality of life if their wounds are persisting. If complete healing is not established the additional costs to the healthcare provider are unknown. A major strength of this study was the 18 month follow-up to maximise the number of pressure ulcers that achieved complete healing.

8.6.3.2 Trends in healing

In section 6.4.3 trends were noted in healing trajectories for the heel pressure ulcers. The main findings of note were the trends in changes in area. While it is generally acknowledged that smaller ulcers heal quicker (O'Meara *et al.*, 2000), no relation between healing and ulcer size was seen in this study. This is probably due to the severity of the ulcers e.g. large blisters usually healed quicker than small necrotic ulcers (this was observed in the current study). In the researchers' clinical experience, ulcers which have non-viable tissue are likely to increase in size due to debridement prior to healing. This could explain some of the increase in sizes noted in this study. Some ulcers may have been subject to further pressure damage which resulted in increasing size. The initial rapid decrease in size followed by a slower rate (noted in some of the study wounds), has been observed by the researcher in many wounds. Van Rijswijk and Polansky (van Rijswijk and Polansky, 1994) noted that after two weeks, the percentage reduction in ulcer area was significantly different between those whose ulcers went on to heal and those whose did not.

Wellenstein and Brem (2004), in their attempt to establish a functional model for pressure ulcer healing rates, observe the variability in changes in area including increases and decreases (plotted as a percentage of the observed to baseline area). They reviewed previous studies on wound healing rates and found that as far back as 1916 it was observed that cicatrization (the process of scar formation) was greater at the beginning than the end of repair. No trends

are specifically identified but Grade 4 ulcers and those smaller than 2 cm^2 were excluded and patients were only followed up for 8 weeks, which makes comparison difficult with the current study.

Bergstrom *et al.* (2005) noted that pressure ulcers do not heal in a linear fashion; that periods of decrease in ulcer area were interspersed with periods of worsening and again by improvement. No studies have been identified, which specifically look at healing rates. However many wound healing studies find that a proportion of patients do not reach full healing at given time point and duration of ulcer is often included as a predictor of non healing (Margolis, Berlin and Strom, 1999)

The feature of a prolonged final stage of healing (see section 6.4.3) is an important finding from this study, which has not been identified in other studies of pressure ulcer healing. If this was subject to further analysis and found to be a common trend, this would raise concerns over studies which do not follow wounds to complete healing. These trends are worthy of further investigation.

8.6.3.3 Tissue type and severity

The need for differentiating between tissue type and severity has been discussed in section 2.6, although the tests of collinearity (section 5.3.2.2) confirm that that they are closely related.

Table 6.5 described the final stages of healing. Most ulcers had a dry scab prior to re-epithelialisation. Where this was not recorded, it is possible that a dry scab did occur with some of the ulcers which had been granulating prior to re-epithelialisation, especially when the data collection interval was a month.

The ‘dry scab’ is not described in any of the classic models of wound healing. It appears to be a build up of epidermal tissue (see figure 6.5), but has not been classified as a healed wound in this study as there is uncertainty over whether intact dermis is present beneath. Although most of these wounds were almost healed and did not have dressings on, they were not the same as ‘dry scabs’ seen on exposed wounds on other areas of the body, where the scab appears to be made up of desiccated wound exudate. Dry scabs were often present for

several weeks or months prior to healing. In the researcher's clinical experience dry scabs are sometimes seen in healing leg ulcers, particularly sited in the malleolar region. It is possible that this is an anomaly of the skin structure on the lower limb. This is also a key finding from this study, which has not been identified in any other studies of pressure ulcer healing and is worthy of further investigation as it may inform the understanding of the prolonged final stage of healing.

This study has raised many questions about the nature of pressure damage to the heel and progress of ulcer healing. Further work is needed to enable the extent of tissue damage to be quantified particularly when blisters (either clear fluid or blood filled) are identified to enable clinicians to have some informed expectations of healing times and instigate appropriate treatment.

8.6.3.4 Surrounding skin

In a third of the 'surrounding skin' observations the skin was found to be normal/ healthy (36%). In 17% of observations skin was dry and flaky. This may have been normal for this mainly elderly population. Section 6.5.5 describes the presentation of the surrounding skin. The condition of the surrounding skin was a candidate variable in the model developed by van Rijswijk and Polansky (1994), but was found not to be significant. No details are given of how this variable was defined. No other descriptions of dry flaky skin in relation to wound healing have been found. The presence of erythema is described as being associated with infection. Further analysis of associations of erythema and infection would be worth considering. Similarly the presence of oedema and associated immobility, may be worthy of further consideration particularly for the heel pressure ulcer population.

