Plan Full title of project

Pain relief strategies for dressing change in chronic wounds: a mixed-methods systematic review and survey of UK practice

Summary of research

Background

Pain is a common experience for people living with chronic wounds and can result from the wound itself, treatments for chronic wounds, including dressing changes; or be anticipatory. Pain during dressing change has been reported as the worst part of living with chronic wounds.(Price et al., 2008)

In 2002 the European Wound Management Association (EWMA) found that: dressing removal is considered to be the time of most pain, followed closely by wound cleansing. Furthermore, that dried out dressings and adherent products are most likely to cause pain and trauma at dressing changes as is gauze, while products such as hydrogels and soft silicone dressings are least likely. EWMA also found that supporting the surrounding skin during dressing removal is not considered a priority, despite evidence that many adhesive products may lead to skin stripping and potential skin trauma and pain.(EWMA Position Document, 2002)

The World Union of Wound Healing Societies 2004 consensus document on procedures for minimising pain at wound dressing suggests that pain at dressing changed can be managed by a combination of accurate assessment, suitable dressing choices, skilled wound management and individualised analgesic regimens procedures.(World Union of Wound Healing Societies, 2004) However, there is currently no up-to-date evidence review of strategies for pain management at dressing change in chronic wounds, what strategies are currently employed in UK practice is unknown, and there is no current UK guidance for patients, carers, and practitioners.

Research questions

For people in the UK living in the community with chronic wounds and experiencing pain at dressing change:

1. What is the current evidence for strategies to relieve pain at dressing change?

2. What are the pain relief strategies currently used in UK practice and what are patients', carers' and healthcare professionals' use and experience of these?

3. What are the requirements for an appropriate pain relief strategy, or strategies, which could be manualised, delivered and evaluated in the community?

The specific objectives are:

1. To undertake an evidence review on interventions for pain prevention and alleviation at dressing change for chronic wounds

2. To undertake a survey of current practice in the UK to document what is being used or not being used for a variety of chronic wounds

3. To examine systems and processes underpinning interventions and outcomes, using a logic model to integrate the different data sources and explore change processes and where contextual factors may influence implementation and outcomes.

4. To provide a map of current practice to help identify variation and consistency across the UK and between practice and evidence in order to identify pain relief strategy or strategies that could be manualised, delivered and evaluated in the UK community

5. To suggest possible future primary research where evidence gaps exist.

In addition, we will prepare clinical guidelines for the management of pain during dressing changes of chronic wounds and adapt these for use across both hospital and community settings

Methods

A mixed methods systematic review of the quantitative evidence on interventions for pain prevention and alleviation at dressing change for chronic wounds together with qualitative evidence reporting experiences of patients, carers and healthcare professionals; will be undertaken. A series of UK surveys of practitioners will be carried out, together with qualitative interviews with patients, healthcare professionals and carers in a sequential mixed methods design to identify current practice and where there is variation and consistency across the UK and differences between practice and evidence. A logic model will be used to integrate the data sources and map out systems and processes underpinning interventions and outcomes. The model will be used to explore where contextual factors may influence implementation, and the pathways of change. Clinical guidelines will be developed. The work will include stakeholder, and patient and public involvement at all stages.

Timelines

The project will take place over 24 months. The mixed methods systematic review will take place in months 1 to 12, and development of the logic model will take place during months 9 to 18. Ethics application and roll out of the UK survey will take place in months 1 to 18 with analysis and write-up results in months 15 to 21. The development of the clinical guidelines will begin in year 1 and the guidelines will be prepared and revised in months 15 to 19. Project dissemination and final write-ups including reports with take place in months 20 to 24.

Impact and dissemination

The findings from this project will be shared with stakeholders, decision-makers and funders to co-develop clinical guidelines for pain management at dressing change of chronic wounds in the community and other UK settings, and identify evidence gaps for future research. We will develop a dissemination plan to identify who needs to hear about the research and how we will achieve reach and impact.

Background and Rationale

A chronic wound (also called an ulcer) is an open sore in the skin that does not heal, or takes a long time to heal, and frequently comes back.(Siddiqui and Bernstein, 2010) Chronic wounds include pressure ulcers (bed sores), venous (vein-related) leg ulcers, and foot ulcers in people who have diabetes.(Frade and Das, 2013) Each of these chronic wounds has a different cause, has different symptoms, and is treated in different ways. However, one thing that is common for chronic wounds is the need for regular dressing changes, sometimes several times per week. These dressing changes are often a painful experience and can cause distress for the person having their dressing changed.(Price et al., 2008)

In 2012/2013, the National Health Service (NHS) managed an estimated 2.2 million adults >18 years of age with a wound, of which 48% were estimated as being chronic.(Guest et al., 2017) At that time the annual prevalence of chronic wounds was estimated as growing by 12% per annum.(Guest et al., 2017) However, for people living with chronic wounds in the United Kingdom (UK), most of the guidelines that are currently available to the National Health Service (NHS) focus on wound management and prevention,(National Institute for Care Excellence, 2014, National Institute for Care Excellence, 2019, National Institute for Care Excellence, Publication date TBC) and there is currently no clear guidance on how people living with chronic wounds, their carer, or people who work in the NHS, should manage pain at dressing change.

The International Association for the Study of Pain defines pain as ‘‘an unpleasant sensory and emotional experience associated with actual or potential tissue damage.’’(International

Association for the Study of Pain, 1979) Wound related pain can also be categorised as one of four categories: background pain which is related to the underlying cause of the wound and is felt at rest, breakthrough pain that can occur during day-to-day activities such as patient mobilisation or dressing slippage, operative pain that is associated with any intervention that requires an anaesthetic (local or general) to manage the pain, and procedural pain which results from a routine intervention such as dressing removal, cleansing or dressing application.(Bechert and Abraham, 2009) Meaume et al, (2004) have reported that 80% of patients with pressure ulcers or venous leg ulcers experience severe and continuous pain, with maximum discomfort occurring during dressing change.

