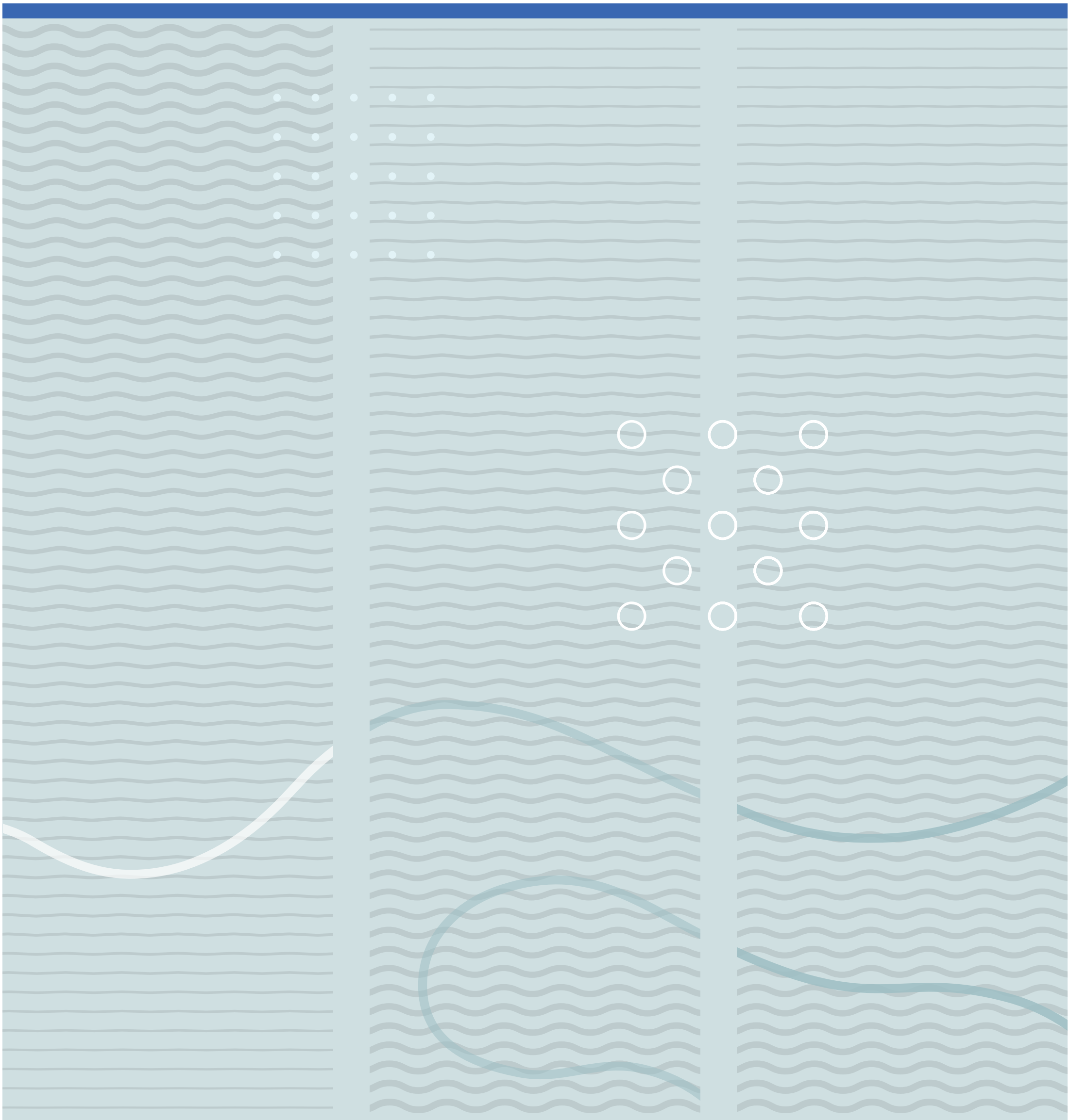
University of South-Eastern Norway
Faculty of Health and Social Sciences
—
Doctoral dissertation no. 128
2022

Lena Leren

A descriptive study of ulcer-related pain characteristics and management



Lena Leren

A descriptive study of ulcer-related pain characteristics and management

A PhD dissertation in
Person-centred Health Care

Faculty of Health and Social Sciences
University of South-Eastern Norway
Drammen, 2022

Doctoral dissertations at the University of South-Eastern Norway no. 128

ISSN: 2535-5244(print)
ISSN: 2535-5252 (online)

ISBN: 978-82-7206-669-6 (print)
ISBN: 978-82-7206-670-2 (online)

Print: University of South-Eastern Norway

Acknowledgements

This project would not have been possible without help and support, and many deserve acknowledgement. I would like to send my special regards to all the persons who participated in the study. Your willingness to spend time and share your experience has been essential.

I would also like to recognize the invaluable assistance of the managers and clinicians at the two outpatient wound care clinics at Vestre Viken HF, for the facilitation of the data collection, and for input and advice.

I especially would like to express my deepest gratitude to my three supervisors, Tone Marte Ljoså, Edda Aslaug Johansen and Hilde Eide. You have all provided invaluable scientific insight in this project. Tone Marte, you have always prioritized me in your busy schedule, and your close and impeccable guidance have helped me advance as a researcher. Edda, your clinical expertise combined with your positive attitude and support have been a safe haven in challenging times. Hilde, you are an academic force, and having you on my team has been very reassuring.

In addition to my fantastic supervisors, I would also like to express my gratitude for the invaluable help from Ragnhild Sørum Falk and Rolf Jelnes. I could not have asked for a better statistician on the team than Ragnhild. You communicate your statistical knowledge in a brilliant way, and your patience has been crucial. Rolf, your advice and your willingness to discuss and share your experience and knowledge have provided me with invaluable perspectives.

I am very grateful to the University of South-Eastern Norway for giving me the opportunity to conduct this PhD project. Many colleagues at USN have helped me along this journey, and I would like to express my gratitude to all of you. I am further grateful for the inspiring network provided by the Science Centre Health and Technology.

Thanks to the PhD Program in Person-centred Health Care. I want to praise all my fellow PhD candidates, who provide an admirable example on how to provide both academic and social support in an inclusive way. In particular, I would like to thank those who have been a part of our regular shut-up-and-write gatherings. These regular meetings have been extremely valuable in providing structure and encouragement in my everyday life as a PhD candidate. I would further like to express my gratitude to my sister and fellow PhD candidate Enid Leren Myhre who literally joined my on this journey.

Thankfully, I have been a part of the research school PROFRES. I am very grateful for the opportunity this has given me to build network and attend both educational gatherings and enlightening writing seminars.

I must also thank all the librarians at the Library Unit, Campus Drammen for their availability and helpfulness. Marit Gjone Sandsleth especially, provided professional assistance in the literature search process, and I am very grateful for her support.

Finally, I would like to pay my special regards to family and friends for support and encouragement in this process. A special thanks to my husband Lars, I could not have done this without you.

Abstract

Background: Chronic leg ulcers are hard-to-heal wounds located below the knee and are increasingly prevalent in the Western population. Irrespective of pathology, chronic leg ulcers are associated with a negative impact on physical and psychosocial function and health status. While all chronic leg ulcers are presumed potentially painful, the prevalence of ulcer related pain is not clearly documented. A thorough description of pain characteristics, impact and management is not present in the available literature. Furthermore, little attention is paid to persistent pain at rest and between ulcer-related procedures such as ulcer-related background pain.

Aim: This thesis aimed to explore the prevalence, characteristics, and management of ulcer-related background pain, as well as factors associated with moderate to severe ulcer-related pain.

Materials and methods: The aims were addressed through a systematic review (Paper I) and a clinical study (Papers II and III). The systematic review was conducted to synthesize available data from both descriptive and effect studies, using the systematic review methodology guided by PRISMA. Random-effects meta-analyses—both overall and stratified by study design—were performed for pain prevalence and pain intensity. A univariable random-effects meta-regression analysis was performed to explore sources of heterogeneity. The clinical study used an exploratory cross-sectional design. Persons with chronic leg ulcers were recruited from two wound care clinics using the consecutive sampling method. Data was obtained through screening interviews, clinical examinations and questionnaires. In Paper II we analysed data from persons with chronic leg ulcers (N = 252) to establish the prevalence of ulcer-related background pain. Logistic regression with stepwise backwards elimination was used to identify factors associated with moderate to severe background pain. In Paper III descriptive analyses were used to explore characteristics (i.e., intensity, localization, temporal pattern, interference) of ulcer related background pain and pain management in participants who reported ulcer related background pain (N = 121).

Main results: In the systematic review and meta-analyses we found a pooled prevalence of ulcer related background pain of 80 % (95% CI 65-92%) in persons with chronic venous leg ulcers. The pain intensity was moderate in average (NRS 4 [(95% CI 3.4-4.5]). The systematic review further confirmed the scarcity of descriptions of ulcer related pain characteristics. The clinical study confirmed that ulcer related background pain was common, with a prevalence of 64 % (95% CI 58-69%). Furthermore, in Paper II we found that older age, female gender, reduced sleep and diminished health status were associated with moderate to severe ulcer-related background pain. In the final model, reduced sleep quality increased the likelihood of having moderate to severe pain in persons with good health status while not in persons with diminished health status. In Paper III we provide a detailed and systematic description of the characteristics and management of ulcer-related background pain. The mean average background pain intensity was 4.5 (SD 2.56) (CI 95% 4.0-5.0), and more than 60% of those who reported ulcer-related background pain had moderate to severe pain (NRS > 4). The ulcer-related pain interfered with daily function to a moderate degree, and most participants reported intermittent pain. Further, the participants reported that pain management provided a mean pain relief of 45.9% (SD 33.9, range 0-100).

Conclusion: Based on the findings from the three included papers, this thesis shows that ulcer-related background pain is a prevalent and intrusive problem that needs further attention, both in research and in clinical practice. Clinicians should pay attention to ulcer-related pain, and provide a thorough pain assessment in all persons reporting ulcer-related background pain. However, this is a single study, and the findings need further confirmation. Furthermore, future research should focus on development of strategies for assessment and management of ulcer-related pain.

Keywords: Pain, Chronic Leg Ulcers, Person-Centred Healthcare, Biopsychosocial Model of Pain, Pain Characteristics, Pain Management

List of papers

Paper I

Leren, L., Johansen, E., Eide, H., Falk, R. S., Juvet, L. K., & Ljoså, T. M. (2020). Pain in persons with chronic venous leg ulcers: A systematic review and meta-analysis. *International Wound Journal*, *17*(2), 466–484. https://doi.org/10.1111/iwj.13296

Paper II

Leren, L., Johansen, E., Eide, H., Falk, R. S., & Ljoså, T. M. (2021). Prevalence and factors associated with ulcer-related pain in persons with chronic leg ulcers—an explorative study. *Journal of Clinical Nursing*, *30*(17-18), 2732–2741. https://doi.org/10.1111/jocn.15787

Paper III

Leren, L., Eide, H., Johansen, E. A., Jelnes, R. & Ljoså, T. M. (2021). Background pain in persons with chronic leg ulcers: An exploratory study of symptom characteristics and management. *International Wound Journal*. Advance online publication. https://doi.org/10.1111/iwj.13730

List of figures and tables

Figures

Figure 1: Number of publications on ulcer-related pain

Figure 2: Methods used in the three dissertation papers, and themes from the aims covered in the papers

Figure 3: Forest plot of prevalence of ulcer-related background pain

Tables

Table 1: Characteristics of Papers I–III

Table 2: Description of participants in Papers II and III

Table 3: Variables and questionnaires used in the clinical study and their use in the respective papers (Papers II and III)

Table 4: Presentation of the software and analyses used in Papers I–III

Table 5: Logistic regression models of factors significantly associated with moderate to severe ulcer-related background pain (N = 192)

Selected abbreviations

CLUs	Chronic leg ulcers
CVLUs	Chronic venous leg ulcers
HQoL	Health-related quality of life
QoL	Quality of life
PCC	Person-centred care
OR	Odds ratio
SD	Standard deviation
CI	Confidence interval
NRS	numeric rating scale
BPI	Brief Pain Inventory
MPQ	McGill Pain Questionnaire
WHO	World Health Organization

Table of contents

Acknowledgements .... **I**

Abstract .... **III**

List of papers .... **V**

List of figures and tables .... **VII**

Selected abbreviations .... **IX**

1 Introduction **1**

1.1 Thesis outline 2

2 Background **3**

2.1 Chronic leg ulcers 3

2.1.1 Prevalence, terminology, and aetiology 3

2.1.2 Living with chronic leg ulcers 5

2.1.3 Management of chronic leg ulcers 6

2.2 Pain and ulcers 7

2.2.1 Research on ulcer-related pain 8

2.2.2 Pain characteristics and assessment of ulcer-related pain 12

2.2.3 Management of ulcer-related pain 13

2.3 Pain and care model perspectives 15

2.3.1 The biopsychosocial model 15

2.3.2 Person-centred care 17

3 Aims and research questions **19**

4 Methods **21**

4.1 Design 21

1.2 Systematic literature review and meta-analysis 22

4.1.1 Identification and selection of relevant literature 23

4.1.2 Appraisal and data extraction 24

4.1.3 Synthesis of data 24

4.2 Clinical study 25

4.2.1 Study samples 25

4.2.2 Participants and settings 26

4.2.3 Data collection..28
4.2.4 Variables and instruments..31
4.3 Statistical analyses..36
4.3.1 Statistical analyses in Paper I..38
4.3.2 Statistical analyses in Paper II..38
4.3.3 Statistical analyses Paper III..40
4.3.4 Analysis of internal consistency (Papers II–III)..40
4.3.5 Analysis of non-responders and handling of missing responses (Papers II–III)..40
4.4 Ethical approvals and considerations..41
5 Findings..45
5.1 Prevalence and characteristics of ulcer-related pain in previous research (Paper I)..45
5.2 Prevalence of and factors associated with ulcer-related pain (Paper II)......47
5.3 Pain characteristics and management of ulcer-related pain (Paper III).......49
6 Discussion..51
6.1 Ulcer-related background pain as a significant problem—prevalence and characteristics..51
6.2 Factors associated with moderate to severe ulcer-related background pain..56
6.3 Management of ulcer-related background pain..58
6.4 Holistic approach to ulcer-related pain..60
6.5 Methodological considerations..62
7 Conclusion..69
7.1 Implications for clinical practice..69
7.2 Concluding remarks and future research..71
8 References..73
Errata..87
Paper I..89
Paper II..111

Paper III **123**

Attachements **139**

1 Introduction

Chronic wounds, including chronic leg ulcers (CLUs), are becoming more frequent due to the ageing population and the concurrent increase in comorbidities and lifestyle diseases, such as diabetes, obesity, venous hypertension and peripheral vascular diseases (Olsson et al., 2019). The prevalence of CLUs, which include venous ulcers, arterial ulcers, mixed ulcers and diabetic ulcers, is estimated at approximately 1.5 per 1000 in developed countries (Martinengo et al., 2019), and have a profound financial impact in terms of health care costs (Nussbaum et al., 2018). These ulcers represent a significant health problem, and can impact individuals' lives physically, psychologically and socially—significantly impacting their quality of life (QoL) (Olsson et al., 2019).

Ulcer-related pain has been described as the worst aspect of having an ulcer (Platsidaki et al., 2017). The prevalence of pain related to CLUs is not well-documented, however, and there is a lack of research and evaluation of the characteristics, impact and management of ulcer-related pain (Jenkins, 2020; Newbern, 2018). While most research focuses on ulcer-related procedural/dressing-related pain, scant attention is paid to chronic background pain. Nevertheless, persistent background pain at rest and between ulcer-related procedures may be just as devastating as the pain at dressing change (Woo & Sibbald, 2008).

Ulcer-related pain is a complex symptom. This type of pain can have numerous and often interlinked causes related to the wound itself, interventions, wound management or other local pathologies (Woo, 2012). Further, many psychological and social factors associated with living with a CLU can exacerbate the pain experience, such as fear of high exudate levels (Vuolo, 2009). Ulcer-related pain can be acute and/or chronic, as well as nociceptive, neuropathic and inflammatory in nature. It can also be classified specifically as background, incident, procedural or operative pain (White, 2008; Woo & Sibbald, 2008; World Union of Wound Healing Society [WUWHS], 2004).

This PhD project focused on background pain related to CLUs. More specifically, we explored pain as a symptom related to CLUs in everyday life. Ulcer-related pain has a direct negative effect on QoL in general, but also specific and cumulative negative effects on sleep, mobility and mood (Frescos, 2018; Phillips et al., 2018). Considering the negative impact of pain, it is important to recognize ulcer-related pain in wound management. However, although we know that ulcer-related background pain is a problem, the prevalence, characteristics and factors associated with background pain related to CLUs are poorly investigated and documented in the literature.

To fill parts of this knowledge gap, the overarching goal of this PhD project was to provide knowledge about ulcer-related background pain. The more specific aims were to explore the prevalence and characteristics of ulcer-related background pain, pain management and identifying factors associated with ulcer-related background pain in adults with CLUs.

1.1 Thesis outline

In the following sections, the theory and perspectives that constitute important background information for the thesis will be presented. I will introduce and delve into leg ulcers as well as pain, providing key definitions and understandings of the central health condition and issue of this study. In addition, wound care practice and the organizations of Norwegian wound care services will be described to illuminate the context. The existing research regarding pain in CLUs will also be explored. Theoretical perspectives related to the biopsychosocial model and person-centredness will be elaborated upon, to ground the thesis within established pain management theory and care models. A detailed description of the thesis’ aims and research questions will also be outlined.

Following these chapters, I will present the material and methods of the study, before providing a summary of the results. These results and methods will then be discussed in light of previous research, theories and models. Finally, implications for practice and further research will be discussed.

2 Background

2.1 Chronic leg ulcers

2.1.1 Prevalence, terminology, and aetiology

Chronic wounds are a worldwide challenge and have been referred to as a silent epidemic (Järbrink et al., 2016; Stein, 2019). In Europe, approximately 50% of all chronic wounds are leg ulcers (Graham et al., 2003). A recent systematic review of the prevalence of CLUs estimates a prevalence rate of 1.51 per 1000 population (95% confidence interval [CI] 0.24–3.84) in the western world (Martinengo et al., 2019). The prevalence data, however, is scarce, the quality of the research is variable, and none appear to have been published for Norway. CLUs are often linked to underlying conditions that are more prevalent in older adults, such as arteriosclerosis, diabetes and venous hypertension (Hahnel et al., 2017). Hence, the prevalence of CLUs is likely to increase as the population continues to age.

In the Norwegian language, one word is primarily used to describe tissue damage involving the dermis: *sår*. In the English vocabulary and in the medical literature, the terms ‘wounds’ and ‘ulcers’ are often used interchangeably. In the traditional non-medical encyclopaedias, wounds are said to be caused by external violence or trauma, whereas ulcers are caused by different kinds of internal aetiology (Hermans, 2010). Further, there is no established consensus on the duration of chronicity of wounds or ulcers that fail to proceed through the healing process in a timely matter (Kyaw et al., 2017). In the medical literature, these wounds are also described as ‘chronic’, ‘hard-to-heal’, ‘complex’ or ‘difficult-to-heal’ (Olsson et al., 2019).

Leg ulcers, or leg and foot ulcers, are referred to as a defect in the skin below the level of the knee (Agale, 2013). CLUs are rarely seen in otherwise healthy people, and most chronic ulcers are caused by comorbidity, such as diabetes or vascular disease (Murray et al., 2018). The leg ulcers may or may not be initially caused by trauma. However, the underlying disease pathology contributes to the chronicity of these ulcers, and the ulcers are often classified as venous, arterial or diabetic. Venous ulcers are caused by venous insufficiency, which is often linked to leg muscular pump dysfunction. This leads to deep and superficial lower limb vein hypertension, which in turn leads to oedema and extravasations of macromolecules and red blood cells, causing wounds (Murray et al., 2018; Paschou et al., 2018). Arterial ulcers are a result of reduced arterial supply to the lower extremities due to diseases such as atherosclerosis and vasculitis (Grey et al., 2006). The development of diabetic foot ulcers is more complex, and a range of factors can influence their development. These factors include neuropathy with hypoalgesia/analgesia, which can lead to injuries remaining undetected; hypoxia in the wound due to insufficient perfusion and angiogenesis, which can lead to reduced tissue oxygenation, reduced nutrient supply, altered immune response and damaged tissue; and high levels of glucose, which can alter immune cells and other functions in the wound (Murray et al., 2018). However, the aetiology of CLUs is often multifactorial and can include both local and systemic factors (Frykberg & Banks, 2015). Several factors—such as wound infection, the person’s social context and health professionals’ competence—may impact the chronicity (Murray et al., 2018). In addition, as several aetiological factors can operate together, it is difficult to classify the ulcers into the traditional categories of venous, arterial and diabetic wounds (Gould et al., 2015). Further, there is no clear consensus regarding the duration of chronicity, and definitions with specific durations range from two weeks to two months (Kyaw et al., 2017). Regardless of the perpetuating cause or duration of the chronic ulcer, some common features are often seen, such as prolonged or excessive inflammation, persistent infections, formation of drug-resistant microbial biofilms, and the inability of dermal and/or epidermal cells to respond to reparative processes (Gupta et al., 2021).

Because of the above-mentioned complex causal factors of chronic tissue damage, often involving both external trauma and internal pathology, choosing between the terms ‘wound’ or ‘ulcer’ and using them consistently seems amiss. In addition, the terms are used interchangeably in the medical literature, making it challenging to choose just one term when referring to existing research and literature. Therefore, both terms—wounds and ulcers—are used in this thesis. However, the primary term used in this thesis is 'chronic leg ulcers' (or 'CLUs'). The operationalization of the definition of CLUs with regards to chronicity and aetiology are described in detail in the methods section (Chapter 4.3.1).

Despite significant advances in the understanding of chronic wounds and the healing process over the last few decades, chronic wounds with slow healing rates continue to be a problem for those living with them (Gethin et al., 2020). Hence, there is a critical clinical need to focus on interventions to improve patient outcomes—not only in terms of wound healing, but also regarding physical, psychological and social function and QoL.

2.1.2 Living with chronic leg ulcers

CLUs can cause various restrictions in the daily life of the person affected. Persons with CLUs often report a range of physical and phycological problems, which in turn impact QoL (Do et al., 2016). In addition to ulcer-related pain, persons with CLUs experience sleep disturbance (Upton & Andrews, 2013), lack of energy (Chase et al., 2000), restriction of leisure activities (Klein et al., 2021), frustration and lack of self-esteem (Jones & Carlisle, 2008).

The symptoms and impacts of chronic wounds are of a physical, psychological and social nature, and are closely linked (Phillips et al., 2018; Upton & South, 2011). Among the physical symptoms and signs, pain, exudate and odour in particular appear to have significant and direct negative effects on QoL, with additional and cumulative effects on sleep, mobility and mood (Phillips et al., 2018). Further, restrictions in social participation are found to be direct and indirect consequences of the wounds. Social support and connections have been found to be impaired when living with a chronic wound (Klein et al., 2021), potentially affecting both mood and physical activity. Closing the circle, the negative psychological consequences of living with a chronic ulcer may have detrimental effects on wound healing, potentially creating a vicious cycle of suffering and a nonhealing wound (Upton & South, 2011). In sum, the impact of living with a chronic ulcer is extensive.

2.1.3 Management of chronic leg ulcers

There are several international guidelines, evidence-based practice (EBP) recommendations and consensus documents pertaining to the management of chronic wounds. Many of these guidelines address specific wound types, and focus on modalities such as offloading, debridement or compression therapy (Munro, 2017). Early identification of factors that impact the formation of and maintenance of the ulcer is important to optimize the potential for healing a CLU. Hence, a holistic and systematic assessment of the person is as important as a thorough assessment of the ulcer itself (Frykberg & Banks, 2015). Indeed, the value of holistic assessment is well-established in the wound care literature (Benbow, 2016; Gupta et al., 2017; Morton & Phillips, 2016; Smith & Sharp, 2019).

Persons living with CLUs may experience a complex organization of health care, receiving care provided at different care levels and meeting different health care professionals. Various models for the treatment of chronic wounds have been created and trialled in the recent decades. In Norway today, most treatment models are based on an outpatient clinic organized under specialized departments, such as plastic, orthopaedic or vascular surgery, general medicine or dermatology. Nevertheless, many persons with CLUs are primarily treated by their general practitioner (GP) or by homecare nurses, and many receive a combination of specialist and primary care services. In addition, it is known that some people engage in self-care: For example, a study from Australia found that 42% of people living with CLUs treat themselves (Edwards et al., 2014). There is no register or study available that describe where persons with CLUs are cared for in Norway. Regardless, wound care is time-consuming, and the products used in wound care are expensive. The total cost is not subsidized by the Norwegian Health Economics Administration (Helseøkonomiforvaltningen [HELFO]) in a way that makes it a financially favourable treatment option for health care providers. The Norwegian wound specialist

Marcus Gürgen stated in a recent interview that wound care is financially an unfavourable treatment offer (Hjelmers, 2019). Hence, this patient group is undesirable for the healthcare providers. Moreover, the (lack of) funding for wound care in Norway leads persons with chronic wounds to be ‘pushed around’ in the health care system (Hjelmers, 2019). In addition, people with chronic wounds often have multiple health problems and are thus often in need of hospitalization. In these instances, they are referred to the relevant specialized department for their current health issue(s), where knowledge about wound treatment may be limited (Welsh, 2018). Hence, the financing and the organization of health care services in Norway may lead to unfavourable management of wound care.

2.2 Pain and ulcers

In 2020—for the first time since 1979—the International Association for the Study of Pain (IASP) introduced a revised definition of pain: namely, that pain is ‘an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage’ (IASP, 2020; Raja et al., 2020). For further valuable context, the definition is expanded with six additional key notes, stating that pain is a personal experience influenced by biological, psychological and social factors. Pain is not merely a sensory signal, and individuals learn the concept of pain through life experience. Pain can also have a functional and adaptive role, but also has a negative impact on function and psychosocial well-being. Moreover, the patient’s self-report of pain should be respected, but the inability to communicate pain does not mean that pain is not experienced (Raja et al., 2020).

Until recently, pain was often classified as nociceptive or neuropathic. *Nociceptive pain* is defined as ‘pain that arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors’, while *neuropathic pain* is defined as ‘pain caused by a lesion or disease of the somatosensory nervous system’ (IASP, 2020). However, this dichotomous classification excluded many patients with no obvious activation of nociceptors nor a proven lesion or disease of the somatosensory nervous system (Trouvin & Perrot, 2019). As a result, the IASP proposed an additional term to describe pain: 'nociplastic pain'. *Nociplastic pain* is defined as 'pain that arises from altered nociception despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain' (IASP, 2020). Although nociceptive, neuropathic and nociplastic pain are divided into separate categories, there is consensus concerning the partial overlap and co-existence of different types of pain (Kosek et al., 2016; Trouvin & Perrot, 2019).

With regards to the duration of pain, pain can further be classified as acute or chronic/persistent. There is no wide consensus on the duration necessary to classify pain as chronic, but definitions of three- or six-months' duration are common in the literature (Steingrímsdóttir et al., 2017). One reason to differentiate between acute and persistent or chronic pain is the function of that pain (Grichnik & Ferrante, 1991): Acute pain draws attention to potential threats and motivates protection, promoting healing; persistent or chronic pain, on the other hand, serves no such apparent function. Hence, some classify chronic pain as a disease on its own, as it can impair function by causing passivity, depression and social isolation (Fine, 2011; Raffaeli & Arnaudo, 2017).

2.2.1 Research on ulcer-related pain

As previously described, ulcer-related pain is often complex and multidimensional in nature. In a consensus document, the WUWHS (2004) proposes the use of the terms 'background', 'incident', 'procedural', and 'operative pain' to describe the cause of ulcer-related pain. The pain experienced may be due to the underlying pathology of the leg ulceration and the wound itself (i.e., background pain), various daily activities (i.e., incident pain), the wound treatment (i.e., procedural and operative pain) and/or complications like skin irritation (Renner et al., 2014). Furthermore, depending on the duration of the pain, ulcer-related pain can be classified as acute or persistent, and persons with CLUs can experience persistent background pain in addition to acute procedure-related pain.

Nociceptive pain related to CLUs can be caused by several factors, such as tissue damage, the inflammatory face of healing, infection, skin irritation due to dressings or exudate, and debriding. Neuropathic ulcer-related pain is a consequence of damaged peripheral nerve fibres, and can be caused by pressure (i.e., oedema, external force), ischemia, exposure, thermal insult and inflammation caused by allergies (Munro, 2017). Persons with CLUs may also have diminished tactile sensation due to other comorbidities, as it is well-documented that diminished tactile sensation is common in healthy older adults (Decorps et al., 2014). Nociplastic pain has not yet been identified and described for CLUs. However, researchers suggest that nociplastic pain may not be a distinct entity, but part of a chronic pain continuum (Trouvin & Perrot, 2019). Nociplastic mechanisms, in combination with mechanisms of nociceptive pain and hypersensitivity, may therefore play a role in the development of persistent ulcer-related pain. In addition, several psychosocial factors related to CLUs—such as embarrassment or feelings of stigmatization due to odour or exudate, depression and social isolation from family and friends—may cause or aggravate ulcer-related pain (Munro, 2017). Ulcer-related pain is a complex symptom, and patients with CLUs often experience multiple types of ulcer-related pain.

Historically, research in wound care has focused predominantly on cure and management rather than on the impact of the ulcers (Green et al., 2014), although chronic wounds may last for several weeks or even months. However, in the 1990s, several researchers began investigating CLUs’ impact on health-related quality of life (HQoL), demonstrating that pain was a substantial problem (Charles, 1995; Flett et al., 1994; Krasner, 1998; Noonan & Burge, 1998; Phillips et al., 1994). This led to the publication of some significant clinical guidelines and consensus documents that drew attention to the extent and treatment of ulcer-related pain (European Wound Management Association, 2002; WUWHS, 2004, 2007). In the following years, there was a slight increase in focus on pain in wound care research, and several studies were published on the prevalence, characteristics, experience, associated factors and management of ulcer-related pain (Mudge et al., 2008; Paschou et al., 2018; Price et al., 2008; Taverner et al., 2014).

In the past decade, the focus on ulcer-related pain seems to have declined, and new research indicates that the reporting of ulcer-related pain is still either not prioritized by health care providers or inappropriately assessed and addressed (Frescos, 2018; Green et al., 2018). A systematic search in health care research databases confirms the trend of a decreasing publication rate on ulcer-related pain. The following CINAHL Headings and Thesaurus terms were used in CINAHL (via EBSCOhost) and MEDLINE (via Ovid), respectively: ‘pain AND wound care’, and ‘pain AND leg ulcer’. This search resulted in a total of 621 (CINAHL) and 238 (MEDLINE) indexed publications over the past 20 years. By looking at the number of publications on a year-to-year basis, a reduction in publications is apparent (Figure 1). If we account for the fact that publications in health science have increased exponentially in this time period (Bornmann & Mutz, 2015), this downward trend is even more alarming. This indicates a reduced interest in ulcer-related pain, which in turn leads to a decrease in available, updated knowledge that health care professionals can use to provide knowledge-based health care.

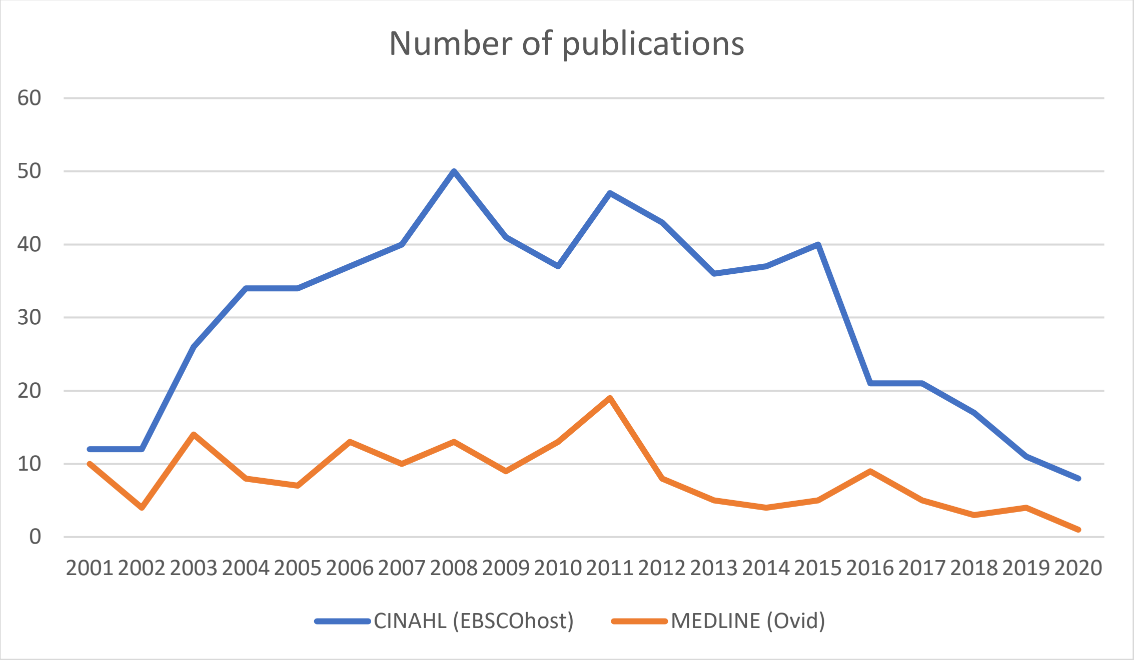


Figure 1: Number of publications on ulcer-related pain

Studies on the impact of CLUs continue to find that ulcer-related pain is the main factor affecting HQoL (Cunha et al., 2017; González-Consuegra & Verdú, 2011; Green et al., 2014; Marczak et al., 2019). Further, wound care experts in an eDelphi study recognized ulcer-related pain as one of the top priorities for wound care research and professional learning needs (Cowman et al., 2012). Investigating ulcer-related pain is important to resume attention on this important topic in wound care in order to provide evidence to inform knowledge-based practise. If pain is appropriately managed, QoL may improve substantially. This, in turn, may lead to increased adherence to treatment and improved mobility, which again may have a positive influence on wound healing (Frescos, 2019).

The available research is not current and shows a varying prevalence of pain related to CLUs (Jenkins, 2020). This variation seems to pertain to both the ulcer diagnoses and the research methodology used. Similarly, ulcer-related pain characteristics are not well-explored in the existing literature. Pain intensity is the most frequent characteristic described, and intensity ranges from mild to intense pain (Sussman & Bates-Jensen, 2011). Only a handful of studies describe other ulcer-related pain characteristics, such as pain interference, pain descriptors and temporal patterns of pain. Furthermore, very few studies provide a more extensive assessment of pain, including descriptions of multiple pain characteristics in a large sample of persons with CLUs. In the available research, ulcer-related background pain is reported to interfere with sleep (Hofman et al., 1997; Noonan & Burge, 1998; Wong et al., 2012), daily activities (Wong et al., 2012) and mood (Noonan & Burge, 1998). Ulcer-related pain's interference with activities is supported in qualitative studies (Heinen et al., 2007; Taverner et al., 2014). Moreover, various descriptors (e.g., 'throbbing', 'tender' and 'burning') are used to describe ulcer-related pain, and sensory descriptors are typically used more often than affective descriptors by persons with CLUs (Gonçalves et al., 2004; Salomé & Ferreira, 2018). In terms of temporal patterns of pain, it has been found that background pain is worse when standing than at rest, and that intermittent or varying pain is more frequent than continuous pain (Kim et al., 2021; Noonan & Burge, 1998; Taverner et al., 2014).

2.2.2 Pain characteristics and assessment of ulcer-related pain

The assessment of pain is an essential part of pain management, and is often a nurse's responsibility (Royal College of Nursing, 2015). The purpose of pain assessment is to detect and describe pain to aid in the diagnostic process; to understand the cause of pain to help determine the best treatment; and to monitor the pain to determine whether a) the underlying disease or disorder is improving or deteriorating, and b) the pain management is working (Swift, 2015). The assessment of pain can be challenging due to pain's subjective nature, making true objective measures of pain impossible (Breivik et al., 2008). As pain is subjective, the gold standard in pain assessment is self-report (Pasero & McCaffery, 2010). However, some may be unable to provide self-report (Herr et al., 2011)—a fact that is recognized in IASPs new definition of pain, where 'described in terms of such damage' has been replaced with 'resembling that associated with', removing the dependence on verbal self-report. Hence, this new definition recognizes that persons who cannot describe or self-report pain may still experience pain. Pain assessment in persons who are unable to self-report calls for different pain assessment methods (Herr et al., 2011). This is relevant here, as persons who are unable to self-report may experience ulcer-related pain.

Furthermore, pain is complex, and the assessment of pain requires a multidimensional and comprehensive approach. There are currently no specific ulcer-related pain-assessment tools available (Frescos, 2019). However, in the Wound Pain Management Model, it is stated that assessment should be based on the following six critical dimensions of the pain experience: intensity, quality, location, duration, onset and impact on activities of daily living (Price et al., 2007). Pain intensity is a quantitative estimate of the severity or magnitude of perceived pain, and is commonly assessed via the verbal rating scale (VRS), visual analogue scale (VAS) or numeric rating scale (NRS) (Jensen & Karoly, 2011). Measures of pain quality are designed to help diagnose the pain problem, describe the pain experience more thoroughly and determine the type and effects of pain management (Jensen & Karoly, 2011). However, the diagnostic value of pain qualities is disputed, and pain qualities alone are not sufficient to identify different types of pain

(Gilron et al., 2011). Localization of pain provide information about where the pain is felt in the body, and is a necessary part of a thorough pain evaluation (Jensen & Karoly, 2011). In combination with information from the medical history, the duration, onset and temporal pattern of pain help determine the possible cause and establish the timing of pain interventions (Ngamkham et al., 2011). Pain interference is assessed to determine the impact of pain on physical and psychological aspects of life (i.e., daily activity and mood) (Cleeland & Ryan, 1994), and might help clinicians determine the effects of pain management. In total, information about these pain characteristics is essential for understanding the patients' pain condition, determining pain mechanisms, choice of pain treatment, and evaluation of the effect of pain management (Turk & Melzack, 2011).

2.2.3 Management of ulcer-related pain

Pain management is an essential nursing intervention. As nurses have the responsibility to effectively treat patients' pain, unrelieved pain can be considered professional misconduct, and nurses have an ethical responsibility to provide optimal, evidence-based care for persons experiencing pain (American Nurses Association Ethics Advisory Board, 2018; International Council of Nurses, 2012; Germossa et al., 2019).

Several studies have aimed to assess the effectiveness of different pharmacological and non-pharmacological interventions to reduce ulcer-related pain in persons with CLUs. Pharmacological interventions include both topical and systemic analgesics. Topical analgesics work locally and often have minimal systemic absorption, thereby minimizing the risk of adverse effects and drug–drug interactions (Mervis & Federman, 2018). Research suggests that lidocaine/prilocaine cream and ibuprofen foam are effective agents for reducing ulcer-related pain (Purcell et al., 2020). Further, even though some small studies and case studies have reported efficacy of topical opioids (Twillman et al., 1999; Zeppetella et al., 2003), they have generally not been proven effective for reducing pain from chronic wounds (Bastami et al., 2012; Vernassiere et al., 2005; Mervis & Federman, 2018). The effect of topical agents with tricyclic antidepressants (TCAs), ketamine, clonidine, cannabinoids, and anticonvulsants, is only supported by anecdotal evidence of efficacy (Mervis & Federman, 2018).

No research has been published assessing the efficacy of traditional systemic analgesics (e.g., paracetamol, NSAIDs and opioids) in persons with chronic wounds. Most guidelines refer to the World Health Organization [WHO] pain ladder with regards to systemic pharmacological pain management of ulcer-related pain (Paschou et al., 2018; Price et al., 2007). Unfortunately, these guidelines do not consider the fact that principles of cancer pain management may be inappropriate—or even harmful—for patients with chronic nonmalignant pain such as ulcer pain.

The 2016 Center for Disease Control guidelines highlight that non-pharmacologic therapy, along with non-opioid pharmacologic therapy, is preferred for chronic pain (Dowell et al., 2016). Dressing selection is perhaps the most essential aspect of preventing and managing most procedural pain (Mervis & Federman, 2018). There is also some evidence that virtual reality can reduce pain caused by dressing change and procedural pain during debridement of burn wounds (Faber et al., 2013; Maani et al., 2011). However, the available research concerns non-pharmacologic therapies aimed at reducing procedural pain, rather than non-pharmacologic therapies aimed at persistent ulcer-related background pain.

Regardless of choice of intervention to reduce pain, all pain management begins with pain assessment. The pain assessment guides the pain management. Nurses and other health care professionals working with patients with CLUs should have up-to-date knowledge and adequate competency in recognizing and evaluating pain type and characteristics, and they must handle suitable interventions to avoid exacerbating procedural pain (e.g., dressing removal, debridement) (Toma et al., 2020). However, research demonstrates that nurses and other health care professionals do not have sufficient knowledge about pain assessment, documentation, and treatment of pain in wound care (Frescos, 2018; Toma et al., 2020).

2.3 Pain and care model perspectives

Person-centred care (PCC) is increasingly becoming a guiding principle of policy-making in federal and state agencies, and professional organizations and societies (WHO, 2013). PCC implies that patients are persons, first and foremost, and that their plans, beliefs, strengths and personality should be carefully considered (Wallström & Ekman, 2018). Regarding pain management, PCC takes into account the biopsychosocial nature of pain, and the individualization of treatment that focuses on the complexity of each person's pain experience as a prerequisite of care (Hush, 2020). However, two persons can experience the same illness or symptom(s) differently (Kusnanto et al., 2018). One must also understand the unique context and individual experience of each person to provide appropriate management. Hence, these PPC and the biopsychosocial model of pain can be seen as complementary.

2.3.1 The biopsychosocial model

The biopsychosocial model is a core element of PCC (Kitson et al., 2013). The model was first introduced in medicine by Engel (1977). Engel proposed that, as a medical illness became more chronic in nature, the psychosocial dimension (e.g., distress, illness behaviour, the sick role) would emerge to complicate assessment and treatment (Engel, 1977). Loeser (1982) adapted the biopsychosocial model to the field of pain management. In his perspective, there were four dimensions related to the idea of pain as a multimodal concept: nociception, pain, suffering and pain behaviour (Gatchel, 2004). Loeser also proposed that social interactions between patients and health care providers had the potential to affect the experience of pain (Loeser, 1991). The biopsychosocial model of pain was introduced by Turk in the 1990s. The model supported the notion of pain as a subjective experience and suggested that individuals experience pain in different ways (Turk, 1996; Turk & Melzack, 2011). In this model, pain was conceptualized as being influenced by biological, psychological and social dimensions (Turk, 1996). These factors—along with their dynamic interactions—shape the experience of pain, with no linear relationship between any of the dimensions (Turk et al., 2011). Thus, while Loeser's (1982) model suggested that psychosocial factors were linear effects caused by biological processes, Turk propose that all dimensions in the biopsychosocial model are integral, and can affect the experience of pain at different times and in different ways (Turk et al., 2011).

Within this understanding of the biopsychosocial model, pain can be impacted by, and can impact on, multiple levels of functioning (e.g., physiological and psychological functioning) and also the family and society (i.e., social and cultural functioning) (Engel 1977). This notion is further in line with the definition of pain as subjective and hence influenced by several physiological, psychological and social and cultural factors (IASP, 2020). The experience of pain will vary between individuals, as it is personal. Accordingly, it is important to consider a variety of subjective factors when assessing and managing pain, as these can play a significant role regarding the severity, duration and recovery of pain. Given that pain is subjective, and recognizing that only those in pain can really know what it is like (McCaffery, 1968), pain assessment entails the involvement of the person in pain and highlights the importance of self-report to be able to assess, diagnose and manage that pain.

The biopsychosocial model has been used in reserach when synthesizing evidence on the effects of chronic ulcers, confirming the severe physical, social and psychological impacts of chronic wounds (Fearns et al., 2017). Further, the model has been adapted to conceptualize the experience of pain related to various diseases (Day et al., 2016; Nelson et al., 2019), and in older adults (Miaskowski et al., 2020). However, research has not yet examined the application of these processes on pain related to CLUs.