8.6.3.5 Pain

In a quality of life study, during interviews with 23 in-patients with pressure ulcers, pain was found to be present in (n=21) 91% of pressure ulcers (Spilsbury *et al.*, 2007). For those patients able to report pain in the current study more than half reported it was present. Some trends were noticed with regard to reducing pain and healing, but no detailed analysis of these trends has been carried out. A systematic review of the literature on pressure ulcer

pain acknowledges that pressure ulcer pain is under-represented in the funded research (Pieper, Langemo and Cuddigan, 2009). However there is no mention of an association of pain levels and healing. This topic is worthy of further investigation.

8.6.4 Adverse sequelae

8.6.4.1 Infection

Although more than half the patients did not experience any sort of infection, both wound infection and infections in other body systems occurred in 42% of patients. A review by Penhallow (2005) concluded that there is no consensus on the impact of bacterial colonisation on wound healing and the difficulties differentiating between colonisation, critical colonisation and infection in chronic wounds such as pressure ulcers mean that it is difficult to attribute association between infection and delayed wound healing. It has face validity due to the increased metabolic demands of an infected wound. Bacteraemia from infected pressure ulcers is a rare but serious complication with a high risk of death (48% mortality in a small study of 21 patients with sepsis from pressure ulcers (Galpin *et al.*, 1976)). Infection is thought not to have been included in the pressure ulcer prognostic factor studies (Berlowitz *et al.*, 1997; Bergstrom *et al.*, 2005; Takahashi *et al.*, 2009). However it has been identified as an independent predictor of non-healing of diabetic foot ulcers (Nather *et al.*, 2008).

8.6.4.2 Length of stay, change of accommodation, readmission rates and ward moves

Data were collected on all of the above and details are recorded in section 6.6 - 6.8 and some particular observations were commented on. Unfortunately no comparative data were available at this time to suggest any associations with the heel pressure ulcers. One study has been identified which reports that orthopaedic patients who develop heel pressure ulcers have an increased length of stay of 3 days, although this was not statistically significant (Campbell, Woodbury and Houghton, 2010).

8.7 Key findings and contributions to knowledge

This study has made an important contribution to the knowledge of healing heel pressure ulcers. Very little was known about pressure ulcer healing and it has been demonstrated that heel ulcers are likely to be different in terms of healing.

Very few studies of prognostic factors for healing pressure ulcers on all body sites have been identified and no previous work has been carried out for specifically for heel ulcers.

The literature review revealed many gaps in knowledge regarding pressure ulcer healing and heel pressure ulcers specifically. The systematic review revealed a lack of evidence for the effectiveness of support surfaces and pressure relieving devices for treating heel pressure ulcer.

The study has been the first to identify the characteristics of the heel pressure ulcer population in acute care settings. It has quantified the event rate for heel pressure ulcer healing and outcomes other than healing such as death or amputation of the affected limb. The long follow-up time and the continued data collection following discharge from hospital, has enabled better estimates of healing rates and mortality rates for this population.

The presence of tissue types such as blisters and blood blisters dry scab during the end stage of healing have not been described in other pressure ulcer sites on the body. The potential time to heal, probability of healing and other outcomes has been quantified. Prognostic factors have been explored and two have been identified that are independent predictors of heel pressure ulcer healing.

Although guidelines exist for management of pressure ulcers, whether these are implemented in clinical practice has been uncertain. This study has found high amount of variability in treatments such as dressings, debridement and support surfaces.

Healing trajectories for pressure ulcers have not previously been studied specifically; this study has contributed to this knowledge (in particular identifying a prolonged final stage of healing) and identified a need to investigate this further.

The study has identified factors such as pain associated with heel pressure ulcers. Details of the pain are also now known such as what triggers it and changes in pain levels that may be associated with the stage of healing.
One of the reasons for carrying out this study was to provide data to inform the planning of a randomised controlled trial of treatment interventions for heel pressure ulcers e.g. for power calculations. The study has achieved this aim.