The European Wound Management Association (EWMA) 2002 position document on pain at wound dressing changes aims to provide practical guidance on managing procedural pain, in particular at dressing removal. Their summary of the available evidence suggests that: pain control methods at wound dressing changes are often under-utilised by practitioners, practitioners should adopt a broad holistic approach to management of wound pain; and that patients should be supported by a combination of techniques to help them through the dressing procedure including good preparation, appropriate choice of dressing materials and adequate analgesia. However, EWMA note that at the time, the research evidence was limited and that few empirical studies had been undertaken.

The World Union of Wound Healing Societies 2004 consensus document on procedures for minimising pain at wound dressing also suggests that pain at dressing changed can be managed by a combination of accurate assessment, suitable dressing choices, skilled wound management and individualised analgesic regimen procedures.(World Union of Wound Healing Societies, 2004)

UK guidance for the management of chronic wounds are tailored to wound healing and only attend to pain as a secondary consideration.(National Institute for Care Excellence, 2016, Scottish Intercollegiate Guidelines Network, 2010) As a result, there is no clear guidance specifically tailored to how patients, carers and healthcare professionals should manage wound-related pain at dressing change.

Whilst an article by Edwards (2013) has summarised evidence on strategies for dressing selection, analgesia, and patient education for wound-related pain at dressing change, it is unclear if the author searched for all available evidence in a systematic manner.(Edwards, 2013)

Our initial scoping searches for this research undertaken in MEDLINE, EMBASE, Web of Science, Cochrane Library CDSR and CENTRAL, CINAHL (and not including searching of other, secondary sources such as trials registers and conference proceedings) has identified a total of 6,902 unique records of which, based on an initial screen of the MEDLINE record set, would identify 78 potentially relevant records on pain relieving strategies for dressing change in chronic wounds. Our proposed research would address the need for an up-to-date evidence review, by obtaining, assessing for relevance, data extracting, quality assessing, and synthesising the evidence from all relevant studies that answer our research questions that we identify through our searching methods for this research, and by applying recognised systematic review conduct guidelines.(Moher et al., 2009)

The EWMA 2002 position document on pain at wound dressing changes also presents an article on an international collaboration that sought to explore health professionals' views on the role that differences in wound care delivery systems have on practitioner performance, patient experience and access to wound care products. Eleven countries took part in the international survey. Main considerations at dressing changes included preventing trauma and pain prevention. Practitioners consistently rated dressing removal to be the time of greatest pain. The results also indicated that practitioners were aware that dried out dressings and products which adhered to the wound were the most important factors leading to wound pain at dressing change.

In a 2008 cross-sectional international survey that assessed that patients' perceptions of their wound pain at dressing change, Price et al. (2008) found that 14.7% of 2,018 participants surveyed experienced dressing-related pain most of the time during dressing change, and 17.2% reported pain all of the time during dressing change. Venous, mixed and arterial ulcers were associated with more frequent pain at dressing change than other wound types. Time for pain to subside following dressing change ranged from <1 hour to >5 hours.

Bell and McCarthy (2010) undertook a survey to investigate nurses' knowledge of wound management in relation to dressing change and wound pain. The country was not reported, but the study authors were based in Ireland. One hundred Registered nurses who had at least one year of clinical experience working on medical or surgical wards were surveyed. The most common methods used by nurses in assessing wound pain at dressing change were talking generally to the patient and monitoring facial expression. Dried-out dressings were rated as being the most common factor contributing to pain at dressing change, followed by adhesive dressing products and wound irrigation. Prescribed analgesia prior to dressing change was the most frequently used method to overcome pain. Soaking old dressings before removal' was the second most frequently used method.

There is at present no published survey on pain relief strategies that are currently being used in the UK for dressing change in chronic wounds that includes patients', carers' and healthcare professionals' (people who work in the NHS) use and experience of these.

Our proposed research will therefore include a UK survey to capture demographic details and explore providers' and recipients' self-reported experiences of chronic wound care, and explore strategies used to reduce pain at dressing change. The survey will also capture the perceived success of these strategies from different participant perspectives, along with how pain is assessed. Perceptions of what factors might contribute to pain at dressing change (e.g., dressing and wound type, skill levels) will be captured along with perceptions of what could improve the management of pain at dressing change.

Our systematic evidence review will help identify research gaps where future research could be planned. Our review and survey will help identify both pain relieving strategies and pain assessment tools which could be both manualised and also assessed for effectiveness in the community. Our evidence review and UK survey will also allow us to view the problems from multiple perspectives leading to the formulation of recommendations for policy and practice.

Aims and objectives

The aims of the research project are to determine:

1. What the current evidence is for strategies to relieve pain at dressing change

2. What pain relief strategies are currently used in UK practice and what are patients', carers' and healthcare professionals' use and experience of these

3. What the requirements are for an appropriate pain relief strategy, or strategies, which could be manualised, delivered and evaluated in the community.

4. What the gaps and limitations of existing research are in order to inform future research

The specific objectives are:

1. To undertake an evidence review on interventions for pain prevention and alleviation at dressing change for chronic wounds

2. To undertake a survey of current practice in the UK to document what is being used or not being used for a variety of chronic wounds

3. To examine systems and processes underpinning interventions and outcomes, using a logic model to integrate the different data sources and explore change processes and where contextual factors may influence implementation and outcomes

4. To provide a map of current practice to help identify variation and consistency across the UK and between practice and evidence in order to identify pain relief strategy or strategies that could be manualised, delivered and evaluated in the UK community; and

5. To suggest possible future primary research where evidence gaps exist

In addition, we will prepare clinical guidelines for the management of pain during dressing changes of chronic wounds and adapt these for use across both hospital and community settings.