The biopsychosocial model of pain informed the development of the studies in this thesis and influenced our method of pain assessment. Hence, to explore and provide a broad biopsychosocial description of ulcer-related background pain, we sought to include variables found to influence pain in other studies.

2.3.2 Person-centred care

There is a wide range of definitions of PCC and closely related concepts, such as patient-oriented, client-centred and person-oriented care. Several authors use the concepts interchangeably and inconsistently (Håkansson Eklund et al., 2019; McCormack & McCance, 2016). Despite the differences in how these concepts are defined and characterized, several common and recurring themes can be identified. Morgan and Yoder (2011) delineated the following four attributes in their concept analysis of PCC: holistic, individualized, respectful and empowering (Morgan & Yoder, 2012). The Person-Centred Nursing Framework was developed by McCormack and McCance (2010), and further updated into the Person-Centred Practice Framework by the same authors in 2017 (McCance & McCormack, 2016). It consists of the following four constructs: prerequisites, the care environment, person-centred processes and outcomes. These constructs enable the delivery of quality care rooted in person-centredness through sharing a culture of values and principles (Gethin et al., 2020). According to McCormack and McCance (2016), prerequisites must be considered first, followed by the care environment—both are necessary in providing effective care through the care processes to deliver person-centred outcomes. This relationship has been validated through the use of the framework in practice and research (McCance & McCormack, 2016). Prerequisites focus on health care workers' attributes (e.g., professional competence), and the care environment focuses on the context in which care is delivered, (e.g., organizational systems that are supportive) (McCance & McCormack, 2016). The definitions of PCC further entail that patients be included as partners in their care and treatment, and that the needs of the individual are at the core of decision-making (Gethin et al., 2020).

Involvement of the person in pain is especially important in pain assessment, given that pain is subjective and that self-report is at the core of pain assessment. In other words, assessment is dependent on patient involvement. This includes a broader perspective on the needs of the person with wounds and pain, and their preferences as well as their experiences with health care. A study on the health care experiences of people living with chronic nonmalignant pain in Norway found that, for these individuals, it was vital that their illness experiences and lifeworld be considered valuable (Gjesdal et al., 2018).

The concept of PCC in wound care is relatively new—indeed, still evolving—and experience and knowledge is sparse (Gethin et al., 2020). Further, pain as an outcome measure to support PCC in wound care is not yet explored. However, quantitative evidence suggests that PCC improves nurses’ ability to provide assessment, anticipatory guidance and coaching to persons with chronic nonmalignant pain (Monsivais & Engebretson, 2011).

One of the main challenges with implementing PPC is that many health professionals do not work in a patient-centred way, failing to listen to patients’ concerns and discuss treatment options with them (Griffin et al., 2004). Research demonstrates that this might also be the case in wound care: In a study using unstructured interviews and non-participant observation to explore the impact of chronic venous leg ulcers (CVLUs) on QoL, researchers found that participants had concerns far beyond their actual wound care, and that these concerns were not fully explored during their nurse consultations (Green et al., 2018).

Although PCC to a greater extent emphasizes the importance of strengthening the relationship between health care provider and patient, the biopsychosocial model and PCC framework overlap in important aspects. Both seek to expand the focus beyond the biomedical model—and both seek to understand how a disease affects the life of the person and vice versa (Turabian, 2018). Further, both recognize the importance of involving the person, which is especially important when exploring the experience of pain, given its subjective nature.

3 Aims and research questions

This PhD project aimed to fill the gap in knowledge of ulcer-related background pain in persons with CLUs. This aim was operationalized by exploring the prevalence, characteristics and management of ulcer-related background pain, as well as factors associated with moderate to severe ulcer-related pain. The specific aims and research questions are outlined below.

Aim 1 was to explore the prevalence of background pain related to CLUs. This aim was answered by two research questions:

- What is the prevalence of background pain related to CVLUs in published studies? (Paper I)
- What is the prevalence of ulcer-related background pain in a sample of persons with CLUs receiving outpatient wound care services? (Paper II)

Aim 2 was to explore the characteristics of background pain related to CLUs. This aim was answered by two research questions:

- What are the characteristics of background pain related to CVLUs as described in published studies? (Paper I)
- What are the characteristics of background pain related to CLUs as described by a sample of persons with CLUs receiving outpatients wound care services? (Paper III)

Aim 3 was to explore factors associated with moderate to severe ulcer-related background pain. This aim was answered by two research question:

- What factors are significantly associated with moderate to severe ulcer-related background pain in persons with CLUs receiving outpatient wound care services? (Paper II)

- What factors are independently associated with moderate to severe ulcer-related background pain in persons with CLUs receiving outpatient wound care services? (Paper II)

Aim 4 was to explore the pain management received by persons with background pain related to CLUs who receive outpatient care. This aim was answered by one research question:

- How do persons with CLUs who receive outpatient care report that their ulcer-related background pain is managed? (Paper III)

The four aims and how these were answered through the thesis' three scientific papers are illustrated in Figure 2.

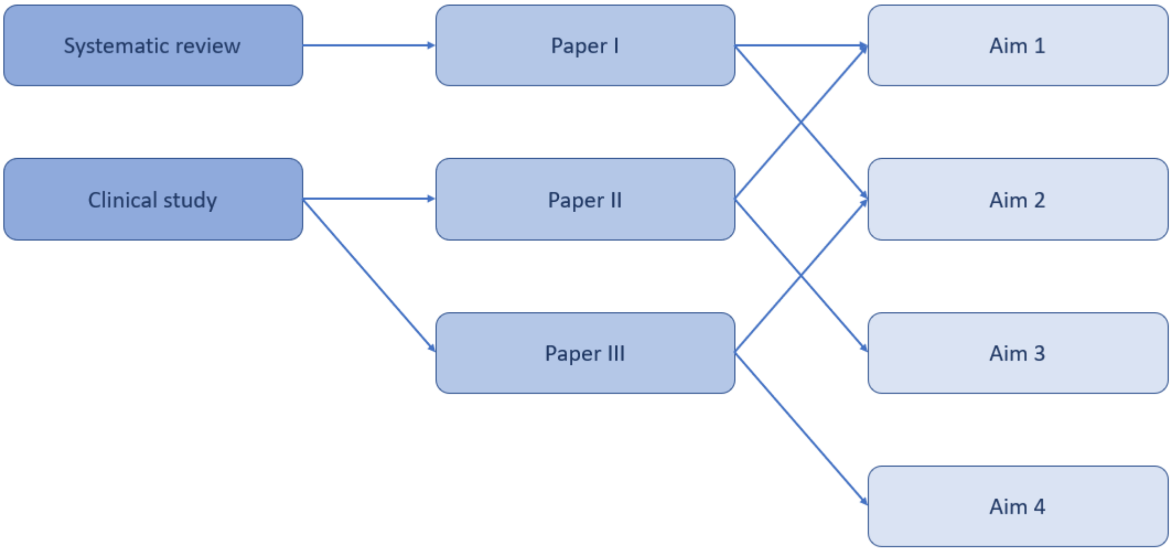


Figure 2: Methods used in the three papers, and themes from the aims covered in the papers

4 Methods

4.1 Design

This thesis is based on a systematic review and meta-analysis (Paper I) and a clinical observational study with a cross-sectional design (Papers II and III).

Systematic reviews 'seek to collate evidence that fits pre-specified eligibility criteria in order to answer a specific research question' (Chandler et al., 2021). A formal pre-specified protocol with explicit criteria for inclusion and exclusion of studies ensures complete coverage of the available evidence, providing an objective, replicable and comprehensive overview (Ranganathan & Aggarwal, 2020). Further, meta-analysis is a statistical approach used to combine the results of several reports to create a single, more precise estimate of an effect or an observation (Barendregt et al., 2013).

A cross-sectional study design involves the collection of data from a sample at a specific point in time (Aggarwal & Ranganathan, 2019). Descriptive studies are designed to describe the distribution of one or more variables. In Paper I, we identified and synthesized the existing research. In Paper II, we assessed the relationship between the presence of several exposures and that of an outcome: Such cross-sectional studies are referred to as analytical. In Paper III, data from the cross-sectional clinical study were analysed only to determine the distribution of one or more variables; hence, the design was descriptive (Aggarwal & Ranganathan, 2019).

The use of several methods strengthens the design of the thesis, as the systematic review provides a synthesis of the existing research, while the clinical observational study generates new, updated evidence from a specific care context. Together, they provide comprehensive knowledge on ulcer-related background pain. An overview of the methodological characteristics of the studies presented in the three papers is presented in Table 1.

Table 1: Characteristics of Papers I–III

Characteristics	Paper I	Paper II (N = 252)	Paper III (N = 121)
Study content	Prevalence of pain Pain characteristics	Prevalence of background pain Factors associated with moderate to severe background pain	Background pain characteristics
Study design	Systematic review	Observational/descriptive Cross-sectional	Observational/descriptive Cross-sectional
Data collection	Literature retrieval	Brief screening interview, clinical examination, questionnaires	Brief screening interview, clinical examination, questionnaires
Analysis	Meta-analysis	Descriptive Inferential (CI, p) Logistic regression	Descriptive Inferential (CI)
Study sample	Persons with CVLUs	Persons with CLUs	Persons with CLUs and ulcer-related background pain
Study setting	Inconclusive*	Outpatient wound clinics	Outpatient wound clinics

Abbreviations: CVLUs = Chronic venous leg ulcers; CLUs = Chronic leg ulcers; CI = confidence index
*Descriptions of the study setting in the included studies are vague and/or missing

1.2 Systematic literature review and meta-analysis

In Paper I, we employed a systematic review methodology. The methods used to identify and select relevant articles, assessing quality and data extraction was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Moher et al., 2015). A review protocol was created based on theory and registered on PROSPERO: an international prospective register of systematic reviews (CRD42017056027).

4.1.1 Identification and selection of relevant literature

In Paper I, we synthesized data from previous quantitative research articles, only including studies reporting on ulcer-related pain in persons with CVLUs. We used a broad search strategy to identify as many relevant studies as possible. In addition, we chose to include both observational studies and baseline data from different design effect studies. This decision was made because we identified few observational studies in scoping searches prior to the search. In addition, the baseline data from effect studies contain relevant information on pain characteristics. This led to the identification of a vast number of publications, however—many of which were not relevant. Furthermore, heterogeneity in the diagnosis criteria made it difficult to synthesize the material in a systematic way if all CLU diagnoses were included. We therefore decided to narrow the scope of the systematic review to patients with venous ulcers, in order to manage and synthesize the available data. CVLUs were chosen as the diagnosis of interest since venous leg ulcers constitute the largest group of CLUs, and most of the research articles identified in the systematic literature search included only CVLUs.

Reflecting the aim of the review, the eligible criteria guided the searches and the assessment of relevance of studies. Quantitative studies were included if they were of sufficient quality and reported original baseline or cross-sectional data on background pain in adult persons with CVLUs. Both effect studies (e.g., randomized controlled trials, non-randomized efficacy studies and randomized prospective studies) and descriptive studies (e.g., register studies and surveys) were considered relevant.

The literature was retrieved by searching five electronic databases covering a broad range of health care research. Searches were restricted to studies published from the year 1990, and were performed in October 2017 and updated in February 2019. The search terms and their combinations in the different databases are presented in the appendix of Paper I. An academic librarian assisted in the development of the search strategy to ensure a rigorous search process. Literature was also retrieved by manually searching relevant conference proceedings and specialist journals, and by hand searching the reference lists of all included studies. References were handled using Covidence (Babineau, 2014).

The searches identified a total of 3412 articles. The identification and selection process are displayed in the flow diagram presented in Figure 1 in Paper I. Assessment of relevance was conducted by screening the title and abstract (N = 2454) and then by assessing full-text articles (N = 556). This left a total of 45 eligible studies for further quality assessment.

4.1.2 Appraisal and data extraction

Two independent reviewers (LL, TML) assessed the quality of eligible studies using the Mixed Methods Appraisal Tool (MMAT), version 2011 (Pluye et al., 2011). Nine articles were excluded based on the quality assessment, resulting in 36 studies being included in the review. Eight of the included studies were descriptive (e.g., descriptive surveys and registry studies) and 28 were effect studies (e.g., randomized controlled trials, non-randomized efficacy studies and prospective uncontrolled trials).

A data extraction form was developed by the research team (LL, TML, HE, EJ). Data were extracted on study design, setting, sample characteristics (e.g., sample-size, age and sex), wound diagnostic criteria, data collection methods/recruitment, type of pain assessment/report as well as pain prevalence and pain characteristics (e.g., intensity, duration and frequency, location and quality). The author of this thesis filled out the data extraction form, and the extracted data were verified by one of the co-authors of the paper (TML).

4.1.3 Synthesis of data

Detailed descriptions of the included studies were presented in Table 2 in Paper I (pp. 471–472). Since there was considerable variety among the included studies regarding methodology, measures were taken to enable a systematic synthesis of the data. Standardized methods for converting different pain rating scales were used to provide mean pain scores with standard deviation (SD) on an NRS ranging from 0–10 (Collins et al., 1997; Hozo et al., 2005; Kahl & Cleland, 2005; Williamson & Hoggart, 2005). However, inclusion criteria in effect studies were generally more detailed than in descriptive studies, typically resulting in more selected samples with fewer comorbidities. The analyses were therefore stratified by study design.

4.2 Clinical study

4.2.1 Study samples

As explained earlier, CLUs are caused by a variety of underlying conditions and can often have multiple causes (cf. Chapter 2.1.1). The emphasis on ulcer diagnosis in the existing literature is based on an intention to treat the ulcer and its underlying and sustaining causes. The focus in this PhD project is on pain, and the ulcer diagnosis is considered of secondary importance when exploring this symptom. It is well-known that all CLUs may cause pain (WUWHS, 2004), and pain assessment and management is needed regardless of ulcer diagnosis. Hence, we chose a wide definition of chronic ulcers, including various aetiologies like venous, diabetic, unspecified and other (e.g., arterial or mixed).

However, burn ulcers, cancer ulcers, radiation ulcers, pressure ulcers caused by immobility, and immunological ulcers were excluded due to a more profound difference in pathophysiology. With regards to the duration of the ulcers, we chose to define chronicity as a wound duration of six weeks or more (Leaper & Durani, 2008). The overall study population in this project consisted of persons with CLUs.

4.2.2 Participants and settings

All participants in the descriptive, cross-sectional study (Papers II and III) were recruited from two specialized outpatient wound clinics. The wound clinics are located in two district hospitals in South-Eastern Norway, organized as part of the surgical department and assessing and treating patients with different types of wounds. Patients are mainly referred to the clinics by their GPs. The clinics are operated by specialized wound care nurses, but vascular surgeons or orthopaedic surgeons consult with the patients at their first visit, and when needed in the follow-up treatment.

Recruitment was consecutive. The author of this thesis approached and recruited eligible patients before their scheduled appointment at the outpatient wound clinics. Participants were recruited if they were over 18 years of age, had an open leg ulcer located below the knee, and the ulcer had persisted for more than 6 weeks. In addition, participants had to understand and read Norwegian, and have no comprehension difficulties. Exclusion criteria included the following ulcer causes: burn injuries, cancer, radiation treatment, pressure due to immobility and immunological diseases.

Recruitment started in March 2017 at the first outpatient wound clinic, located in a regional hospital. This unit was large and organized as a wound clinic five days a week. During the first six weeks, the recruiter (author of this thesis) was present in the clinic four days a week (Monday, Tuesday, Wednesday and Friday), ensuring consecutive recruitment of all eligible patients that were already being treated at the clinic. During this time, patients were not recruited to the study on the one day of the week (Thursday) when new patients were assessed by a doctor. This day was busy, and in agreement with the wound care clinic it was decided to use the first six weeks to obtain experience with and establish good routines for the recruitment process, brief interview and clinical examination. This ensured less disturbance in the already busy schedule when the recruitment of newly referred patients started. After the initial six-week period, recruitment proceeded on the one day of the week when new patients attended the clinic.

There were not as many eligible participants as expected. Hence, in January 2018, recruitment started in the second outpatient wound clinic, located in a different local hospital. This wound clinic was smaller and was organized as a specialized wound clinic one day a week. During this day, both new referrals and follow-up appointments were seen by the wound care nurse, alone or in collaboration with the doctor.

The recruitment process in both wound clinics proceeded throughout 2018, with recruitment two days a week (one day in each clinic); the decision to end recruitment was made based on an evaluation of the number of respondents needed to perform the regression analysis that was originally planned to identify predictors of wound pain. The clinics' medical secretary or a wound care nurse asked the patients for oral consent to be approached by the researcher. Written informed consent was obtained from all those who agreed to participate.

Of the 279 persons who were invited to participate, 252 accepted and signed the written consent form. All 252 participants took part in the data collection, with a screening interview and clinical examination on the day of recruitment, in addition to their scheduled appointment at the outpatient clinic (for more details, see Chapter 4.3.3). The participants received a battery of questionnaires to bring home, complete the following day and return by mail. The questionnaires were returned by 192 participants, resulting in a response rate of 69%. In Paper II, all 252 participants were included in the analysis, whereas in Paper III, only the 121 participants reporting ulcer-related background pain were included. A description of the participants included in the analysis in Papers II and III are presented in Table 2.

Table 2: Description of participants in Papers II and III

	Sample Paper II N = 252	Sample Paper III N = 121
Age, years, mean (SD)	74.4 (12.8)	74.4 (12.5)
Gender		
Male	128 (50.8)	56 (46.3)
Female	124 (49.2)	65 (53.7)
Ulcer duration, weeks, median (IQR)	14.5 (8–26)	15 (8–26)
Ulcer diagnosis		
Unspecified*	67 (26.6)	37 (30.6)
Diabetic foot ulcer	53 (21.0)	20 (16.5)
Venous	50 (19.8)	25 (20.7)
Other**	82 (32.6)	38 (32.2)

Abbreviations: SD = standard mean; IQR = interquartile range

*ICD−10 code L97

**such as traumatic and mixed venous-arterial

4.2.3 Data collection

Data were collected via a brief screening interview, a clinical examination and self-report questionnaires. All screening interviews and clinical examinations were performed by the author of this thesis. The combination of variables collected was determined based on existing research on pain management and wound care, the theoretical framework of the biopsychosocial model of pain, pain as a multidimensional phenomenon and person-centred health care. All variables were thoroughly discussed in the research group, which consisted of experts, researchers and clinicians in both pain management and wound care. For several reasons, it was not feasible to collect data on the full complexity of the person, the pain experience or the ulcers (see Chapter 6.2). However, variables were carefully selected to capture the key aspects related to ulcer-related pain in persons with CLUs.

In the brief screening interview, participants were screened for the presence of ulcer-related pain, background pain and dressing-related pain. Information was gathered on wound duration and reoccurrence, as well as comorbidities. The screening interview took place immediately prior to the scheduled appointment in the clinic.

A clinical examination was performed during the scheduled appointment. Data were collected on ulcer characteristics (e.g., location and size), sensibility of the lower leg/foot and temporal pattern of ulcer-related pain. To assess pain localization, the participants were asked a question with the following response options ('directly in the wound bed'; 'in the wound edges'; 'in the area surrounding the wound'; 'in the entire foot'; 'in the entire leg'; or in a self-determined location). If more than one location was selected, 'multiple locations' was used to describe the location of the pain. The ulcer diagnosis was registered as stated by the medical doctor. Information was also gathered on the participants' use of analgesics, and compliance with prescribed analgesics. It was noted as to whether the pain management was aimed at ulcer-related or other types of pain. Finally, participants were asked to describe other non-medical interventions used to relieve ulcer-related pain.

After the clinical examination, all participants received a battery of self-report questionnaires to complete the following day and return by mail in a pre-paid envelope. All participants received questionnaires regarding demographic information, health status and insomnia symptoms. Participants identified in the screening interview as having ulcer-related background pain also received questionnaires regarding pain characteristics and interference.

An overview of all variables and the questionnaires used in the descriptive, cross-sectional study (Papers II and III) are presented in Table 3.

Table 3: Variables and questionnaires used in the clinical study and their use in the respective papers (Papers II and III)

Variables	Paper II	Paper III
Screening questions		
Ulcer-related background pain	√	√
Dressing-related pain		√
Demographics*	√	√
Clinical characteristics		
Ulcer diagnosis	√	√
Ulcer duration	√	√
Ulcer size	√	√
Reoccurrence		√
Number of ulcers		√
Presumed causal factor		√
Ulcer location		√
Comorbidities	√	√
Sensibility of lower leg		
SWME		√
Tuning fork test		√
Health status (EQ-5D VAS)	√	
Sleep (ISI)	√	√
Pain characteristics	√	
Intensity: worst, least, mean, now (BPI)		√
Interference with function (BPI)		√
Worst pain (BPI3, single item)	√	√
Avoidance of physical activity (study specific)		√
Qualities (SF-MPQ)		√
Location of pain (BPI)		√
Time pattern of pain (PQAS, single item)		√
Pain management (BPI, study-specific)		√

Abbreviations: SWME = Semmes Weinstein monofilament examination; EQ-5D VAS = EuroQol Five Dimensions Visual Analogue Scale; ISI = Insomnia Severity Index; BPI = Brief Pain Inventory; BPR3 = Brief Pain Inventory, item 3; SD-MPQ = short-form McGill Pain Questionnaire; PQAS = Pain Quality Assessment Scale

*Age, gender, marital status, education level, work situation, living arrangements, ethnicity

4.2.4 Variables and instruments

The instruments used in the study are described in this chapter, including an evaluation of their validity and reliability. An instrument's ability to measure what it is intended to measure is referred to as its validity. The overall validity is determined by an instrument's face, content, criterion and construct validity (Polit & Beck, 2020). Face validity is the extent to which an instrument appears to capture the intended phenomenon or construct. Content validity refers to whether the instrument consists of items that can capture all aspects of a construct. Criterion validity is defined as the instrument's ability to predict or correlate with a different measure of the same construct. Finally, construct validity refers to the degree to which an instrument measures the intended construct. The reliability of an instrument relates to the consistency of a measure. The three types of consistency considered are a) over time (test-retest reliability), b) across items (internal consistency), c) and between different researchers (inter-rater reliability) (Heale & Twycross, 2015; Polit & Beck, 2020). The internal consistency expressed by the Cronbach's α analysis indicates how closely related a set of items are as a group, and is considered to be a measure of scale reliability (Polit & Beck, 2020).

4.2.4.1 Demographic and clinical variables

Demographic data were collected on age, gender, work situation, education, living arrangements and ethnicity. These data were collected as part of the self-report questionnaires completed at home the day after recruitment. The clinical data were collected in the brief interview or clinical examination during the scheduled appointment at the wound clinic and registered in a form by the investigator (author of this thesis). Clinical variables that were registered were diagnosis, duration and size of the ulcer(s), reoccurrence of the ulcer(s), number of ulcers, presumed causal factor, ulcer location(s), comorbidities and sensibility of the lower leg (Semmes Weinstein monofilament [5.07/10 g] examination and 128-Hz tuning-fork test).

A pilot evaluation of the face validity and feasibility of the collection of clinical variables was conducted in collaboration with supervisors following the recruitment of 20 participants. Only minor linguistic changes to further specify the variables were made to increase the feasibility.

4.2.4.2 The short-form McGill Pain Questionnaire

The short-form McGill Pain Questionnaire (SF-MPQ) was used to assess different qualities of the pain experience. The initial McGill Pain Questionnaire—developed and published by Melzack et al. in 1975—is aimed at capturing pain as a multidimensional phenomenon, recognizing the shortcomings of simple pain intensity scales (Melzack, 1975). A short-form version (the SF-MPQ) was later developed (Melzack, 1987), as well as translated into and adapted for the Norwegian language (Strand et al., 2008). The SF-MPQ is recommended for use in research and clinical settings when time to obtain information is limited (Strand et al., 2008). The SF-MPQ consists of 15 pain descriptors (11 sensory, 4 affective) with a 4-point intensity scale for each descriptor (none, mild, moderate, severe). Scores are added up for the sensory (0–33) and affective (0–12) subscales, as well as the total scale (0–45). The SF-MPQ also includes a Present Pain Intensity Index, and a VAS ranging from 0 mm (no pain) to 100 mm (worst possible pain) assessing pain intensity during the past week.

The translated Norwegian version of the SF-MPQ (NSF-MPQ) has demonstrated construct validity, a sufficiently high Cronbach’s α (0.74–0.87) (Ljunggren et al., 2007), and acceptable test-retest reliability among persons in Norway with musculoskeletal and rheumatic pain (Strand et al., 2008). The English version of the SF-MPQ has been used in studies to assess ulcer-related pain (Nemeth et al., 2003). However, the validity and reliability of the SF-MPQ have not been specifically evaluated in persons with leg ulcers, and the NSF-MPQ has not previously been used to assess ulcer-related pain. In the present study, the NSF-MPQ was linguistically adjusted to specifically assess ulcer-related pain by adding ‘ulcer-related’ to the word ‘pain’ throughout the questionnaire. The research group reasoned that this would not affect the validity significantly but would ensure that characteristics of ulcer-related pain—and not other types of concurrent pain—were assessed.

4.2.4.3 The Brief Pain Inventory

The Brief Pain Inventory (BPI) was developed to assess the intensity of pain, the interference of pain with daily function, and the type and effect of pain management (Cleeland, 2009).

Pain intensity was assessed by 4 NRSs, from 0 (no pain) to 10 (worst pain imaginable), on pain now, worst pain, least pain, and average pain during the past 24 hours. The 0–10 NRS has demonstrated more validity and strengths than other unidimensional pain scales (Hjermstad et al., 2011). The BPI further consists of a percentage scale (0–100) which quantifies pain relief from current therapies. Zero per cent indicates no relief, while 100% indicates complete relief. A full body map is provided to the participants, on which they can mark the pain location. In the present study, the BPI body map was not used since it was insufficiently detailed to provide accurate description of the location of the ulcer-related pain.

Pain interference was assessed by 7 NRSs, from 0 (does not interfere) to 10 (completely interferes), regarding physical and psychosocial function (Cleeland & Ryan, 1994). The activity cluster of interference items includes general activity, walking ability, work and sleep. The affect cluster of interference items includes mood, enjoyment of life and relations with others.

The translated Norwegian version of the BPI was validated for use in patients with cancer (Klepstad et al., 2002), osteoarthritis (Kapstad et al., 2010), inflammatory bowel disease (Jelsness-Jørgensen et al., 2016) and after cardiac surgery (Gjeilo et al., 2007), demonstrating good validity and reliability. In patients with chronic pain after cardiac surgery, the Norwegian version of the BPI demonstrated acceptable internal consistency

(Cronbach's α 0.84–0.94). An association between the BPI and The *Medical Outcomes Study 36*-item *Short-Form* Health *Survey* (bodily pain) supported the criterion validity, and explorative factor analysis confirmed the two-factor structure of pain interference consistent with the original BPI (Gjeilo et al., 2007). The English version of the BPI was used to assess ulcer-related pain (Pieper et al., 2013). In the present study, the BPI was linguistically adjusted to specifically assess ulcer-related pain by adding 'ulcer-related' to the word 'pain' throughout the questionnaire. As with the Norwegian version of the SF-MPQ (see above), the research group reasoned that this would not affect the validity significantly but would ensure that characteristics of ulcer-related pain—and not other types of concurrent pain—were assessed.

4.2.4.4 Temporal pattern of pain

To assess how pain fluctuated during the day, a question from the Pain Quality Assessment Scale (PQAS) was used in the brief screening interview. The PQAS is a valid tool for assessing various types of nociceptive and neuropathic pain (Jensen et al., 2010; Miaskowski et al., 2017), and has been forward-back translated, linguistically validated and culturally adapted to Norwegian (Ljosaa et al., 2010). The question regarding the temporal pattern of pain is also used in the Oslo Pain Registry (Regional kompetansetjeneste for smerte, 2021): This single item was paraphrased to the participants, and the answer was registered by the recruiter. Additionally, to ensure criterion validity, the participants were asked to fill out a graph stating their level of pain (NRS) every hour during a typical day. Unfortunately, this self-report graph was not completed in most returned questionnaires, making a more detailed assessment of the temporal pattern of pain unreliable.

4.2.4.5 Insomnia Severity Index

The Insomnia Severity Index (ISI) is a seven-item self-report instrument measuring persons' perception of their sleep. The ISI assesses the severity of sleep-onset and sleep maintenance difficulties, contentment with current sleep pattern, interference with daily functioning, impairment attributed to the sleep problem, and degree of distress or concern caused by the sleep problem. Each item is rated on a 0 (no problem) to 4 (very severe problem) scale. The total score ranges from 0 to 28, and a score above 15 is considered to be clinically significant insomnia (Bastien et al., 2001).

The content of the ISI corresponds in part to the diagnostic criteria of insomnia (Direktorat for e-helse, 2021), and the questionnaire is recommended as an outcome measure for insomnia in clinical trials due to its sensitivity to changes in insomnia symptoms and sleep patterns (Morin et al., 2011). The ISI is widely used in Norwegian insomnia practice and research (Hagatun et al., 2019; Kallestad et al., 2010; Kallestad et al., 2015), but formal validation of the translated version is not available. However, a recent study validating the diagnostic properties of the ISI demonstrated good to very good validity against face-to-face interview diagnoses in a random population-based study in Norway (Cohen’s kappa 0.56–0.74) (Filosa et al., 2020).

4.2.4.6 EuroQuol Five Dimensions (EQ-5D-5L)

The EQ-5D-5L is a standardized instrument developed by the EuroQol Research Foundation for use as a measure of health applicable to a wide range of health conditions. The instrument contains two parts. Part 1 (the EQ-5D index) records self-reported problems in five health domains: mobility, self-care, normal activities, pain/discomfort and anxiety/depression. Each domain has five levels of severity corresponding to no, slight, moderate and severe problems, as well as incapacity. Part 2 (the EQ-5D VAS) of the questionnaire derives information about the respondents’ self-rated health, scored on a vertical 20-cm VAS with endpoints labelled ‘the best health you can imagine’ (100) and ‘the worst health you can imagine’ (0) (Rabin et al., 2011). There is currently no Norwegian value set and scoring algorithm for Part 1 available (Hansen et al., 2020). However, only the EQ-5D VAS on self-rated health was analysed and reported on in this study.

A Norwegian translation of the EQ-5D has been used in several Norwegian studies and has been found to have satisfactory measurement properties (Solberg et al., 2005). The original English version of the EQ-5D has been used in studies of patients with CLUs (Renner et al., 2014).

4.3 Statistical analyses

The statistical software package Stata version 15.0 (State College, Texas) and IBM SPSS Statistics Data Editor Software version 26 were used to analyse the data. The software and analyses used in the different papers are displayed in Table 4.

Table 4: The software and analyses used in Papers I–III

Paper I	Paper II	Paper III
Software	**Software**	**Software**
Stata	SPSS Stata	SPSS
To provide pooled estimates of proportion of pain and mean pain intensity	**Descriptive statistics**	**Descriptive statistics**
Random-effect meta-analysis	Frequencies Percentages Mean Standard deviation Range Median Interquartile range	Frequencies Percentages Mean Standard deviation Range Median Interquartile range
Assess heterogeneity and its magnitude	**Inference statistics**	**Inference statistics**
Q-test (not reported) and I-square measure	Logistic regression* Paired t-tests** Chi-square tests** Confidence intervals***	Confidence intervals ***
	Reliability	**Reliability**
	Cronbach's α	Cronbach's α
Explore sources of heterogeneity in pain intensity		
Univariable random-effects meta-regression analysis		
Assess publication bias		
Egger's test		
Statistical significance assumed at $p < 0.05$ level	Statistical significance assumed at $p < 0.05$ level	

*Identify factors associated with moderate to severe ulcer-related background pain, **Investigate differences between responders and non-responders, ***Generalize results from the sample to the population of persons with chronic leg ulcers

4.3.1 Statistical analyses in Paper I

In the systematic review and meta-analysis (Paper I), random-effects meta-analyses (Nyaga et al., 2017) was performed to provide pooled estimates of proportion of pain and mean pain intensities. The *metaprop* and *metan* commands in Stata version 15.0 were applied, respectively. The random-effects meta-analyses were performed overall and stratified by study design.

The proportion of the variance in the estimates due to heterogeneity rather than chance was calculated with heterogeneity statistics I-square. An I-square value > 75% was interpreted as high heterogeneity. To explore sources of heterogeneity, a univariable random-effects meta-regression analysis was performed (Deeks et al., 2011). It was examined as to whether pain intensity scores were affected by publication year, mean age, gender and wound duration. Statistical significance of the random-effects meta-regression was assumed at the $p < 0.05$ level. Due to the small number of publications reporting pain prevalence (N = 10), a random-effects meta-regression analysis could not be performed on prevalence of pain.

Finally, an Egger's test for small-study effects was conducted to check for publication bias (Deeks et al., 2011).

4.3.2 Statistical analyses in Paper II

Descriptive statistics were used to describe demographic data, clinical and wound characteristics, and prevalence of ulcer-related pain in the total sample (N = 252). The results were presented as means with SD for normally distributed continuous variables, as medians with an IQR for skewed continuous variables, and as frequencies with numbers and proportions for categorical variables. The 95% CIs were calculated to estimate the interval of probable values of prevalence in the population.

Univariable and multivariable logistic regression analyses were used to explore factors associated with moderate to severe pain. Initially, a multinomial regression analysis was applied to assess factors associated with no pain, mild pain and moderate to severe pain. The multinomial regression demonstrated no significant association between the suggested factors and mild pain (NRS = 1–3) compared with no pain (NRS = 0) and moderate to severe pain (NRS ≤ 4). However, a significant association was found in persons with moderate to severe pain compared with persons with no and mild pain. Consequently, logistic regression was used to further explore factors associated with moderate to severe pain. The third item of the BPI (NRS 0–10, worst pain in the last 24 hours) was used in this analysis. For the regression analyses, pain intensity was dichotomized into no/mild pain (NRS 0–3.99) and moderate/severe pain (NRS ≤ 4). This procedure was in line with previous research on pain intensity cut-off points for severity (Kapstad et al., 2008; Moore et al., 2013; Zelman et al., 2005).

Although multiple factors are known to be associated with chronic pain, the factors selected in the explorative logistic regression analysis were limited to age (10-year increments), gender (male versus female), health status (EQ-VAS 0–100), sleep quality (ISI total score 0–28), wound diagnosis (venous versus diabetic versus all others), wound size (cm^2), and wound duration (weeks). The variables were selected based on what was considered clinically important, and/or which ones had been found to have a significant association with leg ulcer pain and chronic pain in previous studies. The limited sample size (75 persons with moderate to severe pain and complete data on the selected factors) restricted the number of variables that could be included in the analysis (Vittinghoff & McCulloch, 2007). All variables were tested for multicollinearity, demonstrating low multiple correlations between other variables in the model (Pallant, 2017). Hence, the assumptions were considered not violated. We used stepwise backwards elimination with p = 0.157 as the criteria (corresponding to the Akaike Information Criterion*)* to obtain a subset of sociodemographic variables that were associated with moderate to severe ulcer-related background pain (Heinze et al., 2018). In the final model, we tested for two-way interactions between the included variables (Sommet & Morselli, 2017).

4.3.3 Statistical analyses Paper III

Descriptive statistics were used to describe demographic data, clinical and wound characteristics, types of ulcer-related pain, pain characteristics and pain management in the sample of patients with ulcer-related background pain (N = 121). The results were presented as means with SD for normally distributed continuous variables, as medians with an interquartile range (IQR) for skewed continuous variables, and as frequencies with numbers and proportions for categorical variables. In addition, 95% CIs were used to estimate the interval of probable values of pain intensity in the population.

4.3.4 Analysis of internal consistency (Papers II–III)

The reliability (in terms of internal consistency) of the Norwegian versions of the SF-MPQ, BPI and ISI was explored using Cronbach's α. Cronbach's α estimates the extent to which different items in the instrument reliably measure the same concept or construct. Hence, it is connected to the inter-relatedness of the items. The normal range of Cronbach's α is between .00 and + 1.00, with higher values generally reflecting better internal consistency (Polit & Beck, 2020). A minimum level of .7 is often recommended (Pallant, 2017). However, α is also sensitive to the number of items in a test: A larger number of items can result in a larger α value, while a smaller number of items can result in a smaller α. In addition, a too high α value may indicate redundant items (i.e., assessing the same concept), and a maximum α of .9 has been suggested (Tavakol & Dennick, 2011).

4.3.5 Analysis of non-responders and handling of missing responses (Papers II–III)

No data were gathered on eligible participants who declined participation at the point of recruitment. It was thus impossible to evaluate recruitment bias.

However, non-response analyses were performed on those who signed the written consent form and provided information in the screening interview and clinical examination but did not return the questionnaire battery. Student's t-test and chi-square tests for independence were used to investigate differences between responders and non-responders (Pallant, 2017). In the total sample, those who did not return the questionnaires (N = 60) did not differ significantly from those who did return them, with regards to age (p = 0.14), gender (p = 0.89), number of comorbidities (p = 0.31) or presence of ulcer-related background pain (p = 0.78).

For the logistic regression analyses, participants who did not return the questionnaire battery were not included (Paper II). For these analyses, missing values in the EQ-VAS were imputed using the mean of all respondents, whereas missing values in the ISI were imputed using the median of the nearest point. For the EQ-VAS, missing values were imputed for three respondents, and for the ISI, nine individual items were imputed. The missing values for these variables were assumed to be random.

In Paper III, missing values for the 15 pain descriptors of the SF-MPQ were replaced with 0. The SF-MPQ does not contain a non-applicable alternative, and based on clinical and research experience, patients tend to skip marking the pain descriptors that are not relevant to them, resulting in a large number of missing items.

4.4 Ethical approvals and considerations

Ethical approval was not needed for the literature review and meta-analysis study. The appraisal tool (MMAT) used to critically assess the eligible articles does not include ethical considerations. However, ethical considerations of/in the included studies were discussed in the research group. For more details on ethical considerations, see Chapter 6.

The descriptive, cross-sectional study was approved by the Norwegian Regional Ethical Committee for Medical and Health Research Ethics (South-East region; REK number

2016/1236). The study was also reported to the Norwegian Center for Research Data (NSD). Permission to recruit participants was also obtained from the local data protection officer and the head of the department at the two outpatient wound clinics from which participants were recruited. The Norwegian National Research Ethics Committee’s guidelines and the Helsinki Declaration guided all considerations and decisions in the development, conducting and reporting of the studies in this thesis.

All potential participants received written and oral information about the purpose and nature of the study. Participation was voluntary, and participants were informed that there were no obligations to participate, and no consequences related to health care if they chose not to participate. Those who agreed to participate provided their written informed consent. Participants were informed about their right to withdraw at any time during the study period without providing a reason and without risk of consequences. Confidentiality was maintained through the coding of participants and removal of identifiers in the electronic data material. Completed questionnaires, codebooks and signed consent forms (paper versions) were stored separately in fire-safe, locked safes in an appropriate location at the University of South-Eastern Norway (USN) or digitally on USN’s research server. The completed questionnaires and identifying digital information will be deleted according to the rules and regulations set by the Norwegian National Research Ethics Committee (i.e., five years after the study’s finalization date). Digital copies of the data are saved on the research server at USN.

Importantly, all patients and health care staff involved in the study’s data collection were treated with respect and with good intentions to reduce the burden of participation and workload, as well as avoid interruptions and prolonged treatments and clinical consultations.

The research group considered it very important to ensure that the research had no harmful effects on the participants. The selection of variables included in the battery of questionnaires was carefully considered to minimize the length of the questionnaire battery and the potential burden of participation. Furthermore, the participants were asked to fill out the questionnaire the day after their consultation rather than in the outpatient clinic, allowing them a calmer environment and time to complete the questionnaires. Finally, the clinical examination was performed during an already scheduled dressing change to avoid any extra exposure of the wound (which can potentially cause delayed wound healing).

The staff of the wound care clinics were thoroughly informed about the study and data collection procedures. They were also given the opportunity to express concerns and propose directions regarding the organization of the data collection. Measures were taken to minimize the data collection's impact on the daily work at the clinics. The staff were also given the opportunity to develop parallel studies for educational purposes, as well as for quality improvement of their daily clinical practice and research work.

5 Findings

In this section, the main findings of the three papers are summarized. More detailed findings are presented in the respective papers.

5.1 Prevalence and characteristics of ulcer-related pain in previous research (Paper I)

In this paper, we presented the results of a systematic literature review and meta-analysis on data from empirical studies reporting on the prevalence and characteristics of background pain in persons with CVLUs. A total of 36 quantitative studies, 8 descriptive studies and 28 effect studies were included in the analysis.

The prevalence of background pain was reported in 10 of the 36 studies, ranging from 46.3% to 100%. Random-effect meta-analysis provided an overall pooled estimated proportion of 80%. Subgroup analysis stratified by study design (descriptive and effect studies) demonstrated a higher proportion of background pain in effect studies (90%) compared with descriptive studies (60%) (Figure 3).

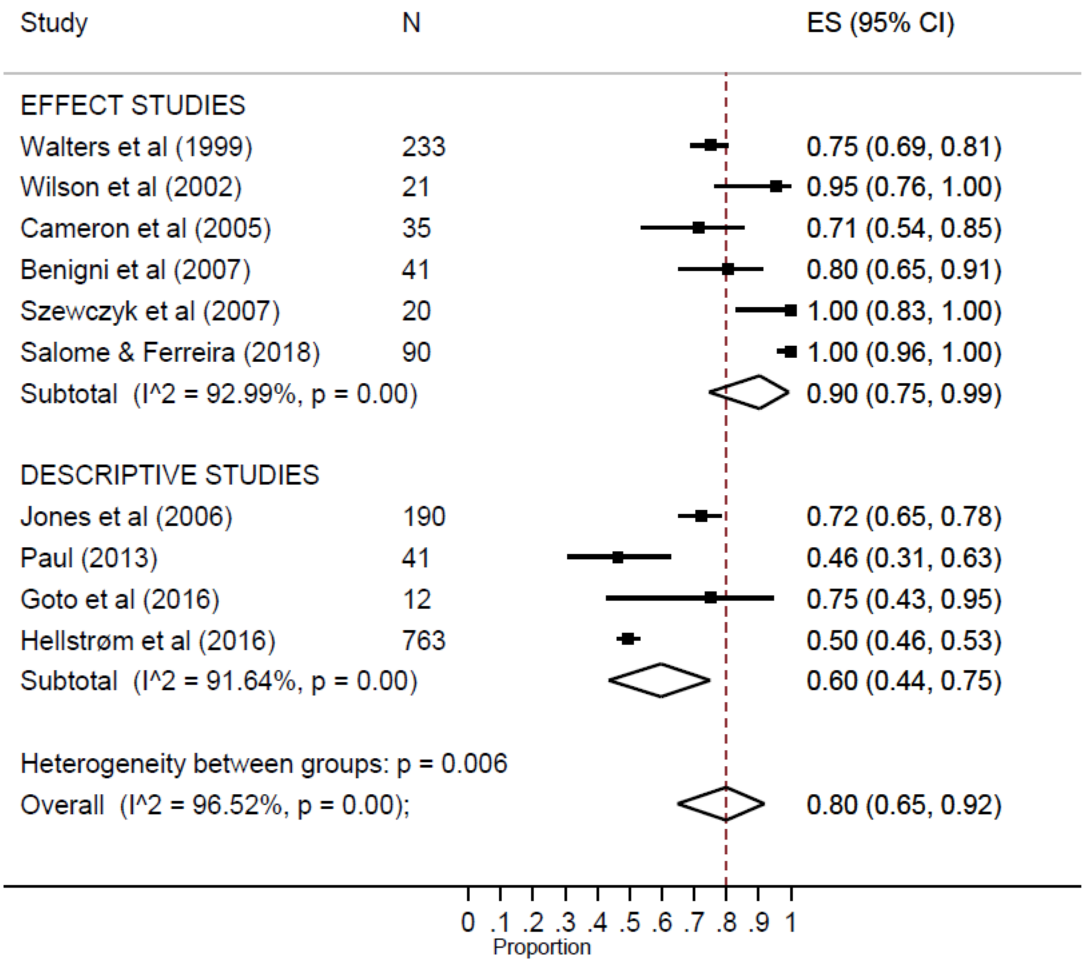


Figure 3: Forest plot of prevalence of ulcer-related background pain

Three descriptive and 24 effect studies (in total, 27 of the included studies) reported intensity, with a mean intensity ranging from 2.3 to 6.6 (all converted to a 0–10 NRS). The random-effect meta-analysis provided an overall pooled estimated mean pain intensity of 4.0. The subgroup analysis resulted in similar pooled estimates in effect studies and descriptive studies, with a mean pain intensity of 4.0 and 3.8, respectively.