Chapter 9 Summary and Recommendations

9.1 Summary

Pressure ulcers occur due to localised injury to the skin and/or underlying tissue usually over a bony prominence, as a result of pressure, or pressure and shear. They are a major health problem estimated to cost £1.2 -2.1 billion annually (4% of total NHS expenditure) (Bennett, Dealey and Posnett, 2004) and have a serious impact on patients in terms of morbidity and their quality of life (Gorecki *et al.*, 2009). The most common body sites for pressure ulcers to develop are the lower trunk and heels (Dealey, 1991a). The lower limb extremities (including the heels) are different from other body sites such as the sacrum, ischeal tuberosity and trochanter areas due to their anatomy (section 1.6.8) and susceptibility to certain diseases (section 1.7.5).

Much of the pressure ulcer research has been in prevention. Many studies have been undertaken which look at factors associated with the development of pressure ulcers (Nixon *et al.*, 2010) but few have been found which look at factors which affect healing. Logically in clinical practice the healthcare professionals primary aim should be prevention, however this is not always achievable. In the unfortunate event of a pressure ulcer occurring, it is important to know about the healing process and identify any factors which will affect healing in order to plan appropriate care. This will allow the clinicians to correct any factors they can to optimise healing.

Existing guidelines for the treatment of pressure ulcers include recommendations for dressings and other treatments, support surfaces and supplementary interventions such as nutrition (EPUAP, 1998; RCN, 2005; NPUAP, 2009). Much of this guidance is based on expert opinion in the absence of good quality trials. There is no specific guidance for pressure ulcers on the heels, although some guidelines advise caution with necrotic pressure ulcers in the presence of peripheral arterial disease. There are two areas here where there are gaps in the evidence: there is a lack of evidence to inform the management of pressure ulcers in general and there is a lack of evidence

specifically for the management of heel ulcers which may well be different in terms of physiology and disease processes.

Good quality epidemiological evidence is needed to inform the planning of intervention studies. This study recognises the differences in heel pressure ulcers and makes a contribution to the epidemiological evidence. Planning a heel pressure ulcer trial will require appropriate heel specific data.

This study set out to initially summarise the evidence for healing of heel pressure ulcers. It was acknowledged that healing pressure ulcers should consider the local wound management, the management of internal risk factors and the relief of pressure. The review of the evidence for the relief of pressure was studied in a systematic process, looking for the effectiveness of support surfaces. Then it proceeded to identify prognostic factors for healing of heel pressure ulcers and describes some of the characteristics of the patients, their ulcers, the treatments and events which occurred while the ulcers were healing.

The systematic review identified only one study for which data for healing heel pressure ulcers could be analysed separately. The number of patients lost to follow-up led to a high risk of attrition bias, other risks of bias were also noted. Although the analysis performed by the authors show statistically significant difference in healing between the two mattress systems studied, these results were viewed with extreme caution. Sensitivity analysis showed that the findings were dependent on what happened to the patients who were lost to follow-up.

Two factors were identified that were independently prognostic for the healing of heel pressure ulcers in a multi-variate analysis. Superficial ulcers (blisters and full thickness skin loss) were likely to heal quicker than severe ulcers (cavities and necrotic ulcers) and ulcers were less likely to heal in patients who had peripheral vascular disease than those who did not. Other factors may be prognostic but were not found to be statistically significant in this small study.

Patients were recruited from specialties within an acute care hospital where the numbers of heel ulcers was known to be high. Most patients recruited were in Care of the Elderly wards, approximately equal numbers of men and women were affected and half had previously smoked. Most patients had several co-morbidities and had reduced mobility and activity.

One hundred and forty patients were recruited with 183 heel pressure ulcers. Of these 77ulcers healed, 88 ulcers were on the heels of 60 patients who died, 5 were on limbs which were amputated, 11 remained unhealed at the end of the study period and 2 were lost to follow-up. For those ulcers that healed, the median time to healing from the point of recruitment was 121 (range 8-440) days.

Information was obtained on the type of tissues that were present on the heel ulcers at different stages of healing; particular note was made of ‘dry scabs’ and the difference between clear fluid and blood filled blisters, which have not previously been described in any of the wound healing literature. Changes in wound area were recorded during follow-up visits, certain trends such as fluctuations in area and rates of change (initial rapid reduction and prolonged final stage reduction) were observed which have been suggested in other healing literature but not studied specifically to complete healing. The condition of the skin surrounding the ulcers was mostly observed to be normal or dry; however erythema and/ or oedema were noted on several occasions, which may have been associated with other pathological processes. Levels of pain (prevalence and severity) were observed, which were not noted in other studies, however the researcher was unable to assess pain according to the protocol for some patients with cognitive impairment. Trends in pain levels and triggers for pain were noticed (see section 6.4.6) which have not been reported elsewhere.