Methods

Health technologies being assessed

The technologies we will assess in our proposed research are any pain relief strategies that are currently being used in the UK for pain relief at dressing change in people living with chronic wounds. As there are currently no UK guidelines on specific technologies, our proposed research will include, but not be limited to, any pain relief strategy in the following broad categories:

- Analgesia and other pharmacological interventions, e.g., Non-steroidal anti-inflammatory drugs (NSAIDs)
- Non-pharmacological interventions, e.g., talking therapy and other anxiety reduction methods
- Wound dressing removal and selection strategies, e.g., soaking dressings prior to removal and selection of dressings which, on removal, will minimise the degree of sensory stimulus to the sensitised wound area.

Methods for the evidence review

Search strategy for the evidence review

Our information specialist has now run preliminary searches in MEDLINE and other bibliographic databases (EMBASE, Web of Science, Cochrane Library CDSR and CENTRAL, CINAHL) on 8 April 2020 which, following de-duplication, identified a total of 6,902 unique records. A single-reviewer screen of titles and abstracts in the MEDLINE record set (n= 1,847), identified 21 potentially relevant records. We would therefore estimate that screening the total 6.9k records (3.7 x more than the MEDLINE only set) would identify 78 potentially relevant records. These numbers do not include searching of other, secondary sources such as trials registers and conference proceedings.

The population terms were informed and adapted from known Cochrane reviews (diabetic ulcers, venous leg ulcers, pressure ulcers, arterial ulcers, neurotropic ulcers, and ischaemic wounds)(O'Meara and Martyn-St James, 2013, Walker et al., 2017, Dumville et al., 2013, Martinez-Zapata et al., 2016). Terms for pain management intervention terms were identified from a previous Cochrane review.(Briggs et al., 2012) The population and pain management terms were be combined with terms for wound dressings.

For our proposed research, a comprehensive and systematic search will be conducted for the reviews. This will include a search of major medical, health-related, nursing and allied health professionals and multidisciplinary electronic databases (MEDLINE and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily [via Ovid SP], Embase [via Ovid SP], Cochrane Central Register of Controlled Trials [via Wiley Cochrane Library], Cumulative Index of Nursing and Allied Health Literature [via EBSCO] and the Web of Science Citation Index Expanded and Social Sciences Citation Index [via Clarivate Analytics]). Ongoing trials will be sought from the U.S. National Library of Medicine and the

WHO International Clinical Trials Registry Platform. Searches will not be restricted by language, geographical location or date.

The reference lists of included studies will be examined for additional relevant references and, where appropriate, forward citation tracking will be conducted using Web of Science and Google Scholar. Authors will be contacted where additional information is required from publications, and where ongoing trials have been identified.

Reference management will be undertaken using EndNote software (Clarivate Analytics) and citation screening will be undertaken using EPPI-reviewer software (Eppi-Centre). Data extraction of the qualitative studies will involve coding using NVIVO software.

Assessment of study quality for the evidence review

We will assess the methodological quality of studies included in the evidence review using quality assessment instruments appropriate for each study design. For randomised controlled trials we will apply Version 2 of the Cochrane Risk of Bias tool. Version 2 of the Cochrane risk-of-bias tool for randomised trials a recommended tool to assess the risk of bias in randomised trials and is structured into a fixed set of domains of bias, focussing on different aspects of trial design, conduct, and reporting.(Higgins et al., 2019) For non-randomised studies we will apply the ROBINS-I (Risk of Bias In Non-randomised Studies of interventions) tool. The ROBINS-I is a tool developed to assess risk of bias in the results of non-randomized studies that compare health effects of two or more interventions.(Sterne et al., 2016) For other study designs (e.g., systematic reviews, cohort studies, case control studies, qualitative studies) we will apply the appropriate CASP (Critical Appraisal Skills Programme) tool.(Critical Skills Appraisal Programme (CASP) Checklists)

Study quality will be assessed by two independent reviewers (FC and MMSJ). Disagreements will be resolved through discussion.

Review strategy for the evidence review

The aims for the evidence review are:

1. To describe the range of interventions used to prevent or alleviate pain at dressing change in chronic wounds and to graphically map the existing evidence in order to highlight where existing interventions have been evaluated and where there are gaps in the research evidence

2. To describe the interventions/practices nurses use to assess patient's experience of pain during chronic wound dressing.

3. To examine if there are variations in practice and pain experience influenced by wound type or setting in which care is delivered.

4. To review the effectiveness of pain relief strategies (alone or in combination) at dressing change in adults with chronic wounds using both quantitative and qualitative evidence

5. To synthesize qualitative evidence and questionnaire data exploring the views and experiences of patients, carers, and/or health care professionals of pain and pain relief strategies during dressing change of chronic wounds.

6. To draw on both evidence of effectiveness and also research of experiences and views to explore potential gaps in the application of evidence in practice, barriers and facilitators to use of pain relief strategies across both hospital and community settings, and the factors that influence nursing practice.

7. To identify gaps and limitations of existing research in order to inform future research

For the evidence review we will conduct a mixed-methods systematic review. The review will be undertaken following the general principles recommended in the Preferred Reporting

Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (http://www.prismastatement.org/)

Two independent reviewers (FC and MMSJ) will undertake study selection, data extraction and quality assessment. Disagreements will be resolved through discussion.

The framework parameters for studies to be included in the evidence review is as follows.

Patient group: Adults with dressing change pain related to chronic wounds. We will define chronic. wounds as pressure ulcers, venous leg ulcers, arterial ulcers, neurotrophic ulcers, and foot ulcers in people with diabetes.

Intervention: Pain-relief strategy, or strategies, to prevent and/or alleviate acute pain at dressing change for chronic wounds.

Setting: Any appropriate setting but must be generalisable to the community setting.

The quantitative component of the review will consider any experimental study design including randomised controlled trials (RCTs), non-randomised controlled trials, quasi-experimental, and before-and-after studies for inclusion. For the qualitative component we will consider studies that focus on qualitative data including designs such as: phenomenology, grounded theory, ethnography, action research and feminist research. In the absence of research studies, other text such as opinion papers, discussion papers, position papers and reports will be considered.