Due to the varied and sparse information on pain characteristics other than pain intensity, a synthesis of other wound characteristics was not possible. In Paper I, these findings were presented in a table and in a narrative summary (pp. 474–475).

In sum, the best available research data were obtained and demonstrate that the majority of persons with CVLUs experience ulcer-related background pain, reporting mild to moderate pain intensity. However, given the poor quality of the assessment and reporting of pain in existing studies, it is likely that the available research paints an inaccurate and simplified clinical picture. We found a lack of standardized methods for defining the aetiology of wounds, as well as for conceptualizing, defining and assessing pain. In addition, the samples were poorly described in terms of demographic and clinical characteristics. Hence, the data available were heterogenous, making it challenging to synthesize the data.

Based on the results, we encourage future studies to adhere to standardized methods for collecting and presenting data on wound and pain characteristics. Researchers and clinicians should also shift focus from mean values of pain intensity to variations and subgroups of mild, moderate and severe pain in order to provide a more person-centred approach to clinical care and pain management for persons with CVLUs. There is a great need for large and methodically sound descriptive studies on self-report of pain prevalence, pain characteristics and related factors in patients with CLUs of venous and other origins.

5.2 Prevalence of and factors associated with ulcer-related pain (Paper II)

Paper II explored the prevalence of background pain in a sample of persons with CLUs of various origins (i.e., venous, diabetic and other), receiving treatment at an outpatient wound clinic (N = 252). In addition, we explored demographic, clinical and psychosocial factors associated with moderate to severe ulcer-related background pain (N = 192).

Background pain was reported by 64% of the total sample, and of those returning the questionnaire (N = 192), 39% reported having moderate to severe pain.

In the univariate analyses, female gender, older age and more insomnia symptoms were factors associated with moderate to severe pain. The final model demonstrated that older females reporting insomnia symptoms had an increased risk of moderate to severe ulcer-related background pain. Interestingly, these participants also perceived their health status to be better (Table 5).

Table 5: Logistic regression models of factors significantly associated with moderate to severe ulcer-related background pain (N = 192)

	Univariate analysis			Multivariate analysis		
	OR	CI (95%)	p	OR	CI (95%)	p
Age (per 10 years)	1.38	1.08–1.76	0.01	1.46	1.10–1.94	< 0.01
Female gender†	3.02	1.65–5.52	< 0.01	2.44	1.28–4.68	< 0.01
Health status (EQ VAS)	1.01	0.99–1.02	0.65	1.02	1.00–1.04	0.02
Sleep quality (ISI)	1.09	1.04–1.15	0.01	1.13	1.06–1.20	< 0.01
Wound diagnosis‡						
Venous	1.39	0.66–2.90	0.38			
Diabetic	0.87	0.42–1.81	0.71			
Wound size (cm^2)	1.10	0.99–1.22	0.08			
Wound duration (weeks)	0.99	0.97–1.01	0.25			

† Male gender served as reference group

‡ All other wound diagnoses (other and unspecified) served as reference group

Abbreviations: EQ VAS = EuroQol visual analogue scale; ISI = Insomnia Severity Index; OR = odds ratio; CI = confidence interval

In the multivariate analyses, we also found an interaction between health status and insomnia symptoms, demonstrating that sleep quality has a modifying effect on health status. The interaction indicates that the importance of sleep is minor for persons with poor health status, while for persons with better health status, sleep quality has greater impact on the predicted probability of having moderate to severe pain. This interaction is illustrated by an interaction plot (p. 2738). We hypothesize that diminished health status has such great impact on a person's life that the insomnia symptoms become secondary; and, vice versa, if a person reports good health status, insomnia symptoms become more noticeable, and in turn influence the likelihood of having moderate to severe pain.

Overall, the findings demonstrated that ulcer-related background pain is a common and continuing problem in persons with CLUs. Further, specific risk factors (e.g., older females with insomnia symptoms and good perceived health status) should draw clinician's attention towards assessing pain, evaluating the need for pain management and offering proper pain-relieving interventions.

5.3 Pain characteristics and management of ulcer-related pain (Paper III)

Paper III provides in-depth knowledge on characteristics of ulcer-related background pain in a sample of participants with CLUs (N = 121). The participants reported on average moderate pain (mean 4.5, CL 95% 4.0–5.0), supporting Paper I's findings on pain intensity. Further, a sub-analysis of pain intensity demonstrated that as many as 61% of the respondents reported moderate or severe pain intensity.

The ulcer-related background pain interfered moderately with daily function. Overall, activity functions, such as general activity, sleep and walking ability, were more affected than the affective functions, such as enjoyment of life and mood.

The most frequent descriptors used to describe the ulcer-related background pain were sensory descriptors, such as 'tender', 'stabbing', 'aching', and 'hot/burning'. A majority of the participants (71%) stated that their pain was intermittent, meaning that they sometimes experienced pain but were pain-free at other times.

A large proportion of the participants (77%) had been prescribed analgesics. However, fewer than 60% had been prescribed analgesics specifically for ulcer-related pain, and 1 out of 4 reported taking fewer doses than prescribed, or not taking the analgesics at all. Additionally, approximately 60% reported using non-medical interventions to relieve ulcer-related pain. The respondents reported that the pain interventions or medications provided a mean pain relief of 45.9%.

The data from this study support the argument that ulcer-related background pain is a significant and interfering problem, and that pain management is not sufficient in persons with CLUs. The use of different sensory descriptors—traditionally associated with both nociceptive and neuropathic pain—may indicate the presence of different types of pain. Further, the temporal pattern and location of the pain described provide interesting implications for pain management; these are discussed in the paper. In addition, almost 60% of the participants had reduced sensation of the monofilament, and over 40% could not detect vibration from a tuning fork, indicating diminished tactile sensation in the lower extremities. This should be a reminder for clinicians not to discard ulcer-related pain in persons with signs of non-painful peripheral neuropathy, and to consider tactile sensation with regards to treatment and prevention in wound care in general.

6 Discussion

To our knowledge, this is the first study exploring multiple aspects of ulcer-related background pain in detail, and providing an elaborative description of the status of ulcer-related background pain in persons with CLUs. Overall, the studies in this dissertation demonstrate that background pain is a significant problem among people with CLUs receiving outpatient wound care services. Ulcer-related background pain has not been well-studied, hence current knowledge regarding its occurrence—and detailed knowledge about associated characteristics and factors—is valuable for wound management in general, and management of ulcer-related background pain specifically. Further, this knowledge contributes to our understanding of the complexity of CLUs in the clinical setting and can thereby promote optimal management.

In the following, the study and principal findings pertaining to each specific research aim are discussed in relation to the available research, the biopsychosocial model of pain and PCC perspectives. Challenges in and recommendations for practice and research are proposed and discussed. This chapter is organized under the following themes: a) ulcer-related pain as a significant problem; b) factors associated with moderate to severe ulcer-related pain; c) management of ulcer-related background pain; d) a holistic approach to ulcer-related pain; e) methodological aspects of the study, including ethical considerations; and f) implications for clinical practice and further research.

6.1 Ulcer-related background pain as a significant problem—prevalence and characteristics

The prevalence of ulcer-related background pain was explored by synthesizing existing research on the prevalence of pain in persons with CVLUs (Paper I), and by exploring the prevalence of pain in a sample of 252 persons with CLUs (Paper II). In Paper I, we discuss potential reasons for the discrepancy of prevalence between effect studies and descriptive studies in the systematic review of the literature (p. 476). The prevalence of ulcer-related background pain of over 60% in the clinical study was concurrent with the pooled prevalence from the descriptive studies in the systematic review.

The intensity of ulcer-related background pain was the only pain characteristic for which we were able to provide a pooled estimate in the systematic review of the literature. Information on other pain characteristics was sparse and varied, and syntheses were not possible. We found a mean pain intensity of mild to moderate, and these findings were similar to the findings in the clinical study (Paper III). It is important to note that pain of mild to moderate intensity is often tolerable, and these findings of mean pain intensity may indicate that the ulcer-related background pain does not always need attention or to be relieved. However, in Paper I we argue that there is a great variation in the mean pain intensity reported by the patients. It is therefore more relevant to look at the percentage share of those persons experiencing moderate to severe pain, rather than mean values of pain intensity for the total sample. Consequently, we performed sub-analyses of pain intensity, and found that approximately 60% of those reporting ulcer-related background pain reported moderate or severe pain intensity. As pain intensity worse than mild should be unacceptable (Moore et al., 2013), this finding should be seen as a clear indicator of the need for better pain management for a large proportion of patients with CLUs. Note, however, that we chose to use the BPI item ‘worst pain intensity’ in our sub-analyses of pain intensity. One could argue that average pain, meaning ‘pain rated as the number that best describes pain on the average’ (Cleeland, 2009) is better-suited than worst pain, as the worst pain measure likely has a profound ceiling effect (i.e., the scores cluster at the higher end of the scale). However, the use of the ‘worst pain intensity’ item is supported in the literature (Atkinson, 2010). From a clinical perspective, health care providers should be concerned with the ‘worst’ pain. Interestingly, the mean average pain and worst pain intensity in our study differed by less than one point on the 0–10 NRS (Paper III, Table 3), indicating only a small difference between pain felt on average and at its worst. These findings demonstrate that individual pain assessment is crucial in clinical practice in order to identify persons in need of pain management. Further, that variation in intensity should be included in a thorough pain assessment to identify individual variations.

A recent observational study (Kim et al., 2021) not included in Paper I from 2020, investigating multidimensional pain characteristics in persons with CVLUs, reported a similar mean pain intensity as that found in Paper I. Previous and current research thus seem to support the findings from our clinical study with regards to pain prevalence and pain intensity—indicating that there has been little change in reported pain prevalence and pain intensity during the last several decades. This is especially interesting given the heightened awareness of ulcer-related pain in the beginning of this century (cf. Chapter 2.3). One might think that the consensus documents and guidelines highlighting the importance of pain would result in lower prevalence rates and lower pain intensity, as these documents are aimed at supporting EBP and improving patients' well-being. The seeming lack of improved wound pain management indicates that wound care professionals have not succeeded in the goal of integrating existing knowledge and changing their practice.

PCC may be a promising venue in this regard, and the Person-Centred Practice Framework should be considered when developing interventions in wound care (Gethin et al., 2020). Some argue that there is a fundamental tension between the goals of EBP and PPC, as they represent opposing tendencies towards standardization, on the one hand, and customization of medical practice around patient preference, on the other (Engle et al., 2021; Weaver, 2015). Further, EBP has been criticized for simplifying the complexity of the person, as studies informing EBP often provide knowledge about the average patient, yet no patient is average (Reach, 2016). The present study can be criticized based on these same arguments. However, we have acknowledged the fact that no patient is average when exploring symptoms of pain, and when interpreting and discussing the results. It is my opinion that by emphasizing interdisciplinary care that includes the patient in the wound care team, EBP and PCC can dovetail effectively. However, if wound care organizations are to create a culture that supports evidence-based PCC, this will require organizational structures and support to aid care delivery (Engle et al., 2021).

A prevalence of ulcer-related background pain of over 60% is substantial. In comparison, in the general Norwegian adult population, about 24–30% report that they have chronic pain (Breivik et al., 2006; Landmark et al., 2012). However, as we did not investigate the duration of the ulcer-related pain, we cannot state based on the data collected that the reported background pain is chronic. Nevertheless, we argue that, given the duration of the wounds (i.e., duration > 4 weeks), it is plausible that ulcer-related background pain is more similar in nature to chronic pain than acute pain (Leren et al., 2020). Hence, the prevalence of background pain related to CLUs is substantially high compared to the prevalence of chronic pain in the general population.

Chronic pain in itself poses a significant socioeconomic burden on society in Nordic countries (Christensen et al., 2011; Gustavsson et al., 2012). Further, the negative impact of chronic pain on the individual is well-established, with evidence demonstrating that chronic pain decreases QoL and interferes with everyday activities (Breivik et al., 2013). There are no available studies investigating the socioeconomic and biopsychosocial burden of ulcer-related background pain. However, the personal impact of ulcer-related pain has been demonstrated, as it impairs QoL and sleep and reduces psychical activity (Cunha et al., 2017; González-Consuegra & Verdú, 2011; Green et al., 2014; Marczak et al., 2019). Therefore, ulcer-related background pain appears to be a significant burden for the person, and may be an added problem on top of living with a CLU and other health problems and painful conditions—which will be discussed further in the following.

In the systematic review of the literature (Paper I), we did not identify enough studies to synthesize any results pertaining to other pain characteristics, such as pain interference, pain qualities, location or temporal fluctuations of pain related to wounds. These pain characteristics were thoroughly explored in the clinical study, and a detailed description and discussion of the importance of these characteristics are provided in Paper III. The findings from the clinical study demonstrated that ulcer-related background pain interfered with daily function to a moderate degree. In addition to ulcer-related pain, other biological factors and comorbidities can also impair daily functions. From previous research, CLUs are known to cause physical as well as psychosocial impairment, such as reduced mobility, an inability to dress appropriately and/or maintain personal hygiene, and embarrassment and challenges caused by odour and bandage appearance (Cunha et al., 2017). Additionally, patients with CLUs are often older, as is the case in the present study, in which the majority of participants were over 70 years of age. Even though biological ageing is only loosely associated with a person's age in years, ageing is known to lead to a gradual decrease in physical and mental capacity, and a growing risk of disease (WHO, 2018). Furthermore, patients with CLUs often suffer from several comorbidities, as confirmed in the clinical studies (Papers II and III, Table 2). Comorbidity is associated with impaired health outcomes (Valderas et al., 2009). All these factors add up to a formidable risk of burden and impaired daily function for persons with wounds. Note also that the BPI questionnaire in this study was altered, and encouraged the participants to specifically rate the interference of their ulcer-related background pain and not pain in general. Therefore, based on the findings from the present study, it seems that ulcer-related pain does have a significant negative impact on patients' daily function. The findings underline the importance of developing holistic strategies and treatment options for improving daily functioning in persons with CLUs. These strategies must include assessment and management of multiple impairing factors in addition to ulcer-related pain, in order to reduce the burden of both the complex health condition and the pain.

The participants used a variety of words to describe the quality of their ulcer-related pain. Additionally, all participants described temporal fluctuations and multiple localizations of the pain. This variability in pain quality descriptors and temporal pattern was also supported in a recent study, in which participants used numerous descriptors and most reported intermittent or periodic pain (Kim et al., 2021). Altogether, the variations in pain characteristics (i.e., intensity, interference, pain qualities, location and temporal fluctuations) indicate that ulcer-related pain is multidimensional and complex. Each pain characteristic provides useful information (cf. Chapter 2.2.3) that should guide the clinician to choose an individually tailored approach to pain assessment and treatment. The information from a comprehensive assessment of ulcer-related pain can guide clinicians on how to individualize care and customize interventions. Moreover, individualization presupposes that the clinician understands the patients' life situation, including the pain experiences (Suhonen et al., 2005): Two important findings in this thesis, however, are that not all persons with CLUs experience ulcer-related pain, and not all pain (i.e., mild and tolerable) needs management. Hence, screening for ulcer-related background pain is essential. If the person reports pain that is intense and/or bothersome, there is a need for a thorough pain assessment, including all aspects of the biopsychosocial model of pain.

As previously argued, these findings support and confirm the claim that ulcer-related background pain is still a significant problem, indicating that the current management of ulcer-related background pain is not optimal. However, it is important to consider that not all persons seek pain management despite experiencing significant pain. We did not investigate tolerable or optimal pain goals in this project. One study found a tolerable pain goal of 4.9 (0–10 scale) on average in persons with CVLUs, and that almost half were satisfied with their pain level (Kim et al., 2021). However, a simple assessment of a tolerable pain goal is likely not sufficient to capture the complexity of optimal and tolerable pain. Here, it is essential to assess expectations and potential barriers in relation to pain goals. For instance, persons with CLUs may expect bothersome ulcer-related pain, consider suffering as inevitable with older age and fear addiction to or side effects of treatment. Barriers to pain management (discussed further in Chapter 6.4) may therefore impact pain goals. A thorough assessment is therefore necessary to establish individual pain goals tailored to each person's needs. Further, following the definitions of PCC (Chapter 2.3.2), all persons should be included as partners in their care and treatment, and the needs of the individual should be at the core of decision-making.

6.2 Factors associated with moderate to severe ulcer-related background pain

The analysis of factors associated with moderate to severe ulcer-related pain showed that female gender, older age, and more severe insomnia symptoms were associated with moderate to severe pain (Paper II). The association between female gender and pain in persons with CLUs is supported by previous research (Guarnera et al., 2007), and the association between higher age and insomnia symptoms with more severe pain is supported by previous research in the general population (Mills et al., 2019). Surprisingly, we also found that having better health status enhanced the risk of having moderate to severe ulcer-related background pain. The interaction found between health status and insomnia symptoms further demonstrates that sleep quality has a modifying effect on health status.

The relationship between gender, age, insomnia, health status and pain is complex. All pain, including ulcer-related pain, is a biopsychosocial phenomenon in which biological, psychological and social factors interact dynamically with each other (Gatchel et al., 2007). Hence, pain and health status can have a bi-directional relationship. While pain can be affected by a person's health status, pain can also be a stressor that exceeds normal coping strategies, which may lead to disability and reduced health status (Wahl et al., 2009). Similarly, the relation between pain and sleep also appears to be bi-directional. Pain may influence a person's ability to sleep and impair sleep quality. In turn, lack of sleep or poor sleep can worsen a person's pain perception, making it even more difficult for them to sleep and/or sleep well (Upton & Andrews, 2013). In Paper II, we hypothesize that diminished health status has such great impact on a person's life that the insomnia symptoms become secondary. However, this intricate relationship between health status, sleep and pain needs to be explored further in future research.

The findings from Paper II indicate that health care providers should pay particular attention to persons at greater risk of having moderate to severe ulcer-related background pain, such as older females with insomnia symptoms and good perceived health status. However, the proposed model only explains a small part of the variance in the sample, and we did not find the association between pain and wound-specific biological factors that has been found by other researchers (Domigues et al., 2016; Guarnera et al., 2007; Paul, 2013). The evidence on factors associated with ulcer-related pain thus remains inconclusive. Nevertheless, these findings also support the need for holistic pain assessment of all persons presenting with ulcer-related background pain. The complexity in the interactions between different biopsychosocial factors—such as the interaction between sleep and health status when it comes to ulcer-related pain—further demonstrates the need for individual biopsychosocial assessment of all persons presenting with CLUs, to identify those in need of pain management.

6.3 Management of ulcer-related background pain

The findings pertaining to pain management demonstrated that few participants had been prescribed analgesics specifically for ulcer-related pain. Additionally, the respondents reported that the pain interventions or medications provided a mean pain relief of less than 50%. Suboptimal pain relief was also demonstrated in a recent study on multidimensional pain characteristics in patients with CVLUs, in which 62% reported that only some pain was relieved by previous pain treatment (Kim et al., 2021). Concerningly, the lack of treatment and poor treatment effects indicate that most patients do not receive individualized pain management for their ulcer-related pain.

Barriers to optimal pain management have not yet been explored in wound care, specifically. However, in the literature on chronic pain, known barriers are classified as health care system-related, caregiver-related or patient-related (Zuccaro, 2012). In Norwegian wound care services, one health care system-related barrier might be the organization of wound care itself. The organization (described in Chapter 2.3), where many persons with CLUs receive health care on multiple levels and by various health care professionals, might result in fragmented responsibility for central aspects of care such as pain management. A typical example is that home-care nurses do not have prescription rights, and hence are unable to initiate and administer analgesics without the doctor’s approval. This system barrier is supported by a survey in the United Kingdom that showed that practitioners (mainly nurses) caring for persons with CLUs had limited therapeutic analgesic options (Atkin & Martin, 2020). Interestingly, ulcer-related pain was recognized as one of the top educational priorities by wound care experts (Cowman et al., 2012). However, when wound care professionals were asked, ulcer-related pain was not recognized as an uncertainty—defined as an aspect of wound care where the wound care professionals were not sure of the best way to proceed (Gray et al., 2017). This seeming lack of uncertainty might be a result of the fragmented care for persons with CLUs, as mentioned above. This fragmented care may in turn result in a lack of responsibility. Moreover, if ulcer-related pain is not seen as the health care providers' responsibility, the health care provider presumably does not feel uncertainty.

Another potential barrier for ulcer pain management is lack of time, which is related to both the health care system and the caregiver (Al-Mahrezi, 2017). When spending time in the outpatient wound clinics, I observed a heavy workload and lack of time that may have affected pain assessment and pain management. A heavy workload has been described in other studies (Gray et al., 2019). If the health care provider experiences a lack of time, they likely prioritize the tasks considered most important—in wound care, such tasks are typically wound cleaning and dressing. This could mean that pain management is not necessarily considered unimportant, but simply cannot be prioritized.

Another important and common patient-related barrier in pain management found in the present study was non-adherence to pain management. In fact, one out of four participants reported some form of non-adherence; and, when asked to state reasons for non-adherence specifically to prescribed analgesics, the participants described well-known patient-related barriers such as fear of adverse effects (Paper III, p. 13). Based on these findings, in Paper III, we briefly discussed potential reasons such as intermittent pain, adverse effects, being afraid of addiction or believing that analgesics should only be used when pain is unbearable (Paper III, page 17). Potential barriers to pain management in wound care thus need to be explored in detail in future research and addressed in clinical practice.

As previously mentioned, the attributes of the care provider and the attributes of the care context need to be considered to provide person-centred processes that result in person-centred outcomes. Some of the barriers to pain management noted above are related to the attributes of the care provider (i.e., prerequisites), such as being professionally competent and being able to demonstrate clarity of beliefs and values. Knowledge about ulcer-related background pain may increase the care provider's ability to provide holistic care for persons with CLUs, and it may help alter the staff's beliefs and values pertaining to the need for a more holistic approach to their care. Further, important pain management barriers are also related to the care context or the organization of care. As noted earlier, the organization of wound care in Norway is fragmented and (arguably) disease-oriented (cf. Chapter 2.1.3). At the organizational or system level of care, integrated models of PCC are based on the coordination of services and elimination of care silos (Santana et al., 2018). In Norway, hospitals are obligated to appoint patient care coordinators for patients requiring complex or long-term coordinated services to secure continuity of care in the individual patient trajectory (Helsedirektoratet, 2013). One can easily argue that many persons with CLUs need such coordinated services. Many already receive care from multiple treatment units and professionals. In addition, as discussed further below, there may be a need for referrals to pain specialist or interdisciplinary pain units. If care coordinators can reduce fragmentation and enhance integration, this may result in more efficient services and support the delivery of health services across the continuum of care. Alternatively, given the extent of the problem, wound care clinics might have to consider integrating pain specialists in wound care. While interdisciplinary collaboration is already considered essential for improved wound care outcomes (Dailey, 2005), to my knowledge, pain specialists are not recognized as part of this collaboration since it is largely focused on wound management.

6.4 Holistic approach to ulcer-related pain

As reported in Papers II and III (Tables 1 and 2), the participants in the clinical study had complex health conditions. The majority of the participants were older adults, which is consistent with findings from previous studies (Guest et al., 2018; Bui, 2019). In older adults, wounds are usually caused by a decline in more than one domain of function (Gould et al., 2020). Research has further demonstrated that frailty is prevalent in older adults in wound care, and that degree of frailty is correlated with wound healing and healing time (Espaulella-Ferrer et al., 2021). Frailty represents a global syndrome of decreased physiologic reserves which lead to increased vulnerability to adverse health outcomes (Clegg et al., 2013). Most of the participants in the clinical study had multiple comorbidities, their overall health status was poor, many reported insomnia symptoms, the mean duration of the CLUs were substantial and many of the participants had experienced reoccurrence of ulcers. In addition, many of the participants lived alone, which could contribute to increased social isolation. We do not know whether persons receiving wound care in specialized wound clinics in Norway are significantly different from those receiving care only through homecare or from the GP or those who self-care. An Australian study that compared persons receiving wound management through homecare and wound clinics found several differences between the two groups. The most important one was that persons receiving homecare services had a greater number of risk factors for delayed healing (Ogrin et al., 2021). Hence, the complexity demonstrated in the studies in this thesis might be even more profound in persons receiving homecare nursing. Further, the range and SD in the demographic and clinical variables of the clinical study, together with the variation in pain characteristics, indicate great heterogeneity. Research demonstrates that older adults are an especially heterogeneous group, differing in their perceptions and needs, interest in their own health and ability to participate in medical decisions (Bastiaens et al., 2007). This should serve as a reminder of the heterogeneity of persons with CLUs.

The complexity and heterogeneity in demographic variables identified in this project strengthen the evidence pointing towards CLUs being complex health conditions (Bui, 2019). This complexity is further exacerbated by challenges with ulcer-related pain. The main issue studied in this thesis—namely, ulcer-related background pain—is arguably complex (as previously discussed). In addition, one must take into consideration that dressing-related pain is frequently a concomitant problem (Price et al., 2008) that further complicates the care. This complexity and heterogeneity clearly indicate the need for a holistic approach in wound care—one that considers all aspects and potential challenges concerning persons living with CLUs.

Due to the complexity of persons with CLUs and the complexity and duration of pain, the management of ulcer-related background pain can be challenging. Pain management consists of assessment, planning, treatment, evaluation and reassessment of pain (IASP, 2020); as previously mentioned, nurses play an important role in this respect. However, if the management of ulcer-related background pain is especially challenging, and management is not successful, nurses and other health care workers providing wound care should consider referring the person to pain specialists and/or interdisciplinary pain clinics.

6.5 Methodological considerations

A systematic review and a descriptive clinical study were carried out in this PhD project. The systematic review provided a synthesis of the existing research, while the clinical observational study generated new and updated knowledge on background pain in persons with CLUs. The two research methods used in the study were thoroughly designed and meticulously carried out, as well as appropriate for answering the research questions. The methodological strengths and limitations will be illuminated and discussed in the following.

The biopsychosocial model of pain and the theory of PCC informed the development of this PhD project and guided the formation of research questions and the selection of variables, in both the systematic review and the clinical study. The findings provide important knowledge about the experience of ulcer-related background pain, and include findings pertaining to biological and psychological factors, as well as sociocultural factors. The sociocultural component of pain is scarcely covered in commonly used pain and QoL measures. Although the MPQ assesses pain as a multidimensional phenomenon (Melzak, 1975), the SF-MPQ does not pose questions about the sociocultural aspects of pain. Similarly, the BPI only covers this aspect by including the pain interference item ‘relation with others’. As a consequence, the sociocultural aspect of ulcer-related background pain was described in this study only to a limited extent. Furthermore, the sample size also prevented us from including sociodemographic variables in the regression analysis (Paper II). We were therefore unable to explore the association between such variables and ulcer-related background pain. Hence, future studies should describe and explore —in detail— sociocultural factors related to ulcer-related background pain.

In our data collection for the systematic review, we used a broad search strategy to capture as many relevant studies as possible. By imposing strict selection criteria, we sought to limit the impact of clinical heterogeneity, hence strengthening the quality of our results. Further, to be included, eligible studies had to meet the MMAT's strict methodological quality criteria. As described in Paper I (p. 468), we initially set out to use a systematic, mixed-studies review methodology, including studies with diverse research designs. Hence, the MMAT was used to assess the quality of eligible studies. Despite our decision to only include quantitative studies, we did not change the appraisal tool. We did not consider this mixed-methods tool to pose a quality problem, as the assessment criteria are as comprehensive as other similar tools used exclusively for quantitative methods. In combination with our use of PRISMA guidelines, these methodological considerations ensured that we obtained the best available research data to explore the prevalence and characteristics of ulcer-related background pain in persons with CVLUs.

A strength of the clinical study is the consecutive sampling we employed. Consecutive recruitment means that all persons treated at the outpatient clinics who met the eligibility criteria over a specific period (here, predefined days when the recruiter was present at the outpatient clinics) were recruited (Polit & Beck, 2017). Although considered non-probability sampling, consecutive sampling is regarded as a better approach than convenience sampling, as it provides structure and thus additional rigour, in that it includes all persons who are accessible within the defined study time period (Mathieson, 2014; Thewes et al., 2018). Furthermore, consecutive sampling in a clinical setting (like that in this project) provides insight into the number of eligible persons, enabling calculation of an accurate response rate (Thewes et al., 2018). In this project, I performed all recruitment, avoiding the potential recruitment bias frequently seen when clinicians invite participants (e.g., greater focus on medical problems and lack of clinician engagement) (Thewes et al., 2018). Although time-consuming, consecutive sampling was considered the best sampling strategy for the purpose of exploring ulcer-related background pain and management, given the limited availability of eligible participants.

Data must be collected from a representative sample of persons with CLUs in order to run inference statistics and generalize the findings to the patient population. In the clinical study, we recruited a sample of persons with CLUs receiving care at the selected outpatient clinics. There is no available research or national guidelines on the organization of wound care in Norway (Heiberg & Langøen, 2019), resulting in uncertainties about differences between persons referred to and treated in wound care clinics, by clinical specialists, and persons treated in primary care by homecare nurses or GPs. To account for potential differences, we originally set out to recruit participants from both specialist and primary care settings. However, the process of obtaining permission from the data protection officer (*personvernombud*) for primary care in the municipalities was challenging. One data protection officer explained that the reason for the tedious permission process was the introduction of the European Union's General Data Protection Regulation (Personopplysningsloven, 2018), which the municipalities were unsure how to interpret. After a long and time-consuming process, we decided to focus on the already established data collection in the outpatient wound care clinics, resulting in a more homogenous recruitment setting. However, from our knowledge about the organization of wound care in Norway, many of those receiving care at outpatient wound clinics also receive homecare nursing. Further, inclusion from additional outpatient clinics would have been preferrable: This would have provided results that could be more generalizable to the population by ensuring diversity more closely related to the population. However, given the time-consuming data collection, it was difficult to find the time and resources within the scope of a PhD project to include participants from more outpatient clinics. While this could have been solved by asking clinicians to contribute to the data collection, in addition to the potential recruitment bias noted above, such a change in the design could also have increased the number of non-responders, as personally distributed questionnaires more often achieve good response rates (Polit & Beck, 2017). Nevertheless, the response rate in the present study was good, the included participants contributed to a rich data set, and the sample was sufficient to provide answers to the research questions.

Furthermore, we chose to only recruit persons who were able to understand and read Norwegian and had no comprehension difficulties. By choosing this inclusion criteria we did not adhere to the new definition of pain, which clearly highlights that a person does not need to be able to express pain to experience pain. However, as previously mentioned, pain assessment in persons who are unable to self-report calls for different pain assessment methods (Herr et al., 2011). We were unable to include this form of assessment in this clinical study; research on ulcer-related pain in persons who are unable to self-report should therefore be prioritized in future studies.

Non-response in cross-sectional studies is a well-known challenge (Sedgwick, 2015). The response rate of 69% for the self-report questionnaires in the present study should be considered good, given the sample's advanced age and serious health conditions. A decreased response rate in older adults due to visual and sensory disorders, fatigue and the impact of multiple comorbidities have been reported (Selmer, 2003). In addition, the fact that we did not register those who refused to participate in the study represents a limitation, as this makes it impossible to assess selection bias. A potential selection bias in this study might be a bias towards relatively healthy participants. This is a recognized challenge (Hébert, 1996) and is difficult to avoid, as older adults who are frailer might have more trouble filling in the questionnaires. To reduce the risk of this form of selection bias, we selected variables and questionnaires with this in mind, ensuring a short and easily comprehensible questionnaire battery.

A combination of methods and tools were used to collect data in the clinical study, such as a screening interview, clinical assessments and self-report questionnaires, including a number of validated instruments. The use of data from patients' self-report and clinicians' assessment contributed to a more comprehensive approach to the exploration of ulcer-related background pain. The instruments used to assess pain intensity, quality descriptors of pain, pain interference, temporal fluctuations, health status and insomnia symptoms are all considered valid measures of the represented construct (cf. Chapter

5.3.3). Most instruments have been used in previous CLU studies but have not been validated specifically for use in persons with CLUs. Note that the instruments assessing pain (the BPI and SF-MPQ) were linguistically adjusted in the present study to ensure assessment of aspects of ulcer-related background pain (the adjustments are described in Chapter 4.3.4). In general, changes made to a questionnaire may affect the validity of the tool. However, the adjustments made in the present study were minor, and were considered by the research group not to pose a considerable threat to the tool's validity. Adjustments were also discussed with and supported by the researcher responsible for the Norwegian SF-MPQ. However, the MD Anderson Cancer Center, who is responsible for the BPI, did not reply to our inquiries regarding the adjustments. Nevertheless, we believe that the changes strengthened the quality of the data obtained, since these specifications ensured that the participants provided answers that reflected characteristics of their ulcer-related pain rather than those of other painful conditions, which indeed were prevalent in the sample.

Concerning the reliability of the questionnaires, Cronbach's α was employed as an estimate for internal reliability (cf. Chapter 5.4.4). The Cronbach's α for the SF-MPQ, BPI and ISI were all high and considered to indicate good consistency between the items comprising the questionnaire (0.9 for all instruments) (Pallant, 2017). However, since the results were at tangent with the Cronbach's α level of redundancy of items (0.9) (Pallant, 2017), the questionnaires should be evaluated for overlapping questions and the need to reduce items. Further, consistency in the data collection was ensured by one person conducting all screening interviews and clinical tests (Polit & Beck, 2017). Initially, and before beginning data collection, we considered including more instruments to provide insight into even more aspects of the complexity related to the person, the pain experience and the ulcer. However, we considered it of utmost importance to reduce the burden of participation for the participants. This was an ethical consideration and especially important given the existing knowledge about the age and frailty of the population under study. By limiting the number of variables, we reduced the burden of participation to a minimum, which was important to ensure that participants were not exhausted. This approach likely also enhanced completion of questionnaires, and presumably prevented missing data in the self-report questionnaires. In addition, we considered it important to use simple and effective measures that can easily be integrated in clinical practice. Hence, the number and types of variables included in the study were carefully considered to enhance the quality of the data.

In addition, and importantly, the assessment method and instruments used to gather data in this project are simple to use and easily available for clinicians. This means that the method should be considered relevant to use in assessment of ulcer-related pain, both in future studies and in clinical practice. The method provides comprehensive information about the characteristics, impact and management of ulcer-related pain: This information should be considered relevant when assessing pain, and when initiating and evaluating management (cf. Chapter 2.2.3).

7 Conclusion

The studies in this thesis have demonstrated that background pain is a prevalent symptom in persons with CLUs. The findings demonstrate that approximately 60% of persons experiencing ulcer-related background pain report moderate to severe pain intensity and that pain interferes with daily function, suggesting that this is a significant and interfering problem. The heterogeneity and variation in the pain characteristics described confirm the complexity of ulcer-related background pain and give support to the importance of thorough pain assessment in all persons reporting ulcer-related background pain. This thesis further suggests that background pain is still undertreated in person with CLUs, despite heightened awareness of and clinical advantages in pain management over the last several decades. Moreover, this indicates that persons with CLUs may need a variety of medical and non-medical treatment options, and that interdisciplinary management might be needed.

7.1 Implications for clinical practice

This thesis provides evidence of the prevalence of ulcer-related background pain in persons with CLUs receiving wound care in outpatient clinics in Norway. Further, a comprehensive description of characteristics of ulcer-related background pain is provided. Such a description can provide useful epidemiological information for planning health care services and for educating health care professionals. The findings can further inform clinical practice on the importance of recognizing ulcer-related background pain. This recognition can play a vital role in providing holistic management of CLUs, improving patients' QoL, reducing the symptom burden and potentially improve wound healing.

PCC is a guiding principle in the organization of care (WHO, 2013). According to the Person-Centred Practice Framework (McCance & McCormack, 2016), one must first consider prerequisites and the care environment in order to facilitate a PCC process and to deliver person-centred outcomes for patients with CLUs. It is my opinion that knowledge generated in this thesis is essential when considering prerequisites and the care environment in wound care. Knowledge about the method used and the findings can make wound care providers more competent, and can support their ability to demonstrate clarity of beliefs and values. More specifically, the pain assessment method in this thesis can be used in clinical practice to improve pain assessment. Furthermore, knowledge of characteristics and factors associated with ulcer-related pain can enhance the staff's ability to choose the most appropriate pain management, and it can help alter the staff's beliefs and values pertaining to the need for a more holistic approach when encountering persons with CLUs.

Increased knowledge may also stimulate change at an organizational level by provoking a shift in focus—from a uniform biomedical focus on wound healing to a multidimensional focus on the consequences of living with a persistent ulcer. This thesis demonstrates the complexity of ulcer-related background pain in particular and confirms the complexity of persons with CLUs in general. This complexity challenges both the health care system and care delivery. Caring for persons with CLUs should involve interpersonal and interdisciplinary collaboration. The evidence from this thesis can assist policy-makers and health care organizers in implementing PCC strategies and enhancing collaboration between different health care specialists. Finally, the knowledge provided in this thesis should be used to inform and prepare future health care professionals in order to improve practice.

This project thus provides knowledge needed in the prerequisite and care environment constructs of the Person-Centred Practice Framework. Hopefully, the findings may contribute to an improved and more person-centred health service for persons with CLUs.

7.2 Concluding remarks and future research

The results presented in this thesis can be used as a starting point for further research and investigation into ulcer-related pain, filling a crucial knowledge gap in the literature. Within the previous chapters, in the discussion of this thesis, and in the three separate papers, recommendations for future research are suggested. I have presented ways in which the findings may be built upon, and I have outlined shortcomings of this project that should be explored further in future research.

This thesis provides new knowledge on factors associated with moderate to severe ulcer-related pain. However, due to the cross-sectional design, we were unable to establish causal relationships, and the intricate relationship between pain, health status and sleep requires further investigation. Furthermore, even though we sought to include biological, psychological and sociocultural variables in our exploration of ulcer-related background pain, a more detailed exploration of sociocultural factors is needed (cf. Chapter 6.5).

The findings in this thesis further indicate that current management of ulcer-related background pain is not successful, indicating a need for further research on the effect of pain management in wound care. In addition, research is also needed on holistic interventions aimed at improving wound care in order to minimize pain, and to improve pain management. Such interventions should be guided by the principles of PCC. Furthermore, interdisciplinary collaboration and the use of tele-health might be a promising venue in this regard.

However, we have also built upon our own research. For instance, in our review of the literature, we found that researchers do not use standardized methods to assess CVLUs and core outcome measures such as pain. Hence, there is a need for valid and standardized assessment methods. In addition, the variation in pain intensity identified in the systematic review calls for a shift in focus from mean pain values to variation and subgroup analyses. In the clinical study, we provided an extensive but easily feasible method to assess pain in clinical studies on persons with CLUs; moreover, we demonstrated clinically relevant analyses to provide information on subgroups (such as persons with moderate to severe ulcer-related pain). However, the method has some limitations (cf. Chapter 6.5), and further validation is needed. Overall, the results from this study provide insight into challenges in wound pain care and can be used to improve wound care in general, as well as pain management in wound care specifically. Persons with CLUs can benefit from the results of this study, as it may lead to better identification and management of their pain. Hence, persons with CLUs, clinicians, researchers and the health care system alike may benefit from the findings of this research project.

8 References

Agale, S. V. (2013). Chronic leg ulcers: Epidemiology, aetiopathogenesis, and management. *Ulcers*, *2013*. https://doi.org/10.1155/2013/413604

Aggarwal, R., & Ranganathan, P. (2019). Study designs: Part 2–descriptive studies. *Perspectives in Clinical Research*, *10*(1), 34–36.

American Nurses Association Ethics Advisory Board. (2018). ANA position statement: The ethical responsibility to manage pain and the suffering it causes. *Online Journal of Issues in Nursing*, *24*(1). https://doi.org/10.3912/OJIN.Vol24No01PoSCol01

Babineau, J. (2014). Product review: Covidence (systematic review software). *Journal of the Canadian Health Libraries Association*, *35*(2), 68–71.

Barendregt, J. J., Doi, S. A., Lee, Y. Y., Norman, R. E., & Vos, T. (2013). Meta-analysis of prevalence. *Journal of Epidemiology and Community Health*, *67*(11), 974–978.

Bastami, S., Frödin, T., Ahlner, J., & Uppugunduri, S. (2012). Topical morphine gel in the treatment of painful leg ulcers, a double-blind, placebo-controlled clinical trial: A pilot study. *International Wound Journal*, *9*(4), 419–427.

Bastiaens, H., Van Royen, P., Pavlic, D. R., Raposo, V., & Baker, R. (2007). Older people's preferences for involvement in their own care: A qualitative study in primary health care in 11 European countries. *Patient Education and Counseling*, *68*(1), 33–42.

Bastien, C. H., Vallières, A., & Morin, C. M. (2001). Validation of the Insomnia Severity Index as an outcome measure for insomnia research. *Sleep Medicine*, *2*(4), 297–307.

Benbow, M. (2016). Best practice in wound assessment. *Nursing Standard*, *30*(27), 40–47.

Bornmann, L., & Mutz, R. (2015). Growth rates of modern science: A bibliometric analysis based on the number of publications and cited references. *Journal of the Association for Information Science and Technology*, *66*(11), 2215–2222.

Breivik, H., Borchgrevink, P.-C., Allen, S.-M., Rosseland, L.-A., Romundstad, L., Breivik Hals, E., Kvarstein, G., & Stubhaug, A. (2008). Assessment of pain. *British Journal of Anaesthesia*, *101*(1), 17–24.

Breivik, H., Collett, B., Ventafridda, V., Cohen, R., & Gallacher, D. (2006). Survey of chronic pain in Europe: Prevalence, impact on daily life, and treatment. *European Journal of Pain*, *10*(4), 287–333.

Breivik, H., Eisenberg, E., & O'Brien, T. (2013). The individual and societal burden of chronic pain in Europe: The case for strategic prioritisation and action to improve knowledge and availability of appropriate care. *BMC Public Health*, *13*. https://doi.org/10.1186/1471-2458-13-1229

Bui, U. T. (2019) Risk factors associated with infection in patients with chronic leg ulcers (Doctoral dissertation, Queensland University of Technology). http://eprints.quit.edu.au/124477/14/Ut_Tui_Bui_thesis.pdf

Chandler, J., Higgins, J., Deeks, J., Davenport, C., & Clarke, M. (2021). Introduction. In J. Higgins, J. Thomas, J. Chandler, M. Cumpston, T. Li, M. Page, & V. Welch (Eds.), *Cochrane handbook for systematic reviews of interventions version* (2nd ed., chap. 1). John Wiley & Sons.

Charles, H. (1995). The impact of leg ulcers on patients' quality of life. *Professional Nurse*, *10*(9), 571–574.

Chase, S. K., Whittemore, R., Crosby, N., Freney, D., Howes, P., & Phillips, T. J. (2000). Living with chronic venous leg ulcers: A descriptive study of knowledge and functional health status. *Journal of Community Health Nursing*, *17*(1). https://doi.org/10.1207/S15327655JCHN1701_01

Christensen, J., Bilde, L., & Gustavsson, A. (2011). *Socio-economic consequences of pain-intensive diseases in Denmark*. Danish Institute for Health Services Research.

Cleeland, C. S. (2009). *The brief pain inventory user guide*. The University of Texas MD Anderson Cancer Center.

Cleeland, C. S., & Ryan, K. M. (1994). Pain assessment: Global use of the Brief Pain Inventory. *Annals of the Academy of Medicine, Singapore, 23*(2), 129–138

Collins, S. L., Moore, R. A., & McQuay, H. J. (1997). The visual analogue pain intensity scale: What is moderate pain in millimetres? *Pain*, *72*(1-2), 95–97.

Cowman, S., Gethin, G., Clarke, E., Moore, Z., Craig, G., Jordan-O'Brien, J., McLain, N., & Strapp, H. (2012). An international eDelphi study identifying the research and education priorities in wound management and tissue repair. *Journal of Clinical Nursing*, *21*(3-4), 344–353.

Cunha, N., Campos, S., & Cabete, J. (2017). Chronic leg ulcers disrupt patients' lives: A study of leg ulcer-related life changes and quality of life. *British Journal of Community Nursing*, *22*(Sup9), S30–S37.