Follow-up data were obtained on treatments such as dressings, bandages, debridement and support surfaces. A large variation in treatment practices was

witnessed in this study that was similar to a previous study (Bergstrom *et al.*, 2005), however this was the first study in the UK to report these finding.

A record was made of any adverse events that affected the patients during the course of the study. The majority of patients had an infection at some point although these were mostly affecting organs or systems away from the heel ulcer e.g. respiratory or urinary tract. Details of patients' pathways were recorded showing in which care environments patients are treated and how frequently they move between them, this information will be most helpful in planning an intervention study.

Overall, this was felt to be a worthwhile study which produced a remarkable amount of new information that will be useful both clinically and to inform future research studies.

9.2 Recommendations for research

A lot of data were collected during the follow-up visits. This was used in this thesis to inform the descriptive analysis, however the data could be used in a further regression model with time-dependent covariates. This process utilises the fact that the variables may change over time and involves constructing a function of time in the model (Fisher and Lin, 1999). The effects of variables such as dressings, bandages, debridement, support surfaces, pain, tissue type, surrounding erythema and oedema and infection could then be considered. This work will require specialised techniques and the involvement of a statistician.

Further similar cohort studies with more patients are required to confirm or strengthen or refute the prognostic factors for heel ulcers identified in this study. A high quality prognostic factor study of healing of all pressure ulcers with data analysed by body site would be valuable. This would enable researchers and clinical staff to understand what might be the similarities and differences in terms of healing according to body site. If these studies were to be carried out, improved definitions of variables are suggested e.g. co-morbidity could be

defined in terms of disease severity and impact e.g. using markers of diabetic control such as HbA1c (Krishnamurti and Steffes, 2001), smoking history should be worked out as ‘pack years smoked’, nutrition should be better defined in terms of adequacy of energy and protein intake and supplementation. Future studies should preferable be inception cohorts or better attempts should be made to improve the accuracy of the estimated start dates of the ulcers and this time point should be used to estimate time to healing. The notion of ‘acute’ or ‘chronic’ skin failure has been suggested by Langemo and Brown (2006), this has good clinical validity. If pressure ulcers could be defined in terms of this variable then it may be prognostic for healing. Studies which look at associations with other organs and/or systems failure and pressure ulcer outcomes may inform this debate.

The systematic review of support surfaces identified a lack of trials in this area. Intervention trials should be undertaken for support surfaces, topical treatments such as dressings and debridement particularly for heel pressure ulcers as there is very little guidance for all these aspects of pressure ulcer care. These could be interventions specific for heel pressure ulcers or treatments for all pressure ulcers with separate data for each pressure ulcer site. The data produced by this study would be useful in informing sample size calculations, recruitment rates, follow-up times, healing rates, dropout rates, types of interventions and potential prognostic factors to be considered in case mix adjustment in the analysis.

The trends in ulcer healing trajectories are worthy of further exploration. The suggestion by van Rijswijk and Polansky (1994) that there may be a cut off time beyond which pressure ulcers are unlikely to heal, would be clinically useful. This would enable health care professionals and patients to plan realistic treatment goals i.e. if healing is unlikely then symptom management (pain, exudate) should be a priority. The actual time to healing and the likelihood of healing would be helpful to patients.

An investigation of the relationship between pain as a time-dependent covariate and ulcer healing has been suggested above. Associations between the level of pain and the stage of healing and the descriptors and trigger factors of pain are worthy of further analysis from the data available.

Information on patient pathways was collected for this study; it may be possible to review case notes of case matched patients without pressure ulcers to identify any sequelae of having a pressure ulcer. Studies of this type have not been identified in the literature.

9.2 Conclusion

Two significant independent prognostic factors have been identified for healing of heel pressure ulcers: these are the severity of the ulcer and the presence of peripheral vascular disease. These have good face validity, the former also been found in other studies of pressure ulcer healing and the later in studies of diabetic foot ulcer healing. Further work is needed to confirm or refute these and indentify other prognostic factors.