Should RCTs be considered similar enough in terms of clinical heterogeneity, and where data permit, Frequentist pair-wise meta-analysis of dichotomous and continuous outcomes across studies will be undertaken using Cochrane Review Manager (RevMan) software. Fixed- and random-effects models will be applied and statistical heterogeneity will be investigated using the I-squared statistic.

The evidence synthesis for our proposed research will depend on the types of evidence that we identify for inclusion, but will be based on applying mixed synthesis methods integrating both quantitative and qualitative evidence in an approach pioneered by the Evidence for Policy and Practice Information and Co-ordinating Centre (EPPI-Centre) (Harden and Thomas, 2005, Thomas et al., 2004). The results for each method of synthesis included in the mixed method review will be extracted and presented in numerical, tabular or textual format. Our proposed research will draw upon our previous experience of undertaking other evidence synthesis employing this approach.(Campbell et al., 2011)

Outcomes for the evidence review

Wound pain assessment methods for the mixed-methods evidence review will include talking, facial expression, body language, and validated tools. Our primary outcomes will include:

- Patient-reported pain scores using visual analogue scales (VAS), verbal rating scales, numerical rating scales, pictorial rating scales.
- Pain scores from pain questionnaires such as the McGill Pain Questionnaire, Brief Pain Inventory (Cleeland 1994).
- Subjective global rating of pain relief (better/unchanged/worse).
- Summary measures such as SPID (Sum of Pain Intensity Differences) and TOTPAR (Total pain relief achieved) (McQuay 1997).
- Narrative, facial and other expressions

Experience of pain and its relationship to both the stage of dressing change (removal, wound preparation, dressing) and the stage of healing

Secondary outcomes will include

- Use of analgesics
- Ulcer healing rates (in relation to dressing change occurrence/visits) as the proportion of ulcers completely healed and/or changes in ulcer size.
- Quality of life measures.
- Adverse effects of pain relief strategies for dressing change.

Whilst this will not be a cost-effectiveness review, any cost data and resource use data that are reported by included studies will also be extracted and summarised.

Methods for the UK survey

The aim of the UK survey is to answer the second research question of what are the current UK wound change pain management strategies and various stakeholder experiences. For this, a series of surveys will be undertaken and also informed and triangulated with a smaller number of initial qualitative interviews with patients, healthcare professionals and carers in a sequential mixed methods design. Initial NHS research ethical approval and HRA governance will be obtained.

Survey Development and Qualitative Interviews

An initial stage of qualitative interviews will be used to explore emerging aspects of the initial logic model, and to inform the later survey content. The qualitative interviews will involve a purposive sample of patients (n=10), carers (n=5) and healthcare staff (n=15) involved in the management of chronic wounds and explore similar topics to those described later for the planned surveys. Additional participant groups may be added based on the initial logic model, and the logic model will also be used, along with the evidence synthesis, to develop an interview schedule. Sampling will be undertaken in one geographical region only for this stage for logistical reasons and it is anticipated that around 30 interviews will be undertaken using the patient, carer and health professional groups described further in the survey stage. A local Clinical Research Network (CRN) and also Sheffield Primary Care (https://www.primarycaresheffield.org.uk/research/) will be used to facilitate this stage and identify local GP practices. Interviews will be conducted either in person of by telephone and digitally audio recorded and anonymously transcribed verbatim. Six stage thematic analysis (Braun and Clarke, 2006)of interviews will be used to identify both semantic and also latent themes. NVivo (QSR version 12) software will be used to facilitate analysis, and a sample of initial coding with be checked with the research team. Respondent validation will also be used where emerging themes are confirmed and discussed with the participants and also advisory group. This stage will also be informed by the concept of trustworthiness (Lincoln and Guba, 1985).

The survey stage will involve an initial pilot, and development of the survey. Content will capture demographic details and explore participant's self-reported experiences of wound care, either as a provider or recipient. Previous surveys exploring dressing change pain (Bell and McCarthy, 2010, Hollinworth and Collier, 2000, Nagy, 1999), will be used to assist survey content, along with the logic model. This will then be piloted, again in one geographical area.

Sampling for the UK survey

The survey will capture demographic details and explore participant's self-reported experiences of wound care, either as a provider or recipient. More specifically, questions will explore what strategies are used to reduce pain, the perceived success of these from different participant perspectives (including self-report intensity of pain for patients using a validated visual analogue scale appropriate for older patients (Edwards, 2013), how pain is

assessed, perceptions of what factors contribute to pain at dressing change (dressing and wound type, patient characteristics, skill) and perceptions of what could improve management. Patient and carer perspectives are specifically included to counter any social desirability self-report bias that may occur when asking health professionals about their dressing change practices and associated pain. The final content will also be determined by the initial logic model (see methods for the logic model section) that emerges from the literature evidence synthesis.

Data collection for the UK survey

The primary data collection stage sampling will involve the identification of a number of case study sites across the UK (see Table 1 below).

Table 1. UK case study site numbers

UK Country	England	Scotland	Wales	Northern Ireland	Total surveys
Number of GP practices randomly sampled	140	10	5	3	158
Patients (10/GP practice)	1400	100	50	30	1580
Carers (10/GP practice)	1400	100	50	30	1580
Practice nurses (up to 2/GP practice	280	20	10	6	316
District nurses (up to 4 per site)	560	40	20	12	632
Local nursing homes (2 local to GP practice)	280	20	10	6	316
Local diabetic foot clinic. Any relevant staff (estimate 4/clinic)	560	40	20	12	632
Local tissue viability service. Any relevant staff (estimate 4/clinic)	560	40	20	12	632
					5688

A disproportionate stratified multi-stage sample will be used to approximately represent the significantly different populations across the four UK countries. Previous sampling methods using surveys of nurses' views of dressing change pain were not considered appropriate, in using only either convenience hospital samples (Bell and McCarthy, 2010, Nagy, 1999) or unrepresentative forums and societies (Hollinworth and Collier, 2000).