Dailey, M. (2005). Interdisciplinary collaboration: Essential for improved wound care outcomes and wound prevention in home care. *Home Health Care Management & Practice*, *17*(3), 213–221.

Day, M. A., Ehde, D. M., Ward, L. C., Hartoonian, N., Alschuler, K. N., Turner, A. P., Kraft, G. H., & Jensen, M. P. (2016). An empirical investigation of a biopsychosocial model of pain in multiple sclerosis. *The Clinical Journal of Pain*, *32*(2), 155–163.

Decorps, J., Saumet, J. L., Sommer, P., Sigaudo-Roussel, D., & Fromy, B. (2014). Effect of ageing on tactile transduction processes. *Ageing Research Reviews*, *13*, 90–99.

Deeks, J. J., Higgins, J. P., & Altman, D. G. (2011). Analysing data and undertaking meta-analyses. In J. P. Higgins & S. Green (Eds.), *Cochrane handbook for systematic reviews of interventions* (2nd ed., chap. 9).

Direktorat for e-helse (2021). *ICD-10: Den internasjonale statistiske klassifikasjonen av sykdommer og beslektede helseproblemer*. https://finnkode.ehelse.no/#icd10/0/0/0/-1

Do, H. T. T., Edwards, H., & Finlayson, K. (2016). Identifying relationships between symptom clusters and quality of life in adults with chronic mixed venous and arterial leg ulcers. *International Wound Journal*, *13*(5), 904–911.

Dowell, D., Haegerich, T. M., & Chou, R. (2016). CDC guideline for prescribing opioids for chronic pain—United States, 2016. *JAMA*, *315*(15), 1624–1645.

Edwards, H., Finlayson, K., Maresco-Pennisi, D., Gibb, M., Parker, C., & Graves, N. (2014). The long and winding road: Health services for clients with chronic leg ulcers in the community. *Wound Practice & Research: Journal of the Australian Wound Management Association*, *22*(4), 226–233.

Engle, R. L., Mohr, D. C., Holmes, S. K., Seibert, M. N., Afable, M., Leyson, J., & Meterko, M. (2021). Evidence-based practice and patient-centered care: Doing both well. *Health Care Management Review*, *46*(3), 174–184.

European Wound Management Association. (2002). *Pain at wound dressing changes* [Position statement]. http://ewma.org/fileadmin/user_upload/EWMA/pdf/Position_Documents/2002/Spring_2002__English_.pdf

Faber, A. W., Patterson, D. R., & Bremer, M. (2013). Repeated use of immersive virtual reality therapy to control pain during wound dressing changes in pediatric and adult burn patients. *Journal of Burn Care & Research*, *34*(5), 563–568.

Fearns, N., Heller-Murphy, S., Kelly, J., & Harbour, J. (2017). Placing the patient at the centre of chronic wound care: A qualitative evidence synthesis. *Journal of Tissue Viability*, *26*(4), 254–259.

Filosa, J., Omland, P. M., Langsrud, K., Hagen, K., Engstrøm, M., Drange, O. K., Knutsen, A. J., Brenner, E., Kallestad, H., & Sand, T. (2020). Validation of insomnia questionnaires in the general population: The Nord-Trøndelag Health Study (HUNT). *Journal of Sleep Research*, *30*(1). https://doi.org/10.1111/jsr.13222

Fine, P. G. (2011). Long-term consequences of chronic pain: Mounting evidence for pain as a neurological disease and parallels with other chronic disease states. *Pain Medicine*, *12*(7), 996–1004.

Flett, R., Harcourt, B., & Alpass, F. (1994). Psychosocial aspects of chronic lower leg ulceration in the elderly. *Western Journal of Nursing Research*, *16*(2), 183–192.

Frescos, N. (2018). Assessment of pain in chronic wounds: A survey of Australian health care practitioners. *International Wound Journal*, *15*(6), 943–949.

Frescos, N. (2019). Pain assessment tools for chronic lower limb wounds: A scoping review. *Wound Practice & Research: Journal of the Australian Wound Management Association*, *27*(1), 27–35.

Frykberg, R. G., & Banks, J. (2015). Challenges in the treatment of chronic wounds. *Advances in Wound Care*, *4*(9), 560–582.

Gatchel, R. J. (2004). Comorbidity of chronic pain and mental health disorders: The biopsychosocial perspective. *American Psychologist*, *59*(8), 795–805.

Germossa, G. N., Hellesø, R., & Sjetne, I. S. (2019). Hospitalized patients' pain experience before and after the introduction of a nurse-based pain management programme: A separate sample pre and post study. *BMC Nursing*, *18*(1). https://doi.org/10.1186/s12912-019-0362-y

Gethin, G., Probst, S., Stryja, J., Christiansen, N., & Price, P. (2020). Evidence for person-centred care in chronic wound care: A systematic review and recommendations for practice. *Journal of Wound Care*, *29*(Sup9b), S1-S22.

Gilron, I., Attal, N., Bouhassira, D., & Dworkin, R. (2011). Assessment of neuropathic pain. In D. C. Turk & R. Melzack (Eds.), *Handbook of pain assessment* (3rd ed.). The Guilford Press.

Gjeilo, K. H., Stenseth, R., Wahba, A., Lydersen, S., & Klepstad, P. (2007). Validation of the brief pain inventory in patients six months after cardiac surgery. *Journal of Pain and Symptom Management*, *34*(6), 648–656.

Gjesdal, K., Dysvik, E., & Furnes, B. (2018). Living with chronic pain: Patients' experiences with healthcare services in Norway. *Nursing Open*, *5*(4), 517–526.

Gonçalves, M. L., de Gouveia Santos, V. L. C., de Mattos Pimenta, C. A., Suzuki, É., & Komegae, K. M. (2004). Pain in chronic leg ulcers. *Journal of Wound Ostomy & Continence Nursing*, *31*(5), 275–283.

González-Consuegra, R. V., & Verdú, J. (2011). Quality of life in people with venous leg ulcers: An integrative review. *Journal of Advanced Nursing*, *67*(5), 926–944.

Gould, L., Abadir, P., Brem, H., Carter, M., Conner-Kerr, T., Davidson, J., DiPietro, L., Falanga, V., Fife, C., Gardner, S., Grice, E., Harmon, J., Hazzard, W. R., High, K. P., Houghton, P., Jacobson, N., Kirsner, R. S., Kovacs, E. J., Margolis, D., McFarland Horne, F., . . . Gardner, S. (2015). Chronic wound repair and healing in older adults: Current status and future research. *Journal of the American Geriatrics Society*, *63*(3), 427–438.

Graham, I. D., Harrison, M. B., Nelson, E. A., Lorimer, K., & Fisher, A. (2003). Prevalence of lower-limb ulceration: A systematic review of prevalence studies. *Advances in Skin & Wound Care*, *16*(6), 305–316.

Gray, T. A., Dumville, J. C., Christie, J., & Cullum, N. A. (2017). Rapid research and implementation priority setting for wound care uncertainties. *PLOS One*, *12*(12). https://doi.org/10.1371/journal.pone.0188958

Gray, T. A., Wilson, P., Dumville, J. C., & Cullum, N. A. (2019). What factors influence community wound care in the UK? A focus group study using the Theoretical Domains Framework. *BMJ Open*, *9*(7). https://doi.org/10.1136/bmjopen-2018-024859

Green, J., Jester, R., McKinley, R., & Pooler, A. (2014). The impact of chronic venous leg ulcers: A systematic review. *Journal of Wound Care*, *23*(12), 601–612.

Green, J., Jester, R., McKinley, R., & Pooler, A. (2018). Chronic venous leg ulcer care: Putting the patient at the heart of leg ulcer care. Part 1: Exploring the consultation. *British Journal of Community Nursing*, *23*(Sup3), S30–S38.

Grey, J. E., Harding, K. G., & Enoch, S. (2006). ABC of wound healing: Venous and arterial leg ulcers. *British Medical Journal*, *332*(7537), 347–350.

Grichnik, K., & Ferrante, F. (1991). The difference between acute and chronic pain. *The Mount Sinai Journal of Medicine*, *58*(3), 217–220.

Griffin, S. J., Kinmonth, A.-L., Veltman, M. W., Gillard, S., Grant, J., & Stewart, M. (2004). Effect on health-related outcomes of interventions to alter the interaction between patients and practitioners: A systematic review of trials. *The Annals of Family Medicine*, *2*(6), 595–608.

Guarnera, G., Tinelli, G., Abeni, D., Di Pietro, C., Sampogna, F., & Tabolli, S. (2007). Pain and quality of life in patients with vascular leg ulcers: An Italian multicentre study. *Journal of Wound Care*, *16*(8), 347–351.

Gupta, S., Andersen, C., Black, J., de Leon, J., Fife, C., Li J. C. L., Niezgoda, J., Snyder, R., Sumpio, B., Tettelbach, W., Treadwell, T., Weir, D., & Silverman, R. P. (2017). Management of chronic wounds: Diagnosis, preparation, treatment, and follow-up. *Wounds: A Compendium of Clinical Research and Practice*, *29*(9), S19–S36.

Gupta, S., Sagar, S., Maheshwari, G., Kisaka, T., & Tripathi, S. (2021). Chronic wounds: Magnitude, socioeconomic burden and consequences. *Wounds Asia*, *4*(1), 8–14.

Gustavsson, A., Bjorkman, J., Ljungcrantz, C., Rhodin, A., Rivano-Fischer, M., Sjolund, K. F., & Mannheimer, C. (2012). Socio-economic burden of patients with a diagnosis related to chronic pain—register data of 840,000 Swedish patients. *European Journal of Pain*, *16*(2), 289–299.

Hagatun, S., Vedaa, Ø., Nordgreen, T., Smith, O. R., Pallesen, S., Havik, O. E., Bjorvatn, B., Thorndike, F. P., Ritterband, L. M., & Sivertsen, B. (2019). The short-term efficacy of an unguided internet-based cognitive-behavioral therapy for insomnia: A randomized controlled trial with a six-month nonrandomized follow-up. *Behavioral Sleep Medicine*, *17*(2), 137–155.

Hahnel, E., Blume-Peytavi, U., Trojahn, C., & Kottner, J. (2017). Associations between skin barrier characteristics, skin conditions and health of aged nursing home residents: A multi-center prevalence and correlational study. *BMC Geriatrics*, *17*(1). https://doi.org/10.1186/s12877-017-0655-5

Håkansson Eklund, J., Holmström, I. K., Kumlin, T., Kaminsky, E., Skoglund, K., Höglander, J., Sundler, A. J., Condén, E., & Merenius, M. S. (2019). "Same" or different? A review of reviews of person-centred and patient-centred care. *Patient Education and Counseling*, *102*(1), 3–11.

Hansen, T. M., Helland, Y., Augestad, L. A., Rand, K., Stavem, K., & Garratt, A. (2020). Elicitation of Norwegian EQ-5D-5L values for hypothetical and experience-based health states based on the EuroQol Valuation Technology (EQ-VT) protocol. *BMJ Open*, *10*(6). https://doi.org/10.1136/bmjopen-2019-034683

Heale, R., & Twycross, A. (2015). Validity and reliability in quantitative studies. *Evidence-Based Nursing*, *18*(3), 66–67.

Heiberg, I. G., & Langøen, A. (2019). Kroniske sår følges ikke opp riktig. *Sykepleien*, *107*(75816). https://doi.org/10.4220/Sykepleiens.2019.75701

Heinen, M., Evers, A., Van Uden, C., Van der Vleuten, C., Van De Kerkhof, P., & Van Achterberg, T. (2007). Sedentary patients with venous or mixed leg ulcers: Determinants of physical activity. *Journal of Advanced Nursing*, *60*(1), 50–57.

Heinze, G., Wallisch, C., & Dunkler, D. (2018). Variable selection—a review and recommendations for the practicing statistician. *Biometrical Journal*, *60*(3), 431–449.

Helsedirektoratet (2013). *Spesialisthelsetjenesteloven med kommentar*. https://www.helsedirektoratet.no/tema/spesialisthelsetjenesteloven

Hermans, M. H. (2010). Wounds and ulcers: Back to the old nomenclature. *Wounds*, *22*(11), 289–293.

Herr, K., Coyne, P. J., McCaffery, M., Manworren, R., & Merkel, S. (2011). Pain assessment in the patient unable to self-report: Position statement with clinical practice recommendations. *Pain Management Nursing*, *12*(4), 230–250.

Hjelmers, A.-K. B. (2019). *Kroniske sår: – Ingen vil egentlig ha disse pasientene, fordi de er økonomisk ugunstige*. https://sykepleien.no/2019/02/kroniske-sar-ingen-vil-egentlig-ha-disse-pasientene-fordi-de-er-okonomisk-ugunstige

Hjermstad, M. J., Fayers, P. M., Haugen, D. F., Caraceni, A., Hanks, G. W., Loge, J. H., Fainsinger, R., Aass, N., & Kaasa, S. (2011). Studies comparing Numerical Rating Scales, Verbal Rating Scales, and Visual Analogue Scales for assessment of pain intensity in adults: A systematic literature review. *Journal of Pain and Symptom Management*, *41*(6), 1073–1093.

Hofman, D., Ryan, T., Arnold, F., Cherry, G., Lindholm, C., Bjellerup, M., & Glynn, C. (1997). Pain in venous leg ulcers. *Journal of Wound Care*, *6*(5), 222–224.

Hozo, S. P., Djulbegovic, B., & Hozo, I. (2005). Estimating the mean and variance from the median, range, and the size of a sample. *BMC Medical Research Methodology*, *5*(1). https://doi.org/10.1186/1471-2288-5-13

Hush, J. M. (2020). Low back pain: It is time to embrace complexity. *Pain, 161*(10), 2248–2251.

International Association for the Study of Pain. (2020). *IASP terminology*. https://www.iasp-pain.org/resources/terminology/

International Council of Nurses. (2012). *The ICN code of ethics for nurses*. https://www.icn.ch/system/files/2021-10/ICN_Code-of-Ethics_EN_Web_0.pdf

Järbrink, K., Ni, G., Sönnergren, H., Schmidtchen, A., Pang, C., Bajpai, R., & Car, J. (2016). Prevalence and incidence of chronic wounds and related complications: A protocol for a systematic review. *Systematic Reviews*, *5*(1). https://doi.org/10.1186/s13643-016-0329-y

Jelsness-Jørgensen, L.-P., Moum, B., Grimstad, T., Jahnsen, J., Opheim, R., Prytz Berset, I., Hovde, Ø., Torp, R., Frigstad, S. O., & Huppertz-Hauss, G. (2016). Validity, reliability, and responsiveness of the brief pain inventory in inflammatory bowel disease. *Canadian Journal of Gastroenterology and Hepatology*, *2016*. https://doi.org/10.1155/2016/5624261

Jenkins, S. (2020). The assessment of pain in chronic wounds (part 2). *Wounds UK*, *16*(4), 36–44.

Jensen, M., Galer, B., & Gammaitomi, A. (2010). *The Pain Quality Assessment Scale (PQAS) and Revised Pain Quality Assessment Scale (PQAS-R): Manual and user guide*. http://www. mapi-trust.org

Jensen, M. P., & Karoly, P. (2011). Self-report scales and procedures for assessing pain in adults. In D. C. Turk & R. Melzack (Eds.), *Handbook of pain assessment* (pp. 19–44). The Guilford Press.

Jones, J. E., & Carlisle, C. (2008). Impact of exudate and odour from chronic venous leg ulceration. *Nursing Standard*, *22*(45), 53–54.

Kahl, C., & Cleland, J. A. (2005). Visual analogue scale, numeric pain rating scale and the McGill Pain Questionnaire: An overview of psychometric properties. *Physical Therapy Reviews*, *10*(2), 123–128.

Kallestad, H., Hansen, B., Langsrud, K., Hjemdal, O., & Stiles, T. C. (2010). Psychometric properties and the predictive validity of the insomnia daytime worry scale: A pilot study. *Cognitive Behaviour Therapy*, *39*(2), 150–157.

Kallestad, H., Jacobsen, H. B., Landrø, N. I., Borchgrevink, P. C., & Stiles, T. C. (2015). The role of insomnia in the treatment of chronic fatigue. *Journal of Psychosomatic Research*, *78*(5), 427–432.

Kapstad, H., Hanestad, B. R., Langeland, N., Rustøen, T., & Stavem, K. (2008). Cutpoints for mild, moderate and severe pain in patients with osteoarthritis of the hip or knee ready for joint replacement surgery. *BMC Musculoskeletal Disorders*, *9*(1). https://doi.org/10.1186/1471-2474-9-55

Kapstad, H., Rokne, B., & Stavem, K. (2010). Psychometric properties of the Brief Pain Inventory among patients with osteoarthritis undergoing total hip replacement surgery. *Health and Quality of Life Outcomes*, *8*(1). https://doi.org/10.1186/1477-7525-8-148

Kim, J., Wilkie, D., Weaver, M., Lyon, D., Kelly, D. L., Millan, S. B., Park, J., & Stechmiller, J. (2021). Multidimensional pain characteristics in older adults with chronic venous leg ulcers. *Advances in Wound Care*, *10*(10), 544–556.

Kitson, A., Marshall, A., Bassett, K., & Zeitz, K. (2013). What are the core elements of patient-centred care? A narrative review and synthesis of the literature from health policy, medicine and nursing. *Journal of Advanced Nursing*, *69*(1), 4–15.

Klein, T. M., Andrees, V., Kirsten, N., Protz, K., Augustin, M., & Blome, C. (2021). Social participation of people with chronic wounds: A systematic review. *International Wound Journal*, *18*(3), 287–311.

Klepstad, P., Loge, J. H., Borchgrevink, P. C., Mendoza, T. R., Cleeland, C. S., & Kaasa, S. (2002). The Norwegian brief pain inventory questionnaire: Translation and validation in cancer pain patients. *Journal of Pain and Symptom Management*, *24*(5), 517–525.

Kosek, E., Cohen, M., Baron, R., Gebhart, G. F., Mico, J.-A., Rice, A. S., Rief, W., & Sluka, A. K. (2016). Do we need a third mechanistic descriptor for chronic pain states? *Pain*, *157*(7), 1382–1386.

Krasner, D. (1998). Painful venous ulcers: Themes and stories about their impact on quality of life. *Ostomy/Wound Management*, *44*(9), 38–42.

Kusnanto, H., Agustian, D., & Hilmanto, D. (2018). Biopsychosocial model of illnesses in primary care: A hermeneutic literature review. *Journal of Family Medicine and Primary Care*, *7*(3), 497–500.

Kyaw, B., Järbrink, K., Martinengo, L., Car, J., Harding, K., & Schmidtchen, A. (2017). Need for improved definition of "chronic wounds" in clinical studies. *Acta Dermato-Venereologica*, *98*(1), 157–158.

Landmark, T., Romundstad, P., Dale, O., Borchgrevink, P. C., & Kaasa, S. (2012). Estimating the prevalence of chronic pain: Validation of recall against longitudinal reporting (the HUNT pain study). *Pain*, *153*(7), 1368–1373.

Leaper, D. J., & Durani, P. (2008). Topical antimicrobial therapy of chronic wounds healing by secondary intention using iodine products. *International Wound Journal, 5*(2), 361–368.

Leren, L., Johansen, E., Eide, H., Falk, R. S., Juvet, L. K., & Ljoså, T. M. (2020). Pain in persons with chronic venous leg ulcers: A systematic review and meta-analysis. *International Wound Journal*, *17*(2), 466–484.

Ljosaa, T. M., Rustoen, T., MøRk, C., Stubhaug, A., Milaskowski, C., Paul, S. M., & Wahl, A. K. (2010). Skin pain and discomfort in psoriasis: An exploratory study of symptom prevalence and characteristics. *Acta Dermato-Venereologica*, *90*(1), 39–45.

Ljunggren, A. E., Strand, L. I., & Johnsen, T. B. (2007). Development of the Norwegian Short-Form McGill Pain Questionnaire (NSF-MPQ). *Advances in Physiotherapy*, *9*(4), 169–180.

Loeser, J. D. (1982). Concepts of pain. In M. Stanton-Hicks & R. Boas (Eds.), *Chronic low back pain* (pp. 145–148). Raven Press.

Loeser, J. D. (1991). What is chronic pain? *Theoretical Medicine*, *12*(3), 213–225.

Maani, C. V., Hoffman, H. G., Morrow, M., Maiers, A., Gaylord, K., McGhee, L. L., & DeSocio, P. A. (2011). Virtual reality pain control during burn wound debridement of combat-related burn injuries using robot-like arm mounted VR goggles. *Journal of Trauma*, *71*(1). https://doi.org/10.1097/TA.0b013e31822192e2

Marczak, J., Rembeck, G., Petersson, E.-L., & Nordeman, L. (2019). Patient experiences of living with chronic leg ulcers and making the decision to seek professional healthcare. *Journal of Wound Care*, *28*(Sup1), S18–S25.

Martinengo, L., Olsson, M., Bajpai, R., Soljak, M., Upton, Z., Schmidtchen, A., Car, J., & Järbrink, K. (2019). Prevalence of chronic wounds in the general population: Systematic review and meta-analysis of observational studies. *Annals of Epidemiology*, *29*, 8–15.

Mathieson, K. (2014). Making sense of biostatistics: Types of nonprobability sampling. *Journal of Clinical Research Best Practice*, *10*(10).

McCaffery, M. (1968). *Nursing practice theories related to cognition, bodily pain, and man-environment interactions*. University of Los Angeles Students’ Store.

McCormack, B., & McCance, T. (2016). *Person-centred practice in nursing and health care: theory and practice*. John Wiley & Sons.

McCormack, B., & McCance, T. (2011). *Person-centred nursing: Theory and practice*. John Wiley & Sons.

Melzack, R. (1975). The McGill Pain Questionnaire: Major properties and scoring methods. *Pain*, *1*(3), 277–299.

Melzack, R. (1987). The short-form McGill Pain Questionnaire. *Pain*, *30*(2), 191–197.

Mervis, J. S., & Federman, D. G. (2018). Pain management in patients with chronic wounds. *Current Dermatology Reports*, *7*(3), 136–146.

Miaskowski, C., Blyth, F., Nicosia, F., Haan, M., Keefe, F., Smith, A., & Ritchie, C. (2020). A biopsychosocial model of chronic pain for older adults. *Pain Medicine*, *21*(9), 1793–1805.

Miaskowski, C., Mastick, J., Paul, S. M., Topp, K., Smoot, B., Abrams, G., Chen, L. M., Kober, K. M., Conley, Y. P., & Chesney, M. (2017). Chemotherapy-induced neuropathy in cancer survivors. *Journal of Pain and Symptom Management*, *54*(2), 204–218.

Mills, S. E., Nicolson, K. P., & Smith, B. H. (2019). Chronic pain: A review of its epidemiology and associated factors in population-based studies. *British Journal of Anaesthesia*, *123*(2), e273–e283.

Moher, D., Shamseer, L., Clarke, M., Ghersi, D., Liberati, A., Petticrew, M., Shekelle, P., Stewart, L. A., & PRISMA-P Group. (2015). Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews*, *4*(1). https://doi.org/10.1186/2046-4053-4-1

Monsivais, D. B., & Engebretson, J. C. (2011). Cultural cues: Review of qualitative evidence of patient-centered care in patients with nonmalignant chronic pain. *Rehabilitation Nursing*, *36*(4), 166–171.

Moore, R., Straube, S., & Aldington, D. (2013). Pain measures and cut-offs—“no worse than mild pain” as a simple, universal outcome. *Anaesthesia*, *68*(4), 400–412.

Morgan, S., & Yoder, L. H. (2012). A concept analysis of person-centered care. *Journal of Holistic Nursing*, *30*(1), 6–15.

Morin, C. M., Belleville, G., Bélanger, L., & Ivers, H. (2011). The Insomnia Severity Index: Psychometric indicators to detect insomnia cases and evaluate treatment response. *Sleep*, *34*(5), 601–608.

Morton, L. M., & Phillips, T. J. (2016). Wound healing and treating wounds: Differential diagnosis and evaluation of chronic wounds. *Journal of the American Academy of Dermatology*, *74*(4), 589–605.

Mudge, E. J., Meaume, S., Woo, K., & Perice, P. E. (2008). Patients' experience of wound-related pain: An international perspective. *EWMA Journal*, *8*(2), 159–171.

Munro, G. (2017). Causes and consideration with chronic wounds: A narrative review of the evidence. *Wound Practice & Research: Journal of the Australian Wound Management Association*, *25*(2), 88–97.

Murray, R. Z., West, Z. E., & McGuiness, W. (2018). The multifactorial formation of chronic wounds. *Wound Practice & Research: Journal of the Australian Wound Management Association*, *26*(1), 38–46.

Nelson, S., Conroy, C., & Logan, D. (2019). The biopsychosocial model of pain in the context of pediatric burn injuries. *European Journal of Pain*, *23*(3), 421–434.

Nemeth, K. A., Graham, I. D., & Harrison, M. B. (2003). The measurement of leg ulcer pain: Identification and appraisal of pain assessment tools. *Advances in Skin & Wound Care*, *16*(5), 260–267.

Newbern, S. (2018). Identifying pain and effects on quality of life from chronic wounds secondary to lower-extremity vascular disease: An integrative review. *Advances in Skin & Wound Care*, *31*(3), 102–108.

Ngamkham, S., Holden, J. E., & Wilkie, D. J. (2011). Differences in pain location, intensity and quality by pain pattern in outpatients with cancer. *Cancer Nursing*, *34*(3) https://doi.org/10.1097/NCC.0b013e3181faab63

Noonan, L., & Burge, S. (1998). Venous leg ulcers: Is pain a problem? *Phlebology*, *13*(1), 14–19.

Nussbaum, S. R., Carter, M. J., Fife, C. E., DaVanzo, J., Haught, R., Nusgart, M., & Cartwright, D. (2018). An economic evaluation of the impact, cost, and Medicare policy implications of chronic nonhealing wounds. *Value in Health*, *21*(1), 27–32.

Nyaga, V. N., Arbyn, M., & Aerts, M. (2017). *METAPROP: Stata module to perform fixed and random effects meta-analysis of proportions*. https://ideas.repec.org/c/boc/bocode/s457781.html

Ogrin, R., Parker, C. N., Finlayson, K. J., Anderson, J., & Edwards, H. E. (2021). Characteristics of people receiving wound care at home versus in a clinic. *Collegian*, *28*(4), 385–392.

Olsson, M., Järbrink, K., Divakar, U., Bajpai, R., Upton, Z., Schmidtchen, A., & Car, J. (2019). The humanistic and economic burden of chronic wounds: A systematic review. *Wound Repair and Regeneration*, *27*(1), 114–125.

Pallant, J. (2017). SPSS survival manual: A step by step guide to data analysis using SPSS for Windows (version 15, 3rd edition). 2007. In: Open University Press.

Paschou, S. A., Stamou, M., Vuagnat, H., Tentolouris, N., & Jude, E. (2018). Pain management of chronic wounds: Diabetic ulcers and beyond. *Maturitas*, *117*, 17–21.

Pasero, C., & McCaffery, M. (2010). *Pain assessment and pharmacologic management e-book*. Elsevier Health Sciences.

Peronopplysningsloven. (2018). *Lov om behandling av personopplysninger* (LOV-2018-06-15-38). Lovdata. https://lovdata.no/dokument/NL/lov/2018-06-15-38

Phillips, P., Lumley, E., Duncan, R., Aber, A., Woods, H. B., Jones, G. L., & Michaels, J. (2018). A systematic review of qualitative research into people's experiences of living with venous leg ulcers. *Journal of Advanced Nursing*, *74*(3), 550–563.

Phillips, T., Stanton, B., Provan, A., & Lew, R. (1994). A study of the impact of leg ulcers on quality of life: Financial, social, and psychologic implications. *Journal of the American Academy of Dermatology*, *31*(1), 49–53.

Pieper, B., DiNardo, E., & Nordstrom, C. K. (2013). A cross-sectional, comparative study of pain and activity in persons with and without injection-related venous ulcers. *Ostomy/Wound Management*, *59*(5), 14–24.

Platsidaki, E., Kouris, A., & Christodoulou, C. (2017). Psychosocial aspects in patients with chronic leg ulcers. *Wounds: A Compendium of Clinical Research and Practice*, *29*(10), 306–310.

Pluye, P., Robert, E., Cargo, M., Bartlett, G., O'Cathain, A., Griffiths, F., Boardman, F., Gagnon, M. P., & Rousseau, M. (2011). *Proposal: A mixed methods appraisal tool for systematic mixed studies reviews*. http://mixedmethodsappraisaltoolpublic.pbworks.com

Polit, D., & Beck, C. (2020). *Essentials of nursing research: Appraising evidence for nursing practice*. Lippincott Williams & Wilkins.

Price, P., Fogh, K., Glynn, C., Krasner, D. L., Osterbrink, J., & Sibbald, R. G. (2007). Managing painful chronic wounds: The Wound Pain Management Model. *International Wound Journal*, *4*, 4–15.

Price, P. E., Fagervik-Morton, H., Mudge, E. J., Beele, H., Ruiz, J. C., Nystrøm, T. H., Lindholm, C., Maume, S., Melby-Østergaard, B., Peter, Y., Romanelli, M., Seppänen, S., Serena, T. E., Sibbald, G., Soriano, J. V., White, W., Wollina, U., Woo, K. Y., Wyndham-White, C., & Harding, K. G. (2008). Dressing-related pain in patients with chronic wounds: An international patient perspective. *International Wound Journal*, *5*(2), 159–171.

Purcell, A., Buckley, T., King, J., Moyle, W., & Marshall, A. P. (2020). Topical analgesic and local anesthetic agents for pain associated with chronic leg ulcers: A systematic review. *World Council of Enterostomal Therapists Journal*, *40*(2), 22–34.

Rabin, R., Oemar, M., Oppe, M., Janssen, B., & Herdman, M. (2011). EQ-5D-5L user guide. *Basic information on how to use the EQ-5D-5L instrument. Rotterdam: EuroQol Group*, *22*.

Raffaeli, W., & Arnaudo, E. (2017). Pain as a disease: an overview. *Journal of Pain Research*, *10*, 2003–2008.

Raja, S. N., Carr, D. B., Cohen, M., Finnerup, N. B., Flor, H., Gibson, S., Keefe, F. J., Mogil, J. S., Ringkamp, M., Sluka, K. A., Song, X. J., Stevens, B., Sullivan, M. D., Tutelman, P. R., Ushida, T., & Vader, T. (2020). The revised International Association for the Study of Pain definition of pain: Concepts, challenges, and compromises. *Pain*, *161*(9), 1976–1982.

Ranganathan, P., & Aggarwal, R. (2020). Study designs: Part 7–systematic reviews. *Perspectives in Clinical Research*, *11*(2), 97–100.

Regional kompetansetjeneste for smerte (2021). *Oversikt over variabler ved OUS smerteklinikk*. https://oslo-universitetssykehus.no/seksjon/Regional-kompetansetjeneste-for-smerte/Documents/Oversikt%20over%20variabler%20ved%20OUS%20smerteregister.pdf

Renner, R., Seikowski, K., & Simon, J. C. (2014). Association of pain level, health and wound status in patients with chronic leg ulcers. *Acta Dermato-Venereologica*, *94*(1), 50–53.

Royal College of Nursing. (2015). *Pain knowledge and skills framework for the nursing team*. https://www.rcn.org.uk/professional-development/publications/pub-004984

Salomé, G. M., & Ferreira, L. M. (2018). The impact of decongestive physical therapy and elastic bandaging on the control of pain in patients with venous ulcers. *Revista do Colegio Brasileiro de Cirurgioes*, *45*(2). https://doi.org/10.1590/0100-6991e-20181385

Santana, M. J., Manalili, K., Jolley, R. J., Zelinsky, S., Quan, H., & Lu, M. (2018). How to practice person-centred care: A conceptual framework. *Health Expectations*, *21*(2), 429–440.

Sedgwick, P. (2015). Bias in observational study designs: Cross sectional studies. *British Medical Journal*, *350*. https://doi.org/10.1136/bmj.h1286

Smith, F., & Sharp, A. (2019). Undertaking a person-centred assessment of patients with chronic wounds. *Nursing Standard*, *34*(10), 77–82.

Solberg, T. K., Olsen, J.-A., Ingebrigtsen, T., Hofoss, D., & Nygaard, Ø. P. (2005). Health-related quality of life assessment by the EuroQol-5D can provide cost-utility data in the field of low-back surgery. *European Spine Journal*, *14*(10), 1000–1007.

Sommet, N., & Morselli, D. (2017). Keep calm and learn multilevel logistic modeling: A simplified three-step procedure using Stata, R, Mplus, and SPSS. *International Review of Social Psychology*, *30*, 203–218.

Stein, R. A. (2019). Predicting infections in chronic leg ulcers: A step ahead. *International Journal of Clinical Practice*, *73*(2). https://doi.org/10.1111/ijcp.13304

Steingrímsdóttir, Ó. A., Landmark, T., Macfarlane, G. J., & Nielsen, C. S. (2017). Defining chronic pain in epidemiological studies: A systematic review and meta-analysis. *Pain*, *158*(11), 2092–2107.

Strand, L. I., Ljunggren, A. E., Bogen, B., Ask, T., & Johnsen, T. B. (2008). The short-form McGill Pain Questionnaire as an outcome measure: Test–retest reliability and responsiveness to change. *European Journal of Pain*, *12*(7), 917–925.

Suhonen, R., Välimäki, M., & Leino-Kilpi, H. (2005). Individualized care, quality of life and satisfaction with nursing care. *Journal of Advanced Nursing*, *50*(3), 283–292.

Sussman, C., & Bates-Jensen, B. (2011). Management of wound pain. In C. Sussman & B. Bates-Jensen (Eds.), *Wound care: A collaborative practice manual for health professionals* (pp. 535–572). Lippincott Williams & Williams.

Swift, A. (2015). Pain management 3: The importance of assessing pain in adults. *Nursing Times*, *111*(41). PMID: 26647478

Tavakol, M., & Dennick, R. (2011). Making sense of Cronbach's alpha. *International Journal of Medical Education*, *2*, 53–55.

Taverner, T., Closs, S. J., & Briggs, M. (2014). The journey to chronic pain: A grounded theory of older adults' experiences of pain associated with leg ulceration. *Pain Management Nursing*, *15*(1), 186–198.

Thewes, B., Rietjens, J., van den Berg, S., Compen, F. R., Abrahams, H., Poort, H., van de Wal, M., Schellekens, M. P. J., Peters, M. E. W. J. , Speckens, A. E. M., Knoop, H, & Prins, J. B. (2018). One way or another: The opportunities and pitfalls of self-referral and consecutive sampling as recruitment strategies for psycho-oncology intervention trials. *Psycho-Oncology: Journal of the Psychological, Social and Behavioral Dimensions of Cancer*, *27*(8), 2056–2059.

Toma, E., Veneziano, M. L., Filomeno, L., Villa, A., Rosato, E., & la Torre, G. (2020). Nursing assessment of wound-related pain: An Italian learning survey. *Advances in Skin & Wound Care*, *33*(10), 540–548.

Trouvin, A.-P., & Perrot, S. (2019). New concepts of pain. *Best Practice & Research Clinical Rheumatology*, *33*(3). https://doi.org/10.1016/j.berh.2019.04.007

Turabian, J. (2018). Patient-centered care and biopsychosocial model. *Trends in General Practice*, *1*(3). https://doi.org/10.15761/TGP.1000114

Turk, D. C. (1996). Psychological aspects of chronic pain and disability. *Journal of Musculoskeletal Pain, 4*(4), 145–154.

Turk, D. C., & Melzack, R. (2011). The measurement of pain and the assessment of people experiencing pain. In D. C. Turk & R. Melzack (Eds.), *Handbook of pain assessment* (pp. 3–16). The Guilford Press.

Turk, D. C., Wilson, H., Swanson, K. S., Ebert, M., & Kerns, R. (2011). The biopsychosocial model of pain and pain management. In M. H. Ebert & R. D. Kerns (Eds.), *Behavioral and Psychopharmacologic Pain Management* (pp. 16–43). Cambridge University Press.

Twillman, R. K., Long, T. D., Cathers, T. A., & Mueller, D. W. (1999). Treatment of painful skin ulcers with topical opioids. *Journal of pain and symptom management, 17*(4), 288–292.

Upton, & Andrews. (2013). Sleep disruption in patients with chronic leg ulcers. *Journal of Wound Care*, *22*(8), 389–394.

Upton, D., & South, F. (2011). The psychological consequences of wounds—a vicious circle that should not be overlooked. *Wounds UK*, *7*(4), 136–138.

Valderas, J. M., Starfield, B., Sibbald, B., Salisbury, C., & Roland, M. (2009). Defining comorbidity: Implications for understanding health and health services. *The Annals of Family Medicine*, *7*(4), 357–363.

Vernassiere, C., Cornet, C., Trechot, P., Alla, F., Truchetet, F., Cuny, J., Commun, N., Granel Brocard, F., Barbaud, A., & Schmutz, J. (2005). Study to determine the efficacy of topical morphine on painful chronic skin ulcers. *Journal of Wound Care*, *14*(6), 289–293.

Vittinghoff, E., & McCulloch, C. E. (2007). Relaxing the rule of ten events per variable in logistic and Cox regression. *American Journal of Epidemiology*, *165*(6), 710–718.

Vuolo, J. C. (2009). Wound-related pain: Key sources and triggers. *British Journal of Nursing*, *18*(15), S22–S225.

Wallström, S., & Ekman, I. (2018). Person-centred care in clinical assessment. *European Journal of Cardiovascular Nursing*, *17*(7), 576–579.

Weaver, R. R. (2015). Reconciling evidence-based medicine and patient-centred care: Defining evidence-based inputs to patient-centred decisions. *Journal of Evaluation in Clinical Practice*, *21*(6), 1076–1080.

Welsh, L. (2018). Wound care evidence, knowledge and education amongst nurses: A semi-systematic literature review. *International Wound Journal, 15*(1), 53–61.

White , R. (2008). Pain assessment and management in patients with chronic wounds. *Nursing Standard*, *22*(32), 62–68.

Williamson, A., & Hoggart, B. (2005). Pain: A review of three commonly used pain rating scales. *Journal of Clinical Nursing*, *14*(7), 798–804.

Wong, I. K., Andriessen, A., Charles, H., Thompson, D., Lee, D., So, W., & Abel, M. (2012). Randomized controlled trial comparing treatment outcome of two compression bandaging systems and standard care without compression in patients with venous leg ulcers. *Journal of the European Academy of Dermatology and Venereology*, *26*(1), 102–110.

Woo, K. Y. (2012). Chronic wound-associated pain, psychological stress, and wound healing. *Surgical Technology International*, *22*, 57–65.

Woo , K. Y., & Sibbald, R. G. (2008). Chronic wound pain: A conceptual model. *Advances in Skin & Wound Care, 21*(4), 175–188.

World Health Organization. (2013). *People-centred healthcare: A policy framework*. World Health Organization.

World Union of Wound Healing Society. (2004). *Principles of best practice: Minimising pain at wound dressing-related procedures. A consensus document*. https://www.google.no/url?sa=t&rct=j&q=&esrc=s&source=web&cd=&cad=rja&uact=8&ved=2ahUKEwiI4eejp-j0AhUWRvEDHTz2BDwQFnoECAcQAQ&url=https%3A%2F%2Fwww.woundsinternational.com%2Fdownload%2Fresource%2F6028&usg=AOvVaw2c7bBak9nV59V7qfC_38-h

World Union of Wound Healing Society. (2007). *Principles of best practice: minimizing pain at dressing-related procedures: "Implementation of pain relieving strategies". Evidence informed practice*. https://www.akademie-zwm.ch/uploads/tx_scpublications/Best_Practice-Pain_WUWHS_2008.pdf

Zelman, D. C., Dukes, E., Brandenburg, N., Bostrom, A., & Gore, M. (2005). Identification of cut-points for mild, moderate and severe pain due to diabetic peripheral neuropathy. *Pain*, *115*(1-2), 29–36.

Zeppetella, G., Paul, J., & Ribeiro, M. D. (2003). Analgesic efficacy of morphine applied topically to painful ulcers. *Journal of Pain and Symptom Management*, *25*(6), 555–558.

Errata

Page	Line	Original Text	Corrected text
V	12	Leren, L., Eide, H., Johansen, E. A., Jelnes, R. & Ljoså, T. M. (2020).	Leren, L., Eide, H., Johansen, E. A., Jelnes, R. & Ljoså, T. M. (2021).
25	11	… have multiple causes (cf. Chapter 2.1.1) The emphasis on ulcer diagnosis …	… have multiple causes (cf. Chapter 2.1.1). The emphasis on ulcer diagnosis …
25	13	The focus if this PhD project is on pain …	The focus in this PhD project is on pain …
64	10	… differences between persons referred to and treated in wound care clinics by clinical specialists and persons treated in primary care by homecare nurses or GPs.	… differences between persons referred to and treated in wound care clinics, by clinical specialists, and persons treated in primary care by homecare nurses or GPs.
65	15-16	In addition, that we did not register those who refused to participate in the study represents …	In addition, the fact that we did not register those who refused to participate in the study represents …

Paper I

Leren, L., Johansen, E., Eide, H., Falk, R. S., Juvet, L. K., & Ljoså, T. M. (2020). Pain in persons with chronic venous leg ulcers: A systematic review and meta-analysis. *International Wound Journal*, *17*(2), 466–484. https://doi.org/10.1111/iwj.13296

Received: 25 October 2019 | Revised: 13 December 2019 | Accepted: 17 December 2019
DOI: 10.1111/iwj.13296

ORIGINAL ARTICLE

IWJ WILEY

Pain in persons with chronic venous leg ulcers: A systematic review and meta-analysis

Lena Leren[1] | **Edda Johansen**[1] | **Hilde Eide**[1] | **Ragnhild S. Falk**[2] | **Lene K. Juvet**[1] | **Tone M. Ljoså**[1]

[1]University of South-Eastern Norway, Drammen, Norway
[2]Oslo University Hospital, University of South-Eastern Norway, Oslo, Norway

Correspondence
Lena Leren, University of South-Eastern Norway, Drammen, Norway.
Email: lena.leren@usn.no

Abstract

Pain is a serious problem for patients with leg ulcers. Research mainly focuses on dressing-related pain; however, chronic background pain may be just as devastating. Our main objective was to describe the prevalence and characteristics of wound-related background pain in persons with chronic venous leg ulcers. We performed a systematic review to synthesise data from quantitative studies. Studies were eligible if they reported original baseline- or cross-sectional data on background pain in chronic venous leg ulcers. The initial search identified 2454 publications. We included 36 descriptive and effect studies. The pooled prevalence of wound-related background pain (from 10 studies) was 80% (95% CI 65-92%). The mean pain intensity score (from 27 studies) was 4 (0-10 numeric rating scale) (95% CI 3.4-4.5). Other pain characteristics could not be synthesised. We identified few sufficiently high-quality studies on prevalence and intensity of wound-related background pain in patients with chronic venous leg ulcers. Four of five persons experience mild to moderate pain. Because of poor quality of pain assessment and report, we believe that the available research does not provide a sufficiently nuanced understanding of background pain in this patient group.

KEYWORDS
pain, systematic review, venous leg ulcer

1 | INTRODUCTION

Pain experienced by people with chronic venous leg ulcers (CVLUs) is complex. In a consensus document, the World Union of Wound Healing Society (2004) proposed the terms background, incident, procedural, and operative pain to describe both the types and causes of wound-related pain. The background pain is caused by the underlying pathology of the leg ulceration and the wound itself. Various daily activities can cause incident pain. The wound treatment causes procedural or operative pain, as well as complications such as skin irritation.[1] Furthermore, wound-related pain can be classified as acute or chronic, nociceptive or neuropathic.[2-4] Wound-related pain is a complex symptom, and patients with persistent leg ulcers often experience multiple types of pain from their ulcer, making this type of pain particularly complex.[5]

Approximately 1% to 2% of the population in western countries suffer from chronic leg ulcers,[6-8] and CVLUs account for 70% to 90% of lower leg ulcers.[9] CVLUs are defined as an open lesion between the knee and the ankle joint that remains unhealed for at least 30 days and occurs in the presence of venous disease.[5] Peak prevalence of CVLUs occurs in the age group 60 to 80 years,[9] and the prevalence rate is expected to increase as the population ages. These ulcers are a particular threat to older individuals as increased age is a major risk factor for impaired wound healing.[10] CVLUs may take months or years to heal and are prone to recurrence because the underlying and wound-provoking factors have not been, or cannot be, adequately addressed.[11] Research shows that CVLUs have a major negative impact on the persons living with them. The ulcers cause pain, social isolation, sleep disturbance, depression, loss of time from work, and financial costs. These biopsychosocial factors can have a major negative impact on the patients' perception of pain.[5] Both the wound itself and the wound-related pain are significant causes of impaired function and quality of life (QoL).[12]

Literature searches identify a limited number of high-quality studies specifically investigating wound-related pain. The existing literature mainly focuses on pain at dressing change, and little attention is paid to chronic background pain. Background pain, sometimes called basal or baseline pain, is related to the underlying cause of the wound, local wound factors such as inflammation, and other related pathologies such as skin irritation. The pain is felt at rest, when there is no tissue manipulation or sudden changes in the patient physical condition, and it may be continuous or intermittent.[5] Persistent background pain at rest and between wound-related procedures might be just as devastating as the procedure-related pain.[13] In this systematic review, we focus on wound-related background pain. Studies reporting on procedural or operative pain are not included.

