Healthcare Improvement Scotland | SIGN Evidence-based clinical guidelines

Management of chronic pain

A national clinical guideline

Peer review draft (Part 2)

February 2026

NHS SCOTLAND

Key to evidence statements and recommendations

Levels of evidence

1^{++}	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
	For a high-quality systematic review of studies with a high risk of bias, the risk of bias will be stated in the text
1^{+}	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1^{-}	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
	Network meta-analyses are given a binary rating (sufficient/insufficient) according to relevance and credibility.
2^{++}	High-quality systematic reviews of case-control or cohort studies
	High-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2^{+}	Well-conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2^{-}	Case-control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, eg case reports, case series
4	Expert opinion

Recommendations

Some recommendations can be made with more certainty than others. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the 'strength' of the recommendation).

The 'strength' of a recommendation takes into account the quality (level) of the evidence. Although higher-quality evidence is more likely to be associated with strong recommendations than lower-quality evidence, a particular level of quality does not automatically lead to a particular strength of recommendation.

Other factors that are taken into account when forming recommendations include: relevance to the NHS in Scotland; applicability of published evidence to the target population; consistency of the body of evidence, and the balance of benefits and harms of the options.

R For '**strong**' recommendations on interventions that **'should'** be used, the guideline development group is confident that, for the vast **majority** of people, the intervention (or interventions) will do more good than harm. For '**strong**' recommendations on interventions that **'should not'** be used, the guideline development group is confident that, for the vast **majority** of people, the intervention (or interventions) will do more harm than good.

R For '**conditiona**l' recommendations on interventions that should be '**considered'**, the guideline development group is confident that the intervention will do more good than harm for **most** patients. The choice of intervention is therefore more likely to vary depending on a person's values and preferences, and so the healthcare professional should spend more time discussing the options with the patient.

Good-practice points

✓ Recommended best practice based on the clinical experience of the guideline development group.

Contents

1 Introduction

1.1 The need for a guideline

Chronic pain is pain that persists for more than three months, or beyond normal injury healing time.[1] It is a major clinical and public health challenge: prevalence figures vary, with estimates in 2016 of between 35.0 and 51.3% in the UK, increasing with age (18–25 years old: 14.3%; 25–64 years: 30–50%; over 75 years old: 62% - age strata did not overlap precisely across the studies).[2] The prevalence of moderate to severely disabling chronic pain is up to 14.3%.

A more recent systematic review of chronic pain in Europe found a point prevalence ranging from 12% to 48%. Factors associated with higher risk included female sex, older age, lower education and unemployment.[3] In Scotland, in 2022, there was an overall prevalence of 38%, with more than 15% of people reporting significant limitations on work or life due to chronic pain. A higher proportion of women compared with men (43% vs 33%) is affected, increasing with age (25–34 years: 23%; 65–74 years: 51%) and deprivation (least deprived: 29%, most deprived: 50%).[4] Chronic pain is projected to increase over the coming years, with a higher rate of increase in more deprived areas, compared with less deprived.

It has a considerable impact on quality of life, resulting in significant suffering and disability.[5-7] Globally, back pain remains the leading cause of years lived with disability.[8] While in many cases it is accepted that a cure is unlikely, the impact on quality of life, mood and function can be significantly reduced by appropriate management. Chronic pain not only has an impact on affected individuals and their families, but also has substantial economic costs, although accurate up-to-date figures for these are hard to obtain. For example, back pain alone was estimated to cost £12 billion per annum in the UK in 1998, and arthritis-associated pain costs around 2.5% of the gross national product of Western nations.[9,10] In 2014, in the National Health Service (NHS), musculoskeletal pain accounted for around 40% of sickness absence.[11] A more recent Norwegian study of healthcare and work absence costs estimated that 4% of gross domestic product (GDP) was spent on chronic pain, although up-to-date, accurate figures in the UK are not available.[12]

While a proportion of patients will require access to specialist secondary and tertiary care pain services, the majority of patients will be managed in the community or primary care. Only 2–3% of people with chronic pain see a specialist, and 22% of general practitioner (GP) consultations focus on pain management.[13] In Scotland, 69% of adults with chronic pain receive support from their GP.[4] It is vital that GPs and other healthcare professionals have the best possible resource and support to manage their patients properly and have facilities for accessing appropriate specialist services when required. Within Scotland, there is evidence of wide variation in clinical practice, service and resource provision, with a general lack of knowledge about chronic pain and the management options that are available.[14,15]

The Scottish Government Framework for Chronic Pain Service Delivery[16] includes approaches to help increase knowledge in the non-specialist setting, through a Chronic Pain Knowledge Hub for health and social care professionals. Further actions include scaling up improved pain service planning and delivery, establishing the NHS pain service managers network to improve co-ordination and planning of specialist services and improving local access to advice and care.

1.1.1 Lived-experience perspective

People with lived experience may have different perspectives on healthcare processes and outcomes from those of healthcare professionals. The involvement of people with lived experience in guideline development is therefore important to ensure that guidelines reflect their needs and concerns and address issues that matter to them.

As the national third-sector intermediary for health and social care, in 2021, the Scottish Government asked the Health and Social Care Alliance Scotland (the ALLIANCE) to conduct a survey that would be used to inform their ongoing work on chronic pain policy. Based on responses gathered from 462 people, the report describes how chronic pain impacts their day-to-day life, the level of importance placed on public information about chronic pain and how to access support. It highlighted the following concerns:[17]

- raising awareness and improving pathways for supported self management in all people affected by chronic pain and ensuring it can be delivered on an ongoing basis to adequately support individuals in the longer term.
- more public information about what chronic pain is, its impact on people in Scotland and how to access support.
- information about the different types of treatment available for chronic pain and when they are used.
- information about what services and health and care teams are available locally and how they might help individuals to manage their pain closer to home.
- access to support to help individuals manage the impact of their pain on their mental health and well-being.