Setting for the UK survey

The locus of the proposed sampling in this study will be GP practices in primary care initially to ensure a community focus is maintained. Practice patient demographic data (https://fingertips.phe.org.uk/profile/general-practice) and dressing prescribing trends

(https://openprescribing.net/) will be checked to ensure practices are broadly representative of national averages. This will ensure there is appropriate representation based on key demographic data such as age (proportion aged 65+), gender, ethnicity and deprivation (Noble et al., 2019).The next stage of the sampling will be to identify a number of further participant groups who will be sampled and involved in the surveys.

Target population for the UK survey

Firstly, a random sample of 10 patients per practice will be identified via searches of practice records (SystmOne or EMIS) as having a relevant diagnosis of a chronic wound (anticipated to be ICD-10 coding E11.621, L89.XXX and L97.XXX for diabetic foot, pressure and non-pressure ulcers respectively). Appropriate screening of patients at each GP practice will then be undertaken to exclude ineligible patients. These stages will supported by the Clinical Research network as part of service support costs. Identified patients with chronic wounds will be sent a paper postal questionnaire using the automated Docmail service which will maintain patient confidentiality within the study, facilitated by practice staff. Docmail allows GP practices to securely upload identified patient contact details online where personalised invitation letters and paper survey copies and return envelopes can also be included. Surveys will also be distributed to a further sample of carers linked to patients at each practice via the first patient survey. Various healthcare practitioners will then be sampled and at a practice level an invitation given to any practice nurses who are involved in chronic wound care and again a paper survey provided for them to complete. After this stage, the sampling will widen to capture relevant additional nursing and other healthcare staff in the geographical area surrounding each GP practice. This will capture data from district nurses, diabetic foot care clinics, tissue viability services and also a sample of local nursing homes. Participant and service details will be obtained either from publicly available information or via Freedom of Information requests. It is anticipated that a total of just over 5000 surveys will be distributed based on a response rate of 30% following one reminder survey; telephone reminders will also be used to increase response rates where ethically permitted. A £5 high street shopping voucher will be provided to respondents as a further incentive. The figure of 30% is based on previous research that used a similar methodology; this related to the Opioid Analgesic Dependence study that similarly sampled GP practices and resulted in 22.5% and 23.3% response rates to 3753 and 3160 patients respectively. This used the Docmail process whereby patients received a personalised letter and invitation to complete a paper questionnaire which could be returned free via post. There was the same £5 high street voucher incentive also and one follow-up reminder letter and questionnaire. We have estimated a slightly higher response rate of 30% in this proposed research as we have costed to include telephone follow-up reminders. These factors represent key influences on response rate in primary care as previous research has indicated.

Survey response and platform

The proposed survey methodology will involve patients initially being identified at GP practices. We will use the Docmail process (https://www.docmail.co.uk/) which has been successfully used in previous research undertaken in ScHARR. GP practices will be given secure access to a practice specific Docmail account and will upload contact details for identified patients with chronic wounds. The Docmail service automates the next stages and prints personalised invitation letters (including GP practice graphics and information and GP signature invitations) as well as a paper copy of the survey; these are then posted out to patients in a letter that is personalised with their name. The envelope pack also contained a Freepost return envelope. One reminder pack will be sent to non-responders, and telephone follow-up will be undertaken. For the other prospective participants, carers will be invited linked to the above patients and although not personalised with their name, will also receive a paper survey and Freepost response envelope. Healthcare practitioners will be identified

linked to the recruited GP practices. This will be done using publicly available contact details of local related services; freedom of information requests will be made to identify staff/services if this is not public information. Similar personalised invitation letters will be sent to identified health-care professionals and again with one reminder pack and telephone reminders where possible. All respondents will receive a £5 high street voucher by post. To check for possible response bias, non-responder analysis will be undertaken (as was previously done in the Opioid Analgesic Dependence study which used similar methods); this will utilise anonymised patient demographic data from each practice (age, gender, ethnicity) and allow comparisons between responders and non-responders to be made. It should also be noted that we consider this study to be eligible for the NIHR Clinical Research Network (CRN) portfolio and will apply for portfolio adoption; This additional CRN support within primary care will further facilitate and support the delivery of the above survey stage.

We aim to capture patient and health professional perspectives as much as possible and to do so inductively. This will be done in various ways: 1) through initial semi-structured qualitative interviews with patients, carers and healthcare staff. Although this will be a relatively small sample size, we will sample to theoretical saturation and anticipate interviews will last between 40-60 minutes. The research team has considerable experience in undertaking such interviews. 2) Analysis of these interviews will be in themes and we anticipate will be operationalised and allow is to ask patients to rank and prioritise issues relating to dressing change wound pain. It is anticipated that some questions will ask about current service provision and capture preferences and logistical aspects 3) We will also include in the survey, a final open response question too which will allow participants the freedom to write additional comments, views and suggestions that may not be captured in the survey.

Data analysis for the UK survey

Descriptive and inferential analysis will be undertaken to report on key findings. Non-responder analysis will be undertaken where data are available to explore any response bias. Returned surveys will be read into Stata (version 16) with appropriate data entry checking. Descriptive and inferential analysis will be undertaken using the most appropriate statistical summary measures and tests based on the assumptions of the data (parametric and non-parametric), supported by informative graphics. Multiple imputation will be used to account for missing data from the respondents

Methods for the logic model development

We will include the use of a logic model throughout the project to integrate the varying forms of data as suggested by the Committee. We have extended the project team to ensure that we have additional expertise in this area to facilitate use of this method. An initial model will be developed from the findings of the mixed-methods systematic review, setting out details of the intervention pathway including types of inputs, key mechanisms, contextual and implementation factors, and where and how these may link to outcomes and impacts. The model will be informed by both quantitative data (particularly in regard to inputs, outcomes and impacts), and qualitative data (particularly in regard to mechanisms, contextual and implementation factors). This model will then inform the subsequent development of the UK survey and interviews, and data analysis by revisiting and further developing the model to produce the final version of the pathway of change based on both the review evidence and the UK survey and interview data. The model will thus act as a mechanism for integrating the varying data sources, but also facilitate the exploration of linkages in the intervention pathway and the influence of factors such as varying contexts and implementation on outcomes.(Baxter et al., 2014, Kneale et al., 2015)