Several studies describe the prevalence and characteristics of pain in relation to CVLUs. However, with prevalence rates varying from 46% up to 100%,[14-16] it is difficult to evaluate the relative impact of pain associated with CVLUs. The most frequent pain characteristic described is pain intensity. Other pain characteristics, such as location of pain, temporal fluctuations of pain intensity, pain interference, and pain quality descriptors, are less frequently described. In the wound-healing literature, pain related to CVLUs is described as constant or intermittent, and pain intensity varies from mild pain to intense pain.[17,18] Pain characteristics are important and necessary factors to assess when considering pain management and when evaluating treatments.

To date, little effort has been made to systematically review these studies to determine the overall prevalence and characteristics of wound-related background pain. A lack of information and knowledge about this type of pain may have negative consequences for wound treatment as it is likely that adequate pain recognition and management are important in improving both QoL and adherence to treatment.[19] Hence, the purpose of this review was to synthesise existing studies reporting the prevalence and characteristics of wound-related background pain in order to provide a much needed and accurate estimate.

Key Messages

- wound-related background pain may be just as devastating as the procedure-related pain at dressing change
- a systematic review identified 36 studies on prevalence and characteristics of background wound-related pain
- meta-analysis showed that 80% had wound-related background pain, with moderate pain intensity (4/10 numeric rating scale)
- wound-related background pain is a common and severe symptom that needs to be recognised in clinical practice and in future research

2 | METHODS

2.1 | Aim

Our main objectives were to (a) systematically review the literature to describe the prevalence of wound-related background pain in published studies that focus specifically on CVLUs in samples from both community and hospital care settings and (b) describe characteristics of this wound-related background pain (eg, intensity, qualities, location, and temporal fluctuations).

The secondary objectives were to perform a meta-analysis on pain prevalence and pain characteristics and to identify factors associated with pain intensity.

2.2 | Design

A systematic review was conducted to synthesise data from both descriptive and effect studies.[20,21] We used a systematic review methodology, using the guidance of PRISMA.[22] A review protocol was created a priori and was registered on PROSPERO international prospective register of systematic reviews (CRD42017056027).

2.3 | Search strategy

A systematic search was performed in the following electronic bibliographic databases: MEDLINE, EMBASE, CINAHL, The Cochrane Library (the Cochrane Database of Systematic Reviews, the Cochrane Central Register of Controlled Trials [CENTRAL], the Cochrane Methodology Register), and The British Nursing Index.

The search strategy included terms relating to different wound diagnoses and to pain. A detailed list of search terms was prepared and adapted to each database. The list consisted of a combination of medical subject headings (eg, MeSH) and free terms related to pain and ulcers. Data on pain as a subdomain of QoL were not included. The complete search strategy is described in Appendix.

We identified additional studies by manually searching relevant conference proceedings and specialist journals. The reference lists of all relevant studies and systematic reviews were hand searched for additional relevant studies.

The search was restricted to studies published between 1st January, 1990 and 31st October, 2017. Searches were rerun before the final analyses were completed (1st February, 2019) in order to retrieve and include the latest relevant studies in the review.

2.4 | Changes in protocol

To begin with, we chose a systematic mixed-studies review method to synthesise data from studies with diverse research designs.[20,21,23] In the present study, we present the quantitative data obtained from the literature search.[24]

Furthermore, we initially set out to establish the prevalence and characteristics of wound-related pain in persons living with various diagnoses of chronic leg and foot ulcers. We found a great deal of heterogeneity in the diagnosis criteria, which made the synthesis of data complex. This led us to narrow the scope further and include only data on wound-related background pain in persons with CVLUs. This decision was based on the argument that CVLUs make up the largest group of patients with chronic wounds and that the majority of studies focused on these patients.[9]

We initially also set out to include studies of all languages, but we realised that it was too resource-demanding to translate all abstracts in other languages. As a result, we decided to include only studies published in English or Scandinavian languages.

2.5 | Study selection

Two of the authors (L.L. and T.M.L.) independently assessed titles and abstracts of all potentially relevant publications identified from the literature search.

Inclusion and exclusion criteria are presented in Table 1. Pain measures included in generic health-related QoL instruments were not included as the scope of this review was wound-related pain. If the same data were analysed in multiple publications, the publication with the more complete or more extensive data was included.

The initial search identified 2454 unique publications. The abstracts were screened, and the inclusion and exclusion criteria were applied. This left 556 articles, of which another 514 were excluded, resulting in a total of 43 articles. The updated search identified 164 publications, which was reduced to 118 after removing duplicates. After applying inclusion and exclusion criteria, three articles were included. In the quality assessment, 45 studies were evaluated, and 9 studies were excluded. A total of 36 studies were included in the synthesis, and 33 of these

TABLE 1 Inclusion and exclusion criteria

	Inclusion criteria	Exclusion criteria
Publication year	Published between January 1990 and February 2019	
Language	English, Scandinavian	
Study design	Effect studies and descriptive studies (with cross-sectional, longitudinal, prospective/retrospective design)	Qualitative studies Case studies/series Reviews Conference papers Discussion papers Editorials Consensus documents Expert opinions Other non-research publications
Study sample	Adult persons >18 years with active venous leg ulcer, duration >4 weeks	Not reporting on pain in persons with active CVLUs separately
Pain data	Original self-reported data on pain prevalence or pain characteristics	Pain assessment/instrument not defined/described Insufficient pain report (eg, only changes in pain score reported) Pain as an inclusion criterion in the study Procedure-related pain reports only

studies presented data eligible for the meta-analyses. The PRISMA flow diagram in Figure 1 depicts the flow of information through the different phases of a systematic review.

2.6 | Quality assessment

Six authors paired up and evaluated the quality of eligible studies using the Mixed Method Appraisal Tool MMAT-v2011.[25] The tool permits appraisal of studies across a range of designs, where different sections of the tools are used for the appraisal of the different study types.[21,26] Hence, each study design is judged within its methodological domain. The MMAT scores range from 0% (no criterion is met) to 100% (all four criteria are met). Disagreement on the score of the MMAT-v2011 was resolved by discussion among the authors.

The quality score of nine studies was 0%, and these studies were thus excluded because of poor methodological quality or inadequate report of pain prevalence and characteristics.

2.7 | Data extraction

One author (L.L.) summarised the study characteristics and pain findings in a table, and a second author (T.M. L.) verified this extracted data. The extracted data included information on author(s), year of publication, country, study purpose, design, sample characteristics (eg, sample size, age, gender, and wound duration), wound diagnostic criteria, data collection methods/recruitment, and type of pain assessment/report, as well as pain prevalence and characteristics (ie, intensity, duration and frequency, location, and quality). In addition, the respondents' use of pain medication and compression therapy was extracted.

2.8 | Synthesis of data and analysis

There was a large diversity among the included studies regarding aim and focus of research. All studies assessed pain in persons with CVLUs and were considered sufficiently homogenous to provide a meaningful summary. Only baseline data were extracted from the studies with

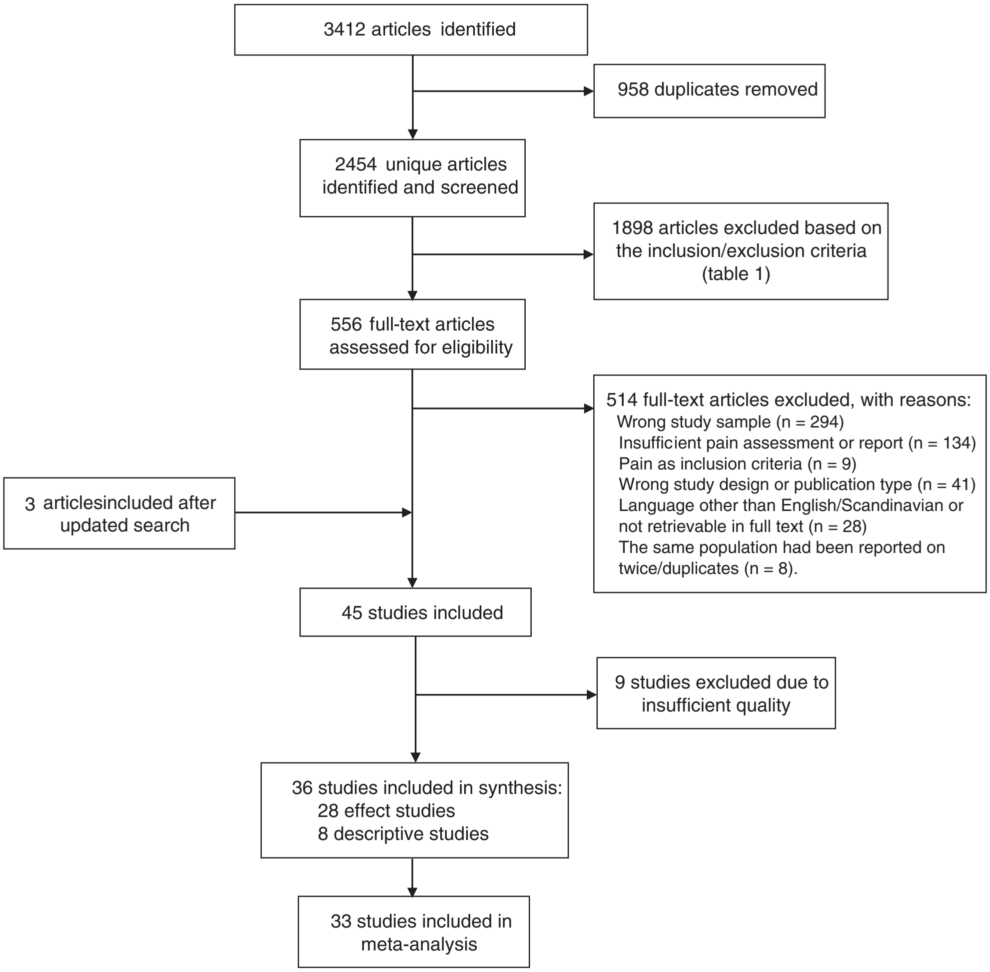


FIGURE 1 PRISMA flow diagram

repeated measures. The inclusion criteria in effect studies were generally more detailed than in descriptive studies, typically resulting in more selected samples with fewer comorbidities. Therefore, we stratified the analysis by study design.

In the studies reporting pain intensity, a great variation of tools (ie, different numeric rating scales [NRS], different verbal rating scales [VRS], various anchor points) were used to assess pain intensity. Data were synthesised using standardised methods for converting different pain rating scales,[27-29] providing an NRS of pain ranging from 0 to 10. In studies only providing information about median pain score and range, mean pain score and SD were calculated as described by Hozo et al.[30]

We performed a random-effects meta-analysis overall and stratified by study design for pain prevalence and pain intensity. Summary estimates were calculated to provide pooled estimates of proportion of pain and mean pain intensities in the included studies[31] and were presented with accompanying 95% confidence intervals (CI). Heterogeneity between the studies was assessed with the Q-test, and its magnitude was quantified using the I-squared measure. This describes the proportion of the total variation because of heterogeneity rather than chance. We interpreted a value ≥75% as high heterogeneity.[32]

To explore sources of heterogeneity in pain intensity, we performed univariable random-effects meta-regression analyses. We considered the following variables: study design; year of publication; and participant's age, gender, and wound duration. Meta-regression analyses were not performed for pain prevalence because of the small number of publications (n = 10).

We used the forest plot to present the summary estimates overall and stratified by study design. Publication bias was assessed by Egger's test.

All analyses were conducted using Stata 15.0 (State College, Texas). The *metaprop* and the *metan* commands were used to perform meta-analysis of the prevalence data and the intensity data, respectively.

3 | RESULTS

3.1 | Selected studies

The included studies contained original data on pain prevalence, intensity, and/or characteristics. All these studies met the minimum quality score criteria of 25% on the MMAT. Publication year ranged from 1993 to 2018. A total of 36 studies were included. Ten studies were descriptive (ie, descriptive survey, registry study), and 26 were effect studies (ie, randomised controlled trials, non-randomised efficacy studies, prospective uncontrolled trials). Detailed descriptions of the included studies are presented in Table 2.

3.2 | Pain prevalence

Pain prevalence was reported in 10 of the 36 studies. Six were effect studies (two randomised controlled trials, three non-randomised efficacy studies, one controlled randomised prospective study), and four were descriptive studies (one registry study, three surveys). Four of these studies were conducted in the United Kingdom, and one was conducted in each of Czech Republic, Sweden, Poland, United States, Japan, and Brazil.

Prevalence of pain was determined by self-report in all included studies, and various tools and descriptions were used to assess and report pain. "No pain" was used as a reference point to determine pain prevalence. The prevalence ranged from 46.3% to 100%. The pooled estimated proportion was 80% (ES 0.80 [95% CI 0.65-0.92]), with high heterogeneity (I-squared 96.5%). Subgroup analysis by design demonstrated a higher proportion in effect studies (90%) compared with descriptive studies (60%), both with high heterogeneity. The meta-analysis of the prevalence of background wound-related pain is illustrated in the forest plot in Figure 2.

3.3 | Pain intensity

Pain intensity was reported in 27 of the included studies. Three of these studies were descriptive studies, while 24 were effect studies (ie, randomised controlled trials and non-randomised efficacy studies). The studies were conducted in 13 different countries spread over four continents (Table 1). The mean age of most of the patient samples ranged from 50.3 to 74.6 years. One study[48] reported on a noticeably younger sample with a mean age of 38 years.

The mean pain intensity scores ranged from 2.3 to 6.6 (all converted to NRS 0–10). The overall pooled estimate of mean pain intensity was 4.0 (CI 95% 3.5, 4.5), with high heterogeneity. Subgroup analysis showed similar pooled estimates of mean pain intensity in effect studies (4.0) and in descriptive studies (3.8), both with high heterogeneity. The meta-analysis of the intensity of background wound-related pain is illustrated in the forest plot in Figure 3.

The meta-regression showed that there was an association between the observed effect size and the mean age of participants in the studies; for each year increase in age, the mean pain intensity decreased by 0.09 ($P = .005$).

TABLE 2 Included studies in the meta-analysis sorted by study design and publication year

Author(s), year	Country	Study design	No. of participants	Mean age (years)	Tool used to assess pain prevalence	Pain assessment tools	Prevalence of pain	Pain intensity	MMAT Quality score (%)
Effect studies									
Teepe et al, 1993[33]	No info	Randomised controlled trial	43	71.6		VAS (0-5)		✓	25
Morrell et al, 1998[34]	UK	Randomised controlled trial	223	73.5		SF-MPQ		✓	75[c]
Santilli et al, 1999[35]	No info	Non-randomised efficacy study	17	67.7		NRS (0-10)		✓	25
Walters et al, 1999[36]	UK	Randomised controlled trial	233	74.6	Not reported ("... 25% said they had no leg ulcer pain")	SF-MPQ	✓	✓	50[c]
Wilson et al, 2002[37]	UK	Non-randomised efficacy study	21	74	Verbal rating scale (0-5), 0 = no pain	VRS	✓		50
Navratilova et al, 2004[38]	Czech republic	Randomised controlled trial	50	62.9		VAS (0-10)	✓		50
Mermet et al, 2007[39]	France	Prospective uncontrolled study	15	79		VAS (0-100)		✓	25
Cameron et al, 2005[40]	UK	Randomised controlled trial	35	73.2	Verbal rating scale (0-5), 0 = none	VRS	✓		50
Benigni et al, 2007[41]	France	Non-randomised efficacy study	42	70.5	Pain during previous compression system (y/n)	VRS	✓		25
Szewczyk et al, 2007[16]	Poland	Non-randomised efficacy study	20	62.2	Numeric pain scale (0-10), 0 = no pain	NRS (0-10)	✓	✓	50
Jünger et al, 2008[42]	No info	Prospective controlled trial	39	67.2		Pain scale (0-10)		✓	50
Edwards et al, 2009[43]	Australia	Randomised controlled trial	67			MOS pain measures (0-10)		✓	50
Brizzio et al, 2010[44]	No info	Randomised controlled trial	55	61.7		NRS (0-100)		✓	75[c]
Schumann et al, 2011[45]	Germany	Randomised controlled trial	51	74		VAS (0-100)		✓	75
Escadon et al, 2012[46]	No info	Non-randomised efficacy study	10			VAS (0-10)		✓	50[c]
Wong et al, 2012[47]	China	Randomised controlled trial	321	71.7		BPI (0-10)		✓	50[c]
Olyaie et al, 2013[48]	Iran	Randomised controlled trial	90	38		NRS (0-20)		✓	100
Park et al, 2013[49]	Korea	Non-randomised efficacy study	16	50.3		Subjective (0-4)		✓	50
Behesthi et al, 2014[50]	Iran	Randomised controlled trial	90	58.5		NRS (0-20)		✓	75
Brown et al. 2014[51]	Germany and USA	Randomised controlled trial	120	68.3		NRS (0-100)		✓	75

(Continues)

TABLE 2 (Continued)

Author(s), year	Country	Study design	No. of participants	Mean age (years)	Tool used to assess pain prevalence	Pain assessment tools	Prevalence of pain	Pain intensity	MMAT Quality score (%)
Bradbury et al. 2015[52]	No info	Non-randomised controlled trial	15	64.4		NRS (0-10)		✓	50
Brehmer et al, 2015[53]	Germany	Randomised controlled trial	14	67		VAS (0-100)		✓	25
Gibbons et al, 2015[54]	USA	Randomised controlled trial	80	60.1		VAS (150 mm)		✓	75
White et al, 2015[55]	UK	Randomised controlled trial	36	69		VAS (0–5)		✓	100
Harding et al, 2016[56]	UK and Poland	Non-randomised efficacy study	42	71.4		VAS (0–10)		✓	50
Vitse et al, 2017[57]	France	Prospective randomised controlled trial	71	67		VAS (0–100)		✓	100
Salome & Ferreira, 2018[15]	Brazil	Randomised controlled trial	90		Numeric pain scale (0–10), 0 = no pain		✓		100
Domingues et al, 2018[58]	Brazil	Randomised controlled trial	71	66.5		NRS (0–10)		✓	50
Descriptive studies									
Jones et al, 2006[59]	UK	Explorative survey	190	69	Verbal rating scale (0-4), 0 = no pain	VRS	✓		50
Cwajda-Bialasik et al, 2012[60]	Poland	Descriptive questionnaire survey	101	66.2		NRS (0-10)		✓	50
Paul, 2013[14]	US	Descriptive survey	41^a	67^b	Wound-related pain (y/n)	NRS (0-10)	✓		100
Goto et al, 2016[61]	Japan	Observational survey	13	67.5	Numeric rating scale (0–10), 0 = no pain	NRS (0-10)	✓	✓	25
Hellström et al, 2016[62]	Sweden	Register study	763^a		Experienced pain (y/n)	NRS (0-10)	✓	✓	25

Note: Ticked boxes indicate that the data (prevalence and/or intensity) are included in the meta-analyses.

Abbreviations: BPI, Brief Pain Inventory, MOS, Medical Outcomes Study; NRS, Numeric Rating Scale, SF-MPQ2, Short Form McGill Pain Questionnaire-2, VRS, Verbal Rating Scale.

[a] Venous leg ulcer only.

[b] Total sample.

[c] One criterion not applicable.

FIGURE 2 Forest plot of prevalence of wound-related background pain

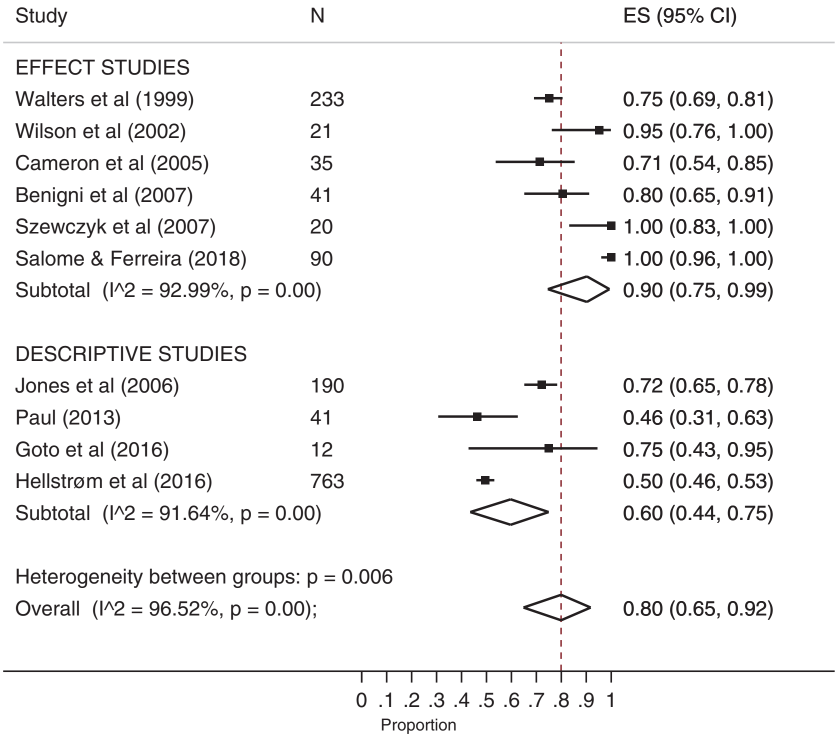


FIGURE 3 Forest plot of intensity of wound-related background pain

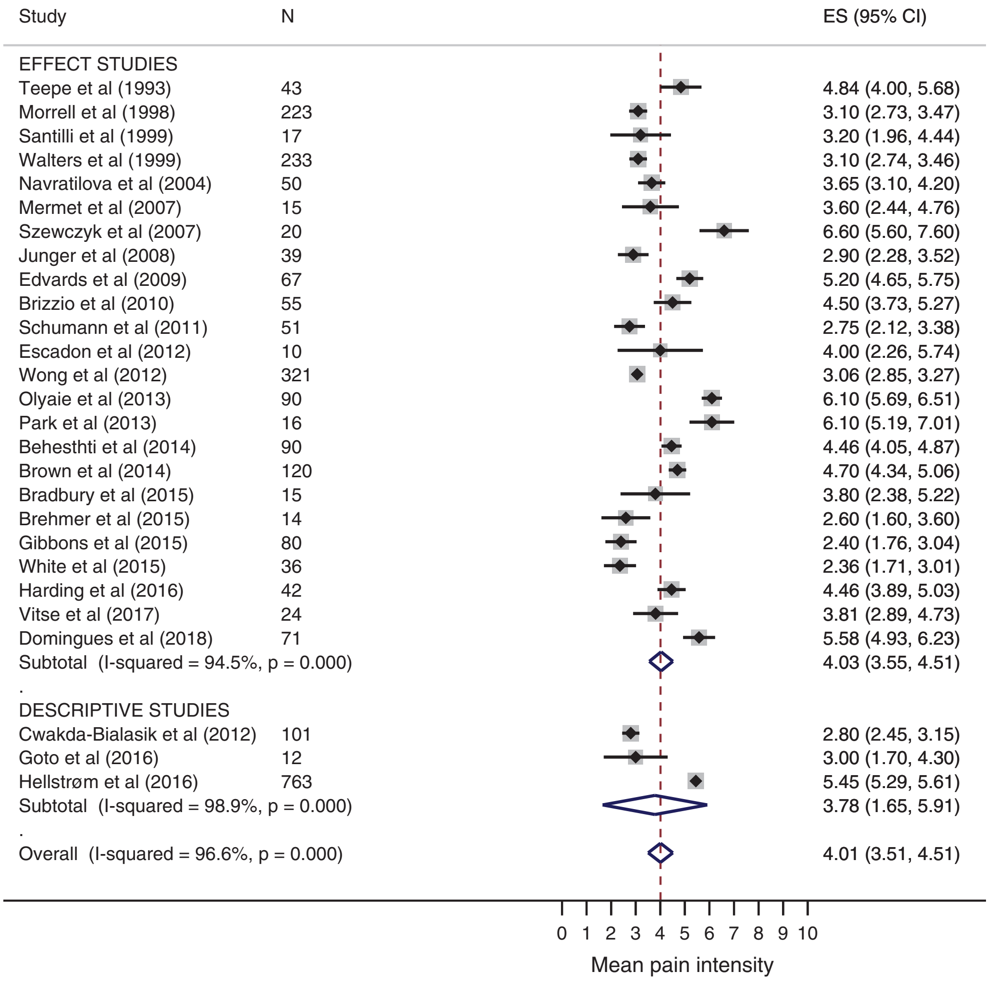


TABLE 3 Pain characteristics not included in the meta-analysis

Author(s), Year Sample size	Measures	Pain intensity	Pain quality	Pain pattern	Pain interference
Morell et al, 1998[34] N = 233	SF-MPQ		Pain rating index (mean): Sensory (0-33): 9.1 Affective (0-12): 2.0 Number of words chosen (0-15): 5.5		
Cameron et al, 2005[40] N = 35	VRS (6 items) MPQ modified version	Percentage of sample reporting graded pain intensity: None: 14.3% Mild: 36.4% Uncomfortable: 20.2% Distressing: 11.3% Horrible: 14.5% Excruciating: 3.3%			
Benigni et al, 2007[41] N = 33	VRS (minor, moderate, intense, very intense)	Percentage of sample reporting graded pain intensity: Minor: 18% (n = 6) Moderate: 37% (n = 12) Intense: 40% (n = 13) Very intense: 6% (n = 2)		Percentage of sample reporting various degrees of spontaneous pain at baseline: Absent: 10% (n = 4) Minor: 19% (n = 4) Moderate: 38% (n = 16) Intense: 33% (n = 14) Experience of previous treatment with compression bandages: 81% (n = 33) had experienced pain, which was "intense" in 40% (n = 13)	
Closs et al, 2008[63] N = 79	NRS (0-5) MPQ	Average rating of pain intensity (median): Average pain = 1 Worst pain = 2 Least pain = 0,5 Pain now = 0	MPQ pain rating index (mean ± SD): 17 ± 5 Number of words chosen (mean ± SD): 7 ± 5 Percentage of patients using the following pain sensory pain descriptors: Itchy: 50% Tender: 43% Throbbing 37% Burning: 33% Stinging: 33%		
Wong et al, 2012[47] N = 321	BPI				Pain interference (mean ± SD): 3.3 ± 2.5
Eusen et al, 2016[64] N = 81	DN4	Percentage of sample having neuropathic pain: 57.1%			

(Continues)

TABLE 3 (Continued)

Author(s), Year Sample size	Measures	Pain intensity	Pain quality	Pain pattern	Pain interference
Goto et al, 2016[61] N = 13	SF-MPQ2		Scores on the SF-MPQ-2 scale (median and interquartile range): Continuous pain: 18.5 (6.5–30.0) Intermittent pain: 11.5 (0.0–28.5) Neuropathic pain: 13.5 (3.0–22.3) Affective descriptors: 0.0 (0.0–10.0) Total pain score: 54.0 (13.3–78.5)		
Hellström et al, 2016[62] N = 763					38% of those reporting pain also reported pain interference with sleep
Salome and Ferreira (2018)[15] N = 90	MPQ NPS classified as: absence (0), mild (0–3), moderate (4–6), intense (7–10), pain		Moderate pain: 53.3% Intense pain: 46.7% Percentages of descriptors used (MPQ): None: 8.9% Sensory: 60% Affective: 51.1% Evaluative: 27.8% Miscellaneous: 32.2%		

Abbreviations: BPI, Brief pain inventory, DN4, DN4 Questionnaire (neuropathic pain questionnaire); MPQ, McGill Pain; NRS, Numeric Rating Scale, SF-MPQ2, Short form McGill Pain Questionnaire-2, VRS, Verbal Rating Scale.

Year of publication, gender distribution, and mean ulcer duration were not statistically significantly associated with mean pain intensity.

We found no significant indication of publication bias (Egger's test $P = .34$).

3.4 | Other pain characteristics

Information on pain characteristics was diverse and sparse. Therefore, a synthesis of wound pain characteristics (other than pain intensity) was not plausible. We present these studies' findings in Table 3 and describe them in a narrative way in the following. Seven studies reported on pain characteristics other than pain intensity. Three studies reported on characteristics assessed with the McGill Pain Questionnaire (MPQ), and one study used the neuropathic pain questionnaire Douleur Neuropathique 4 (DN4). One study reported on pain interference from the Brief Pain Inventory (BPI), and one reported on pain interference with sleep. One study reported on the temporal pattern of pain, without describing the means of assessment. Some studies reported pain intensity in a way that made it improper to include the data in the meta-analysis. Most of these excluded studies reported pain intensity corresponding to mild to moderate,[40,63] which is similar to results found in the studies included in the meta-analysis. Note that one excluded study[41] report a high prevalence (40%) of intense pain.

4 | DISCUSSION

To our knowledge, this is the first study attempting to synthesise prevalence and characteristics of wound-related background pain in persons with CVLU. The main findings in the present study suggest that as many as 80% of persons with CVLU have wound-related background pain. These patients report having mild to moderate pain intensity on average. Other characteristics of wound-related pain were not possible to synthesise from available research.

4.1 | Prevalence of wound-related pain

The prevalence of wound-related background pain in the studies included in this meta-analysis varies from 46% to 100%.[14,15,65] Possible reasons for this large variety of pain prevalence may be related to different research methods (eg, assess, report, define, and classify pain) that provide either lower or higher prevalence rates among studies. In the present meta-analysis, we excluded a number of studies because of such methodological inconsistencies that we believe contribute to an even greater variety of pain prevalence rates.

On one hand, lower estimates may occur as a result of the chosen pain assessment method. For instance, research shows that staff-administered instruments provide lower pain prevalence rates compared with oral or written self-report instruments.[66] Lower estimates may also occur because studies apply different definitions of pain. In some studies, no pain was defined as 3 or less (NRS 0–10), providing lower and faulty pain prevalence rates as they excluded patients with mild pain. Furthermore, studies only reporting on one type of pain, such as neuropathic pain,[64] likely under-report pain prevalence because they do not account for the fact that the patients may just as well have nociceptive or inflammatory pain, without a neuropathic component.

On the other hand, falsified high pain prevalence rates may occur when researchers do not explicitly assess wound-related pain. With general pain questions, the respondents may report pain caused by other pathologies. Therefore, studies that assessed pain with health-related QoL measures (eg, EQ-5d, SF-36) were excluded in this meta-analysis as it is likely that the patients report pain other than wound-related pain. However, even though all included studies imply that the pain reported is wound-related pain, it is not always clear if the patients have been explicitly asked about wound-related pain, and the patients do not report other frequent conditions such as musculoskeletal pain.

An additional interesting finding related to the prevalence of wound-related pain is the significantly larger prevalence rates reported by the effect studies compared with the descriptive studies. This was a somewhat surprising finding as the inclusion and exclusion criteria in the effect studies are generally stricter. This rigour may result in study samples that are healthier with fewer comorbidities, possibly leading to a lower pain prevalence. However, the strict selection of participants in the effect studies may also lead to study samples with more severe or larger wounds, potentially increasing the pain prevalence rates. Note that the number of studies included in this meta-analysis was small, with just six effect studies and four descriptive studies. Therefore, the variation of pain prevalence might also be the result of chance.

4.2 | Intensity of wound-related pain

The second main finding in this meta-analysis is the mean pain intensity of background wound-related pain of 4 (NRS 0–10), which is equivalent to mild to moderate pain.[67] Note that persons with mild to moderate pain usually do not need pain management. The finding of low pain intensity levels in this meta-analysis is surprising, considering that QoL studies show that pain may be the most bothersome symptom of having a CVLU.[68-70] A number of methodological factors may explain the discrepancies reported in the research literature. First, it is important to recognise the great variation in pain intensity (ie, standard deviations, interquartile ranges, etc.) reported within the different studies. We believe it is more relevant to look at the percentage share of the patient samples experiencing moderate to severe pain rather than mean values of pain intensities. Future studies should rather report pain characteristics and evaluate treatment effects based on pain intensity in these subgroups.

Second, another main concern regarding the low pain intensity reported in the literature is that few studies report pain prevalence. Furthermore, many studies do not inform whether they calculate the mean pain intensity score of only those patients who have pain (ie, score greater than 0 on the NRS) or include all patients in their intensity calculations regardless the pain score (ie, NRS 0 to the highest score). If the latter scenario is the case, the inclusion of scores of no pain (NRS 0) leads to a lower mean pain intensity score for the sample. In future studies, more detailed information on the assessment and calculation of pain intensity is needed.

It is challenging to extract an estimate of wound pain intensity because of the great variations of pain assessment tools used in the research literature. Ideally, researchers should strive towards using the recommended common standard of 0 to 10 NRS of pain intensity.[71] In 32 studies, we found eight different NRSs and three different VRSs for assessing pain intensity, with even more variation in anchors related to the different scales. Not all studies used 0 as the lowest anchor point of their pain scale, but all stated that the lowest point equals no pain. The highest anchor point, however, had various descriptions, including intense pain, extreme pain, unbearable pain, worst pain ever experienced, worst pain imaginable, extremely painful, severe pain, never felt such pain before, excruciating pain, most pain, and maximum pain. As all the included studies applied "no pain" as the lowest point and a descriptor of extreme pain as the highest point, as well as including enough options for participants to choose between different levels of pain intensity, we do believe that the studies included in this meta-analysis are comparable in terms of pain intensity measures.

The most frequent pain intensity assessment methods used in the included studies were visual analogue scales (VAS), NRS, and VRS. Note that most of the pain intensity measures in the included studies are crude and do not state whether the pain assessed is of maximum or average intensity or at rest vs in activity. Furthermore, all of these assessment methods have potential problems in this population of older persons. They all require some degree of abstract thinking and fine discrimination among the response alternatives. Such tasks may be difficult for the elderly because of cognitive changes, as well as lack of experience with psychometric tests. In addition, the VAS may be especially difficult to administer to frail patients or those with limited vision.[72] We assume that the studies have strived towards including persons with normal cognitive abilities. However, frailty and limited vision is still a potential risk of bias given the samples' high mean age and the limited methodology description in the included studies. In future research, and especially in clinical settings, it is important to carefully consider the assessment tool used and make sure to use methods suitable for the individual abilities of the person of interest. In general, research indicates that the NRS is proper to use in older people.[73]

4.3 | Wound pain characteristics

In this meta-analysis, we also aimed at describing a broad range of wound pain characteristics. However, we did not identify enough studies to synthesise any results regarding pain quality descriptors, temporal fluctuations, and pain interference with function. This is in itself an important finding, suggesting a knowledge gap in pain experienced by persons with CVLUs. It is of utmost importance that future studies apply validated and similar pain measures. Using common and standardised instruments provides the opportunity to investigate wound pain in subgroups of patients, as well as compare pain measures in persons with CVLUs with other patient groups. Therefore, we recommend using the NRS (0-10) for pain intensity. The BPI should be used for variations in pain intensity (ie, pain now, worst, least, average), pain localisation, and pain interference with physical and psychosocial functions. MPQ should preferably be used to assess pain qualities.[45,74] All of these instruments are frequently used to assess pain in numerous patient groups. For clinical purpose, these instruments can be applied in wound pain assessment; however, the clinical assessment must be individually customised to the patient's resources and needs.

An understanding of these pain characteristics may in fact be of great clinical benefit in the treatment of CVLUs. The location of pain can help identify the cause of the pain (eg, pain caused by oedema, fixation of bandages, tissue damage, and inflammation). Temporal fluctuations of pain can guide the clinicians in choosing the appropriate pain management (eg, patients with no pain during night time should not receive analgesics around the clock). In addition, pain interference with both physical, emotional, and social function is a better metric of suffering than pain intensity[75] and can help the clinician to tailor non-pharmacological pain management according to the patients' individual needs. Hypothetically, the wound-related background pain impact on function may be associated with the findings of pain as the most bothersome symptom of CVLUs in QoL studies. In future studies, the assessment of characteristics and consequences of wound-related pain are needed.

4.4 | Methodological discussion

Some methodological aspects of the existing research literature and the present meta-analysis need to be elucidated and discussed. First, the concept and definition of chronic wound-related background pain is often not clearly conceptualised and defined in research studies and the wound literature. While procedure-related and operative pain is often differentiated from other wound-related pain, we find no differentiation of background pain from incidence pain (eg, pain caused by activities[3,76]). From a clinical point of view, different types of pain experienced in everyday life (other than procedure related pain) is likely difficult for the person with CVLUs to segregate into different categories. As a result, in this systematic review, wound-related pain not caused by dressing change or other procedures are referred to as background pain.

We also need to be aware of the fact that we cannot state, based on the findings in this review and meta-analysis, that the pain reported by persons with chronic

CVLUs is a type of chronic pain. However, it is plausible that wound-related background pain because of chronic wounds (ie, duration >4 weeks) is, in its nature, more similar to chronic pain than acute pain. When pain is chronic, the measure of mean pain intensity alone is not sufficient.[75] A meaningful assessment of chronic pain is more demanding than assessing acute pain in both clinical practice and in research.[71] Taking into account that persons with CVLUs often experience acute procedure-related pain in addition to the more long-lasting background pain, they must be recognised as a patient group that is highly exposed to pain. The complex pain picture in persons with CVLUs needs to be recognised in both future studies and in clinical practice.

In the present meta-analysis, we used a broad search strategy in order to capture as many relevant studies as possible. In order to strengthen our results, we limited the impact of clinical heterogeneity by imposing strict selection criteria. The studies had to clearly identify wound diagnosis of CVLU, specify wound duration of at least 4 weeks, describe the pain measurement method used, and sufficiently report on relevant pain outcomes. In addition, eligible studies had to meet strict methodological quality criteria of the MMAT tool. This procedure left us with 36 sufficiently high-quality articles reporting on pain prevalence and pain characteristics. Several identified studies were excluded because of poor quality, and a vast number was excluded because of insufficient report of wound-related pain. Still, the tests for statistical heterogeneity in the included studies demonstrated substantial heterogeneity among the studies (I-squared >90%). Because of the small number of included studies, as well as limited data obtained from the studies, further statistical analyses of study variance were not possible to perform. However, we can speculate that the diversity of clinical and methodological factors may lead to the great differences of pain prevalence and intensity among the included studies. For instance, the use of compression therapy and pain medication may relieve pain and thereby influence both pain prevalence and pain characteristics. In addition, differences in when pain was assessed (ie, at rest, with activity, at its worst or average) may influence the results. Furthermore, studies that include patients with larger ulcer size likely report higher prevalence and intensity of wound pain. Note, however, that the size of the tissue injury is not always linearly related to the level of pain.[77] Likewise, patients recruited from hospital wards rather than outpatient clinics or community settings may have more serious disease and wound prognosis, thus experiencing wound-related pain more often and with higher intensity. The random sampling method used in effect studies may also lead to greater variability of wound pain among patient rather than convenience sampling from a more homogenous patient group often used in descriptive studies. Finally, the inconsistent use of different pain assessment tools, as well as the fact that these tools are not well suited for the older patient group, might have an impact on the variability of pain prevalence and intensity reported in the studies included in this meta-analysis.

It is crucial to be aware that only 10 studies on pain prevalence were included in the meta-analysis. Considering the vast number of studies assessed for eligibility, this is a small number of studies. This finding demonstrates a lack of high-quality research reporting pain prevalence in persons with CVLUs. One should therefore be careful to draw firm conclusions on wound-related pain prevalence based on this small number of studies but should also be aware that this is the best available current estimate.

Finally, despite setting strict inclusion and exclusion criteria, we found it complicated to synthesise the data obtained on wound-related pain in people with CVLUs. We argue that the lack of standardised methods for defining aetiology of wounds, as well as conceptualising, defining, and assessing core outcome measures such as pain, in combination with a lack of descriptions of the study samples, result in a heterogeneity that makes the synthesis of data very difficult. In general, there is a lack of high-quality evidence in the field of wound management. Researchers and clinicians do not use standardised methods for assessing wounds and core outcome measures such as pain.[77,79,80] Studies often have methodological flaws such as inadequate sample sizes, and they test pain-relieving interventions without focusing particularly on wound-related pain.[78-80] Our review of the literature demonstrates a need for valid and standardised assessment methods and tools of this important patient-reported outcome measure and more in-depth research on characteristics of background pain related to CVLUs.

In conclusion, we have obtained the best available research data to demonstrate that the majority of persons with CVLU experience wound-related background pain, reporting mild to moderate pain intensity. Because of the poor quality of the assessment and reporting of pain, it is likely that the research available underestimates the severity of wound pain and provides an inaccurate and simplified clinical picture. In the interest of improving the quality and reporting of data on pain prevalence and pain characteristics, we would encourage future studies to adhere to standardised methods for collecting and presenting data on wound and pain characteristics. Furthermore, the findings of pain intensity in this meta-analysis indicate a need for a shift in focus from mean values to variations and subgroups in order to provide a person-centred approach to clinical care and pain management for persons with CVLUs.

With the growing number of individuals living with CVLUs, it is crucial that we develop a better understanding of the pain that accompanies the ulcers. More importantly, it is imperative that clinicians are aware of the great extent and impact of background wound-related pain and know how to accurately assess, evaluate, and initiate an individualised pain management regimen to meet the patient's needs.

ACKNOWLEDGEMENTS

We thank academic librarian Marit Gjone Sandsleth at the department of Research and Internationalization, Library Unit at University of South-Eastern Norway (USN) who provided professional assistance in the literature-search process in this study. USN has funded the project based on funding from Norwegian Ministry of Education and Research. None of these institutions has had any roles in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

CONFLICT OF INTEREST

We declare that we have no competing interests.