Healthcare Improvement Scotland gathered information from people in Scotland living with chronic pain to support the Framework for Pain Management Service Delivery.[18] The work involved gathering lived experience from people living with chronic pain by asking questions about the care and support they had experienced through health and social care services and local support groups. The report summarises feedback from 92 people with chronic pain and includes recommendations for improved service delivery in the following areas:

- staff understanding and attitudes
- access to support services

- different types of support
- self management
- feedback from people with lived experience.

The Framework for Chronic Pain Service Delivery aims to better meet the needs of people living with chronic pain in Scotland by improving timely and equitable access to a range of evidence-based treatments through a person-centred approach. The Framework acknowledges current inequity of access.[16]

Realistic Medicine puts people affected by health conditions at the centre of their care and encourages healthcare professionals to find out what matters most to people. The initiative treats those who use services and those working in health and social care as equal partners in decision making, promotes sharing information about treatment options and supports informed choice about what's right for individuals.

SIGN will publish a plain language version of this guideline alongside the full version to:

- help people understand the latest evidence around diagnosis, treatment, and self care
- empower people to actively participate in decisions about managing their condition in discussions with health and social care professionals
- highlight areas of uncertainty for people, making them aware of where more information or research is needed.

1.2 Remit of the guideline

1.2.1 Overall objectives

This guideline provides recommendations based on current evidence for best practice in managing adults with chronic non-malignant pain in non-specialist settings, defined as any setting where the training and infrastructure is not specifically designed for treating chronic pain. This might include management in the community, primary care or secondary care. The guideline is structured according to interventions used to manage chronic pain.

Where evidence is available on populations with particular needs (for example in women, pelvic pain, people with substance dependency or older people) this is included. This guideline aims to synthesise the available evidence on chronic pain management to inform patient-centred choices.

It does not cover:

- interventions which can only be delivered in secondary or tertiary care.
- treatment of patients with migraine or headache (see SIGN 155,

Pharmacological management of migraine).[19]

- pain caused by cancer.
- management of chronic pain in children (see the Scottish Government guideline Management of chronic pain in children and young people[20] and World Health Organization (WHO) guideline on the management of chronic pain in children.[21])
- underlying conditions. Chronic pain is caused by many underlying conditions. The treatment of these conditions is not the focus of this guideline.

1.2.2 How this guideline has been developed

This guideline has been developed in line with SIGN methodology (see section 15.1) and is being published in two parts to make recommendations available as quickly as possible. The order in which this is being done does not reflect the relative importance of the questions, nor strength of available evidence. This document is the second part of the guideline and contains information on:

- muscle relaxants
- simple analgesics
- topical analgesics
- anti-epileptics
- combination pharmacological therapies
- hands-on physical therapies
- hands-off physical therapies
- electrotherapies
- alternative interventions
- dietary interventions.

The first part of the guideline has been published[22] and contains information on:

- opioids
- naloxone
- medicinal cannabis
- antidepressants
- pain management programmes
- psychological interventions
- self-help interventions, and
- occupation-based interventions.

SIGN methodology involves an iterative systematic literature search, which

means that systematic reviews and meta-analyses are identified first due to their ability to minimise risk of bias better than other types of study. If insufficient evidence is identified at this level to support development of recommendations, the searches investigate lower levels of primary study evidence. For this guideline, a very large volume of systematic reviews was identified and evidence has been restricted to this type of study for most questions. Where SIGN has carried out searches for additional evidence, this is explained in the body of the guideline. The use of systematic reviews maximises the overall quality of evidence for each question, and allows the certainty of evidence to be stated for each effect, but also means that primary studies involving people with specific pain types, or with specific characteristics (such as men, women, older people, younger people or those with disabilities or with similar levels of socioeconomic deprivation) are pooled within the systematic reviews in order to provide estimates of effect synthesised from a broad body of relevant evidence. This means that it has not been possible to develop separate recommendations for these groups based on the evidence reviewed in this guideline. Where relevant, the guideline development group has used their clinical experience to provide guidance for specific groups when it may have different implications from the general recommendations.

The use of systematic reviews may limit the estimation of clinical effectiveness to interventions with a more mature body of published evidence, as such reviews may not yet exist for new and emerging treatment options.

1.2.3 Comorbidities to consider when managing patients with chronic pain

The prevalence of chronic pain increases with age (see section 1.1). Older adults are at increased risk of multimorbidity, including cardiovascular disease, diabetes, dementia and renal disease, with consequential increased risk of experiencing pain and incapacity. Multimorbidity in the ageing population can also impact on overall medication safety.[23] Chronic pain is experienced with higher prevalence among socially, economically and historically marginalised groups, and multiple factors are involved in the development, maintenance and exacerbation of these inequalities.[24,25] Further information on inequalities associated with chronic pain and the person-centred 7-Steps medication review process, which matches therapeutic objectives to life priorities for the individual, is included in the Scottish Government Quality Prescribing for Chronic Pain Guide.

Common comorbidities and coexisting health issues that were considered when reviewing the evidence for this guideline are:

- mood disorders (including depression and anxiety)
- cardiovascular disease and stroke
- diabetes
- surgical and medical interventions
- obesity.[26]

1.2.4 Target users of the guideline

This guideline will be of particular interest to all healthcare professionals involved in the assessment and management of people with chronic pain, including general practitioners, pharmacists, anaesthetists, psychologists, psychiatrists, physiotherapists, rheumatologists, occupational therapists, and nurses. Importantly, this guideline is also for people with chronic pain, carers and voluntary organisations with an interest in chronic pain.

1.3 Definitions and classification of chronic pain and other terms

1.3.1 Chronic pain

Pain is defined by the International Association for the Study of Pain (IASP) as 'an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage'.[27] The IASP notes that pain is complex and nuanced and has expanded on the definition with the following key points:

- Pain is always a personal experience that is influenced to varying degrees by biological, psychological, and social factors.
- Pain and nociception are different phenomena. Pain cannot be inferred solely from activity in sensory neurons.
- Through their life experiences, individuals learn the concept of pain.
- A person's report of an experience as pain should be respected.
- Although pain usually serves an adaptive role, it may have adverse effects on function and social and psychological well-being.
- Verbal description is only one of several behaviours to express pain; inability to communicate does not negate the possibility that a human or a non-human animal experiences pain.