The median time to complete healing of heel pressure ulcers has been identified for this cohort of patients. Few studies have used the outcome of time to complete healing of the ulcer; proportion of ulcers healed at a given time is more commonly reported. When compared to other pressure ulcer healing studies, it is likely that similar healing times would be demonstrated with similar case mix and follow-up. This information will be useful in planning intervention studies.

The effectiveness of appropriate pressure relieving aids for heel ulcers has yet to be established. Clinically a variety of devices are used with associated costs to the health service and possible discomfort and inconvenience to the patients with no assurance of their benefits. Intervention studies of pressure relieving devices are needed.

The healing trajectory for heel pressure ulcers has been found to vary with many ulcers having an initial rapid reduction in ulcer size, others having temporary increases in size, which may be associated with debridement and most importantly a prolonged final stage of healing. Other studies have suggested similar findings. Further work needs to be done specifically looking at factors associated with the end stage of healing.

Tissue types found in heel pressure ulcers are not well documented for ulcers in other sites e.g. clear fluid and blood filled blisters at the start of the ulcer and dry scabs at the end stage of healing. The relationship with severity (Grade) and tissue type and the significance of these has yet to be defined.

The relationship with the condition of the surrounding skin and wound healing e.g. dry and flaky, erythema or oedema has not been explored. Whether these presentations are frequently occurring or significant has not been well documented.

Pain has been found to be frequently reported in heel pressure ulcers, the impact of this on the patients' quality of life is likely to be different to pain in other body sites as mobility will be affected. Any association of pain with wound healing has yet to be established.

There will now be opportunity and motivation to publish not only the main findings of the prognostic factor analysis but also information which may help to stimulate and inform future research. Topics will include:

- The findings of the prognostic factor analysis
- The impact of the mental capacity act on recruitment of cognitively impaired patients
- Illustrated process of wound healing: heel ulcers
- Pathophysiology of heel pressure ulceration
- The relationship between pain and wound healing
- SR of support surface for treating heel ulcers

- Patient characteristics, pathways and treatments for healing of heel pressure ulcers

9.3 Implications for practice

As severe pressure ulcers are likely to take longer to heal than superficial ulcers, long term care plans should reflect their needs for ongoing ulcer management e.g. the provision of aids and adaptations, care setting suitable for long term health care.

The need for the assessment of the severity/grade of the pressure ulcer to be accurate is essential. In the researchers clinical experience many general nurses do not reliably assess the Grade of the ulcer. This study has identified the gaps in knowledge regarding the relative importance of the Grade of the ulcer (the anatomical structures affected), the tissue types such as slough and necrosis, the size (area) of the ulcer and other presenting features such as blisters and dry scabs. Until their role in wound healing is fully understood it is important for clinical staff to record these details. This will be used to develop empirical knowledge and contribute towards future research.

The presence of PVD is also likely to delay healing; it is desirable that all heel pressure ulcer patients should have their peripheral arterial status established to inform ongoing ulcer management.

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Appendices

Appendix 1: Patient information sheet

A Study of Wound Healing in Heel Pressure Ulcers

Patient Information Sheet

Please read this document carefully.

I would like to invite you to take part in a research study. Before you decide whether to take part it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Feel free to discuss this with anyone else you wish to, for example, friend / nurse / doctor or relative. Ask me if there is anything that is not clear. I am happy to provide more information. Take as much time as you need to decide whether your relative would want to take part.

Thank you for reading this.

What is the purpose of this study?

This is a study of the treatment of pressure ulcers (pressure sores) found on people's heels. The study will not introduce any new treatments. It is an observation of the progress of the heel ulcers and the treatments used.

Pressure ulcers can occur on different areas of the body, usually when someone is immobile for long periods of time and are caused by the pressure on the parts of the body which are supporting the person. Pressure ulcers usually start as a reddened area on the skin. They may develop into blisters or wounds; it is these ulcers which will be studied. Although in most cases where the immobility is anticipated measures are taken by nurses to prevent pressure ulcers occurring, these are not always successful or possible.

Why have I been chosen?

You have been identified as having a heel pressure ulcer. Within the hospitals in Leeds over the next 2 years, about 200 people with heel pressure ulcers will be asked to take part in this study.

Do I have to take part?

Participation in this study is entirely voluntary. It is up to you to decide whether or not to take part. If you decide they will take part you will be given this information sheet to keep and asked to sign a consent form. If you do decide to take part you can still change your mind at any time. Their future care and treatment will not be influenced by your decision for them to take part or not. If you do agree to take part in this study and decide at a later time to withdraw then you are free to do so at any time without influencing your future care or treatment.