ORCID

Lena Leren https://orcid.org/0000-0001-9083-5615

REFERENCES

1. Renner R, Seikowski K, Simon JC. Association of pain level, health and wound status in patients with chronic leg ulcers. *Acta Derm Venereol*. 2014;94(1):50-53.
2. Woo KY, Sibbald RG. Chronic wound pain: a conceptual model. *Adv Skin Wound Care*. 2008;21(4):175-188.
3. WUWHS. Principles of best practice: minimising pain at wound dressing-related procedures. *A Consensus Document: World Union of Wound Healing Societies*; 2004. London: Medical Education Partnership. Retrieved from: http://www.woundsinternational.com/media/issues/79/files/content_39.pdf.
4. White R. Pain assessment and management in patients with chronic wounds. *Nurs Stand*. 2008;22(32):62-68.
5. Stechmiller JK, Lyon D, Schultz G, et al. Biobehavioral mechanisms associated with nonhealing wounds and Psychoneurologic symptoms (pain, cognitive dysfunction, fatigue, depression, and anxiety) in older individuals with chronic venous leg ulcers. *Biol Res Nurs*. 2019;407-419.
6. Nussbaum SR, Carter MJ, Fife CE, et al. An economic evaluation of the impact, cost, and medicare policy implications of chronic nonhealing wounds. *Value Health*. 2018;21(1):27-32.
7. Heyer K, Herberger K, Protz K, Glaeske G, Augustin M. Epidemiology of chronic wounds in Germany: analysis of statutory health insurance data. *Wound Repair and Regen*. 2016;24(2):434-442.
8. Guest JF, Ayoub N, McIlwraith T, et al. Health economic burden that wounds impose on the National Health Service in the UK. *BMJ Open*. 2015;5(12):e009283.
9. Margolisa DJ, Bilkerb W, Santannab J, d Baumgartenc M. Venous leg ulcer: incidence and prevalence in the elderly. *J Am Acad Dermatol*. 2002;46(3):381-386.
10. Guo S, DiPietro LA. Factors affecting wound healing. *J Dent Res*. 2010;89(3):219-229.
11. Werdin F, Tennenhaus M, Schaller H-E, Rennekampff H-O. Evidence-based management strategies for treatment of chronic wounds. *Eplasty*. 2009;9:169-179.
12. Vishwanath V. Quality of life: venous leg ulcers. *Indian Dermatol Online J*. 2014;5(3):397-399.
13. Woo KY, Sibbald RG, Fogh K, et al. Assessment and management of persistent (chronic) and total wound pain—Reprinted courtesy of Blackwell publishing, who retains the copyright. It first appeared in the international wound J 2008;5(2). *W Council Enter Ther J*. 2009;29(2):8-17.
14. Paul J. A cross-sectional study of chronic wound-related pain and itching. *Ostomy Wound Manage*. 2013;59(7):28-34.
15. Salome G, Ferreira L. The impact of decongestive physical therapy and elastic bandaging on the control of pain in patients with venous ulcers. *Rev Col Bra Cir*. 2018;45(2):e1385.
16. Szewczyk MT, Moscicka P, Cwajda J, Piotrowicz R, Jawien A. Evaluation of the effectiveness of new polyurethane foam dressings in the treatment of heavily exudative venous ulcers. [polish, English]. *Acta Angiologica*. 2007;13(2):85-93.
17. Sussman C, Bates-Jensen BM. Management of wound pain. Wound care: a collaborative practice manual: Lippincott Williams & Wilkins; 2007.
18. Charles H. Venous leg ulcer pain and its characteristics. *J of Tissue Viability*. 2002;12(4):154-158.
19. McMullen M. The relationship between pain and leg ulcers: a critical review. *Br J Nurs*. 2004;13(Sup4):S30-S36.
20. Grant MJ, Booth A. A typology of reviews: an analysis of 14 review types and associated methodologies. *Health Info Libr J*. 2009;26(2):91-108.
21. Pluye P, Hong QN. Combining the power of stories and the power of numbers: mixed methods research and mixed studies reviews. *Annu Rev Public Health*. 2014;35:29-45.
22. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev*. 2015;4(1):1.
23. Pope C, Mays N, Popay J. *Synthesising Qualitative and Quantitative Health Evidence: A Guide to Methods*. UK: McGraw-Hill Education; 2007.
24. Pearson A, White H, Bath-Hextall F, et al. Methodology for JBI mixed methods systematic reviews. *Adelaide: The Joanna Briggs Institute*. 2014;2014:5-34.
25. Pluye P, Robert E, Cargo M, Bartlett G, O'Cathain A, Griffiths F, et al. Proposal: A mixed methods appraisal tool for systematic mixed studies reviews 2011 29.05.2018.
26. Pace R, Pluye P, Bartlett G, et al. Testing the reliability and efficiency of the pilot mixed methods appraisal tool (MMAT) for systematic mixed studies review. *Int J Nurs Stud*. 2012;49(1):47-53.
27. Collins SL, Moore RA, McQuay HJ. The visual analogue pain intensity scale: what is moderate pain in millimetres? *Pain*. 1997;72(1–2):95-97.
28. Kahl C, Cleland JA. Visual analogue scale, numeric pain rating scale and the McGill pain questionnaire: an overview of psychometric properties. *Phys Ther Rev*. 2005;10(2):123-128.

29. Williamson A, Hoggart B. Pain: a review of three commonly used pain rating scales. *J Clin Nurs*. 2005;14(7):798-804.
30. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med Res Methodol*. 2005;5(1):13.
31. Nyaga VN, Arbyn M. *Aerts M*. Stata module to perform fixed and random effects meta-analysis of proportions: METAPROP; 2017.
32. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327(7414):557-560.
33. Teepe RG, Roseeuw DI, Hermans J, et al. Randomized trial comparing cryopreserved cultured epidermal allografts with hydrocolloid dressings in healing chronic venous ulcers. *J Am Acad Dermatol*. 1993;29(6):982-988.
34. Morrell CJ, Walters SJ, Dixon S, et al. Cost effectiveness of community leg ulcer clinics: randomised controlled trial. *BMJ*. 1998;316(7143):1487-1491.
35. Santilli SM, Valusek PA, Robinson C. Use of a noncontact radiant heat bandage for the treatment of chronic venous stasis ulcers. *Adv Wound Care*. 1999;12(2):89-93.
36. Walters SJ, Morrell CJ, Dixon S. Measuring health-related quality of life in patients with venous leg ulcers. *Qual Life Res*. 1999;8(4):327-336.
37. Wilson J, Arseculeratne Y, Yang Y, Cherry G. Healing venous ulcers with cycloidal multidirectional vibration therapy. *J Wound Care*. 2002;11(10):395-398.
38. Navratilova Z, Slonkova V, Semradova V, Adler J. Cryopreserved and lyophilized cultured epidermal allografts in the treatment of leg ulcers: a pilot study. *J Eur Acad Dermatol Venereol*. 2004;18(2):173-179.
39. Mermet I, Pottier N, Sainthillier JM, et al. Use of amniotic membrane transplantation in the treatment of venous leg ulcers. *Wound Repair Regen*. 2007;15(4):459-464.
40. Cameron J, Hoffman D, Wilson J, Cherry G. Comparison of two peri-wound skin protectants in venous leg ulcers: a randomised controlled trial. *J Wound Care*. 2005;14(5):233-236.
41. Benigni J, Lazareth I, Parpex P, et al. Efficacy, safety and acceptability of a new two-layer bandage system for venous leg ulcers. *J Wound Care*. 2007;16(9):385-390.
42. Jünger M, Arnold A, Zuder D, Stahl HW, Heising S. Local therapy and treatment costs of chronic, venous leg ulcers with electrical stimulation (Dermapulse®): a prospective, placebo controlled, double blind trial. *Wound Repair Regen*. 2008;16(4):480-487.
43. Edwards H, Courtney M, Finlayson K, Shuter P, Lindsay E. A randomised controlled trial of a community nursing intervention: improved quality of life and healing for clients with chronic leg ulcers. *J Clin Nurs*. 2009;18(11):1541-1549.
44. Brizzio E, Amsler F, Lun B, Blättler W. Comparison of low-strength compression stockings with bandages for the treatment of recalcitrant venous ulcers. *J Vasc Surg*. 2010;51(2):410-416.
45. Schumann H, Calow T, Weckesser S, Müller M, Hoffmann G. Water-filtered infrared a for the treatment of chronic venous stasis ulcers of the lower legs at home: a randomized controlled blinded study. *Br J Dermatol*. 2011;165(3):541-551.
46. Escandon J, Vivas AC, Perez R, Kirsner R, Davis S. A prospective pilot study of ultrasound therapy effectiveness in refractory venous leg ulcers. *Int Wound J*. 2012;9(5):570-578.
47. Wong IK, Andriessen A, Lee DT, et al. Randomized controlled trial comparing treatment outcome of two compression bandaging systems and standard care without compression in patients with venous leg ulcers. *J Eur Acad Dermatol Venereol*. 2012;26(1):102-110.
48. Olyaie M, Rad FS, Elahifar M-A, Garkaz A, Mahsa G. High-frequency and noncontact low-frequency ultrasound therapy for venous leg ulcer treatment: a randomized, controlled study. *Ostomy Wound Manage*. 2013;59(8):14-20.
49. Park KY, Kim IS, Yeo IK, Kim BJ, Kim MN. Treatment of refractory venous stasis ulcers with autologous platelet-rich plasma and light-emitting diodes: a pilot study. *Journal of Dermatological Treatment*. 2013;24(5):332-335.
50. Beheshti A, Shafigh Y, Parsa H, Zangivand AA. Comparison of high-frequency and MIST ultrasound therapy for the healing of venous leg ulcers. *Advances in Clinical and Experimental Medicine: Official Organ Wroclaw Medical University*. 2014;23(6):969-975.
51. Brown A, Augustin M, Jünger M, et al. Randomized standard-of-care-controlled trial of a silica gel fibre matrix in the treatment of chronic venous leg ulcers. *Eur J Dermatol*. 2014;24(2):210-216.
52. Bradbury S, Walkley N, Ivins N, Harding K. Clinical evaluation of a novel topical negative pressure device in promoting healing in chronic wounds. *Adv Wound Care*. 2015;4(6):346-357.
53. Brehmer F, Haenssle H, Daeschlein G, et al. Alleviation of chronic venous leg ulcers with a hand-held dielectric barrier discharge plasma generator (PlasmaDerm® VU-2010): results of a monocentric, two-armed, open, prospective, randomized and controlled trial (NCT 01415622). *J Eur Acad Dermatol Venereol*. 2015;29(1):148-155.
54. Gibbons GW, Orgill DP, Serena TE, et al. A prospective, randomized, controlled trial comparing the effects of noncontact, low-frequency ultrasound to standard care in healing venous leg ulcers. *Ostomy Wound Manage*. 2015;61(1):16-29.
55. White J, Ivins N, Wilkes A, Carolan-Rees G, Harding KG. Non-contact low-frequency ultrasound therapy compared with UKstandard of care for venous leg ulcers: a single-Centre, assessor-blinded, randomised controlled trial. *Int Wound J*. 2015;13(5):833-842.
56. Harding KG, Szczepkowski M, Mikosiński J, et al. Safety and performance evaluation of a next-generation antimicrobial dressing in patients with chronic venous leg ulcers. *Int Wound J*. 2016;13(4):442-448.
57. Vitse J, Bekara F, Byun S, Herlin C, Teot L. A double-blind, placebo-controlled randomized evaluation of the effect of low-level laser therapy on venous leg ulcers. *Int J Low Extrem Wounds*. 2017;16(1):29-35.
58. Domingues EAR, Kaizer UAO, Lima MHM. Effectiveness of the strategies of an orientation programme for the lifestyle and wound-healing process in patients with venous ulcer: a randomised controlled trial. *Int Wound J*. 2018;15(5):798-806.
59. Jones J, Barr W, Robinson J, Carlisle C. Depression in patients with chronic venous ulceration. *Br J Nurs*. 2006;15(Sup2):S17-S23.
60. Cwajda-Białasik J, Szewczyk MT, Mościcka P, Cierzniakowska K. The locus of pain control in patients with lower limb ulcerations. *J Clin Nurs*. 2012;21(23–24):3346-3351.

61. Goto T, Tamai N, Nakagami G, et al. Can wound exudate from venous leg ulcers measure wound pain status?: a pilot study. *PLoS One*. 2016;11(12):e0167478.
62. Hellström A, Nilsson C, Nilsson A, Fagerström C. Leg ulcers in older people: a national study addressing variation in diagnosis, pain and sleep disturbance. *BMC Geriatr*. 2016;16(1):25.
63. Closs SJ, Nelson EA, Briggs M. Can venous and arterial leg ulcers be differentiated by the characteristics of the pain they produce? *J Clin Nurs*. 2008;17(5):637-645.
64. Eusen M, Brenaut E, Schoenlaub P, Saliou P, Misery L. Neuropathic pain in patients with chronic leg ulcers. *J Eur Acad Dermatol Venereol*. 2016;30(9):1603-1605.
65. Szewczyk MT, Mościcka P, Cwajda J, Piotrowicz R, Jawień A. Evaluation of the effectiveness of new polyurethane foam dressings in the treatment of heavily exudative venous ulcers. *Acta Angiologica*. 2007;13(2):85-93.
66. Kappesser J. Williams ACdC. Pain estimation: asking the right questions. *Pain*. 2010;148(2):184-187.
67. Woo A, Lechner B, Fu T, et al. Cut points for mild, moderate, and severe pain among cancer and non-cancer patients: a literature review. *An Pall Med*. 2015;4(4):176-183.
68. Parker K. Psychosocial effects of living with a leg ulcer. *Nurs Stand*. 2012;26(45):50-6,60,2.
69. Briggs M, Flemming K. Living with leg ulceration: a synthesis of qualitative research. *J Adv Nurs*. 2007;59(4):319-328.
70. Persoon A, Heinen MM, Van Der Vleuten CJ, De Rooij MJ, Van De Kerkhof P, Van Achterberg T. Leg ulcers: a review of their impact on daily life. *J Clin Nurs*. 2004;13(3):341-354.
71. Breivik H, Borchgrevink P, Allen S, et al. Assessment of pain. *BJA: British Journal of Anaesthesia*. 2008;101(1):17-24.
72. Woo K, Sibbald G, Fogh K, et al. Assessment and management of persistent (chronic) and total wound pain. *Int Wound J*. 2008;5(2):205-215.
73. Hjermstad MJ, Fayers PM, Haugen DF, et al. Studies comparing numerical rating scales, verbal rating scales, and visual analogue scales for assessment of pain intensity in adults: a systematic literature review. *J Pain Symptom Manage*. 2011;41(6):1073-1093.
74. The British Pain Society (2019) Outcome measures. London: Faculty of Pain Medicine of the Royal College of Anaesthetists. Retrieved from: https://www.britishpainsociety.org/static/uploads/resources/files/Outcome_Measures_January_2019.pdf. 2011;41(6):1073-1093.
75. Ballantyne JC, Sullivan MD. Intensity of chronic pain—the wrong metric? *New Eng J Med*. 2015;373(22):2098-2099.
76. EWMA. *Pain at Wound Dressing Changes*. Medical Education Partnership: Position Document; 2002 http://ewma.org/fileadmin/user_upload/EWMA/pdf/Position_Documents/2002/Spring_2002__English_.pdf.
77. Pain IAFTSo. IASP terminology. https://www.iasp-pain.org/Education/Content.aspx?ItemNumber=1698#Pain2017
78. Gottrup F, Apelqvist J, Price P. Outcomes in controlled and comparative studies on non-healing wounds: recommendations to improve the quality of evidence in wound management. *J Wound Care*. 2010;19(6):237-268.
79. Gethin G, Killeen F, Devane D. Heterogeneity of wound outcome measures in RCTs of treatments for VLUs: a systematic review. *J Wound Care*. 2015;24(5):211-226.
80. Lazarus G, Valle MF, Malas M, et al. Chronic venous leg ulcer treatment: future research needs. *Wound Repair Regen*. 2014;22(1):34-42.

How to cite this article: Leren L, Johansen E, Eide H, Falk RS, Juvet LK, Ljoså TM. Pain in persons with chronic venous leg ulcers: A systematic review and meta-analysis. *Int Wound J*. 2020;17:466–484. https://doi.org/10.1111/iwj.13296

APPENDIX 1: COMPLETE SEARCH STRATEGY

#	Search
1	exp *Leg ulcer/*
2	*(”chronic wound*” or “chronic ulcer*” or “leg wound*” or “leg ulcer” or “foot ulcer*” or “foot wound*” or “venous ulcer*” or “venous wound*” or “venous foot” or “varicose ulcer*” or "varicose wound*” or “diabetic foot” or “diabetic wound*” or “diabetic ulcer*” or “diabetic foot ulcer*” or “stasis wound*” or “stasis ulcer*”).tw.*
3	1 or 2
4	*(MH "Pain") OR (MM "Acute Pain") OR (MM "Neuralgia") OR (MM "Nociceptive Pain") OR (MM "Chronic Pain") OR (MM "Breakthrough Pain")*
5	exp *Hyperalgesia/*
6	exp *Pain Perception*
7	exp *Pain measurement/*
8	*(“pain prevalence” or “pain intensit*” or “pain qualit*” or “pain characteristic*” or “nociceptive pain” or “nociception” or “chronic pain” or “neuropathic pain” or “hyperalgesia” or “pain perception” or “neuralgia” or “acute pain” or “allodynia” or “pain assessment” or “pain measurement” or “breakthrough pain” or “background pain” or “persistent pain” or “inflammatory pain”).tw.*
9	4 or 5 or 6 or 7 or 8
10	2 and 9
11	Limit 10 to (yr="1990 - 2016" and (classical article or clinical study or clinical trial, all or comparative study or controlled clinical trial or "corrected and republished article" or evaluation studies or journal article or meta-analysis or multicenter study or observational study or pragmatic clinical trial or randomized controlled trial or "review" or "scientific integrity review" or systematic reviews or validation studies))

Medline search strategy

#	Search
1	exp *leg ulcer/*
2	exp *wounds, chronic/*
3	*(“chronic wound*” or “chronic ulcer*” or “leg wound*” or “leg ulcer*” or “foot ulcer*” or “foot wound*” or “venous ulcer*” or “venous wound*” or “varicose ulcer*” or “varicose wound*” or “venous foot” or “diabetic foot” or “diabetic wound*” or “diabetic ulcer*” or “diabetic foot ulcer*” or “stasis wound*” or “stasis ulcer*”).tw.*
4	1 or 2 or 3
5	*(MH "Pain") OR (MM "Breakthrough Pain") OR (MM "Neuralgia") OR (MM "Nociceptive Pain")*
6	exp *allodynia/*
7	exp *chronic pain/*
8	exp *hyperalgesia/*
9	exp *pain measurement/*
10	*(“pain prevalence” or “pain intensit*” or “pain qualit*” or “pain characteristic*” or “nociceptive pain” or “nociception” or “chronic pain” or “neuropathic pain” or “hyperalgesia” or “pain perception” or “neuralgia” or “acute pain” or “allodynia” or “pain assessment” or “pain measurement” or “breakthrough pain” or “background pain” or “persistent pain” or “inflammatory pain”).tw.*
11	5 or 6 or 7 or 8 or 9 or 10
12	4 and 11
13	Limit 12 to: Published Date: 19900101-20161231; Publication Type: Brief Item, Clinical Trial, Corrected Article, Journal Article, Meta Analysis, Meta Synthesis, Questionnaire/Scale, Randomized Controlled Trial, Research, Research Instrument, Review, Statistics, Systematic Review

Cinahl search strategy

#	Search
1	exp _leg ulcer/_
2	exp _foot ulcer/_
3	exp _diabetic foot/_
4	exp _chronic wound/_
5	_("chronic wound*" or "chronic ulcer*" or "leg wound*" or "leg ulcer*" or "foot ulcer*" or "foot wound*" or "venous ulcer*" or "venous wound*" or "varicose ulcer*" or "varicose wound*" or "venous foot" or "diabetic foot" or "diabetic wound*" or "diabetic ulcer*" or "diabetic foot ulcer*" or "stasis wound*" or "stasis ulcer*").tw._
6	1 or 2 or 3 or 4 or 5
7	Pain (ink. Acute pain)/ or allodynia/ or breakthrough pain/ or chronic pain/ or hyperalgesia/ or neuralgia/ or nociceptive pain/
8	_nociception/_
9	pain assessment/ or brief pain inventory/ or mcgill pain questionnaire/ or visual analog scale/
10	exp _pain measurement/_
11	_Pain intensity/_
12	_("pain prevalence" or "pain intensit*" or "pain qualit*" or "pain characteristic*" or "nociceptive pain" or "nociception" or "chronic pain" or "neuropathic pain" or "hyperalgesia" or "pain perception" or "neuralgia" or "acute pain" or "allodynia" or "pain assessment" or "pain measurement" or "breakthrough pain" or "background pain" or "persistent pain" or "inflammatory pain"). tw._
13	7 or 8 or 9 or 10 or 11 or 12
14	6 and 13
15	Limit 14 to (yr="1990 - 2016") and (article or report or "review" or short survey)

Embase search strategy

#	Search
1	exp _Leg ulcer/_
2	_("chronic wound*" or "chronic ulcer*" or "leg wound*" or "leg ulcer" or "foot ulcee*" or "foot wound*" or "venous ulcer*" or "venous wound*" or "venous foot" or "varicose ulcer*" or "varicose wound*" or "diabetic foot" or "diabetic wound*" or "diabetic ulcer*" or "diabetic foot ulcer*" or "stasis wound*" or "stasis ulcer*").tw._
3	1 or 2
4	_(MH "Pain") OR (MM "Acute Pain") OR (MM "Neuralgia") OR (MM "Nociceptive Pain") OR (MM "Chronic Pain") OR (MM "Breakthrough Pain")_
5	exp _Hyperalgesia/_
6	exp _Pain Perception_
7	exp _Pain measurement/_
8	_("pain prevalence" or "pain intensit*" or "pain qualit*" or "pain characteristic*" or "nociceptive pain" or "nociception" or "chronic pain" or "neuropathic pain" or "hyperalgesia" or "pain perception" or "neuralgia" or "acute pain" or "allodynia" or "pain assessment" or "pain measurement" or "breakthrough pain" or "background pain" or "persistent pain" or "inflammatory pain"). tw._
9	4 or 5 or 6 or 7 or 8
10	2 and 9

Cochrane search strategy

#	Search
1	SU.EXACT("Wounds") OR SU.EXACT("Leg Ulcers") OR "leg ulcer*" OR "foot ulcer*" OR "diabetic foot" OR "varicose ulcer*" OR "chronic wound*" OR "chronic ulcer*" OR "leg wound*" OR "leg ulcer*" OR "foot ulcer*" OR "foot wound*" OR "venous ulcer*" OR "venous wound*" OR "venous foot*" OR "varicose ulcer*" OR "varicose wound*" OR "diabetic foot" OR "diabetic wound*" OR "diabetic ulcer*" OR "diabetic foot ulcer*" OR "stasis wound*" OR "stasis ulcer*"
2	SU.EXACT("Pain: Measurement") OR SU.EXACT("Pain and Pain Management") OR "pain prevalence" OR "pain qualit*" OR "pain intensit*" OR "pain characteristic*" OR "Nociceptive pain" OR Nociception OR "Chronic pain" or "Neuropathic pain" OR Hyperalgesia OR "pain perception" OR Neuralgia OR "Acute pain" OR Allodynia OR "Pain assessment" OR "Pain measurement" OR "background pain" OR "breakthrough pain" OR "persistent pain" OR "inflammatory pain"
3	1 AND 2
4	Limit 3 to (Date: After January 01 1990) and (Document type: Article, Case Study, Evidence Based Healthcare, Interview, Literature Review, Review)

British Nursing Index search strategy

Paper II

Leren, L., Johansen, E., Eide, H., Falk, R. S., & Ljoså, T. M. (2021). Prevalence and factors associated with ulcer-related pain in persons with chronic leg ulcers—an explorative study. *Journal of Clinical Nursing*, *30*(17-18), 2732–2741. https://doi.org/10.1111/jocn.15787

Received: 3 November 2020 | Revised: 19 March 2021 | Accepted: 23 March 2021

DOI: 10.1111/jocn.15787

Journal of Clinical Nursing WILEY

ORIGINAL ARTICLE

Prevalence and factors associated with ulcer-related pain in persons with chronic leg ulcers—an explorative study

Lena Leren RN, MSc, PhD, Candidate[1] | Edda Aslaug Johansen RN, PhD, Associated Professor[1] | Hilde Eide RN, PhD, Professor[1] | Ragnhild Sørum Falk PhD, Statistician[2] | Tone Marte Ljoså RN, PhD, Associated Professor[1]

[1]Faculty of Nursing and Health Sciences, University of South-Eastern, Notodden, Norway

[2]Oslo Center for Biostatistics and Epidemiology, University of Oslo, Oslo, Norway

Correspondence

Lena Leren, USN, Faculty of Nursing and Health Sciences, University of South-Eastern Norway.
Email: lena.leren@usn.no

Funding information

The University of South-Eastern Norway has funded the project based on funding from Norwegian Ministry of Education and Research. None of the above-mentioned institutions has any roles in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

Abstract

Aims and Objectives: The aims of this study were to explore the prevalence of background pain and identify demographic, clinical and psychosocial factors associated with moderate to severe background pain in persons with leg ulcers.

Background: All chronic leg ulcers are potentially painful. Research indicates that 80% of persons with chronic leg ulcers experience wound-related background pain. However, studies on factors associated with pain have small samples and findings are inconclusive.

Design: Exploratory cross-sectional study.

Method: This quantitative study recruited persons with chronic leg ulcers (N = 252) from two wound care clinics using consecutive sampling method. Data were obtained through screening interview, clinical examination and questionnaires. Logistic regression with stepwise backwards elimination was used to identify factors associated with moderate to severe background pain. The STROBE checklist for cross-sectional studies was used for reporting this study.

Results: Background pain was reported by 64% of the participants. Inferential statistical analyses suggest that between 58% and 69% of persons with chronic leg ulcers suffer from this type of pain. Factors associated with moderate to severe pain were older age, female gender, reduced sleep quality and diminished health status. In the final model, reduced sleep quality increased the likelihood of having moderate to severe pain in persons with good health status while not in persons with diminished health status.

Conclusion: Ulcer-related background pain is common in persons with chronic leg ulcers. Older females reporting insomnia symptoms also had increased risk of moderate to severe ulcer-related background pain. These participants also perceived their health status to be better.

Relevance to clinical practice: This study demonstrates that ulcer-related background pain and associated factors needs more attention in clinical practice. Furthermore, nurses and other healthcare professionals should integrate biopsychosocial strategies to assess and manage ulcer-related background pain.

KEYWORDS
biopsychosocial pain model, chronic leg ulcer, pain, pain prevalence, ulcer-related pain

What does this paper contribute to the wider global clinical community?

- Ulcer-related background pain is a common and significant problem that needs to be addressed in clinical practice.
- The results suggest that nurses and other healthcare providers should be especially aware of pain in older females with insomnia symptoms and perceived good health status.
- This study demonstrates the need for an individual and holistic pain assessment of all persons presenting with a chronic leg ulcer to identify those in need of pain management.

1 | INTRODUCTION

Leg ulcers are hard-to-heal wounds localised on the lower leg or foot commonly caused by venous insufficiency, arterial insufficiency, diabetes and rheumatoid arthritis (Tollow & Ogden, 2019). The chronicity of wounds is defined as a failure 'to proceed through an orderly and timely process to produce anatomic and functional integrity' (Lazarus et al., 1994). The prevalence of chronic leg ulcers in the general population is estimated to be 1.5 per 1000 persons (Martinengo et al., 2019). Since the incidence of wounds rise with age, the prevalence is likely to rise as the population ages (Atkin et al., 2019). All types of chronic leg ulcers, irrespective of pathology, are associated with a negative impact on patients' physical and psychosocial function and health status which may result in a significant decline in quality of life (Cunha et al., 2017; Franks & Morgan, 2003; Herber et al., 2007). In addition, chronic wounds are a major financial burden to the society (Olsson et al., 2019). Finally, research report that all chronic leg ulcers are potentially painful (WUWHS, 2007; Zaidi et al., 2019). Most available research on ulcer-related pain focus on procedure related pain. Ulcer-related background pain, and factors associated with this pain have not been adequately studied.

2 | BACKGROUND

Pain is defined as 'An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage' (IASP, 2020). This definition covers both physical and emotional components of the pain experience and reflects the definition that 'pain is whatever the experiencing person says it is' (McCaffery and Beebe, 1996). Persons with chronic leg ulcers may experience various types of pain. Ulcer-related pain can be nociceptive, neuropathic or inflammatory in nature, as well as acute and/or persistent (White, 2008; Woo & Sibbald, 2008). The World Union of Wound Healing Society (2004) classifies ulcer-related pain as background, incident, procedural and operative pain. Ulcer pain can be caused by the underlying pathology of the leg ulceration and the wound itself, various daily activities, the ulcer treatment, as well as complications such as skin irritation and infection (Renner et al., 2014).

The present study focusses on ulcer-related background pain defined as pain related to wounds experienced in everyday life (other than procedural/operative pain) (Leren et al., 2020). This type of pain is highly prevalent and reduces quality of life (Olsson et al., 2019). A recently published systematic review and meta-analysis reported that up to 80% of persons with chronic wounds experience mild to moderate pain (mean pain intensity of 4 out of 10, 95% CI 3.5, 4.5) between dressing changes (Leren et al., 2020).

According to the existing literature, several demographic and clinical factors that are associated with pain and common across the general population and in persons with ulcers. Female gender (Fillingim et al., 2009), older age (Gibson & Farrell, 2004) and reduced quality of life (Breivik et al., 2006) are factors typically associated with more severe pain in the general population. Female gender (Guarnera et al., 2007), poorer health status (Guarnera et al., 2007; Renner et al., 2014), disturbed sleep (Hellström et al., 2016), as well as wound aetiology (Domingues et al., 2016; Guarnera et al., 2007; Paul, 2013) and size (Salvetti et al., 2014) are factors associated with presence of or more severe ulcer-related pain in persons with chronic ulcers. However, other studies found no such association between ulcer-related pain and female gender (Domingues et al., 2016; Renner et al., 2014; Salvetti et al., 2014), or age (Domingues et al., 2016; Renner et al., 2014; Salvetti et al., 2014). Clearly, the literature on factors associated with ulcer-related pain is inconclusive, and typically small and underpowered studies show no significant associations among relevant factors and ulcer-related pain. Further exploration is warranted to identify risk factors for vulnerable patient groups, so that adequate prevention and management of pain can be provided.

In an e-Delphi study from 24 countries and 360 experts, pain management is listed as one of the top educational priorities in wound care (Cowman et al., 2012). While there are differences in nurses' legislated scope of practice across nations and continents, nurses have an overall responsibility to ensure that persons experiencing pain are adequately assessed and provided with effective pain management (American Nurses Association, 2018). Furthermore, pain assessment and management are identified as a main category of the 'wound management and assessment' area for registered nurses providing care for chronic wounds (Kielo et al., 2019). However, wound care researchers report that persistent ulcer-related pain is either dismissed by healthcare providers or inappropriately assessed (Frescos, 2018; Green et al., 2018). Presumably, lack of knowledge (Green et al., 2018) or time (Frescos, 2018; Green et al., 2018) may be reasons for inadequate pain assessment. Increased knowledge about ulcer-related background pain and associated factors can support nurses in the provision of holistic and person-centred care to persons with chronic leg ulcers.

There is a need for larger and methodologically sound studies to provide research-based knowledge and identify risk factors of ulcer-related background pain and vulnerable persons. Therefore, the objectives of the present study are to explore the prevalence of background pain, and identify the demographic, clinical and psychosocial factors associated with moderate to severe background pain.

3 | METHOD

3.1 | Design and recruitment

This exploratory cross-sectional study used a consecutive sampling method to recruit participants who attended out-patient wound clinics. Participants were approached and recruited on the day of a scheduled appointment. Inclusion criteria were as follows: (a) presence of an open wound located below the knee, (b) wound duration of 6 weeks or longer, (c) age 18 years or older, (d) ability to understand and read Norwegian and (e) no comprehension difficulties. Exclusion criteria included the following ulcer causes: burns, cancer, radiation treatment, pressure due to immobility and immunological factors. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline (Von Elm et al., 2014) (see Data S1).

3.2 | Sample size and data collection

A traditional power analysis was not performed for this study, since there were scarce data on the prevalence of background pain in persons with chronic leg ulcers at the time of recruitment. However, we aimed at recruiting at least 170 respondents to be able to explore the association of 6–8 factors with moderate to severe pain. We assumed a small proportion of missing data and a response-rate of approximately 70%. To reach the sample size, we collected data at two wound care outpatient clinics in South-Eastern Norway over a period of 22 months (from March 2017 to December 2018). Information was gathered by means of screening interviews, clinical examinations and self-administered questionnaires.

3.2.1 | Screening interview

An initial screening interview with each patient was carried out by one of the authors (LL), and took place before scheduled appointment at the wound care clinic. Participants were screened for presence and type of wound pain. All participants were asked 'Do you experience any pain in relation to your ulcer?'. If participants confirmed having pain, the following questions were posed: 'Do you experience wound pain in relation to dressing change?' and 'Do you experience wound pain unrelated to dressing change?'. These three questions were answered using a yes-no format. Data on wound duration and comorbidities was also gathered in the brief interview.

3.2.2 | Clinical examination

During the scheduled appointment at the clinic, a medical doctor assessed the ulcer, and stated the diagnosis (i.e., venous leg ulcer, diabetic foot ulcer, traumatic ulcer, unspecified ulcer). One of the authors (LL) performed all clinical wound examinations and collected data on wound characteristics to avoid inter-rater variability. Wound size was estimated by measuring the width (millimeters at the widest) and height (millimeters at the highest) of the wound. The area was calculated using the formula for an ellipse.

3.2.3 | Questionnaires

All participants received a battery of self-report questionnaires on the day of recruitment. They were asked to answer the questionnaires the following day and return them by mail in a pre-paid envelope. The questionnaires contained items regarding demography, insomnia symptoms and health status. Participants with wound-related background pain also received questionnaires regarding pain.

Demography

Information was collected on age, gender, work situation, education, living arrangements and ethnicity.

EuroQuol Visual Analogue Scale (EQ VAS)

The EQ VAS (0–100) was used to obtain information on the respondents' self-reported health status (Oppe et al., 2007). Higher scores indicate better self-perceived health status. The Norwegian translation of the EQ-5D, including EQ VAS, has demonstrated satisfactory measurement properties (Solberg et al., 2005). The original English version of the EQ VAS has been used in studies of persons with chronic leg ulcers (Renner et al., 2014). Missing values in EQ VAS (n=3) were replaced by mean imputation.

Insomnia Severity Index (ISI)

The ISI is a brief self-report instrument measuring the patient's perception of their sleep. The ISI targets the subjective symptoms and consequences of insomnia as well as the degree of concerns or distress caused by those difficulties (Bastien et al., 2001; Morin et al., 2011). Its content corresponds in part to the diagnostic criteria of insomnia (Helsedirektoratet, 2016). Each of the seven items in ISI is rated on a 0–4 scale, where zero indicates no problem and four indicates severe problems. The total score ranges from 0 to 28. The total score is interpreted as follows: absence of insomnia (0–7), sub-threshold insomnia (8–14), moderate insomnia (15–21) and severe insomnia (22–28) (Bastien et al., 2001). The ISI has been translated into several languages and has demonstrated acceptable psychometric properties in studies of the general population with primary insomnia or normal sleeping (Bastien et al., 2001). The Norwegian version of the ISI is widely used, and has demonstrated satisfactory validity (Filosa et al., 2020). Missing values in ISI were replaced by median of nearest point (in total nine individual items). The Cronbach's alpha for ISI was.92 in this study.

The Brief Pain Inventory (BPI)

The BPI is a self-report questionnaire regarding pain characteristics.

The 0 (no pain) to 10 (worst pain imaginable) numeric rating scale (NRS) for worst pain in the last 24 hours was used to gather information about the intensity of ulcer related pain (Cleeland, 2009). The translated Norwegian version of BPI has been validated for use in persons with cancer and osteoarthritis, and has demonstrated good validity and reliability (Gjeilo et al., 2007; Jelsness-Jørgensen et al., 2016; Kapstad et al., 2010; Klepstad et al., 2002). Studies have used the English version of the BPI to assess wound-related pain (Pieper et al., 2013). For the purpose of this study, the BPI was linguistically adjusted to specifically assess ulcer related pain by replacing the word 'pain' with 'ulcer related pain' throughout the questionnaire. The BPI was scored according to the official user guide (Cleeland, 2009). In the analysis, we used pain intensity as a dichotomised variable, no and mild pain (NRS 0–3) versus moderate to severe pain (NRS ≥4). This cut-off point is in line with previous research of pain intensity (Kapstad et al., 2008).

3.3 | Ethical considerations

The Norwegian Regional Ethical Comity South East Norway approved the study (REC number 2016/1236).). In addition, the Data Inspectorate, the research managers and the heads of department at the local hospitals approved the study. Participants were informed about the aims and procedures of this study, and written informed consent was obtained from all participants before inclusion. They were informed that the information they provided would be anonymised in publications, and they could withdraw from the study at any time before publication of the study.

3.4 | Analysis

Descriptive statistics were presented as frequencies with proportions for categorical variables, as means with standard deviation (SD) for normally distributed continuous variables and as medians with interquartile range (IQR) for skewed continuous variables. Comparison of responders versus non-responders in the sample was performed using t tests and chi-squared tests.

To identify factors associated with moderate to severe wound related background pain, we performed logistic regression analyses. The BPI item worst ulcer-related pain (0–10 NRS), dichotomised as moderate to severe pain (NRS 4–10) versus no or mild pain (NRS 0–3), was used as the dependent variable. Participants reporting no wound-related background pain in the screening interview did not receive the BPI in the battery of questionnaires and were therefore scored as 0 on this item. Variables considered for inclusion in the model were factors that were deemed clinically important, or that had a significant association with chronic pain in previous studies. Both univariable and multivariable regression analyses were performed. Results were presented as odds ratios (ORs) with 95% confidence intervals (CIs) and p values. Due to the restricted sample size (75 individuals with moderate to severe pain), we included no more than eight factors in the multivariable model. The included variables were age (per 10 years), gender (male versus female), health status (EQ VAS 0–100), sleep quality (ISI total score 0 – 28), wound diagnosis (venous versus diabetic versus all others), wound size (cm^2) and wound duration (weeks). No multicollinearity between the variables was observed. We used stepwise backwards elimination with $p= 0.157$ as criteria (corresponding to *Akaikes Information Criteria)* to obtain a subset of sociodemographic variables that were associated with moderate to severe wound-related background pain. In the final model, we tested for two-way interactions between the included variables. Because of the complexity in interpretation of odds ratio in interaction terms, a significant interaction is presented by an interaction plot.

All tests were two-sided, and with significance level of 5%. Data were mainly analysed using Statistical Package for the Social Sciences (SPSS) version 26. For the purpose of creating the interaction plot Stata 16.0 was used (State College, Tx, USA).

4 | RESULTS

4.1 | Response rate

A total of 279 persons were invited to participate in the study, where of 252 persons accepted and signed the written consent form. The main reason for declining participation was lack of energy. All 252 participants took part in the screening interview and the clinical examination. The questionnaire was returned by 192 participants, leaving a response rate of 69%. Non-responders and responders were compared on important sociodemographic (i.e., age, gender) and clinical variables (i.e., number of comorbidities, presence of ulcer-related background pain), and the groups did not differ significantly (Table S1).

4.2 | Demographic data

The mean age of the total sample was 74.4 years (SD 12.8). The sample consisted of equal parts of men and women. One third lived alone, and two thirds were not working (i.e., on sick leave, retired) (Table 1).

4.3 | Clinical- and wound characteristic

All participants had at least one active wound located at the leg, ankle or foot. The median wound duration was 14.5 weeks (IQR 8–26), and the median wound size of the largest lesion was 1.2 cm^2 (IQR 0.2–4.7). Unspecified ulcer in lower extremities (ICD-10 diagnosis code L97) was the most frequent wound diagnosis (27%). A total of 76% reported more than one comorbidity. The most frequent comorbidities were coronary diseases, including hypertension and atherosclerosis (77%), painful conditions such as musculoskeletal pain (50%), and diabetes (35%) (Table 2).

4.4 | Prevalence of ulcer related background pain

Ulcer-related background pain was reported by 64% (95% CI 58–69) in the total sample (N = 252). Of those returning the questionnaire (N = 192), 42% reported no ulcer-related background pain, 19% reported mild ulcer-related background pain, while 39% reported moderate to severe ulcer-related background pain during the last 24 h (Figure 1).

4.5 | Factors associated with moderate to severe ulcer related background pain

In univariate analyses, older age, female gender and reduced sleep quality were significantly associated with moderate to severe wound-related background pain (Table 3). After backward elimination, age was associated with pain (OR per 10 years 1.47, 95% CI 1.10–1.97), as well as female gender (OR 2.44, 95% CI 1.28–4.68). Quality of sleep was also associated with the risk of moderate to severe pain (OR for 1 unit increase 1.13, 95% CI 1.06–1.20). Health status was not significant in the univariate analysis but reached significant in the multivariable analysis (OR 1.02, 95% CI 1.00–1.04). The pseudo R^2 indicated that the model explained 13% of the variance in the variable moderate to severe pain. In the final model, we found an interaction between health status and sleep quality. The interaction plot demonstrates that sleep quality has a modifying effect on health status, that is for persons with diminished health status the importance of sleep was minor, while for persons with better health status the sleep quality has great impact of the predicted probability of moderate to severe pain (Figure 2). The ORs of age and gender were similar in the models with and without the interaction term.

TABLE 1 Demographic data of total sample (N = 252) and respondents stratified by pain (N = 192).

	Total sample N = 252		Respondents stratified by pain N = 192			
			No/mild pain N = 117		Moderate/severe pain N = 75	
	n	%	n	%	n	%
Age						
<49	10	4.0	8	6.9	1	1.3
50–59	23	9.1	13	11.1	5	6.7
60–69	42	16.7	21	17.9	10	13.3
70–79	84	33.3	41	35.0	27	36.0
80–89	69	27.4	26	22.2	25	33.3
>90	24	9.5	8	6.8	7	9.3
Total	252	100	117	100	75	100
Gender						
Male	128	50.8	72	61.5	26	34.7
Female	124	49.2	45	38.5	49	65.3
Total	252	100	117	100	75	100
Marital status						
Single	34	13.5	25	21.4	9	12.0
Married/cohabitant	112	44.4	69	59.0	43	57.3
Widowed	46	18.3	23	19.7	23	30.7
Total	192	76.2	117	100	75	100
Educational level						
Primary school	72	28.6	40	34.2	32	42.7
Secondary school	66	26.2	41	35.0	25	33.3
University <4 years	35	13.9	23	19.7	12	16.0
University >4 years	15	5.9	11	9.4	4	5.3
Total	188	74.6	115	98.3	73	97.3
Work situation						
Working	19	7.5	11	9.4	8	10.7
Retired/sick leave	171	67.9	105	89.7	66	88.0
Total	190	75.4	116	99.1	74	98.7
Living arrangements						
Alone	76	30.2	45	38.5	31	41.3
With spouse/other family	116	46.0	72	61.5	44	58.7
Total	192	76.2	117	100	75	100
Ethnicity						
Norwegian	187	74.2	115	98.3	72	96.0
Other	4	1.6	2	1.7	2	2.7
Total	191	75.8	117	100	74	98.7

5 | DISCUSSION

This study estimated that the pain prevalence in the population of persons with chronic leg ulcer was between 58% and 69%. This confidence interval is relatively narrow and similar to the prevalence of 60% found in descriptive studies in a recent meta-analysis (95% CI 44%–75%) (Leren et al., 2020). The pain prevalence found in this study is, however, lower than the prevalence of 90% demonstrated in effect studies from the same meta-analysis (Leren et al., 2020). Note that there is a great variation in how ulcer related pain is assessed,

TABLE 2 Clinical- and wound characteristics of the total sample (N = 252).

	Median	IQR	Mean	SD	n	(%)
Wound diagnosis						
Unspecified (ICD–10 code L97)					67	26.6
Diabetic					53	21
Venous					50	19.8
Other					82	32.6
Wound duration (weeks)	14.5	8–26				
Wound size (cm^2)	1.19	0.20–4.71				
Number of comorbidities			3.1	1.48		
Type of comorbidities						
Coronary disease					193	76.6
Other painful conditions					125	49.6
Diabetes					87	34.5
Malnutrition					68	27
Renal disease					47	18.7
Cancer (previous or present)					44	17.5
Arthritis					43	17.1
Stroke					22	8.7
Asthma/COPD					20	7.9
Pain intensity (BPI, item 3, 0–10 NRS)	2.5	0–6				
Sleep quality (ISI, total score, 0–28)	7	3–12				
Health status (EQ VAS)			60.2	21.0		

Abbreviations: BPI: Brief Pain Inventory, COPD: Chronic Obstructive Pulmonary Disease, NRS: Numeric rating scale, ISI: Insomnia Severity Index, IQR, interquartile range; EQ VAS: EuroQol Visual Analogue Scale item; SD, standard deviation.

and studies are rarely explicit on the type of ulcer pain they have investigated. In fact, persons with ulcers are likely not aware of the differentiation between background and procedural ulcer pain, unless this differentiation is explicitly addressed. We believe that the screening procedure of ulcer-related background pain used in this study, provides a lower but more precise prevalence rate of background pain in a sample of persons with various types of leg ulcers.