The Scottish Government recognised chronic pain as a long-term condition in 2009.[28] However, it is only in the most recent International Classification of Diseases (ICD-11) that a comprehensive and systematic classification has been developed for chronic pain.[29,30] The ICD is the main tool used in many countries for coding diagnoses and interventions but the lack of effective coding for chronic pain to date has led to major deficiencies in epidemiological understanding of chronic pain and its impact. The new ICD-11 chronic pain coding is a significant advance, which will help to increase the recognition of chronic pain in primary care as an important condition, supporting service planning, education and research for chronic pain.[31]

In this guideline, chronic pain is defined as pain that has been present for more than three months, consistent with the World Health Organization's definition in ICD-11.[29]

1.3.2 Overdose

An overdose can occur when a drug is administered in quantities greater than can be physically tolerated and/or is taken in combination with other

substances that increase adverse effects. Overdoses can be accidental or deliberate and involve prescribed, over-the-counter and illicit drugs.[32]

1.3.3 Treatment duration

For recommendations on treatment duration, short term is defined as less than three months, medium term as three to 12 months and long term as over 12 months.

1.4 Reporting in pain trials

Difficulties in reporting make the interpretation of the evidence base challenging. Chronic pain is a complex phenomenon with consequent challenges for its assessment and management both in clinical trials and routine clinical practice. This is further complicated by the fact that even in the same condition the underlying pain mechanisms may differ significantly between individuals. While changes in peripheral pain processing might predominate in one patient, central changes may be much more important in the next patient with implications for the most effective treatment approaches in each case.[33-35]

These limitations have been recognised internationally, leading to the development of the Initiative on Methods, Measurement and Pain Assessment in Clinical Trials (IMMPACT, www.immpact.org) in 2002. In clinical trials, unless there is careful assessment of the chronic pain syndrome in each patient, potentially useful treatments may be discarded as being ineffective when the average response is considered. Even good quality, adequately powered double-blind randomised controlled trials may not provide the best approach for developing a strong evidence base for pain management.[36-38]

To allow comparison between studies, a standardised approach to outcome measures is recommended by IMMPACT.[36] Four key domains were recommended to adequately assess outcomes:

1. Pain intensity. A numerical rating scale 0–10 is recommended as the most practical and sensitive.
2. Physical functioning. Assessment with validated self-report questionnaires such as the Multidimensional Pain Inventory or Brief Pain Inventory interference scales is recommended.
3. Emotional functioning. The Beck Depression Inventory and the Profile of Mood States are recommended.
4. Patient rating of overall improvement. The Patient Global Impression of Change (PGIC) scale can be used.

Side effects and detailed information about patient recruitment and progress through the trial should also be recorded.[39,40]

In addition to the limitations of assessment and trial design, concerns have been raised about how analysis methods may either obscure clinically important positive outcomes, or overestimate treatment effects. This is further discussed in the SIGN methodology supplement. If the average response is considered, a treatment may appear ineffective, whereas it

could have the potential to be effective in a particular subgroup of the patients being studied. It may, therefore, be useful to analyse responders to a particular treatment separately from non-responders.[38]

While there are numerous good quality systematic reviews and meta-analyses that provide an evidence base for managing patients with chronic pain, the published primary literature has some limitations. This has been taken into consideration by the guideline development group (GDG) when appraising the evidence and, where there are areas of potential doubt, recommendations have been downgraded accordingly. Research recommendations have been made where clear gaps and limitations in the evidence were identified (see section 15.2).

1.4.1 What is a clinically important difference?

While proof of the statistical significance of trial results may be established, a more directly applicable question for healthcare professionals is whether or not results are also clinically important. The minimum clinically important difference (MCID) determines and communicates whether there is clinical relevance associated with the observed differences between treatments in a clinical trial. It has been defined as "the smallest difference in score in the domain of interest which patients perceive as beneficial and which would mandate, in the absence of troublesome side effects and excessive cost, a change in the patient's management."[41] There is no agreement on a single MCID for people living with chronic pain as it is recognised to vary between different patient populations and the various health outcome measures used in clinical trials. Variability may also be seen among studies examining the same patient population as a result of differences in study design, study location, and treatment administered.

A systematic review, including 66 studies of treatments for chronic pain found a median absolute MCID of 23 mm on a 0–100 mm scale (interquartile range (IQR) 12–39), with very high heterogeneity (I^2 = 99%) around two-thirds of which was associated with baseline pain.[42] The authors note that MCID for chronic pain relief varied considerably among published studies and was influenced by the operational definition of relevant pain relief and clinical condition of participants in the studies.

1.4.2 Interpreting effect sizes

The Agency for Healthcare Research and Quality (AHRQ) whose evidence reviews are cited in this guideline has summarised their definitions for magnitude of effects in meta-analyses of chronic pain trials as follows:

- A small effect was defined for pain as a mean between-group difference following treatment of 0.5 to 1.0 points on a 0- to 10-point numeric rating scale or visual analogue scale (VAS) and for function as a standardised mean difference (SMD) of 0.2 to 0.5 or a mean difference of 5 to 10 points on the 0–100-point Oswestry Disability Index (ODI), 1 to 2 points on the 0 to 24-point Roland-Morris Disability Questionnaire (RMDQ), or equivalent.
- A moderate effect was defined for pain as a mean difference of 10 to 20 points on a 0- to 100-point VAS and for function as an SMD of

0.5 to 0.8, or a mean difference of 10 to 20 points on the ODI, 2 to 5 points on the RMDQ, or equivalent.

- Large/substantial effects were defined as greater than moderate.

1.5 Statement of intent

This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results.

The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at through a process of shared decision making with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be documented in the patient's medical records at the time the relevant decision is taken.

1.5.1 Influence of financial and other interests

It has been recognised that financial or academic interests may have an influence on the interpretation of evidence from clinical studies.