What will happen to me if I agree to take part?

If you agree to take part I will collect some information about you and the treatment of your heel ulcers at our first meeting. I will then visit you every week to collect more details about the progress of your heel ulcer until it heals. When you are discharged from hospital, if the ulcer is still present, I will visit you once a month.

Most of the information I need I will be able to get from medical and nursing records, for example, the reason for admission, any other medical conditions such as diabetes and the dressings which are used. Sometimes I will carry out a change of dressing as part of your normal treatment to enable me to measure and photograph the wound. I will carry out two extra tests which the nurses may not routinely do, these are to assess your circulation and nerve sensation, these 2 tests will only be carried out every 3 months. I will also take a photograph of the heel ulcer at the first meeting then again after every month.

What will I have to do?

You will continue to be treated for the heel pressure ulcer according to the normal practice of the staff that are caring for you. I will identify some additional information about your activity, mobility and any pain. The dressing change may take up to 5 minutes longer if I am taking a photograph of the wound.

Why do the study?

Pressure ulcers usually take a long time to heal (often months) and are often cared for in different places by different people, for example in hospital and at home. Because of this, information about how they are treated and studies to identify what works best are not easily available.

Are there any implications for me taking part?

There will be no personal advantages to you taking part; I will only be observing the standard treatment you are receiving. However the information derived from the study will be used to inform future management of heel pressure ulcers. The information will

be shared locally, nationally and internationally so that it will benefit as many people as possible.

Being involved in the study will not affect your care at all. At our first meeting I would like to carry out a couple of extra tests: a Doppler test to assess the circulation in your legs and a Monofilament test to assess sensation in your legs and feet. If your relative still has a heel ulcer after 3 months I will repeat these tests. These tests can sometimes cause slight discomfort. If you wish to take part in the study but don't want to have these tests then this can be arranged.

All subsequent visits may take slightly longer than usual while I complete the paperwork.

Will my taking part in this study be kept confidential?

All information that is collected about you during the course of the research will be kept strictly confidential. Any information about you that leaves the hospital/ your home will have your name and address removed so that you cannot be recognised from it. Your hospital Consultant and GP will be notified of your participation in the trial.

What happens to the results of the study?

The results of the study will be used as part of a PhD thesis. It is also planned to publish in medical and nursing journals. You will not be identified in any publication arising from this study. If you wish to receive a copy of the study report on completion, then please let me know.

Who is organising and funding the research?

The study is being funded by a Leeds Teaching Hospitals Trust Charitable Trustee Fellowship. The Fellowship has provided funds for my time to undertake the research and for the equipment I use e.g. the camera and the wound tracing maps. I am being supported with the study by the University of Leeds.

Who has reviewed the study?

The Leeds (West) Trust Research Ethics Committee and Leeds Teaching Hospitals and Leeds Primary Care Trust's Research Governance Committees have reviewed the study.

What do I do now?

If you are interested in taking part let me know when I return and we can discuss this further.

Where can I get more information about the study?

If you do not understand anything on this information sheet or would like further information please contact me on the telephone number below or ask the ward staff to contact me.

Research Investigator: Elizabeth McGinnis, Nurse Consultant – Tissue Viability
Leeds Teaching Hospitals Trust. c/o Nursing Directorate, Old Trust HQ, Leeds General Infirmary, Great George Street, Leeds LS1 3EX
Telephone: 0113 3926238 or mobile 07717 573 956

If you wish to discuss this with someone who is not involved in the study, you can contact: Ms Alison Raycraft, Matron Specialist Acute Care for Older People
Leeds Teaching Hospital Trust c/o Ground Floor, Old Trust Headquarters, Leeds General Infirmary, Great George Street, Leeds LS1 3EX
Tel: 0113 3923641 or mobile 07786250841

Thank you for taking the time to read this information sheet

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Appendix 2: Honorary contract for Leeds Primary Care Trust

Appendix 3: Leeds West Research Ethics Committee Approval (June 2006)

Appendix 4: Leeds Teaching Hospitals NHS Trust R&D approval (April 2006)

Appendix 5: Leeds PCT (Bradford South & West) R&D approval (June 2006)

Appendix 6: Leeds West Research Ethics Ammendment 2 approval (Sept 2008)

Appendix 7: Leeds West Research Ethics ammendment 3 approval (Sept 2008)