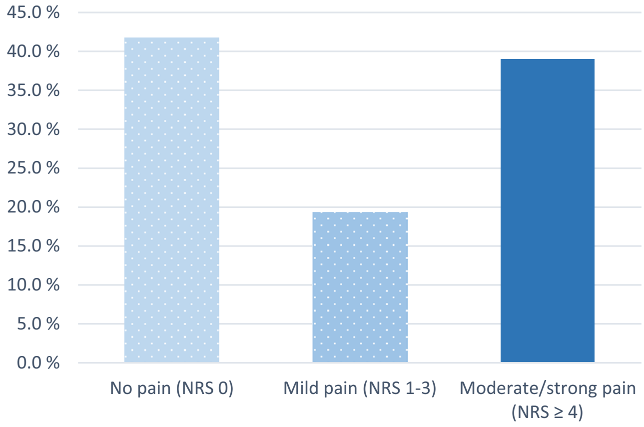


FIGURE 1 Ulcer-related background pain intensity, based on questionnaire respondents (N = 192). [Colour figure can be viewed at wileyonlinelibrary.com]

Of those returning the questionnaire (N = 192) almost one third reported moderate to severe pain intensity. In this study, we grouped the NRS pain intensity score into no pain, mild pain and moderate to severe pain. This procedure is in line with previous research on pain intensity cut points (Kapstad et al., 2008). In most studies of pain in persons with chronic leg ulcers, prevalence of pain and mean pain intensity scores are reported (Leren et al., 2020). From a clinical perspective, it is often more relevant to look at the percentage share of the persons experiencing moderate to severe pain. While people often tolerate mild pain and do not need analgesics, moderate to severe pain can reduce quality of life and requires pain management including both non-opioids and weak or strong opioids. There may be numerous reasons for the high percentage of severe pain in the present study, but inadequate pain management is probably a major contribution. Research indicates healthcare professionals do not comply with well-established guidelines for best practice of wound care when it comes to pain assessment (Franck & Bruce, 2009; Frescos, 2018), and are insecure about the optimum pharmacological management of non-malignant pain in older persons (Barber & Gibson, 2009). In addition, stoicism and fear of addiction among

TABLE 3 Logistic regression models of factors significantly associated with moderate to severe wound-related background pain (N = 192).

	Univariate analysis			Multivariate analysis		
	OR	CI (95%)	p	OR	CI (95%)	p
Age (per 10 years)	1.38	1.08–1.76	0.01	1.46	1.10–1.94	<0.01
Female gender[a]	3.02	1.65–5.52	<0.01	2.44	1.28–4.68	<0.01
Health status (EQ VAS)	1.01	0.99–1.02	0.65	1.02	1.00–1.04	0.02
Sleep quality (ISI)	1.09	1.04–1.15	0.01	1.13	1.06–1.20	<0.01
Wound diagnosis[b]						
Venous	1.39	0.66–2.90	0.38			
Diabetic	0.87	0.42–1.81	0.71			
Wound size (cm^2)	1.10	0.99–1.22	0.08			
Wound duration (weeks)	0.99	0.97–1.01	0.25			

Abbreviations: EQ VAS: EuroQol Visual analogue scale, ISI: Insomnia Severity Index. OR: Odds Ratio, CI: Confidence Interval.

[a] male gender served as reference group; [b] all other wound diagnosis (other and unspecified) served as reference group

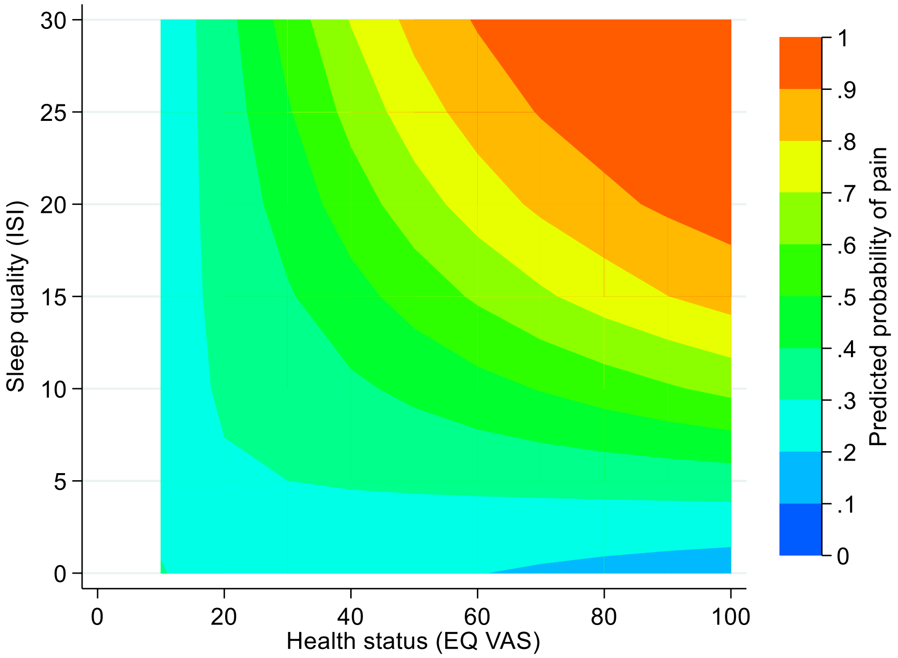


FIGURE 2 Plot demonstrating the interactions effect between health status (EQ VAS) and sleep quality (ISI) for moderate to severe ulcer-related background pain. [Colour figure can be viewed at wileyonlinelibrary.com]

patient with chronic venous ulcers, may lead to a tendency to take analgesics less frequently or at a lower dose than prescribed (Sale et al., 2006). Regardless, findings from this study indicate that there is a need to address pain management in chronic ulcer wound care.

In the univariate analysis in the present study, female gender, older age and more insomnia symptoms were factors associated with moderate to severe ulcer-related background pain. The association between gender and pain is consistent with the previous study on patients with chronic ulcers by Guernera and colleagues (2007), and the association between age and pain is supported by previous research in the general population (Gibson & Farrell, 2004). The reason for these associations not being more apparent in previous studies on chronic ulcers, might be due to small sample sizes as well as using different pain intensity scores.

In the multivariate analysis, older females reporting insomnia symptoms also have increased risk of having moderate to severe ulcer-related background pain. Interestingly, these participants also perceived their health status to be better. We also found an interaction between health status and insomnia symptoms in the multivariate analysis. We hypothesise that the importance of sleep depends on the level self-perceived health status when investigating the risk of moderate to severe ulcer-related pain. This means that for people with diminished health status, sleep does not have a significant impact. It is possible that diminished health status has such great impact on a person's life, that insomnia symptoms becomes secondary. However, if a person reports good health status, insomnia symptoms becomes more noticeable and in turn influence the likelihood of having moderate to severe pain. Note that our cross-sectional data offer limited information about the mechanism affecting the relationship between insomnia symptoms, health status and moderate to severe pain. This relationship should be subject for further research. Despite the limited knowledge about the mechanisms in play, we would assert that it is imperative to screen for insomnia symptoms and impact on health status in persons presenting with chronic leg ulcers. The findings are a reminder that nurses need to pay attention to sleep and pain in persons reporting good health status, as well as those reporting diminished health status.

Unlike previous studies of factors associated with ulcer-related pain, we found no significant association between several biological factors (i.e., wound diagnosis, ulcer size, ulcer duration) and moderate to severe ulcer-related background pain. Even though there are differences in the pathologies and clinical characteristics of different types of chronic leg ulcers, all chronic leg ulcers are associated with a profound impact on persons' physical, functional and psychological status (Cunha et al., 2017; Franks & Morgan, 2003; Herber et al., 2007). Pain is a biopsychosocial phenomenon (IASP, 2020), and it is acknowledged that the size and severity of an injury is not always related to the pain experienced (Chapman et al., 2000). The experience of pain related to a chronic ulcer can be affected by biological, psychological and social factors (Gatchel et al., 2007). Note that the proposed model only explains a small part of the variance in the sample. It is reasonable to assume that psychological and social factors account for a substantial part of the remaining variation. In addition, the lack of clear associations with regards to the biological variables demonstrates the need for an individual and holistic pain assessment of all persons presenting with a chronic leg ulcer to identify those in need of pain management.

Some limitations of this study need to be addressed, and generalisation of results is not straight forward since we recruited only hospital outpatients. Our sample may therefore not be representative of a community sample of persons living with chronic leg ulcers. Additionally, because of the explorative nature of this study, we included participants with a variety of wound diagnosis, and almost 60% had 'unspecified' or 'other' wound diagnoses. This makes generalisation to one specific wound patient group, as well as comparison of research findings, a challenging task. However, from a clinical perspective the participants in the present study do represent the population attending outpatient clinics. Even with careful systematic assessment, wound diagnostics can be challenging in cases with multiple underlying factors, borderline diagnostic indicators and mixed aetiologies (Gupta et al., 2017). The heterogeneity in ulcer diagnosis is representative for the clinical practice, making the results from this study relevant. However, the lack of diagnostic specificity is the reason why we did not explore these groups (others and unspecified) as risk factors for moderate to severe ulcer-related background pain in the regression analyses.

Furthermore, a cross-sectional design only allows for observing factors associated with moderate to severe ulcer-related background pain, and determining an established causal relationship is not possible. In the future, the association between gender, age, health status, insomnia symptoms and pain should be explored using longitudinal data. In addition, more confounding factors, such as socioeconomic status should be included and adjusted for. For instance, in previous studies, education, income and occupation were associated with ulcer-related pain (Domingues et al., 2016; Salvetti et al., 2014). However, the variables describing socioeconomic status in our study were not suitable to accentuate distinctions in the population.

Finally, the use of a single variable of pain intensity to assess persistent ulcer-related pain is questionable, since the assessment of persistent pain requires a holistic approach, including numerous pain characteristics, physical- and psychological factors (Tauben & Stacey, 2020). However, for the purpose of demonstrating associated factors we found pain intensity to be the best available and comparable option. In addition, the use of the 3rd item in the BPI (strongest ulcer-related pain in the last 24 h) might have led to higher pain intensity reports, compared to studies using the mean pain intensity score. However, the worst pain intensity item presumably provides information of the most bothersome pain and gives a stronger indication of a person's need for pain management.

6 | CONCLUSIONS

This study shows a high prevalence of ulcer-related background pain in persons with chronic leg ulcers. As many as 29% reported having moderate to severe background pain. These findings indicate that pain assessment and management still need more attention in ulcer care. Furthermore, our analysis indicates that being female of older age, as well as having better health status and more insomnia symptoms, enhance the risk of having moderate to severe ulcer-related background pain. The intricate relationship between health status, insomnia symptoms and moderate to severe pain is interesting, but further research is needed. This study demonstrates the need for an individual and holistic pain assessment of all persons presenting with a chronic leg ulcer to identify those in need of pain management.

7 | RELEVANCE TO CLINICAL PRACTICE

This study highlights that ulcer-related background pain is a common and ongoing problem in persons with chronic leg ulcers. Awareness of the extent of ulcer-related background pain is the first step—but alone not sufficient to improve practice. Nurses and other healthcare professionals need to integrate biopsychosocial strategies to assess ulcer-related background pain. Particular attention must be paid to those patients who demonstrate a greater risk of having moderate to severe ulcer-related pain, such as older females with insomnia symptoms and good perceived health status. The presence of a chronic ulcer, as well as the aforementioned risk factors, should draw clinician's attention to assess pain, evaluate the need of pain management, and offer proper pain-relieving interventions.

ACKNOWLEDGEMENTS

We thank all the clinicians at the two outpatient wound care clinics at Vestre Viken HF for the facilitation of the data collection, and for input and advice.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research report.

AUTHOR CONTRIBUTION

All authors contributed significantly in the conception and design of the study. Leren performed the data collection. Leren, Falk and Ljoså performed the data analysis. Leren and Ljoså drafted the work. Eide, Johansen and Falk revised it critically for important intellectual content. All authors read and approved the final manuscript. All authors agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORCID

Lena Leren https://orcid.org/0000-0001-9083-5615

REFERENCES

American Nurses Association, A. N. (2018). The ethical responsibility to manage pain and the suffering it causes. ANA Position Statement, https://www.nursingworld.org/~495e9b/globalassets/docs/ana/ethics/theethicalresponsibilitytomanagepainandthesufferingitcauses2018.pdf.

Atkin, L., Bućko, Z., Montero, E. C., Cutting, K., Moffatt, C., Probst, A., Romanelli, M., Schultz, G. S., & Tettelbach, W. (2019). Implementing TIMERS: The race against hard-to-heal wounds. *Journal of Wound Care*, *28*(Sup3a), S1–S50. https://doi.org/10.12968/jowc.2019.28.Sup3a.S1.

Barber, J. B., & Gibson, S. J. (2009). Treatment of chronic non-malignant pain in the elderly. *Drug Safety*, *32*(6), 457–474. https://doi.org/10.2165/00002018-200932060-00003.

Bastien, C. H., Vallières, A., & Morin, C. M. (2001). Validation of the Insomnia Severity Index as an outcome measure for insomnia research. *Sleep Medicine*, *2*(4), 297–307. https://doi.org/10.1016/s1389-9457(00)00065-4.

Breivik, H., Collett, B., Ventafridda, V., Cohen, R., & Gallacher, D. (2006). Survey of chronic pain in Europe: Prevalence, impact on daily life, and treatment. *European Journal of Pain*, *10*(4), 287–333. https://doi.org/10.1016/j.ejpain.2005.06.009.

Chapman, C. R., Nakamura, Y., & Flores, L. Y. (2000). A constructivist framework for understanding individual differences in pain. *Individual Differences Conscious Experience*, *20*, 17.

Cleeland, C. S. (2009). The brief pain inventory: user guide. Houston, TX: The University of Texas MD Anderson Cancer Center, 1–11. https://www.mdanderson.org/documents/Departments-and-Divisions/Symptom-Research/BPI_UserGuide.pdf.

Cowman, S., Gethin, G., Clarke, E., Moore, Z., Craig, G., Jordan-O'Brien, J., McLain, N., & Strapp, H. (2012). An international eDelphi study identifying the research and education priorities in wound management and tissue repair. *Journal of Clinical Nursing*, *21*(3–4), 344–353. https://doi.org/10.1111/j.1365-2702.2011.03950.x.

Cunha, N., Campos, S., & Cabete, J. (2017). Chronic leg ulcers disrupt patients' lives: A study of leg ulcer-related life changes and quality of life. *British Journal of Community Nursing*, *22*(Sup9), S30–S37. https://doi.org/10.12968/bjcn.2017.22.Sup9.S30.

Domingues, E. A. R., da Costa, P. C. P., de Moraes Lopes, M. H. B., Monteiro, I., & Alexandre, N. M. C. (2016). Pain prevalence, socio-demographic and clinical features in patients with chronic ulcers. *Journal of Tissue Viability*, *25*(3), 180–184. https://doi.org/10.1016/j.jtv.2016.03.005.

Fillingim, R. B., King, C. D., Ribeiro-Dasilva, M. C., Rahim-Williams, B., & Riley, J. L. III (2009). Sex, gender, and pain: a review of recent clinical and experimental findings. *The Journal of Pain*, *10*(5), 447–485. https://doi.org/10.1016/j.jpain.2008.12.001.

Filosa, J., Omland, P. M., Langsrud, K., Hagen, K., Engstrøm, M., Drange, O. K., & Sand, T. (2020). Validation of insomnia questionnaires in the general population: The Nord-Trøndelag Health Study (HUNT). *Journal of Sleep Research*, *30*, e13222. https://doi.org/10.1111/jsr.13222.

Franck, L. S., & Bruce, E. (2009). Putting pain assessment into practice: Why is it so painful? *Pain Research and Management*, *14*,), 13–20. https://doi.org/10.1155/2009/856587.

Franks, P. J., & Morgan, P. A. (2003). Health-related quality of life with chronic leg ulceration. *Expert Review of Pharmacoeconomics & Outcomes Research*, *3*(5), 611–622. https://doi.org/10.1586/14737167.3.5.611

Frescos, N. (2018). Assessment of pain in chronic wounds: A survey of Australian health care practitioners. *International Wound Journal*, *15*(6), 943–949. https://doi.org/10.1111/iwj.12951.

Gatchel, R. J., Peng, Y. B., Peters, M. L., Fuchs, P. N., & Turk, D. C. (2007). The biopsychosocial approach to chronic pain: scientific advances and future directions. *Psychological Bulletin*, *133*(4), 581. https://doi.org/10.1037/0033-2909.133.4.581.

Gibson, S. J., & Farrell, M. (2004). A review of age differences in the neurophysiology of nociception and the perceptual experience of pain. *The Clinical Journal of Pain*, *20*(4), 227–239. https://doi.org/10.1097/00002508-200407000-00004.

Gjeilo, K. H., Stenseth, R., Wahba, A., Lydersen, S., & Klepstad, P. (2007). Validation of the brief pain inventory in patients six months after cardiac surgery. *Journal of Pain and Symptom Management*, *34*(6), 648–656. https://doi.org/10.1016/j.jpainsymman.2007.01.010.

Green, J., Jester, R., McKinley, R., & Pooler, A. (2018). Chronic venous leg ulcer care: Putting the patient at the heart of leg ulcer care. Part 1: Exploring the consultation. *British Journal of Community Nursing*, *23*(Sup3), S30–S38. https://doi.org/10.12968/bjcn.2018.23.Sup3.S30.

Guarnera, G., Tinelli, G., Abeni, D., Di Pietro, C., Sampogna, F., & Tabolli, S. (2007). Pain and quality of life in patients with vascular leg ulcers: an Italian multicentre study. *Journal of Wound Care*, *16*(8), 347–351. https://doi.org/10.12968/jowc.2007.16.8.27856.

Gupta, S., Andersen, C., Black, J., de Leon, J., Fife, C., Lanti li, J. C., Niezgoda, J., Snyder, R., Sumpio, B., Tettelbach, W., Treadwell, T., Weir, D., & Silverman, R. P. (2017). Management of Chronic Wounds: Diagnosis, Preparation, Treatment, and Follow-up. *Wounds: a Compendium of Clinical Research and Practice*, *29*(9), S19–S36.

Hellström, A., Nilsson, C., Nilsson, A., & Fagerström, C. (2016). Leg ulcers in older people: a national study addressing variation in diagnosis, pain and sleep disturbance. *BMC Geriatrics*, *16*(1), 25. https://doi.org/10.1186/s12877-016-0198-1.

Helsedirektoratet. (2016). ICD-10: Den internasjonale statistiske klassifikasjonen av sykdommer og beslektede helseproblemer. Retrieved from https://finnkode.ehelse.no/#icd10/0/0/0/-1

Herber, O. R., Schnepp, W., & Rieger, M. A. (2007). A systematic review on the impact of leg ulceration on patients' quality of life. *Health and Quality of Life Outcomes*, *5*(1), 44. https://doi.org/10.1186/1477-7525-5-44.

IASP. (2020). IASP Terminology. IASP Terminology: Retrieved from. https://www.iasp-pain.org/Education/Content.aspx?ItemNumber=1698.

Jelsness-Jørgensen, L.-P., Moum, B., Grimstad, T., Jahnsen, J., Opheim, R., Prytz Berset, I., Hovde, Ø., Torp, R., Frigstad, S. O., Huppertz-Hauss, G., & Huppertz-Hauss, G. (2016). Validity, reliability, and responsiveness of the brief pain inventory in inflammatory bowel disease. *Canadian Journal of Gastroenterology and Hepatology*, *2016*, https://doi.org/10.1155/2016/5624261.

Kapstad, H., Hanestad, B. R., Langeland, N., Rustøen, T., & Stavem, K. (2008). Cutpoints for mild, moderate and severe pain in patients with osteoarthritis of the hip or knee ready for joint replacement surgery. *BMC Musculoskeletal Disorders*, *9*(1), 55. https://doi.org/10.1186/1471-2474-9-55.

Kapstad, H., Rokne, B., & Stavem, K. (2010). Psychometric properties of the Brief Pain Inventory among patients with osteoarthritis undergoing total hip replacement surgery. *Health and Quality of Life Outcomes*, *8*(1), 148. https://doi.org/10.1186/1477-7525-8-148.

Kielo, E., Suhonen, R., Salminen, L., & Stolt, M. (2019). Competence areas for registered nurses and podiatrists in chronic wound care, and their role in wound care practice. *Journal of Clinical Nursing*, *28*(21–22), 4021–4034. https://doi.org/10.1111/jocn.14991.

Klepstad, P., Loge, J. H., Borchgrevink, P. C., Mendoza, T. R., Cleeland, C. S., & Kaasa, S. (2002). The Norwegian brief pain inventory questionnaire: Translation and validation in cancer pain patients. *Journal of Pain and Symptom Management*, *24*(5), 517–525. https://doi.org/10.1016/s0885-3924(02)00526-2.

Lazarus, G. S., Cooper, D. M., Knighton, D. R., Margolis, D. J., Percoraro, R. E., Rodeheaver, G., & Robson, M. C. (1994). Definitions and guidelines for assessment of wounds and evaluation of healing. *Wound Repair and Regeneration*, *2*(3), 165–170. https://doi.org/10.1046/j.1524-475X.1994.20305.x.

Leren, L., Johansen, E., Eide, H., Falk, R. S., Juvet, L. K., & Ljoså, T. M. (2020). Pain in persons with chronic venous leg ulcers: A systematic review and meta-analysis. *International Wound Journal*, *17*(7), 466–484. https://doi.org/10.1111/iwj.13296.

Martinengo, L., Olsson, M., Bajpai, R., Soljak, M., Upton, Z., Schmidtchen, A., Car, J., & Järbrink, K. (2019). Prevalence of chronic wounds in the general population: systematic review and meta-analysis of observational studies. *Annals of Epidemiology*, *29*, 8–15. https://doi.org/10.1016/j.annepidem.2018.10.005

Morin, C. M., Belleville, G., Bélanger, L., & Ivers, H. (2011). The Insomnia Severity Index: Psychometric indicators to detect insomnia cases and evaluate treatment response. *Sleep*, *34*(5), 601–608. https://doi.org/10.1093/sleep/34.5.601.

Olsson, M., Järbrink, K., Divakar, U., Bajpai, R., Upton, Z., Schmidtchen, A., & Car, J. (2019). The humanistic and economic burden of chronic wounds: A systematic review. *Wound Repair and Regeneration*, *27*(1), 114–125. https://doi.org/10.1111/wrr.12683.

Oppe, M., Devlin, N., & Szende, A. (2007). EQ-5D value sets: Inventory, comparative review and user guide: Springer. https://doi.org/10.1007/1-4020-5511-0.

Paul, J. (2013). A cross-sectional study of chronic wound-related pain and itching. *Ostomy/Wound Management*, *59*(7), 28–34. https://doi.org/10.1016/j.maturitas.2018.08.013.

Pieper, B., DiNardo, E., & Nordstrom, C. K. (2013). A cross-sectional, comparative study of pain and activity in persons with and without injection-related venous ulcers. *Ostomy/Wound Management*, *59*(5), 14–24.

Renner, R., Seikowski, K., & Simon, J. C. (2014). Association of pain level, health and wound status in patients with chronic leg ulcers. *Acta Dermato-Venereologica*, *94*(1), 50–53. https://doi.org/10.2340/00015555-1635.

Sale, J. E., Gignac, M., & Hawker, G. (2006). How "bad" does the pain have to be? A qualitative study examining adherence to pain medication in older adults with osteoarthritis. *Arthritis Care & Research: Official Journal of the American College of Rheumatology*, *55*(2), 272–278. https://doi.org/10.1002/art.21853.

Salvetti, M. D. G., Costa, I. K. F., Dantas, D. V., Freitas, C. C. S. D., Vasconcelos, Q. L. D. D. A., & Torres, G. D. V. (2014). Prevalence of pain and associated factors in venous ulcer patients. *Revista Dor*, *15*(1), 17–20. https://doi.org/10.5935/1806-0013.20140005.

Solberg, T. K., Olsen, J.-A., Ingebrigtsen, T., Hofoss, D., & Nygaard, Ø. P. (2005). Health-related quality of life assessment by the EuroQol-5D can provide cost-utility data in the field of low-back surgery. *European Spine Journal*, *14*(10), 1000–1007. https://doi.org/10.1007/s00586-005-0898-2.

Tauben, D., & Stacey, B. R. (2020). Evaluation of chronic non-cancer pain in adults. In S. Fishman (Ed.), *UpToDate*. Retrieved from: https://www.uptodate.com/contents/evaluation-of-chronic-non-cancer-pain-in-adults?search=chronic%20pain&source=search_result&selectedTitle=3~150&usage_type=default&display_rank=3

Tollow, P., & Ogden, J. (2019). The importance of relationships in treatment for chronic leg ulceration. *Journal of Health Psychology*, *24*(13), 1839–1849. https://doi.org/10.1177/1359105317705984.

Von Elm, E., Altman, D. G., Egger, M., Pocock, S. J., Gøtzsche, P. C., Vandenbroucke, J. P., & Initiative, S. (2014). The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for reporting observational studies. *International Journal of Surgery*, *12*(12), 1495–1499. https://doi.org/10.1016/j.ijsu.2014.07.013.

White, R. (2008). A multinational survey of the assessment of pain when removing dressings. *Wounds UK*, *4*(1), 14.

Woo, K. Y., & Sibbald, R. G. (2008). Chronic wound pain: A conceptual model. *Advances in Skin & Wound Care*, *21*(4), 175–190. https://doi.org/10.1097/01.ASW.0000305430.01413.2e.

WUWHS. (2007). Principles of best practice: Minimizing pain at dressing-related procedures:"Implementation of pain relieving strategies". Evidence informed practice. Retrieved from: http://less-pain.com/Documents/PainAwareness/WUWHS%202008%20Best%20Practice%20Document%20English.pdf

Zaidi, Z., Hussain, K., & Sudhakaran, S. (2019). In Z. Zaidi, K. Hussain, & S. Sudhakaran (eds). *Treatment of Skin Diseases* (pp. 251–257). Springer, Cham. https://doi.org/10.1007/978-3-319-89581-9.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Leren L, Johansen EA, Eide H, Sørum Falk R, Ljoså TM. Prevalence and factors associated with ulcer-related pain in persons with chronic leg ulcers—an explorative study. *J Clin Nurs*. 2021;30:2732–2741. https://doi.org/10.1111/jocn.15787

Paper III

Leren, L., Eide, H., Johansen, E. A., Jelnes, R. & Ljoså, T. M. (2020). Background pain in persons with chronic leg ulcers: An exploratory study of symptom characteristics and management. *International Wound Journal*. Advance online publication. https://doi.org/10.1111/iwj.13730

Received: 1 July 2021 | Revised: 22 November 2021 | Accepted: 1 December 2021

DOI: 10.1111/iwj.13730

ORIGINAL ARTICLE

Background pain in persons with chronic leg ulcers: An exploratory study of symptom characteristics and management

Lena Leren[1] | **Hilde Eide**[1] | **Edda Aslaug Johansen**[2] | **Rolf Jelnes**[3] | **Tone Marte Ljoså**[1]

[1]Centre for Health and Technology, Faculty of Nursing and Health Sciences, University of South-Eastern Norway, Drammen, Norway

[2]Faculty of Nursing and Health Sciences, University of South-Eastern Norway, Drammen, Norway

[3]Medical Department, Hospital of Southern, Sonderborg, Denmark

Correspondence
Lena Leren, Centre for Health and Technology, Faculty of Nursing and Health Sciences, University of South-Eastern Norway, Notodden, Norway.
Email: lena.leren@usn.no

Funding information
University of South-Eastern Norway

Abstract

This exploratory descriptive study aimed to describe characteristics and management of background pain related to chronic leg ulcers. A total of 121 participants were recruited from two wound care clinics using a consecutive sampling method. Data were obtained through screening interview, clinical examination, and questionnaires. The mean average background pain intensity was 4.5 (SD 2.56) (CI 95% 4.0-5.0). Pain interfered mostly with general activity (mean 4.3), sleep (mean 4.1), and walking ability (mean 4.0) (0-10 NRS). The most frequently reported descriptors of background pain were 'tender', 'stabbing', 'aching', and 'hot-burning'. Most of the participants stated that the pain was intermittent. Less than 60% had analgesics prescribed specifically for ulcer related pain, and the respondents reported that pain management provided a mean pain relief of 45.9% (SD 33.9, range 0-100). The findings indicate that ulcer related background pain is a significant problem that interferes with daily function, and that pain management in wound care is still inadequate.

KEYWORDS

chronic leg ulcers, holistic wound care, pain, pain characteristics, pain management

Key Messages

- a thorough pain assessment procedure is the cornerstone of successful pain management in persons with CLUs
- this cross-sectional explorative study aimed to describe characteristics and management of ulcer related pain in 121 persons with chronic leg ulcers
- ulcer related background pain is a significant problem, and the participants report moderate pain intensity, which interferes with general activity, sleep, and walking ability
- pain management seems to be inadequate, with less than 60% of the participants receiving analgesics for their ulcer related background pain

---

1 | INTRODUCTION

Chronic leg ulcers (CLUs) are hard-to-heal wounds localised on the lower leg or foot, persisting for more than 6 weeks.[1] CLUs are common, and affect approximately 0.1% to 2% of the adult population in Western countries.[2] Ulcer related pain is a significant problem, and all CLUs are potentially painful.[3-5] Pain is defined as 'an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage'.[6] Ulcer related pain can be classified as background, incident, procedural, and operative.[7] Background pain is caused by the underlying pathology of the leg ulceration and the wound itself, incidence pain stems from various daily activities, while procedural and operative pain is caused by wound treatment and debridement.[8] From a clinical perspective, it is probably difficult for persons with CLUs to separate the experience of background pain from incidence pain.[9] Hence, in this study, background pain is defined as ulcer related pain experienced in everyday life (other than procedural/operative pain).[9] Ulcer related pain is often multi-causal in nature, and can be further classified as nociceptive, neuropathic, inflammatory, as well as acute and/or chronic.[10-13] In addition, persons with CLUs are often old and may have multiple painful comorbidities.[14,15] Consequently, persons with CLUs can have very complex pain conditions with the ulcer related background pain as an additional problem on top of living with a CLU and other painful comorbidities.

In the beginning of this century, several consensus statements based on expert opinion drew attention to the extent – and treatment of ulcer related pain.[5,7,16] And the well-known concept of holistic wound bed preparation paradigm emphasises patient comfort and relieving pain in wound care.[17] Effective pain management in wound care depends on detailed and accurate assessment and documentation of the pain experience, and a mix of psychosocial approaches together with local and systemic pain management should be implemented to control it.[17,18] Most research studies on pain management in wound care have focused on the effects of different low-adherent or non-adherent dressings and topical analgesics and local anaesthetic agents mainly aimed to reduce dressing related pain.[19,20] Larger studies assessing more extensive and holistic management are not available. However, despite the publication of clinical guidelines, consensus documents and research, ulcer related background pain is still not effectively assessed nor addressed in leg ulcer care,[21,22] and background pain continues to be a frequent and substantial problem.[23]

Most research studies on CLUs report on diagnosis, prevention, treatment, and healing rates.[24,25] Few studies report on ulcer related pain, and this research often concentrates on acute procedure-related pain and pain at dressing change. Knowledge is therefore scarce on the characteristics of ulcer related background pain. Intensity is the most commonly reported pain characteristic, and mean background pain intensity in CLUs is estimated at 3 to 4 (0-10 numeric rating scale).[9,23,26] A limited number of studies describe other characteristics of ulcer related pain than intensity, such as pain descriptors, interference, and temporal pattern. Throbbing, tender, and burning were the most common descriptors of background pain.[26-28] Sensory descriptors were typically used more often than affective descriptors.[26,29] Ulcer related background pain can interfere with sleep,[30,31] and one study found moderate pain interference in a sample with venous leg ulcers.[32] Finally, background pain was worse during standing than at rest, and intermittent pain was more frequent than continuous pain.[33] Qualitative studies also support the use of sensory descriptors, varying intensity, and pain interference.[34] However, no previous studies provide a methodologically sound and comprehensive description of several characteristics of ulcer related background pain in a large sample of persons with CLUs.

CLUs are a substantial problem, and ulcer related background pain is a frequent and bothersome symptom disrupting quality of life. Knowledge about characteristics of ulcer related background pain is scarce and little is known about the pain management persons with CLUs receive. A thorough evaluation of the pain symptomatology in these persons is necessary for a better understanding of the pain experience and addressing the pervasive impact on function. Hence, the aim of the current study was to explore and describe characteristics of ulcer related background pain and pain management as reported by persons with CLUs.

2 | METHODS

2.1 | Design and participants

The current study is a descriptive analysis of cross-sectional data. The data collection was conducted from May 2017 to the end of December 2018. Consecutive sampling method was used to recruit participants attending two outpatient clinics for wound care in South-Eastern Norway. Inclusion criteria were: (a) presence of an open wound located below the knee; (b) wound duration of 6 weeks or longer; (c) age 18 years or older, (d) ability to understand and read Norwegian; and (e) no cognitive impairment causing comprehension difficulties. Exclusion criteria included the following ulcer diagnosis: burn-ulcer, cancer-ulcer, radiation-ulcer, pressure ulcers caused by immobility, and immunological ulcers.

The present study sample was selected from a larger sample of persons with CLUs (reference deleted for blinded review). To explore pain characteristics, we analysed data from 121 persons who reported presence of ulcer related background pain in the screening interviews, and who returned the self-report questionnaires.

2.2 | Data collection

Data were gathered with an initial screening interview, and a clinical examination at the wound outpatient clinic, as well as a self-report questionnaire filled in at home within 24 hours after the hospital visit.

2.2.1 | Screening interview

The initial brief interview was conducted by LL before the scheduled appointment at the wound care clinic. Participants were asked for the presence and type of ulcer related pain, and a structured questionnaire was used to gather data on wound duration and reoccurrence, as well as comorbidities.

2.2.2 | Clinical examination

During the scheduled appointment at the wound clinic, an examination was conducted by LL. Data were collected on ulcer characteristics, sensibility of the foot, location and temporal pattern of ulcer related pain, and pain management. Both participants self-report and patient records of pain management were incomplete in some cases. To ensure consistency of the clinical test, all tests were performed by one researcher LL.

Wound characteristics: The medical doctor assessed the ulcer and stated the ulcer diagnosis (ie, venous, diabetic, traumatic, unspecified). In addition, the researcher LL asked the participants about the presumed causal factor (eg, trauma, pressure), and identified and marked the localization of the ulcer on a body map of the lower leg. Wound size was estimated by multiplying the width and height (millimetres at the widest and highest) of the wound, calculating the area using the formula of an ellipse.

Sensibility of the lower leg: Tactile static mechanical sensation was assessed using Semmes-Weinstein monofilament (5.07/10 g) examination (SWME).[35] Two pricks with the monofilament were applied on each of four plantar sites on the forefoot (great toe, and base of first, third, and fifth metatarsals). Inability to detect one prick is used as a diagnostic threshold when screening for diabetic peripheral neuropathy.[36] Vibration sense was assessed using a 128-Hz tuning fork. The vibrating tuning fork was first placed on bony prominence where neuropathy is unlikely (eg, hand). Once the participant was familiar with the vibration, the vibrating fork was applied to the bony prominence situated at the dorsum of the first toe just proximal to the nail bed.[37,38] The respondents indicated whether they could feel the vibration with their eyes closed. Reduced or lost sense of vibration stimuli may indicate neuropathy.[39]

Location of pain: Participants were asked to identify the pain location, such as directly in the wound bed; in the wound edges; in the area surrounding the wound; in the entire foot; in the entire leg, or a self-determined location. If more than one location was selected, ‘multiple locations’ were used to describe the location of the pain.

Temporal pattern of pain: To assess how pain fluctuated during the day, a question from the pain quality assessment scale (PQAS)[40] was used. PQAS is a valid tool for assessing various types of nociceptive and neuropathic pain,[40,41] and is linguistically validated and culturally adapted in Norwegian.[42] The participants were asked whether their pain was intermittent (feel pain sometimes, pain free at other times), variable (pain all the time, but also moments of more severe/different pain), or stable (constant pain that does not change).

Pain management: Participants were asked about their use of analgesics, and compliance to prescribed analgesics. Supplemental/confirmatory information was gathered from the patients' records when available. It was differentiated whether the pain management was aimed at ulcer related or other types of pain. Finally, participants were asked to describe other non-medical interventions used to relieve ulcer related pain.

2.2.3 | Questionnaires

All participants received a battery of self-report questionnaires on the day of recruitment and scheduled appointment at the wound clinic. The questionnaires were completed the following day and returned by mail in a prepaid envelope. The questionnaires contained questions regarding demography and pain characteristics. Participants were specifically asked to keep in mind their ulcer related pain when answering questions regarding pain.

Demography: Information was obtained on age, gender, work situation, education, living arrangements, and ethnicity.

Short-form McGill pain questionnaire (*SF-MPQ*) was used to assess qualities of present ulcer related background pain. The SF-MPQ contains 15 pain descriptors (11 sensory, four affective) with a four-point intensity scale for each word (ie, none, mild, moderate, severe). In addition, the SF-MPQ contains a present pain intensity index and a 0 to 100 mm visual analogue scale (VAS) to assess present pain intensity.[43] The Norwegian version of SF-MPQ has demonstrated reliability and validity in a Norwegian sample with musculoskeletal pain.[44,45] The English version of SF-MPQ has been used to assess ulcer related pain.[46] The SF-MPQ was linguistically adjusted to specifically assess ulcer related pain by adding 'ulcer related' to the word 'pain' throughout the questionnaire. The Cronbach's alpha for all the descriptors were 0.87, and the Cronbach's alpha for the sensory and affective descriptors were 0.84 and 0.68, respectively.

The brief pain inventory (*BPI*) was used to provide information about the location, intensity, treatment, and interference of ulcer related pain on function in the last 24 hours. BPI consists of four 0 (no pain) to 10 (worst pain imaginable) numeric rating scales (NRS) on the intensity of pain in general, at its worst, at its least, and right now. A percentage scale (0-100) quantifies pain relief from current therapies, and a bodymap is provided to mark the pain location. Furthermore, seven questions address whether pain interferes with physical and psychosocial function.[47] The activity cluster of interference items (WAW) includes general activity, walking ability, work, and sleep, while the affect cluster of interference items (REM) includes mood, enjoyment of life, and relations with others. The translated Norwegian version of the BPI was validated for use in patients with cancer and osteoarthritis, demonstrating good validity and reliability.[48-51] The English version of the BPI was used to assess ulcer related pain.[52] The BPI was linguistically adjusted to specifically assess ulcer related pain by adding 'ulcer related' to the word 'pain' throughout the questionnaire. Cronbach's alpha for both the activity cluster and the affect cluster of interference items were 0.89, and the Cronbach's alpha for all interference items was 0.93 in this study.

Avoidance of physical activities: The participants were asked if they avoided certain activities because of ulcer related pain using a yes/no format. If yes, the participants were asked to describe the activities in own words.

2.3 | Research ethics

Approval for the study was granted by the Norwegian Regional Ethical Comity for Medical and Health Research Ethics, region South-East (REK number 2016/1236). In addition, the Norwegian Center for Research Data (NSD), as well as the research manager and the head of department at the local hospitals, approved the study. Participants were informed both orally and written about the aims and procedures of this study, and written consent was obtained from all participants. They were informed that the information they provided would be deidentified, and they could withdraw from the study at any time before the publication of the study.

2.4 | Data analysis

SPSS version 26 was used to perform descriptive statistical analyses. Categorical data are presented as frequencies with proportions, and continuous data are presented as means with standard deviation (SD) or medians with range. Chronbach's alpha was calculated for assessing the reliability of the BPI interference sub-scales and the NSF-MPQ total, affective, and sensory descriptors.

BPI and MPQ-SF were both scored according to the developers' recommendations.[43,53] In the analysis, the BPI item number three (worst pain intensity) was transformed to an ordinal variable where 0 to 3.99 correspond to no/mild pain, ≥4 to 6.99 correspond to moderate pain, and ≥7 to 10 correspond to severe pain. These cut-off points are in line with previous studies.[23,54,55]

Responses to open-ended questions were quantified into categories. Categories for avoidance of physical activity were walking, household chores, social activities, bending/crouching, and sitting with legs down. Categories for non-medical interventions were elevating the feet, activity, reduced activity, lowering feet, and other (ie, massage, ulcer care, aids to protect the ulcer).

There were few missing values on single items overall in the dataset. However, one single item, the SF-MPQ VAS present pain intensity item, had 27.3% missing values. Missing items on the 15 pain descriptors of SF-MPQ were replaced by 0. By experience, participants skip marking the pain descriptors that are not relevant to them, causing an inaccurate and high number of missing items.

3 | RESULTS

3.1 | Sample characteristics

The mean age of participants was 74.4 years (SD 12.75), and 53.7% were female. A total of 39.7% were living alone, and 87.5% were not working (ie, on sick leave, retired) (Table 1).

3.2 | Clinical characteristics

The participants had at least one active ulcer located at the leg, ankle, or foot. Unspecified ulcer in lower extremities (ICD-10 diagnosis code L97) was the most frequent diagnosis (30.6%). Most ulcers (48%) were triggered by a trauma, but most ulcers were further diagnosed based on physiological factors such as underlying diseases and vascular conditions. The mean wound size was 4.2 cm^2 (SD 8.8), and mean wound duration was of 28.5 weeks (SD 47.8) (Table 2).

For 46%, the present ulcer was not the first CLU they suffered from. A total of 94% reported at least one comorbidity. The most frequent comorbidities were coronary diseases (74%) including hypertension and arteriosclerosis, other painful conditions (52%) such as musculoskeletal pain, and diabetes (31%). Loss of tactile and vibration sensation was common: 59% obtained >8 on the SWME, and 51% did not detect vibration from the tuning fork (Table 2).

TABLE 1 Demographic data (N = 121)

	N (%)
Age	
<49	5 (4.1)
50-59	11 (9.1)
60-69	17 (14.0)
70-79	44 (36.4)
80-89	34 (28.1)
>90	10 (8.3)
Gender	
Male	56 (46.3)
Female	65 (53.7)
Marital status	
Single	19 (15.7)
Married/cohabitant	72 (59.5)
Widowed	30 (24.8)
Educational level	
Primary school	48 (39.7)
Secondary school	37 (30.6)
University <4 years	24 (19.8)
University >4 years	9 (7.4)
Work situation	
Working	13 (10.8)
Retired/sick leave	106 (87.5)
Living arrangements	
Alone	48 (39.7)
With spouse/other family	73 (60.3)
Ethnicity	
Norwegian	118 (97.5)
Other	2 (1.7)

Note: N, number of participants.

3.3 | Types of pain

In this sample, all participants reported having ulcer related background pain. One in five reported having only ulcer related background pain, while four in five reported both background pain and pain at dressing change (procedural) (Figure 1).

3.4 | Characteristics of ulcer related background pain

Ulcer pain intensity: The mean average pain intensity was 4.5 (SD 2.56) (CI 95% 4.0-5.0), and the mean worst pain intensity was 4.9 (SD 2.88) (CI 95% 4.4-5.5) (0-10 NRS). Mean present pain intensity was 38.65 mm (SD 27.23) (0-100 VAS) (Table 3). Divided into categories, 37% reported no or mild pain (NRS 0-3), 28% moderate pain (NRS 4-6), and 35% severe pain (NRS 7-10) (Figure 2).

Ulcer pain interference: Pain interfered mostly with general activity (mean 4.3), sleep (mean 4.1), and walking ability (mean 4.0) (0-10 NRS). The average activity pain interference (WAW) was 4.1 (SD 2.8), and the average affective pain interference (REM) was 3.1 (SD 2.7).

Avoidance of physical activities: As many as 37% of the sample reported that they avoided certain activities (eg, walking, household chores, social activities, bending/crouching, sitting with legs down) to escape ulcer related pain.

Ulcer pain qualities: The mean score on the sensory sub-scale of SF-MPQ was 6.95 (SD 6.66). The most frequently reported sensory descriptors were ‘tender’ (50.4%), ‘stabbing’ (49.6%), ‘aching’ (46.3%), and ‘hot-burning’ (45.5%). On the affective sub-scale, the mean score was 1.36 (SD 2.19). The most frequently reported affective descriptor was ‘tiring-exhausting’ (32.2%).

Ulcer pain location: Most respondents (51.7%) stated that the ulcer related pain was located in multiple locations, and few (22.3%) reported that the pain was only located in the ulcer itself. The most frequent pain locations were the ulcer itself (74.4%), the surrounding area of the wound (55.4%) and the entire leg (10.7%).

Time pattern of ulcer pain: The majority stated that the ulcer related pain was intermittent (71.1%). None reported that the pain was stable.