It is not possible to completely eliminate any possible bias from these sources, nor even to quantify the degree of bias with any certainty. SIGN requires that all those involved in the work of guideline development should declare all financial and academic interests, whether direct or indirect, annually for as long as they are actively working with the organisation. By being explicit about the influences to which contributors are subjected, SIGN acknowledges the risk of bias and makes it possible for guideline users or reviewers to assess for themselves how likely it is that the conclusions and guideline recommendations are based on a biased interpretation of the evidence.

Signed copies of declaration of interests forms are retained by the SIGN Executive and a register of interests is available in the supporting material section for this guideline at **www.sign.ac.uk**

1.5.2 Prescribing of licensed medicines outwith their marketing authorisation

Recommendations within this guideline are based on the best clinical evidence. Some recommendations may be for medicines prescribed outwith the marketing authorisation (MA) also known as product licence. This is known as 'off-label' use.

Medicines may be prescribed 'off label' in the following circumstances:

- for an indication not specified within the MA

- for administration via a different route
- for administration of a different dose
- for a different patient population.

An unlicensed medicine is a medicine which does not have MA for medicinal use in humans.

Generally 'off-label' prescribing of medicines becomes necessary if the clinical need cannot be met by licensed medicines within the MA. Such use should be supported by appropriate evidence and experience.[43]

"Prescribing medicines outside the conditions of their marketing authorisation alters (and probably increases) the prescribers' professional responsibility and potential liability".[43]

The General Medical Council (GMC) recommends that when prescribing a medicine 'off label', doctors should:[44]

- be satisfied that there is no suitably licensed medicine that will meet the patient's need
- be satisfied that there is sufficient evidence or experience of using the medicine to show its safety and efficacy
- take responsibility for prescribing the medicine and for overseeing the patient's care, including monitoring the effects of the medicine, and any follow-up treatment, or ensure that arrangements are made for another suitable doctor to do so.
- make a clear, accurate and legible record of all medicines prescribed and, when not following common practice, the reasons for prescribing an unlicensed medicine.

Non-medical and medical prescribers should ensure that they are familiar with the legislative framework and the Royal Pharmaceutical Society's Competency Framework for all Prescribers.[45]

Prior to any prescribing, the licensing status of a medication should be checked in the Summary of Product Characteristics (SmPc) (www.medicines.org.uk). The prescriber must be competent, operate within the professional code of ethics of their statutory bodies and the prescribing practices of their employers.[46]

1.5.3 Health technology assessment advice for NHSScotland

Specialist teams within Healthcare Improvement Scotland issue a range of advice that focuses on the safe and effective use of medicines and technologies in NHSScotland.

The Scottish Medicines Consortium (SMC) provides advice to NHS boards and their Area Drug and Therapeutics Committees about the status of all newly licensed medicines, new formulations of existing medicines and new indications for established products. NHSScotland should take account of this advice and ensure that medicines accepted for use are made available to meet clinical need where appropriate.

SMC advice relevant to this guideline is summarised in section 14.4.

2 Key principles in managing chronic pain

2.1 Introduction

Chronic pain is a complex and personal experience, and objective measurements do not show its full impact. The management of chronic pain requires a considered, person-centred approach, drawing from a range of options rather than relying on any one treatment. Realistic goal setting in partnership with people experiencing pain, empowering self management early, and using non-pharmacological methods are central. The use of medication sits alongside these principles, when appropriate. Each management plan should be tailored to what matters to the individual, with a focus on improving function and quality of life, rather than an exclusive focus on complete pain removal, which is often unattainable.[27]

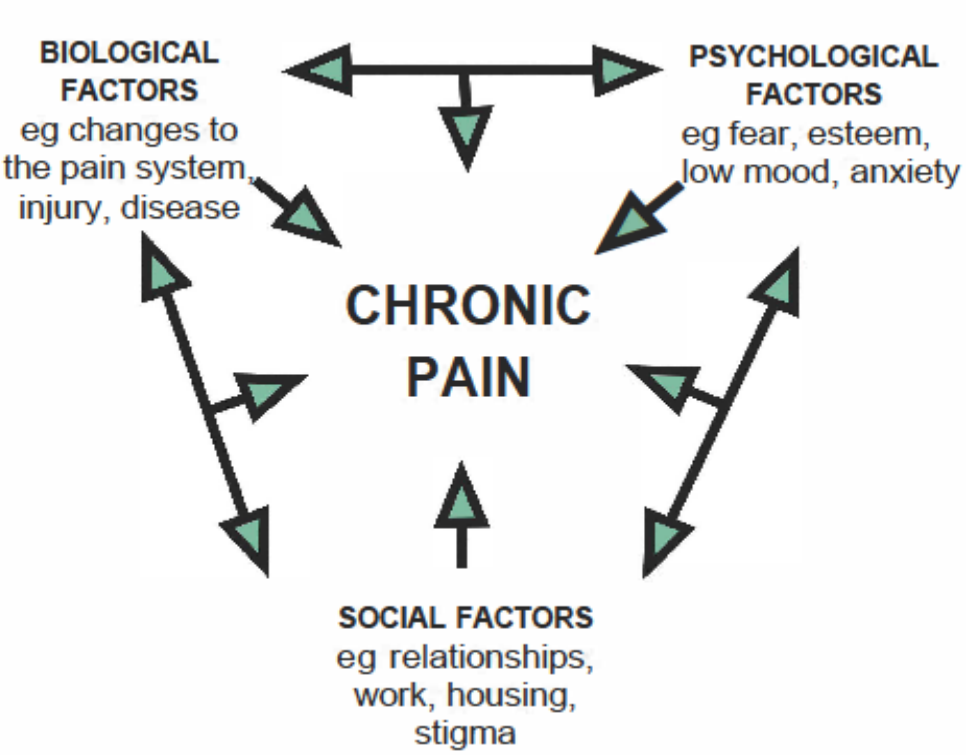
Scottish Government's Realistic Medicine aligns closely with this approach and encourages open discussion between people and healthcare professionals, shared decision making and care that is guided by each person's values.