Patient and Public Involvement for the project

We have engaged with Sheffield Teaching Hospitals Foundation Trust Online Patient Advisory Panel regarding the proposal. The main purpose of the Panel is to ensure that research is patient focused. Responses that we received and will use in our research include: wound dressing and management outcomes in addition to pain relief ones, including pain-relieving strategies that do not work, availability of pain-relieving strategies, including in our research people who manage their own dressing change, including family members, including outcomes on practitioners' assessment of the patient's pain, the convenience / inconvenience to the practitioner, and recommendation for further trials of particular strategies, amongst others.

Our patient and public involvement (PPI) co-applicant (DS) for the proposed research, has helped inform how PPI involvement during the project should take place, including dissemination. As a member of the research team, DS will provide input at the scheduled project management meetings and she will also act as a representative of the public advisory group that we will set up for this project. The public advisory group will be formed of patients and the public from across the country, we will aim for diversity in terms of age, gender, ethnicity and services used. We will advertise for members using local and national patient networks, and also the People In Research Website.

Given that the group will have national representation it is anticipated that most meetings will be virtual (using telephone/video conferencing with members' costs reimbursed), and one of the co-applicants (SB) has substantial experience in forming and facilitating public advisory groups run in this way. The public advisory group will be involved at all stages of the project. During the evidence review, the group will contribute to finalising the research questions and protocols to ensure that priorities of patients are fully included in the evidence review for this project. Members will also input to the analysis and synthesis for the evidence review, by providing a patient perspective on the data and advising on the most relevant and important outcomes to patients.

In the second phase, the advisory group members will contribute to the development of the UK survey by ensuring that the methods of identification and recruitment are conducted in a manner which is sensitive, ethical and appropriate for those managing and living with chronic wounds. Their input will ensure that the survey is designed to capture outcomes important to patients; and that the content is appropriate and worded in Plain English so that it is acceptable and accessible to diverse groups of participants. The advisory group will have a key role in interpreting the findings of the survey, in terms of what the results may mean for patients.

Towards the final stages of the project the advisory group will be involved in developing and reviewing outputs from the project so they are relevant and comprehensible to patients and the public. The project includes the co-development of outputs from the study via focus groups and workshops, and members of the advisory group will be involved in helping to plan and develop these alongside our PPI co-applicant. If we have members who are willing to help run these workshops this may offer them a good opportunity for personal development. We anticipate that PPI members will also be interested in taking part in other dissemination activities such as co-authoring publications, giving talks to relevant groups and co-developing a short online (YouTube) presentation.

We will offer our co-applicant and advisory group members reimbursement for their time spent during meetings and any reading of documentation at rates recommended by INVOLVE (currently £25 per hour). We will aim to ensure that meetings are at convenient times by using doodle polls to seek advisory members' preferences. As we expect most of the meetings to be virtual, we may not need to recompense for travel expenses, although we have found from previous studies that a meeting to develop outputs may work better as an in-person session. We anticipate that there will be meetings every three to four months however, from previous studies we have found that it is optimal to arrange meetings when

input is needed rather than at regular intervals. We will offer advisory group members support such as online training or signposting to relevant resources to facilitate their involvement. Subject to data protection requirements, we have in the past “buddied up” members new to a public advisory role with those who are more experienced for telephone or email support. Our PPI co-applicant will provide strategic oversight to our involvement processes.

We will provide feedback to our PPI co-applicant and advisory group members throughout the process so that people know their involvement is valued and has made a difference.

For all PPI involvement, we will use a webinar platform which enables either computer access to meetings or telephone input. We have previously used this platform with varying user groups and found it to be easy to access by clicking on a link with no downloading of software. We will be sending out any information that will be discussed/presented prior to each meeting so that people joining from phone will be able to access it during discussions. We will also invite input on these documents via written comments/feedback either prior to or following each meeting.

Methods for preparation of the clinical guidelines

The clinical guidelines will be co-developed with practitioners, patients and decision makers via workshops. Data from the evidence review and UK survey components of the project will be used to inform the clinical guidelines.

The guideline development process will be overseen by FC, who was a member of the National Institute for Care Excellence (NICE) Guidelines Development Unit, and has supported the development of a range of NICE guidance including management of hypertension in primary care and identification and management of harmful sexual behaviour in children and young people. FC has also published on methods underpinning national clinical guidelines.(Campbell et al., 2006)

We will prepare an initial scope for the clinical guidelines which will set out the need for the guidelines, the areas that the guidelines will cover, and what the guidelines intend to achieve. The scope will be sent to organisations with an interest in the topic in order to inform a final scope. These organisations will include candidates for a Guideline Committee that we will form for the project. We will seek representatives on this committee from the Royal College of Nursing, Royal College of General Practitioners, Royal College of Physicians and the Royal College of Pharmacists; along patients, practitioners and care providers from across the country.

The Guideline Committee will meet for three clinical guidelines workshops that we will prepare, and we will seek a chair for these workshops from our committee members.