3.5 | Ulcer pain management

A total of 76.9% confirmed they had analgesics prescribed. Of those, 58.7% had analgesics for ulcer related pain (Table 4). Analgesics were not used as prescribed by 25.8% of those with prescribed analgesics. The main

TABLE 2 Clinical characteristics (N = 121)

	Median (IQR)	N (%)
Wound diagnosis (as specified by doctor)		
Unspecified (L97)		37 (30.6)
Venous		25 (20.7)
Diabetic foot ulcer		20 (16.5)
Traumatic		17 (14.0)
Arterial		9 (7.4)
Other		13 (10.8)
Wound size (cm^2)	1.2 (0.46-4.32)	
Wound duration (weeks)	15 (8-26)	
Reoccurring wound		
Yes		55 (45.5)
No		57 (47.1)
Number of wounds		
1		62 (51.2)
2-5		38 (31.4)
>5		12 (9.9)
Presumed primary causal factor		
Trauma		123 (48)
Pressure/friction		50 (19.8)
Venous insufficiency		16 (6.3)
Arterial insufficiency		5 (2)
Unknown/other		58 (23)
Wound location		
Leg		44 (36.4)
Foot		36 (29.8)
Ankle		23 (19.0)
Multiple locations		18 (14.9)
Number of comorbidities		2 (1.5-3)
No of comorbidities		6 (5.0)
One comorbidity		24 (19.8)
Two comorbidities		35 (28.9)
Three comorbidities		30 (24.8)
Four or more comorbidities		26 (21.5)
Comorbidities		
Coronary disease		90 (74.4)
Other painful conditions[a]		63 (52.1)
Diabetes		37 (30.6)
Malnutrition		25 (20.7)
Arthritis		22 (18.2)
Renal disease		20 (16.5)
Cancer (previous or present)		20 (16.5)
Stroke		12 (9.9)
Asthma/COPD		8 (6.6)
SWME		
0-3/8		42 (34.7)
4-7/8		29 (23.9)
8/8		42 (34.7)
Tuning fork test		
Positive		62 (51.2)
Negative		49 (40.5)

Abbreviations: IQR, interquartile range; SD, standard deviation; SWME, Semmes-Weinstein monofilament examination.

[a] Such as musculoskeletal pain and neuropathies.

compliance issue was not using the analgesic at all (n = 10) or using less analgesics than prescribed (n = 13). The reasons for not using/using less analgesics were several: adverse effects (drowsiness, constipation) (n = 8), fear of adverse effects (n = 6), no effect (n = 3), and no need for analgesics (n = 2), or a combination of these.

As many as 61.2% reported using non-medical interventions to show ulcer related pain, and most frequently they elevated the feet (23.1%) (Table 4). The respondents reported that the pain treatments or medications provided a mean pain relief of 45.9% (SD 33.9, range 0-100).

4 | DISCUSSION

This is one of the first research studies to provide solid knowledge of the characteristics of ulcer related background pain in persons with CLU's. While most other studies report on one or a few characteristics, this study describes the variety of pain characteristics of relevance for a holistic pain assessment and thereby effective pain management.

In the present study, the participants reported on average moderate ulcer related background pain (mean 4.5, CI 95% 4.0-5.0). This finding is supported our previous systematic review of pain in chronic venous ulcers (reference blinded for review), where we found an overall pooled estimate of mean pain intensity of 4.0 (CI 95% 3.5, 4.5). Interestingly, the SF-MPQ present pain intensity 0 to 100 VAS had almost 30% missing answers, which supports previous reports that VAS may

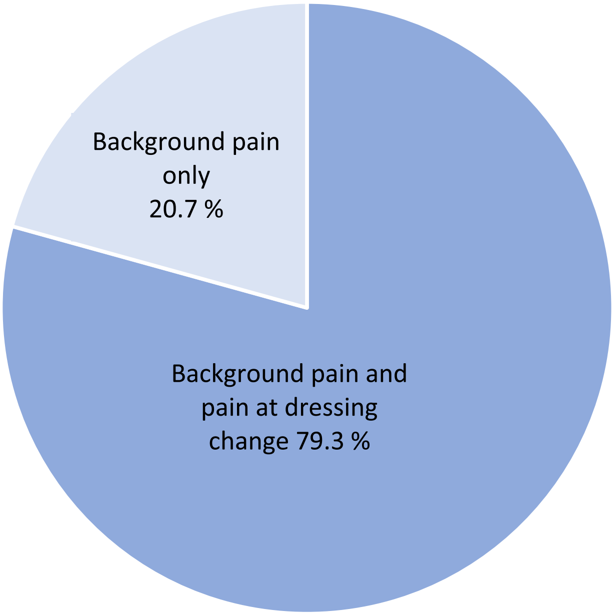


FIGURE 1 Background pain and pain at dressing change

not be an appropriate measure for pain intensity in the elderly.[56] Sub-analyses of the worst pain intensity scores in the present study demonstrated that 61% of the respondents reported moderate or severe pain intensity indicating a need for better pain management. Pain intensity worse than mild should be unacceptable.[57] The fact that as many as 34% of the respondents reported severe background pain intensity highlights the importance of looking further into existing pain management practice in wound care.

This study further demonstrates that ulcer related background pain interfered with daily function. In particular, activity functions (WOW) such as general activity, sleep, and walking ability were affected to a moderate degree.[58] In addition, 37% of the participants reported that they avoided certain activities, such as walking and daily chores. To a lesser extent, ulcer related pain interfered with affective functions such as enjoyment of life and mood (REM). However, enjoyment of life was moderately interfered with by ulcer pain. These findings are supported by previous research showing that chronic pain is associated with reduced physical activity[59,60] and can lead to emotional and behavioural reactions.[61] Note that pain interference does not necessarily provide an acceptable surrogate for physical and psychosocial function, and participants may have impaired function because of other factors than pain.[62] In fact, in the present study, more than half of the participants had other painful comorbidities such as musculoskeletal pain, joint pain, and neuropathies. Previous research also shows that the ulcer itself,[63] older age,[64] and comorbidities[65] are associated with impaired function and health outcomes. Recognising that ulcer related pain in addition to other factors can interfere with several aspects of a person's life are reasons to use biopsychosocial approaches in wound management. Biopsychosocial approaches might offset important negative consequences of a developing chronic pain problem. It is therefore essential to consider both the activity and affective dimension of pain interference as it allows assessing which aspects of the individuals' life (activity or affectivity) are affected by pain, and provide interventions accordingly.[66] Furthermore, it allows estimating the contribution of interventions in each of these aspects. Since physical activity is essential for wound healing,[67,68] pain management for promoting physical activity should be an integrated part of holistic wound care.

The most frequent descriptors used to describe ulcer related background pain were ‘tender’, ‘stabbing’, ‘aching’, and ‘hot-burning’, which are all sensory descriptors. Tender and aching are traditionally associated with nociceptive pain caused by inflammation and tissue damage, while hot-burning and stabbing are often associated with neuropathic pain caused by injury and sensitization of the peripheral or central nervous system.[69] Several pathophysiological mechanisms of CLUs, such as tissue damage, inflammation, and nerve damage, may contribute to the manifestations and different types (eg, nociceptive, neuropathic) of ulcer related background pain.[13] The fact that the participants reported different types of pain descriptors may indicate the presence of different types of pain. Note, however, that no descriptor is particular for either nociceptive or neuropathic pain, and therefore type of pain cannot be determined by pain descriptors alone. The use of descriptors in combination with a thorough history taking and clinical examination can guide clinicians in determining type of pain and choosing appropriate pain management.[69,70]

The fact that nine participants reported ‘no pain’ in the last 24 hours is in concordance with the finding that most participants (71.1%) stated that their pain was intermittent, meaning that they experience pain sometimes, but are pain free at other times. Further, this finding indicates that at least some of the participants have pain free periods that exceed 24 hours. The remaining sample reported that their pain was variable, meaning that they had ‘background’ pain all the time, but also periods of less as well as more pain (eg, incident pain, pain attacks). Note that none of the participants described their pain as stable. The temporal fluctuation is important to recognise when assessing and treating ulcer related pain, in order to provide appropriate pain management. Persons with long pain free periods do not need continuous analgesia

TABLE 3 Ulcer pain characteristics (N = 121)

	N (%)	Mean	SD
BPI pain intensity (0-10 NRS, past 24 hours)			
Worst		4.9	2.88
Average		4.5	3.56
Now		3.0	3.64
Least		2.1	2.04
BPI pain interference (0-10 NRS, past 24 hours)			
General activity		4.3	3.16
Sleep		4.1	3.18
Walking ability		4.0	3.11
Normal work		3.9	3.14
Enjoyment of life		3.6	3.09
Mood		3.3	2.96
Relations with others		2.4	2.69
Activity pain interference (WAW)		4.1	2.8
Affective pain interference (REM)		3.1	2.7
Total interference score		3.6	2.6
SF-MPQ			
Descriptors			
SF-MPQ sensory		6.90	6.66
SF-MPQ affective		1.36	2.19
SF-MPQ total		8.24	8.35
VAS present pain intensity (0-100)		38.65	27.23
Present pain intensity index			
No pain	10 (8.3)		
Mild pain	22 (18.2)		
Discomforting	28 (23.1)		
Distressing	45 (37.2)		
Horrible	7 (5.8)		
Excruciating	2 (1.7)		
PQAS pain pattern			
Intermittent pain	86 (71.1)		
Variable pain	31 (25.6)		
Stable pain	0 (0)		
Localization of ulcer related pain			
Multiple locations	69 (57.0)		
Only the wound itself (wound bed or edges)	27 (22.3)		
The wound bed	90 (74.4)		
The wound edges	15 (12.4)		
The area surrounding the wound	67 (55.4)		
The entire foot	7 (6.0)		
The entire leg	13 (10.7)		

Abbreviations: BPI, brief pain inventory; NRS, numeric rating scale; PQAS, pain quality assessment scale; REM, affective pain interference; SD, standard derivation; SF-MPQ, Short-form Mc Gill pain questionnaire; WAW, activity pain interference.

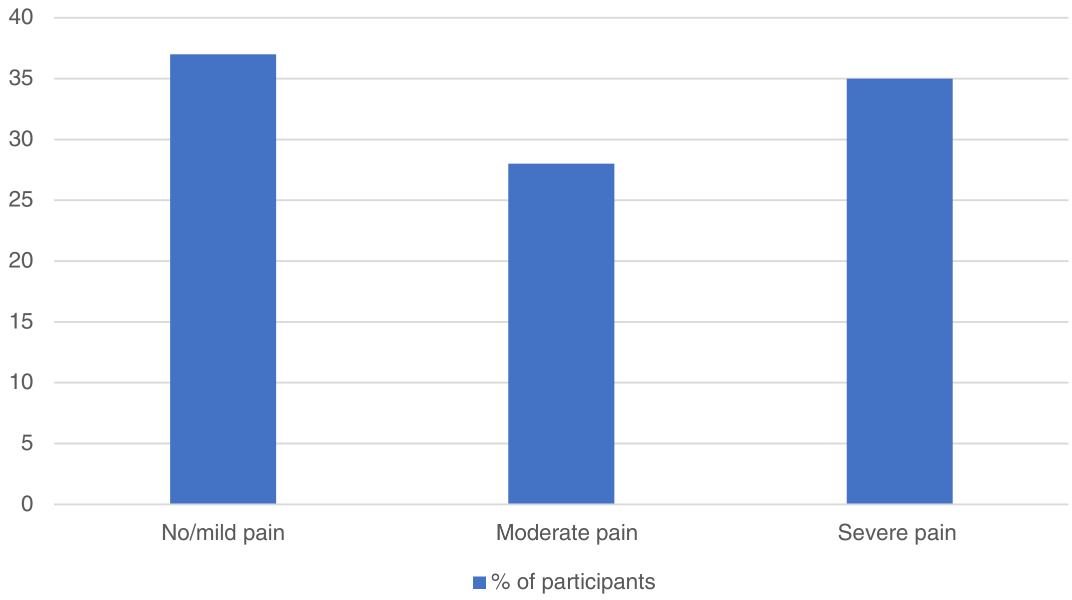


FIGURE 2 Brief pain inventory worst ulcer pain intensity divided into categories (N = 117)

TABLE 4 Ulcer pain management

	n (%)
Prescribed analgesics	
Yes	93 (76.9)
No	28 (23.1)
Prescribed analgesics for ulcer related pain	
Yes	71 (58.7)
No	50 (41.3)
Use of non-medical interventions	
Yes	74 (61.2)
No	47 (38.8)
Type of non-medical interventions	
Elevating feet	28 (23.1)
Activity	16 (13.2)
Reduced activity	13 (10.7)
Lowering feet	9 (7.4)
Other[a]	8 (6.6)

[a] Massage, ulcer care, aids to protect the ulcer.

administered around the clock (ATC), but rather administration per needed (PRN).[71] Likewise, persons with variable pain may need ATC in addition to PRN to achieve pain relief. The temporal fluctuations of pain and pain intensity are especially important when taking into consideration that almost three out of four of the respondents reported both ulcer related background pain and dressing related pain.

A majority of the participants reported that their ulcer related pain had multiple locations. The present study does not provide further information about differences in pain characteristics based on the location. However, pain in other locations than the ulcer itself might be primary hyperalgesia because of inflammation,[72] referred pain from the ulcer,[73] or caused by other pathological factors associated with having a CLU (eg, ischaemia, oedema, swelling, skin irritation, diabetic neuropathy). Interestingly, less than one out of four participants reported that the pain was located only in the ulcer itself. This finding indicates that local pain-relieving measures applied in the wound bed (eg, analgesic gels, analgesic-releasing dressings) are most likely inadequate to relieve pain. The location of pain should therefore be thoroughly examined when assessing ulcer related pain, as it could inform clinicians of the best combination of systemic and local pain management.

An interesting finding from the present study pertains to the assessment of tactile mechanical sensation. Only 30% of the respondents were diagnosed with diabetes, and only 16% had a diabetic foot ulcer. Yet almost 60% of the participants had reduced sensation and were unable to detect one or more pricks using SWME. Note that inability to detect one prick is used as a diagnostic threshold when screening for diabetic peripheral neuropathy.[36] In addition, over 40% could not detect vibration from the tuning fork. These findings demonstrate that many persons with other ulcer-diagnoses than diabetic ulcers (eg, traumatic, venous, and mixed aetiology ulcers) also had diminished tactile sensation in the lower leg.

Interestingly, studies have showed an alteration of nerve function in persons with both arterial- and venous ulcers,[74-76] and vascular microangiopathy that lead to nerve ischaemia may result in neuropathy in persons with CLUs.[77] Note that lost sense of touch and vibration may indicate presence of peripheral neuropathy.[39] However, it is also well documented that diminished tactile sensation is common in healthy older adults.[78] Our present study cannot state whether the findings of diminished tactile sensation in persons with CLUs is a sign of peripheral neuropathy because of disease, or a normal alteration in the peripheral nervous system with increasing age. However, previous research also shows that ulcer related pain is prevalent despite diminished tactile sensation.[79] Therefore, the present study's findings are relevant in clinical practice, and should be a reminder for clinicians not to discard ulcer related pain in persons with CLUs and signs of non-painful peripheral neuropathy. The high prevalence of diminished tactile sensation is also important to consider with regards to treatment and prevention of CLUs, regardless of ulcer diagnosis. SWME and tuning fork tests are non-invasive, low-cost, rapid, and easy-to-apply in clinical practice. And even though there are several uncertainties in the diagnostics properties of the tests, the monofilament and tuning fork are important evidence-based tools for predicting the prognosis of persons with CLUs.[36,38,80]

Interestingly, while a large proportion of the participants (77%) had prescribed analgesics, less than 60% had prescribed analgesics specifically for ulcer related pain. One out of four reported using doses less than prescribed or not taking the analgesic at all for several reasons. The fact that participants had intermittent pain and some pain-free periods of more than 24 hours may explain some of the non-adherence to prescribed analgesics. However, this study's findings of a large proportion of persons with moderate to severe pain with substantial impact on function may also indicate that the clinicians did not succeed in providing proper pain management. Previous research supports this study's findings that persons with CLUs experience different pain severity and relief, and they have different impact of pain on activity, sleep and negative emotions. In addition, they may experience different adverse effects of analgesics (eg, nausea, drowsiness).[81] They may also have the same barriers to pain management as other patients, such as being afraid of addiction or believing that analgesics should only be used when pain is unbearable.[82,83] All these factors may in turn affect adherence to treatment. Good quality pain management must involve assessment and evaluation of the response to treatment and be individualised to meet a person's various needs.

The present study has strengths and limitations that need to be recognised. First of all, this study is the first of its kind to investigate a number of pain characteristics in depth in a large sample of persons with CLU's. The findings are relevant for persons with CLU's with various diagnoses, making the study clinically relevant for clinicians managing a variety of CLUs. However, since we only recruited hospital outpatients, our sample may not be representative of a community sample of persons with ulcer related pain caused by CLUs. Furthermore, we recruited persons with various ulcer diagnosis and therefore one should be careful when generalising the results to one specific wound patient group. However, the sample should be representative for persons with ulcer related background pain attending outpatient wound clinics.

This study provides detailed and systematic quantitative data concerning ulcer related background pain experienced by persons living with CLUs. The data support previous research that suggests that ulcer related background pain is a significant and interfering problem. Over 60% of the participants reported moderate to severe pain intensity and that pain interfered with daily function. Unfortunately, despite heightened awareness of and clinical advantages in pain management over the past 15 years, our study suggests that background pain is still undertreated in person with CLUs. Considering the other pain characteristics presented, we further emphasise the importance of thorough pain assessment in all persons presenting with CLUs, and especially in all persons reporting ulcer related background pain, to provide effective pain management. Persons with CLUs might need a variety of treatment strategies including analgesics (aimed at both nociceptive and neuropathic pain) and non-medical treatment aimed at chronic pain conditions. Pain management should be a high priority in wound management to avoid negative consequences of pain.

ACKNOWLEDGEMENTS

We thank all the clinicians at the two outpatient wound care clinics at Vestre Viken HF for the facilitation of the data collection, and for input and advice. The University of South-Eastern Norway has funded the project based on funding from Norwegian Ministry of Education and Research. None of the above-mentioned institutions has any roles in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research report.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are not available due to privacy or ethical restrictions.

ORCID

Lena Leren https://orcid.org/0000-0001-9083-5615

REFERENCES

1. Agale SV. Chronic Leg Ulcers: epidemiology, aetiopathogenesis, and management. *Ulcers*. 2013;2013:1-9.
2. Martinengo L, Olsson M, Bajpai R, et al. Prevalence of chronic wounds in the general population: systematic review and meta-analysis of observational studies. *Ann Epidemiol*. 2019;29:8-15.
3. Sibbald RG, Armstrong DG, Orsted HL. Pain in diabetic foot ulcers. *Ostomy Wound Manage*. 2003;49(4 Suppl):24-29.
4. Zaidi Z, Hussain K, Sudhakaran S. Leg Ulcers. *Treatment of Skin Diseases*. New York City: Springer; 2019:251-257.
5. WUWHS. Principles of best practice: minimizing pain at dressing-related procedures: "Implementation of pain relieving strategies". Evidence informed practice. 2007; 1–25. http://lesspain.com/Documents/PainAwareness/WUWHS%202008%20Best%20Practice%20Document%20English.pdf
6. IASP. IASP Terminology. IASP Terminology. 2020. https://www.iasp-pain.org/Education/Content.aspx?ItemNumber=1698
7. WUWHS. Principles of best practice: minimising pain at wound dressing-related procedures. A consensus document. 2004. http://www.woundsinternational.com/media/issues/79/files/content_39.pdf
8. Renner R, Seikowski K, Simon JC. Association of pain level, health and wound status in patients with chronic leg ulcers. *Acta Derm Venereol*. 2014;94(1):50-53.
9. Leren L, Johansen E, Eide H, Falk RS, Juvet LK, Ljoså TM. Pain in persons with chronic venous leg ulcers: a systematic review and meta-analysis. *Int Wound J*. 2020;17:466-484.
10. White R. A multinational survey of the assessment of pain when removing dressings. *Wounds*. 2008;4(1):14–22.
11. Woo KY, Sibbald RG. Chronic wound pain: a conceptual model. *Adv Skin Wound Care*. 2008;21(4):175-190.
12. Briggs M. Minimising pain at wound dressing-related procedures: a consensus document. WUWHS Consensus Statement. 2004: p. 1–10.
13. Woo KY, Abbott LK, Librach L. Evidence-based approach to manage persistent wound-related pain. *Curr Opin Support Palliat Care*. 2013;7(1):86-94.
14. Guest JF, Fuller GW, Vowden P. Venous leg ulcer management in clinical practice in the UK: costs and outcomes. *Int Wound J*. 2018;15(1):29-37.
15. Hall J, Buckley HL, Lamb KA, et al. Point prevalence of complex wounds in a defined United Kingdom population. *Wound Repair Regen*. 2014;22(6):694-700.
16. EWMA. Pain at wound dressing changes. Position Document 2002. http://ewma.org/fileadmin/user_upload/EWMA/pdf/Position_Documents/2002/Spring_2002__English_pdf
17. Sibbald RG, Elliott JA, Persaud-Jaimangal R, et al. Wound bed preparation 2021. *Adv Skin Wound Care*. 2021;34(4):183-195.
18. Jenkins S. The assessment of pain in chronic wounds (part 2). *Wounds*. 2020;16(4):37-44.
19. Paschou SA, Stamou M, Vuagnat H, Tentolouris N, Jude E. Pain management of chronic wounds: diabetic ulcers and beyond. *Maturitas*. 2018;117:17-21.
20. Purcell A, Buckley T, King J, Moyle W, Marshall AP. Topical analgesic and local anesthetic agents for pain associated with chronic leg ulcers: a systematic review. *Adv Skin Wound Care*. 2020;33(5):240-251.
21. Green J, Jester R, McKinley R, Pooler A. Chronic venous leg ulcer care: putting the patient at the heart of leg ulcer care. Part 1: exploring the consultation. *Br J Community Nurs*. 2018; 23(Sup3):S30-S38.
22. Frescos N. Assessment of pain in chronic wounds: a survey of Australian health care practitioners. *Int Wound J*. 2018;15(6): 943-949.
23. Leren L, Johansen EA, Eide H, Sørum Falk R, Ljoså TM. Prevalence and factors associated with ulcer-related pain in persons with chronic leg ulcers—an explorative study. *J Clin Nurs*. 2021;30:2732-2741.
24. Roth RS, Lowery JC, Hamill JB. Assessing persistent pain and its relation to affective distress, depressive symptoms, and pain catastrophizing in patients with chronic wounds: a pilot study. *Am J Phys Med Rehabil*. 2004;83:827-834.
25. Parker K. Psychosocial effects of living with a leg ulcer. *Nurs Stand*. 2012;26(45):50–56, 60, 62, 52.
26. Gonçalves ML, de Gouveia Santos VLC, de Mattos Pimenta CA, Suzuki É, Komegae KM. Pain in chronic leg ulcers. *J Wound Ostomy Cont Nurs*. 2004;31(5):275-283.
27. Closs SJ, Nelson EA, Briggs M. Can venous and arterial leg ulcers be differentiated by the characteristics of the pain they produce? *J Clin Nurs*. 2008;17(5):637-645.
28. Park SH, Ferreira K, Santos VL. Understanding pain and quality of life for patients with chronic venous ulcers. *Wounds*. 2008;20(11):309-320.
29. Salome G, Ferreira L. The impact of decongestive physical therapy and elastic bandaging on the control of pain in patients with venous ulcers. *Rev Col Bras Cir*. 2018;45(2):e1385.
30. Hellström A, Nilsson C, Nilsson A, Fagerström C. Leg ulcers in older people: a national study addressing variation in diagnosis, pain and sleep disturbance. *BMC Geriatr*. 2016;16(1):25.
31. Hofman D, Ryan TJ, Arnold F, et al. Pain in venous leg ulcers. *J Wound Care*. 1997;6(5):222-224.
32. Wong IK, Andriessen A, Charles HE, et al. Randomized controlled trial comparing treatment outcome of two compression bandaging systems and standard care without compression in patients with venous leg ulcers. *J Eur Acad Dermatol Venereol*. 2012;26:102-110.
33. Noonan L, Burge S. Venous leg ulcers: is pain a problem? *Phlebology*. 1998;13(1):14-19.
34. Taverner T, Closs SJ, Briggs M. The journey to chronic pain: a grounded theory of older adults' experiences of pain associated with leg ulceration. *Pain Manag Nurs*. 2014;15(1): 186-198.
35. Singh N, Armstrong DG, Lipsky BA. Preventing foot ulcers in patients with diabetes. *JAMA*. 2005;293(2):217-228.
36. Feng Y, Schlösser FJ, Sumpio BE. The Semmes Weinstein monofilament examination as a screening tool for diabetic peripheral neuropathy. *J Vasc Surg*. 2009;50(3):675-682.e1.
37. Assosiation, C.D. Appendix 11B - Rapid Screening for Diabetic Neuropathy Using the 128 Hz Vibration Tuning Fork Canadian

Journal of Diabetes 2018 April 1, 2018. http://www.sciencedirect.com/science/article/pii/S1499267117308791

38. Oyer D, Saxon D, Shah A. Quantitative assessment of diabetic peripheral neuropathy with use of the clanging tuning fork test. *Endocr Pract*. 2007;13(1):5-10.
39. Dyck PJ, Herrmann DN, Staff NP, Dyck PJB. Assessing decreased sensation and increased sensory phenomena in diabetic polyneuropathies. *Diabetes*. 2013;62(11):3677-3686.
40. Jensen M, Galer B, Gammaitomi A. The Pain Quality Assessment Scale (PQAS) and Revised Pain Quality Assessment Scale (PQAS-R): Manual and User Guide. Mapi Research Trust website. 2010. http://www.mapi-trust.org
41. Miaskowski C, Mastick J, Paul SM, et al. Chemotherapy-induced neuropathy in cancer survivors. *J Pain Symptom Manag*. 2017;54(2):204-218.e2.
42. Ljosaa TM, Rustoen T, Mørk C, et al. Skin pain and discomfort in psoriasis: an exploratory study of symptom prevalence and characteristics. *Acta Derm Venereol*. 2010;90(1):39-45.
43. Melzack R. The short-form McGill pain questionnaire. *Pain*. 1987;30(2):191-197.
44. Ljunggren AE, Strand LI, Johnsen TB. Development of the Norwegian short-form McGill pain questionnaire (NSF-MPQ). *Adv Physiother*. 2007;9(4):169-180.
45. Strand LI, Ljunggren AE, Bogen B, Ask T, Johnsen TB. The short-form McGill pain questionnaire as an outcome measure: test–retest reliability and responsiveness to change. *Eur J Pain*. 2008;12(7):917-925.
46. Nemeth KA, Graham ID, Harrison MB. The measurement of leg ulcer pain: identification and appraisal of pain assessment tools. *Adv Skin Wound Care*. 2003;16(5):260-267.
47. Cleeland CS, Ryan K. The Brief Pain Inventory. Pain Research Group. 1991.
48. Jelsness-Jørgensen L-P, Moum B, Grimstad T, et al. Validity, reliability, and responsiveness of the brief pain inventory in inflammatory bowel disease. *Can J Gastroenterol Hepatol*. 2016; 2016:1-10.
49. Klepstad P, Loge JH, Borchgrevink PC, Mendoza TR, Cleeland CS, Kaasa S. The Norwegian brief pain inventory questionnaire: translation and validation in cancer pain patients. *J Pain Symptom Manag*. 2002;24(5):517-525.
50. Kapstad H, Rokne B, Stavem K. Psychometric properties of the brief pain inventory among patients with osteoarthritis undergoing total hip replacement surgery. *Health Qual Life Outcomes*. 2010;8(1):148.
51. Gjeilo KH, Stenseth R, Wahba A, Lydersen S, Klepstad P. Validation of the brief pain inventory in patients six months after cardiac surgery. *J Pain Symptom Manag*. 2007;34(6):648-656.
52. Pieper B, DiNardo E, Nordstrom CK. A cross-sectional, comparative study of pain and activity in persons with and without injection-related venous ulcers. *Ostomy Wound Manage*. 2013; 59(5):14-24.
53. Cleeland CS. *The Brief Pain Inventory: User Guide*. Houston, TX: The University of Texas MD Anderson Cancer Center; 2009:1-11.
54. Zelman DC, Dukes E, Brandenburg N, Bostrom A, Gore M. Identification of cut-points for mild, moderate and severe pain due to diabetic peripheral neuropathy. *Pain*. 2005;115(1–2):29-36.
55. Kapstad H, Hanestad BR, Langeland N, Rustøen T, Stavem K. Cutpoints for mild, moderate and severe pain in patients with osteoarthritis of the hip or knee ready for joint replacement surgery. *BMC Musculoskelet Disord*. 2008;9(1):55.
56. Hjermstad MJ, Fayers PM, Haugen DF, et al. Studies comparing numerical rating scales, verbal rating scales, and visual analogue scales for assessment of pain intensity in adults: a systematic literature review. *J Pain Symptom Manag*. 2011;41(6):1073-1093.
57. Moore R, Straube S, Aldington D. Pain measures and cut-offs–'no worse than mild pain' as a simple, universal outcome. *Anaesthesia*. 2013;68(4):400-412.
58. Shi Q, Mendoza TR, Dueck AC, et al. Determination of mild, moderate, and severe pain interference in patients with cancer. *Pain*. 2017;158(6):1108-1112.
59. Stubbs B, Binnekade TT, Soundy A, Schofield P, Huijnen IPJ, Eggermont LHP. Are older adults with chronic musculoskeletal pain less active than older adults without pain? A systematic review and meta-analysis. *Pain Med*. 2013;14(9):1316-1331.
60. Ellingson LD, Shields MR, Stegner AJ, Cook DB. Physical activity, sustained sedentary behavior, and pain modulation in women with fibromyalgia. *J Pain*. 2012;13(2):195-206.
61. Linton SJ, Shaw WS. Impact of psychological factors in the experience of pain. *Phys Ther*. 2011;91(5):700-711.
62. Karayannis NV, Sturgeon JA, Chih-Kao M, Cooley C, Mackey SC. Pain interference and physical function demonstrate poor longitudinal association in people living with pain: a PROMIS investigation. *Pain*. 2017;158(6):1063-1068.
63. Cunha N, Campos S, Cabete J. Chronic leg ulcers disrupt patients' lives: a study of leg ulcer-related life changes and quality of life. *Br J Community Nurs*. 2017;22(Sup9):S30-S37.
64. WHO. Aging and Health. 2018. https://www.who.int/news-room/fact-sheets/detail/ageing-and-health
65. Valderas JM, Starfield B, Sibbald B, Salisbury C, Roland M. Defining comorbidity: implications for understanding health and health services. *Ann Family Med*. 2009;7(4):357-363.
66. Atkinson TM, Halabi S, Bennett AV, et al. Measurement of affective and activity pain interference using the brief pain inventory (BPI): cancer and leukemia group B 70903. *Pain Med*. 2012;13(11):1417-1424.
67. Mutlak OO. The influence of exercise on ulcer healing in patients with chronic venous insufficiency. 2015.
68. Eraydin Ş, Avşar G. The effect of foot exercises on wound healing in type 2 diabetic patients with a foot ulcer. *J Wound Ostomy Continence Nurs*. 2018;45(2):123-130.
69. Finnerup NB, Haroutounian S, Kamerman P, et al. Neuropathic pain: an updated grading system for research and clinical practice. *Pain*. 2016;157(8):1599-1606.
70. Holtan A, Kongsgaard UE. The use of pain descriptors in cancer patients. *J Pain Symptom Manag*. 2009;38(2):208-215.
71. Pasero C. Around-the-clock (ATC) dosing of analgesics. *J Perianesth Nurs*. 2010;25(1):36-39.
72. Gögenur I, Rosenberg J. In: Mads Utke Werner NBF, Arendt-Nielsen L, eds. *Smerte, inflammation og kirurgisk stress-respons, in Smerter: baggrund, evidens og behandling*. København: FADL's Forlag; 2019:170-182.
73. Arendt-Nielsen L, Laursen R, Drewes AM. Referred pain as an indicator for neural plasticity. *Progress in Brain Research*. 2000; 129:343-356.
74. McDermott MM, Sufit R, Nishida T, et al. Lower extremity nerve function in patients with lower extremity ischemia. *Arch Intern Med*. 2006;166(18):1986-1992.

75. Stücker M, Schöbe MC, Hoffmann K, Schultz-Ehrenburg U. Cutaneous microcirculation in skin lesions associated with chronic venous insufficiency. *Dermatol Surg*. 1995;21(10):877-882.
76. Yim E, Vivas A, Maderal A, Kirsner RS. Neuropathy and ankle mobility abnormalities in patients with chronic venous disease. *JAMA Dermatol*. 2014;150(4):385-389.
77. Eusen M, Brenaut E, Schoenlaub P, Saliou P, Misery L. Neuropathic pain in patients with chronic leg ulcers. *J Eur Acad Dermatol Venereol*. 2016;30(9):1603-1605.
78. Decorps J, Saumet JL, Sommer P, Sigaudo-Roussel D, Fromy B. Effect of ageing on tactile transduction processes. *Ageing Res Rev*. 2014;13:90-99.
79. Bengtsson L, Jonsson M, Apelqvist J. Wound-related pain is underestimated in patients with diabetic foot ulcers. *J Wound Care*. 2008;17(10):433-433, 435.
80. Feng Y, Schlösser FJ, Sumpio BE. The Semmes Weinstein monofilament examination is a significant predictor of the risk of foot ulceration and amputation in patients with diabetes mellitus. *J Vasc Surg*. 2011;53(1):220-226.e5.
81. Hayes K, Gordon DB. Delivering quality pain management: the challenge for nurses. *AORN J*. 2015;101(3):327-337.
82. Jacobsen R, Møldrup C, Christrup L, Sjøgren P. Patient-related barriers to cancer pain management: a systematic exploratory review. *Scand J Caring Sci*. 2009;23(1):190-208.
83. Gunnarsdottir S, Serlin RC, Ward S. Patient-related barriers to pain management: the Icelandic barriers questionnaire II. *J Pain Symptom Manag*. 2005;29(3):273-285.

How to cite this article: Leren L, Eide H, Johansen EA, Jelnes R, Ljoså TM. Background pain in persons with chronic leg ulcers: An exploratory study of symptom characteristics and management. *Int Wound J*. 2021;1-13. doi:10.1111/iwj.13730

Attachements

1. Approval from the Norwegian Regional Ethical Committee for Medical Health Research Ethics
2. Approval from the local data protection officer VVHF

REK
REGIONALE KOMITEER FOR MEDISINSK OG HELSEFAGLIG FORSKNINGSETIKK

Region:	Saksbehandler:	Telefon:	Vår dato:	Vår referanse:
REK sør-øst	Claus Henning Thorsen	22845515	07.09.2016	2016/1236/REK sør-øst C
			Deres dato:	**Deres referanse:**
			14.06.2016	

Vår referanse må oppgis ved alle henvendelser

Tone Marte Ljoså
Høgskolen i Sørøst-Norge
Postboks 235
3603 Drammen

2016/1236 Sårsmerte hos pasienter med kroniske legg- og fotsår

Forskningsansvarlig: Høgskolen i Sørøst-Norge
Prosjektleder: Tone Marte Ljoså

Vi viser til søknad om forhåndsgodkjenning av ovennevnte forskningsprosjekt. Søknaden ble behandlet av Regional komité for medisinsk og helsefaglig forskningsetikk (REK sør-øst) i møtet 18.08.2016. Vurderingen er gjort med hjemmel i helseforskningsloven (hfl.) § 10, jf. forskningsetikkloven § 4.

Prosjektomtale

Prosjektet gir ny kunnskap om pasienters beskrivelse av sårsmerte. Smerte synes å være et av de mest plagsomme symptomene hos dem med kroniske sår. Likevel er det lite forskning på området, og vi mangler en dypere forståelse av pasientenes opplevelse av sårsmerte. Med spørreskjema gjør vi en tverrsnittsundersøkelse på forekomst av sårsmerte, hvordan pasienter beskriver sårsmerte (intensitet, kvalitet, lokalisasjon, døgnvariasjon), hvordan sårsmerte påvirker fysisk og psykososial funksjon (livskvalitet og søvn), og om det er betydelig forskjell i smerteopplevelsen hos pasienter med ulike typer sår. Spørreskjema vil gis til 350 pasienter med ulike kroniske legg- og fotsår. Respondentene vil rekrutteres fra poliklinikker og hjemmesykepleie som yter tjenester knyttet til sårbehandling. Deskriptive analyser og regresjonsanalyse vil bli brukt til dataanalysen. Økt forståelse og innsikt i temaet kan bidra til bedre lindrende behandling til pasienter med smerter relatert til kroniske sår.

Vurdering

Prosjektets formål er å gi økt forståelse og innsikt i pasienters sårsmerter og kan bidra til bedre lindrende behandling til pasienter med smerter relatert til kroniske sår.

Studien er en tverrsnittsundersøkelse på 1) forekomst av sårsmerte 2) pasienters beskrivelse av sårsmerte (intensitet, kvalitet, lokalisasjon, døgnvariasjon 3) hvordan sårsmerte påvirker fysisk og psykososial funksjon (livskvalitet og søvn 4) og om det er forskjeller i smerteopplevelsen hos pasienter med ulik såretiologi.

Man tar sikte på å inkluderer 350 pasienter > 18 år med ulike kroniske legg-fotsår. Pasientene rekrutteres av sykepleiere ansatt på poliklinikker/hjemmesykepleie som yter tjenester knyttet til sårbehandling

Demografiske data og kliniske opplysninger innhentes via spørreskjema. Kliniske opplysninger relatert til såret, basert på sykepleieres undersøkelse og kliniske vurdering under sårskift, innhentes fra ansvarlig sykepleier og nedtegnes på skjema av forsker. Andre kliniske opplysninger om såret vil innhentes ved at forskeren spør pasienten, og nedtegnes i skjema. I tillegg vil det tas bilde av såret og foten/leggen med kamera som kun brukes til dette formålet. Bildet vil gi klinisk informasjon om hva slags type sår pasienten har.

Komiteen mener dette er en gjennomarbeidet søknad med gode etiske vurderinger. Ulempene må anses som ubetydelige, ettersom undersøkelse av såret skjer under sårskift og således ikke innebærer noen ekstra belastning for pasienten. Tidsbruk ved utfylling av spørreskjemaer ligger innenfor det akseptable, komiteen bemerker dog i den forbindelse at de i informasjonsskrivet anførte 20 minutter synes å være et noe knapt estimat.

Komiteen mener samtykkekompetanse bør vurderes av den/de som kjenner pasientene best, og ikke den enkelte pleier som kommer for å foreta sårskiftet. Komiteen forutsetter derfor at det i prosjektet finnes/etableres rutiner for vurdering av samtykkekompetanse.

Vedtak
Prosjektet godkjennes, jf. helseforskningslovens §§ 9 og 33.

Tillatelsen er gitt under forutsetning av at prosjektet gjennomføres slik det er beskrevet i søknaden og protokollen, og de bestemmelser som følger av helseforskningsloven med forskrifter.

Tillatelsen gjelder til 31.01.2020. Av dokumentasjons- og oppfølgingshensyn skal opplysningene likevel bevares inntil 31.01.2025. Opplysningene skal lagres avidentifisert, dvs. atskilt i en nøkkel- og en opplysningsfil. Opplysningene skal deretter slettes eller anonymiseres, senest innen et halvt år fra denne dato.

Komiteens avgjørelse var enstemmig.

Sluttmelding og søknad om prosjektendring
Dersom det skal gjøres endringer i prosjektet i forhold til de opplysninger som er gitt i søknaden, må prosjektleder sende endringsmelding til REK. Prosjektet skal sende sluttmelding på eget skjema, se helseforskningsloven § 12, senest et halvt år etter prosjektslutt.

Klageadgang
Komiteens vedtak kan påklages til Den nasjonale forskningsetiske komité for medisin og helsefag, jfr. helseforskningsloven § 10, tredje ledd og forvaltningsloven § 28. En eventuell klage sendes til REK sør-øst C. Klagefristen er tre uker fra mottak av dette brevet, jfr. forvaltningsloven § 29.

Med vennlig hilsen

Britt-Ingjerd Nesheim
prof.dr.med.
leder REK sør-øst C

Claus Henning Thorsen
Rådgiver

Kopi til: *Høgskolen i Sørøst-Norge ved øverste administrative ledelse: postmottak@usn.no*

REK
REGIONALE KOMITEER FOR MEDISINSK OG HELSEFAGLIG FORSKNINGSETIKK

Region:	Saksbehandler:	Telefon:	Vår dato:	Vår referanse:
REK sør-øst	Claus Henning Thorsen	22845515	16.11.2016	2016/1236/REK sør-øst C
			Deres dato:	**Deres referanse:**
			23.10.2016	

Vår referanse må oppgis ved alle henvendelser

Tone Marte Ljoså
Postboks 235

2016/1236 Sårsmerte hos pasienter med kroniske legg- og fotsår

Forskningsansvarlig: Høgskolen i Sørøst-Norge
Prosjektleder: Tone Marte Ljoså

Vi viser til søknad om prosjektendring datert 23.10.2016 for ovennevnte forskningsprosjekt. Søknaden er behandlet av leder for REK sør-øst C på fullmakt.

Vurdering

De omsøkte endringene er beskrevet i skjema for prosjektendringer.

Det søkes om endringer i skjema for klinisk informasjon og spørreskjemapakken. I tillegg er det gjort endring med hensyn til hvem som foretar den kliniske undersøkelsen.

Informasjonsskrivet er revidert i henhold til de ovenfor beskrevne endringer.

Komitéen har ingen forskningsetiske innvendinger til prosjektet slik det nå foreligger, og godkjenner omsøkte endringer slik disse beskrives i endringsmelding med vedlegg.

Vedtak

Komitéen har vurdert endringsmeldingen og godkjenner prosjektet slik det nå foreligger med hjemmel i helseforskningslovens § 11.

Tillatelsen er gitt under forutsetning av at prosjektendringen gjennomføres slik det er beskrevet i prosjektendringsmeldingen og endringsprotokoll, og de bestemmelser som følger av helseforskningsloven med forskrifter.

Forskningsprosjektets data skal oppbevares forsvarlig, se personopplysningsforskriften kapittel 2, og Helsedirektoratets veileder for Personvern og informasjonssikkerhet i forskningsprosjekter innenfor helse og omsorgssektoren.

Komiteens vedtak kan påklages til Den nasjonale forskningsetiske komité for medisin og helsefag, jf. helseforskningsloven § 10, 3 ledd og forvaltningsloven § 28. En eventuell klage sendes til REK sør-øst C.

Klagefristen er tre uker fra mottak av dette brevet, jf. forvaltningsloven § 29.

Vi ber om at alle henvendelser sendes inn via vår saksportal: http://helseforskning.etikkom.no eller på e-post til: post@helseforskning.etikkom.no

Vennligst oppgi vårt referansenummer i korrespondansen.

Med vennlig hilsen

Britt-Ingjerd Nesheim
Prof.dr.med.
Leder REK sør-øst C

Claus Henning Thorsen
Rådgiver

Kopi til: *tone.marte.ljosaa@hbv.no; postmottak@usn.no*

Lena Leren

Fra: Henriette Henriksen
Sendt: mandag 9. januar 2017 12:25
Til: Anders Bjørneboe
Kopi:
Emne: SV: Ang forskningsprosjekt smerte og sår

Hei og takk for informasjon.

Studien innehar de nødvendige godkjenninger fra REK, samt baserer seg på pasientens samtykke.
Personvernombudet tar informasjonen til orientering og har ingen innvendinger mot prosjektet.
Prosjektet må også forankres hos klinikkens forskningsansvarlig, Jeanette Koht.

Lykke til med deltakelsen.

Henriette

Med vennlig hilsen
Henriette Henriksen
Personvernombud / Informasjonssikkerhetsansvarlig | Teknologi og eHelse
Vestre Viken HF | www.vestreviken.no

Fra: Anders Bjørneboe
Sendt: 6. januar 2017 15:57
Til: Henriette Henriksen
Kopi:
Emne: VS: Ang forskningsprosjekt smerte og sår

Hei,
Prosjektet er forankret og godkjent i kir avdelingsledelse. Oversendes Personvernombudet i VV for godkjenning.
Saken har ligget litt hos meg, det beklages.

Mvh
Anders Bjørneboe

Doctoral dissertation no. 128
2022

—

A descriptive study of ulcer-related pain characteristics and management

Dissertation for the degree of PhD

—

Lena Leren

—

ISBN: 978-82-7206-669-6 (print)
ISBN: 978-82-7206-670-2 (online)

usn.no