2.2 Understanding chronic pain

The International Association for the Study of Pain (IASP) definition of chronic pain (see section 1.3) reinforces that pain is more than a physical sensation.[27] While acute pain often accompanies illness or injury and resolves with healing, chronic pain may persist after tissues have healed and its intensity may not appear to correlate with the degree of damage. It can often arise without any obvious injury.

Chronic pain has been recognised as a long-term condition by the Scottish Government[28] and should be considered a complex condition requiring a compassionate, comprehensive and targeted approach that acknowledges the reality of each person's experience of pain, regardless of cause.

Figure 1: The biopsychosocial model of chronic pain



Chronic pain is understood within the biopsychosocial model of health. This considers the complex interaction of biological, psychological, social and cultural factors, advocating for a more holistic approach to management and the use of multidisciplinary treatment programmes that integrate medical, psychological, and social support.[47]

Biological factors may include the mechanism of injury or disease process, ageing, sex, hormonal factors, sleep, and the dynamic nature of the nervous system in processing pain (neuroplasticity). Psychological influences involve thoughts, beliefs emotions and coping patterns, including fear, low mood, catastrophising and confidence in managing symptoms. Social and cultural factors include relationships, work demands, financial pressures, housing, deprivation, race, ethnicity, stigma and support.

Recognising these interacting influences provides the basis for a co-ordinated approach, combining physical rehabilitation and medical treatments, psychological therapies and education, and attention to social, cultural and work-related challenges. This partnership-based model supports autonomy, encourages self management, and aims to reduce the day-to-day impact of pain.

2.3 Limitations of medical treatments

The biopsychosocial approach is not offered as an alternative to medical treatment, but in recognition of the complex and multifactorial nature of chronic pain. Persistent pain rarely responds to a single intervention.

Medications that are usually effective for acute pain (such as opioids and anti-inflammatory drugs) are shown in this guideline to be of limited value if pain persists beyond a few months. For many, this may be due to tolerance (in the case of opioids) or unacceptable side effects (in the case of anti-inflammatories). Medications designed for long-term use, such as antiepileptic or antidepressant drugs, help a minority of those with persistent pain. When they do help, they are often limited by adverse effects.

A minority of people may benefit from injections or neuromodulation techniques following specialist assessment, but these procedures are helpful for specific conditions and are limited by potential complications and a short duration of effect. These treatments are not considered in this guideline but are being evaluated by the Scottish Health Technologies Group.

Recognising these limitations can help healthcare professionals set realistic expectations, emphasise non-pharmacological strategies and prioritise medicines where the balance of benefit and harm is clearly favourable.

2.4 Aims and principles of care

The primary aim of pain management is to enhance quality of life, reduce distress, improve function and participation, and support self efficacy, rather than to achieve complete pain elimination, which is often not possible. This is reflected in research where pain studies often use a 30% and 50% reduction in pain scores as a measure of moderate and substantial improvement in pain. These and other descriptions can be conveyed in individual conversations to clarify expectations and support realistic goals from therapies.

Key principles of management include:

- diagnosing (and coding) chronic pain, and recognising its status as a long-term condition that requires ongoing, adaptive support
- working in partnership with the person (and their family or carers, where appropriate) to understand what matters to them
- using education to support shared decision-making about realistic, meaningful goals
- prioritising interventions with a clear evidence base and a favourable balance of benefit and harm as set out in this guideline.

These principles are consistent with those of Realistic Medicine: reducing unnecessary interventions, minimising avoidable harm and working to reduce unwarranted variation in care, particularly in primary-care settings where most chronic pain is managed.

2.5 Healthy lifestyle changes to mitigate chronic pain and its impact

Chronic pain is influenced by how the body and brain process signals of threat or safety. Body and brain systems that respond to threat tend to

become more reactive when someone is physically depleted, stressed, socially isolated or sleeping poorly.

Conversely, good physical health, psychological well-being and strong social connections can support healthier pain processing and reduce the overall burden of symptoms. Although lifestyle changes do not cure chronic pain, they can lessen its impact, improve function and enhance resilience in day-to-day life.

While direct evidence for pain reduction from individual lifestyle changes varies, people should be supported, where possible, to:

- eat a healthy, balanced diet
- engage in regular physical activity
- avoid smoking and limit alcohol use
- adopt comfortable and sustainable postures at work and at home
- prevent and manage stress
- seek timely support for physical or mental health concerns
- maintain good sleep hygiene
- build and sustain social connections.

2.6 Person-centred approach with shared decision making

A person-centred approach begins with exploring each person's perspective on their pain: what it feels like, how it affects their daily life, and their priorities for change. Care planning should use collaborative goal-setting methods (for example, specific, measurable, achievable, relevant, and time bound (SMART) goals), focusing on valued activities, roles and participation rather than pain scores alone.

Shared decision making is central. Clinicians should offer clear, balanced information about potential benefits and harms of reasonable options (including deprescribing, appropriate levels of investigation and 'watchful waiting' strategies), explore the person's preferences and context, and arrive at a joint plan. Tools such as BRAN (Benefits, Risks, Alternatives, doing Nothing) questions, pain diaries and accessible written or digital information can facilitate these conversations and help people prepare for reviews.

People with chronic pain may feel dismissed or disbelieved. Acknowledging this and being transparent about the balance of modest benefits with well-known risks of interventions are important for building trust in the long term.

2.7 Multimodal and multidisciplinary approach

In practice, most physical, psychological and pharmacological interventions are co-ordinated within primary care. This might involve pharmacists, practice nurses, community link workers, physiotherapists and mental health professionals as well as primary-care clinicians.