The guidelines will be prepared to include the recommendations made by our Guideline Committee. The processes and methods used to develop the guidelines will be informed by the National Care and Clinical Excellence (NICE).(National Institute for Care Excellence, 2018). We will ensure that the guidance incorporates, references and updates aligned accredited UK guidance for the management of chronic wounds such as, ‘Chronic wounds: advanced wound dressings and antimicrobial dressings (ESMPB2),(National Institute for Care Excellence, 2016) (March 2016) and the Scottish Intercollegiate Guidelines Network (SIGN) guidance on ‘Management of chronic venous leg ulcers’(Scottish Intercollegiate Guidelines Network, 2010)

We will assess the strength of the evidence used to inform the guidelines, by applying a GRADE (Grading of Recommendations Assessment, Development and Evaluation) assessment. Many international organisations have provided input into the development of the GRADE approach which is now considered the standard in guideline development.(https://www.gradeworkinggroup.org/). The guidelines will be reported in

accordance with the Appraisal of Guidelines for Research & Evaluation (AGREE) II instrument.(The AGREE Next Steps Consortium, 2017)

Dissemination, Outputs and anticipated Impact

The key audiences for our research dissemination will include, but not be limited to, academia in wound care research, people living with chronic wounds, wound care practitioners, and guideline developers for wound care and management.

We plan to publish our findings in open-access, peer-reviewed publications. Our target journals will include Advances in Skin and Wound Care, Chronic Wound Care Management and Research; and Wounds UK. We also plan to present our findings at wound care conferences, including the Wounds UK annual conference. These will be tailored to the academic and wound care practitioner communities. We will monitor and measure the impact of these outputs through citation tracking of the publications. We will track whether other guidelines reference the study, and record requests for further information from decision-makers/researchers/practitioners.

We will, in collaboration with our public advisors, provide accessible summaries for the public, patients, and clinicians about our project findings on effective pain-relieving strategies for dressing change for people living with chronic wounds UK. We will explore with the PPI advisors, potential formats for this dissemination, including the use of promotional flyers; the creation of a website/web-pages and other user-friendly interfaces; interactive media, and podcasts and co-develop these outputs with the advisory group.

We will consider any interaction with broadcast media, including press briefing/releases, press conferences/interviews, and radio/TV appearance, where relevant. Our lead reviewer (FC) has previous experience of undertaking knowledge exchange in this format.

Based on our findings, we will co-develop with stakeholders, clinical guidelines for the management of pain during dressing changes of chronic wounds, that can be adapted for use across both hospital and community settings. We will consider the additional development of outputs such as evidence briefings to facilitate uptake and impact of our study findings as advised by our stakeholder colleagues.

Project / research timetable

The project will take place over 24 months, with the mixed methods systematic review taking place in months 1 to 12. Logic model development will take place in months 9 to 11 with revision in months 16 to 18.

Ethics application for the UK survey will take place in months 1 to 6. Interviews, including transcribing and analysis will take place in months 9 to 11. Piloting roll out of the UK survey will take place in months 13 to 18, with analysis and write-up of the UK survey results in months 15 to 21.

The development of the clinical guidelines will begin in year 1 in order to clarify the scope of the guidelines and to recruit the guideline committee. Guideline workshops will be undertaken when preliminary results are available to inform the guidance and will be will be scheduled in year two of the project. The guidelines will be prepared and revised in months 15 to 19 allowing time to promote and disseminate these in months 20 to 24.

Project dissemination, including these guidelines, along with peer-review and final reports will also take place in months 20 to 24. A Gannt chart for our proposed research is presented in Table 2.

Table 2. Project Gannt chart

	Year 1												Year 2											
Activity	Apr 21	May 21	Jun 21	Jul 21	Aug 21	Sept 21	Oct 21	Nov 21	Dec 21	Jan 22	Feb 22	Mar 22	Apr 22	May 22	Jun 22	Jul 22	Aug 22	Sept 22	Oct 22	Nov 22	Dec 22	Jan 23	Feb 23	Mar 23
Evidence Review:																								
Run searches																								
Study selection																								
Data extraction																								
Evidence review synthesis and write-up																								
Logic model																								
Logic model development																								
Revised logic model development																								
Survey																								
NHS research ethics committee approval																								
HRA approval																								
Qualitative interview recruitment																								
Qualitative interviews, transcribing and analysis																								

	Year 1												Year 2											
Activity	Apr 21	May 21	Jun 21	Jul 21	Aug 21	Sept 21	Oct 21	Nov 21	Dec 21	Jan 22	Feb 22	Mar 22	Apr 22	May 22	Jun 22	Jul 22	Aug 22	Sept 22	Oct 22	Nov 22	Dec 22	Jan 23	Feb 23	Mar 23
Survey design and pilot																								
Participant recruitment and survey																								
Survey data entry and analysis																								
Survey write-up																								
Project management																								
Project meetings																								
PPI																								
Public advisory group meetings																								
Clinical Guidelines																								
Develop guideline scope / recruit committee																								
Guideline workshops																								
Guideline consultation / revisions																								

	Year 1												Year 2										
Activity	Apr 21	May 21	Jun 21	Jul 21	Aug 21	Sept 21	Oct 21	Nov 21	Dec 21	Jan 22	Feb 22	Mar 22	Apr 22	May 22	Jun 22	Jul 22	Aug 22	Sept 22	Oct 22	Nov 22	Dec 22	Jan 23	Feb 23	Mar 23
Write-up and dissemination																								
Dissemination activities: planning / drafting publications and other outputs, final guidelines write-up																								
NIHR reports																								
NIHR reports																								
Final NIHR report write-up																								

Project management

The lead applicant (MMSJ) will take overall responsibility for delivering the study. MMSJ will act as second systematic reviewer on the evidence review, with FC leading on the evidence review and RC leading on the UK survey. We have extended the project team to include SB who will act as advisor on the logic model throughout the study and contribute expertise in public involvement and engagement. MW will be responsible for clinical input on pain management and assessment, and our partner organisation, Accelerate CIC will provide topic advice on tissue viability. PPI representation on the project team will be provided by DS who will be responsible for overseeing the PPI elements within the project. A project management group consisting of all co-applicants will meet in person or by tele / videoconference a total of eight times over the 24-month project to oversee day-to-day management of the study.