Multidisciplinary pain services, typically involving physiotherapy, psychological input, pharmacy and medical review, are a key resource when further support is required. From these services, more intensive multidisciplinary pain management programmes (see SIGN 173: Management of chronic pain, section 8)[22] and selected specialist interventions can be accessed, where appropriate.[48]

2.8 Supported self management

The aim of supported self management is to empower people to become active participants in their own care, abandoning strategies that are not helping, and adopting approaches that may improve physical and mental well-being in the presence of ongoing medical issues. Although these strategies do not cure chronic pain, they can reduce its impact and support a life more closely aligned with the person's values.

Supporting people to manage their own medication is an important part of any supported self management approach to persistent pain. Resources such as the Pain Toolkit and the NHSScotland Manage My Meds app can help with this (see section 13.2).

2.9 Addressing psychosocial factors

Psychological and social pressures shape how people experience and cope with chronic pain. Low mood, anxiety, sleep difficulties, financial strain, caring responsibilities, loneliness or unstable housing can all make pain more intrusive and harder to manage. These influences do not suggest the pain is psychological in origin, but remind us that people live in circumstances that can amplify or ease their symptoms.

In primary care, it is rarely possible to explore every aspect in depth, but small, compassionate steps can have a meaningful impact. Simple questions about sleep, stress, relationships, work, or day-to-day hurdles can help identify where support might be most needed. Compassion and avoiding judgement are important, including explaining that stress, worry and exhaustion are common consequences of long-term pain, and not failings. Practical support might involve utilising third sectors or signposting to psychological therapies, such as cognitive behavioural therapy (CBT) or acceptance and commitment therapy (ACT), when appropriate (see SIGN 173: Management of chronic pain, section 9).[22]

2.10 Quality Prescribing for Chronic Pain 2026–2029 Guide

Scottish Government and multidisciplinary teams across primary and secondary care in NHSScotland, supported by individuals with lived experience and patient organisations, have jointly developed a guide to enable understanding and assessment of chronic pain, improve communication and highlight the benefits and harms of non-pharmacological approaches alongside the appropriate use of medication. The guide provides a practical resource for practitioners who help people living with chronic pain.

In addition to reinforcing key messages from this guideline on the safe and effective management of chronic pain, the Quality Prescribing Guide provides further information on topics which are not included in this guideline, such as implementation of medication reviews, health inequalities in chronic pain, a primary care consultation model, information on deprescribing and clinical case studies.

The guide is informed by evidence from this guideline and the clinical and non-clinical experience of clinicians, academics, experts by experience, patient groups and policy makers in Scotland, and is designed to be complimentary to this guideline.

3 Simple analgesics

3.1 Introduction

Chronic pain is a common condition which can be difficult to manage with medicines. Many patients use multiple medications to try to manage their condition, often with little evidence of benefit to support their use, particularly in the long term. The use of these medicines may also present a risk of harm to the patient, particularly when they are used alongside other medicines (which is often the case) or in patients with multiple comorbidities (such as cardiovascular conditions, renal impairment and gastrointestinal conditions). It is important to identify new evidence (or lack thereof) that could impact practice. Increasing concerns regarding the safety and long-term effectiveness of opioids means it is important to fully understand the benefits and harms of using simple analgesics in managing chronic pain.

Simple analgesics include paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs) and nefopam.

Non-steroidal anti-inflammatories have both an analgesic and an anti-inflammatory effect which makes them particularly useful for the treatment of chronic pain associated with inflammation. These medications reduce pain and inflammation by inhibiting enzymes, called cyclo-oxygenases (COX). There are two main types of NSAIDs, non-selective and selective, which refer to different NSAIDs' ability to inhibit specific types of COX enzymes. Non-selective NSAIDs (such as diclofenac, ibuprofen or naproxen) inhibit both COX-1 and COX-2 enzymes to a significant degree. Medications which target COX-2 enzymes only (such as celecoxib or etoricoxib) are selective NSAIDs.

It is important that people living with chronic pain and the clinicians guiding their treatment can differentiate between medicines that may be beneficial in chronic pain management and medication that is unlikely to bring benefit. Benefit can be measured by improvements in pain, function and/or quality of life. This will avoid patients taking ineffective medication and thus avoid unnecessary polypharmacy. It is also important for patients and clinicians to be aware of the potential harms from medication, the likelihood of these harms occurring and any scenarios where the risk of harm is increased (for example, use alongside other medicines, individual patient risk factors). This will support a risk/benefit assessment of using simple analgesics in individual patients for chronic pain management.

In Scotland, paracetamol and NSAIDs are frequently used for the management of various conditions that cause chronic pain. They are often used long term. Which NSAIDs are prescribed has some variation between health boards and is largely determined by the local prescribing formulary. Nefopam is not used as widely, but there is variation across Scotland. Many health boards have guidance against prescribing nefopam in place.

3.2 Evidence of benefit

3.2.1 Pain

ORAL NSAID v PLACEBO

Osteoarthritis

A well conducted systematic review and meta-analysis of RCTs carried out by AHRQ explored the effectiveness and harms of non-opioid pharmacological treatments for chronic pain. In the short term (three to less than six months), NSAIDs resulted in a small reduction in pain compared with placebo (mean difference (MD) -0.73 on a 10-point scale, 95% confidence interval (CI) -0.84 to -0.62; 27 RCTs, 13,478 participants: moderate certainty evidence). Most trials were in patients with knee or hip osteoarthritis and the main drugs were celecoxib and naproxen. The proportion of study participants reporting a pain response to NSAIDs was significantly greater than placebo (56% vs 46%, relative risk (RR) 1.23, 95% CI 1.18 to 1.31; 15 RCTs, 8,253 participants: high-certainty evidence).[49] In the intermediate term (six to <12 months), pain reduction was sustained, based on a single study in patients with knee osteoarthritis taking celecoxib compared with placebo (MD -0.63, 95% CI -1.10 to -0.16; one RCT, 345 participants: no evidence certainty rating). The relative risk of reporting a pain response was not statistically significant (RR 1.13, 95% CI 0.94 to 1.35; one RCT, unclear participants: no evidence certainty rating).	1++
A network meta-analysis (NMA) explored the long-term outcomes (≥12 months) of medications for people with knee osteoarthritis. When expressed in terms of mean difference compared with placebo on a 0–100 scale there was no NSAID which offered a benefit over placebo as long-term effect (based on a network of 42 RCTs, 22,037 participants).[50]	sufficient

Inflammatory arthritis

The AHRQ systematic review reported that NSAIDs reduced pain severity compared with placebo at short-term follow-up (MD -0.97, 95% CI -1.33 to -0.74; nine RCTs, 4,543 participants: moderate certainty evidence). The proportion of patients who recorded a short-term pain response was significantly higher with NSAIDs than with placebo (45% vs 32%, RR 1.58, 95% CI 1.34 to 2.06; seven RCTs, 3,434 participants: moderate certainty evidence). Statistically significant responses were also reported at intermediate and long-term follow-up, but based on single studies in each case.[49]	1++

Lower back pain

The same systematic review identified two short-term RCTs (654 participants) comparing effects of naproxen with placebo in people with chronic lower back pain. The authors noted that results were inconsistent, it was not possible to determine a pooled effect and that the certainty of the evidence was insufficient.[49]	1++

ORAL NSAID v ORAL NSAID

Osteoarthritis

There was only low certainty evidence from trials in which different NSAIDs were compared with each other. Most comparisons had only one or two trials contributing and there were no differences between drugs in pain or function outcomes for osteoarthritis patients in the short, intermediate, or long term with the exception of the comparison between diclofenac and celecoxib which showed a moderate effect in favour of diclofenac for pain (MD -12.2 on a 0–100 point Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scale, 95% CI -22.1 to -2.2; one RCT, participants not reported: low certainty evidence).[49]	1++

Inflammatory arthritis

In short-term follow-up there was no evidence of a difference in pain reduction between any two NSAIDs studied (low to moderate certainty evidence). For intermediate-term pain outcomes there was low certainty evidence for no difference in outcomes between meloxicam and naproxen and nabumetone and naproxen in single studies.[50]	sufficient

PARACETAMOL

Osteoarthritis

The AHRQ systematic review evaluated the effects of paracetamol (acetaminophen) on outcomes for people with chronic osteoarthritis pain. Paracetamol did not have an impact on osteoarthritis pain in the short term (MD -0.34, 95% CI -0.66 to 0.03; three RCTs, 1,082 participants: low certainty evidence) or intermediate term (MD -0.30, 95% CI -0.77 to 0.17; one RCT, 212 participants: low certainty evidence).[49]	1++
A NMA found no evidence of long-term effect of paracetamol for pain reduction in people with knee osteoarthritis compared with placebo (MD 7.00, 95% credible interval (CrI) -10.86 to 23.95; one RCT, 27 participants: no evidence certainty rating).[50]	sufficient

CROSS CLASS COMPARISONS

The AHRQ systematic review identified one small short-term RCT (85 participants) which compared diclofenac (150 mg daily) with paracetamol (4,000 mg daily) and found diclofenac to be superior for improvement in pain (-53.9 vs -23.8 difference from baseline on WOMAC pain subscale (lower numbers indicate greater relative effect); p=0.003).[49]	1++

3.2.2 Function

ORAL NSAID v PLACEBO

Osteoarthritis

The AHRQ systematic review reported that NSAIDs resulted in a small improvement in function in people with osteoarthritis compared with placebo in the short term (3 to <6 months) (SMD -0.32, 95% CI 0.37 to 0.28; 28 RCTs, 13,473 participants: high certainty evidence) and intermediate term (SMD -0.25, 95% CI -0.47 to -0.04; one RCT, 345	1++

participants: no evidence certainty rating).[49]	
A NMA reported on long-term effects of NSAIDs on physical function in people with knee osteoarthritis. Data was only reported for celecoxib which did not significantly improve physical function compared with placebo (SMD -0.13, 95% CrI -0.32 to 0.07; two RCTs, 232 participants: no evidence certainty rating).[50]	sufficient
<u>Inflammatory arthritis</u>	
The AHRQ systematic review reported that NSAIDs improved function in people with chronic pain due to inflammatory arthritis compared with placebo at short-term follow-up (SMD -0.34, 95% CI -0.51 to -0.20; seven RCTs, 4,284 participants: moderate certainty evidence).[49]	1++
There were only single trials reporting on function at intermediate- and long-term follow-up. One trial reported a small improvement in function compared with placebo at intermediate term. In the other trial (365 participants) the review reported that meloxicam "did not improve function in the long term compared with placebo", although there was a very small statistically significant effect. For each trial the certainty of evidence was assessed as low.[49]	
ORAL NSAID v ORAL NSAID	
The same systematic review reported no evidence of a difference in effect on function between any NSAID, except the comparison between diclofenac and celecoxib, where a single RCT found that diclofenac had a moderate improvement in function over celecoxib (RR 2.06, 95% CI 1.37 to 3.08; low certainty evidence).[49]	1++
PARACETAMOL	
<u>Osteoarthritis</u>	
The AHRQ systematic review reported that paracetamol did not have an impact on osteoarthritis function in the short term compared with placebo (SMD -0.14, 95% CI -0.29 to 0.04; three RCTs, 1,082 participants). A very small, clinically insignificant improvement in function was reported in the intermediate term compared with placebo (MD -3.7 on a 1–100-point scale, 95% CI -6.9 to -0.5; one RCT, 212 participants: low certainty evidence).[49]	1++
CROSS CLASS COMPARISONS	
The same systematic review identified one small short-term RCT (85 participants) which compared diclofenac (150 mg daily) with paracetamol (4,000 mg daily) and found a significant improvement in function in those taking diclofenac (mean difference from baseline on WOMAC function subscale -163.0 (24.4% improvement), p<0.001) but not in those taking paracetamol (-41.8, p=0.28: insufficient evidence certainty).[49]	1++
3.2.3 Quality of life	
ORAL NSAID v PLACEBO	
<u>Osteoarthritis</u>	
Based on short-term trials in the AHRQ systematic review, there was no	1++

evidence of an effect on quality of life (QoL) of oral NSAIDs as measured by the short form-36 (mental component scale). There was an improvement in the physical component scale which did not reach the three-point minimal clinically important difference stipulated by the review authors (MD 2.95 on a standardised 0–100-point scale, 95% CI 1.79 to 4.18; three RCTs, 1,027 participants: moderate certainty evidence).[49]

Inflammatory arthritis

The same systematic review identified two RCTs which reported quality of life data associated with NSAIDs in people with inflammatory arthritis. One small trial (55 participants) reported moderate improvement in QoL in people with ankylosing spondylitis who received naproxen. A larger trial (1,148 participants) found some improvements in QoL with naproxen and celecoxib. The authors note that for most doses these improvements were statistically significant, but not clinically significant.[49] 1++

ORAL NSAID v ORAL NSAID

No evidence was identified which reported on QoL in head-to-head comparisons of NSAIDs.