In addition, a Project Advisory Group will provide independent oversight and input to the project. This group will consist of independent experts in chronic wounds, along with MMSJ, RC, DS and FC from the study team. Independent members will be recruited to the Project Advisory Group by the lead applicant (MMSJ) with advice taken on suitable candidates from other co-applicants. The Project Advisory Group will be responsible for providing independent oversight of the UK survey in addition to providing expert input as required to the evidence review and will meet in person or by tele / videoconference a total of eight times over the 24-month project. Key points for the Project Advisory Group will be when finalising the UK survey questions, when determining the topics for further research based on the findings of the evidence review. Given that the group will have national and international representation it is anticipated that meetings will be virtual (using telephone/video conferencing).

A Clinical Guideline Committee will provide expert input to the development of the clinical guidelines. This group will consist of representatives from clinical membership organisations, clinical practitioners and care providers, along with FC, MMSJ and RC from the study team. Members will be recruited to the Clinical Guideline Committee by FC. The Clinical Guideline Committee will be responsible for input to the clinical guidelines we plan to prepare. To facilitate the development of the clinical guidelines, a series of three workshops for Clinical Guideline Committee will be scheduled in year two of the project. Key points for the Clinical Guideline Committee will be the development and finalisation of the clinical guidelines.

A project administrator will contribute to the day-to-day running of the project and will also assist in the administrative tasks related to organising the project team, PPI, and advisory group meetings.

Ethics

There are no Ethical issues related to the evidence review part of the project.

As this research involves NHS patients and searches of their patient records, NHS research ethics committee (REC) and Health Research Authority governance approvals will be obtained prior to empirical data collection (i.e., qualitative interviews and quantitative survey). This will be done via the online IRAS application process. Research sites will be confirmed once the research begins and added via the HRA minor amendments process.

Project / research expertise

In addition to being Principal Investigator, Marrissa Martyn-St James will be involved as second reviewer for the systematic. Marrissa has 17 years of systematic review experience, including Cochrane reviews of treatments for chronic wounds.

Fiona is an experienced systematic reviewer and Cochrane reviewer. She has undertaken and published mixed methods systematic reviews and presents internationally on this methodology, including realist, meta-synthesis and ethnographic approaches in the synthesis of mixed methods reviews. Fiona previously trained and worked as a nurse, health visitor and district nurse in the UK. In addition to leading the evidence review, Fiona will lead on the preparation of the clinical guidelines.

Richard Cooper will lead the UK survey of current UK practice and more specifically the research ethics and HRA governance application, the design and piloting of the survey, as well as sampling and subsequent survey analysis. Richard is a senior lecturer in public health and has 17 years of experience undertaking health-related research and evaluation. His research focus includes ethics in healthcare and technologies in healthcare. He is an experienced mixed methods researcher with a particular interest in qualitative methods.

Ruth Wong will undertake the searches for the systematic review. Ruth Wong is an information specialist since 2010 with experience in systematic literature searching for the NIHR Health Technology Assessment Programme, NICE Decision Support Unit and the Department of Health Policy Research Unit in Economic Evaluation of Health and Care Interventions.

Susan Baxter will lead on development of the logic model. She has been a healthcare researcher for over 20 years with expertise in theories of change, evidence synthesis, qualitative research and public involvement.

Dan Green will design and undertake the statistical analysis plan for the UK survey. Dan is a lecturer in Epidemiology and Statistics

Matthew Wilson is a clinical academic with more than 20 years of experience in Health Technology Assessment and leading quantitative randomised trials in anaesthesia/pain medicine. He is acknowledged as an international expert on analgesic interventions providing acute pain relief. He has provided clinical oversight, methodological and strategic input. He will contribute to the day-to-day management of the study and fulfil senior writing duties, in the production of peer review papers and reports.

Karen Staines will be involved in an advisory role to support this study. Her remit will be use of expertise within the field of Tissue Viability. Karen has been working within this specialism since 2008 and leads on Education/Research and Wound Care within Accelerate.

Deb smith is our PPI co-application. In addition to having lived experience of the research topic, Deb has eight years of experience of being a public and patient contributor in health and social care research.

The project also includes two primary care contributions:

Dr Caroline Mitchell who will be involved in the project from the Academic Unit of Primary Medical Care at the University of Sheffield and will contribute actively to steering group meetings and other activities for the duration of the project. Dr Mitchell has an excellent level of research experience in primary care and also continues to work as a GP in primary care;

Dr Jon Dickson as clinical lead of the Sheffield Primary Care Research group (https://www.primarycaresheffield.org.uk/research/) has agreed to support the project and in particular the recruitment of GP practices in the initial qualitative interview exploratory stage.

The integrated Tissue Viability team at Sheffield Teaching Hospitals NHS Foundation Trust are also able to collaborate with us on this project, to provide input to project meetings and advice on the evidence review, UK survey, and production of the UK guidelines

Success criteria and barriers to proposed work

The benefit of our proposed research is that we will be able to quantify any uncertainty regarding the current evidence using robust systematic review and survey methods which will allow decision makers and guideline developers to make informed decisions about whether to change current practice now or wait for further research to be completed. Funding of future research based on our research recommendations would also be required to maximise the impact of our project.

A potential barrier to further research would be a lack of knowledge among clinicians, patients and researchers regarding the limitations in the current evidence-base that we may identify. However, our dissemination plan aims to address this by ensuring rapid dissemination of our findings to a

wide community of clinicians, researchers and patient organisations, in PPI informed accessible formats.

We anticipate that there may also be some resistance from wound care practitioner communities to changing current practice based solely on the evidence from our work, due to a lack of knowledge regarding the limitations in the current evidence-base that we may identify. Our dissemination includes preparing clinical guidelines for the management of pain during dressing changes of chronic wounds, and adaption of these for use across both hospital and community settings. These will evidence-based and developed with clinical membership organisations to help mitigate this.

How the research will make a difference

The research will identify effective interventions to reduce recurrent, acute pain from dressing changes. Implementation of the most effective analgesic strategies has the potential to substantially lessen distress and discomfort suffered by patients. Similarly, treatments demonstrating no benefit can be confidently abandoned with a commensurate disinvestment of resources

References

See associated 'References' file uploaded