CROSS CLASS COMPARISONS

No evidence was identified which reported on QoL in cross class comparisons.

3.3 Evidence of harms

3.3.1 NSAIDs

The AHRQ systematic review reported estimates of harmful effects of non-opioid pharmacological therapies for chronic pain based on their own meta-analyses of individual RCTs and on narrative review of published systematic reviews. In the following sections, where identified, systematic reviews cited within the AHRQ review have not been reanalysed or critically appraised although relevant results will be reported.[49]

Serious Adverse Events

A meta-analysis of short-term RCTs (including evidence from surveillance up to 2022) concluded there was no increased risk of serious adverse events (SAEs) with NSAIDs compared with control (RR 0.96, 95% CI 0.73 to 1.27; 25 RCTs, 13,736 participants: low certainty evidence).[49]

In the intermediate term, a single RCT (563 participants) did not find an increased risk of SAEs with naproxen (RR 0.51, 95% CI 0.05 to 5.58), but this evidence was insufficient to draw conclusions. The authors of the AHRQ review cite a further Cochrane review which evaluated celecoxib 200 mg daily versus any non-selective NSAID or placebo in people with osteoarthritis.[51] It found no significant differences in the incidence of SAEs with celecoxib compared with non-selective NSAIDs (nine RCTs) or placebo (32 RCTs, participants varied according to comparison: very low-certainty evidence). The AHRQ review found no significant increase in SAEs with topical diclofenac compared with placebo (RR 1.03, 95% CI 0.29 to 27.01; two RCTs, 912 participants: very low-certainty evidence).[49] 1++

Withdrawals due to adverse events	
In the AHRQ systematic review, which pooled data for harms across all chronic pain types, withdrawals due to adverse events (WAE) were increased with NSAIDs overall in the short term (RR 1.30, 95% CI 1.14 to 1.49; 38 RCTs, 20,060 participants: moderate certainty evidence).[49]	
Subgroup analysis showed that the size and direction of effect varied by individual drug. The review reported a moderate increase in WAE in the short term with diclofenac (RR 1.71, 95% CI 1.22 to 2.65; six RCTs), ibuprofen (five RCTs, RR 1.96, 95% CI 1.42 to 2.69), and naproxen (15 RCTs, RR 1.50, 95% CI 1.23 to 1.84), while celecoxib (16 RCTs, RR 1.05, 95% CI 0.86 to 1.24) and meloxicam (three RCTs, RR 1.16, 95% CI 0.51 to 2.32) showed no statistically significant increased risk (number of participants for subgroup analyses was not reported).	1++
Three RCTs did not find that NSAIDs significantly increased risk of WAE in the intermediate or long term. There was not a significant increase in WAEs with topical diclofenac compared with placebo (RR 1.03, 95% CI 0.29 to 27.01; four RCTs, 1,549 participants: low certainty evidence). The authors of this review report a further Cochrane review of celecoxib 200 mg daily versus any non-selective NSAID or placebo in patients with osteoarthritis.[51] It reported no significant differences in the incidence of WAEs in groups using celecoxib compared with nonselective NSAIDs (nine RCTs) or placebo (32 RCTs).	
Cardiovascular events	
The AHRQ systematic review notes the availability of a large number of RCTs which provide data on cardiovascular risks of NSAIDs.[49] The authors of this review cite a further systematic review of 639 RCTs which evaluated cardiovascular harms using individual patient data and standard meta-analysis.[52] While not limited to individuals with chronic pain, the authors note that the indication for an NSAID in around four fifths of the participants was rheumatoid arthritis or osteoarthritis. The analyses combined data on four selective COX-2 inhibitor drugs; celecoxib, rofecoxib, etoricoxib, and lumiracoxib (“coxibs”). This review found an increased risk in major vascular events with a coxib (adjusted RR (aRR) 1.37, 95% CI 1.14 to 1.66; 190 RCTs, 88,605 participants: evidence certainty not reported) and with diclofenac (aRR 1.41, 95% CI 1.12 to 1.78; estimate based on indirect comparison, total number of participants not reported) compared with placebo. Major coronary events were increased with coxibs, diclofenac, and ibuprofen, and increased risk of hospitalisation for heart failure was found with all NSAIDs (*see Table 1*). This review reported that there may be increased risk of major vascular events in the first six months of treatment with diclofenac (but no evidence of increased risk over longer treatment periods for any NSAID or coxib studied), and that, for all drugs analysed, higher doses were associated with greater risk.	1++

Table 1: Individual patient data meta-analysis of NSAID cardiovascular risks compared with placebo

Event	Diclofenac Adjusted RR (95% CI)	Ibuprofen Adjusted RR (95% CI)	Naproxen Adjusted RR (95% CI)	Coxibs Adjusted RR (95% CI)
Major vascular events[a]	**1.41 (1.12 to 1.78)**	1.44 (0.89 to 2.33)	0.93 (0.69 to 1.27)	**1.37 (1.14 to 1.66)** Celecoxib 1.36 (1.00 to 1.84)
Vascular mortality	1.65 (0.95 to 2.85)	1.90 (0.56 to 6.41)	1.08 (0.48 to 2.47)	1.58 (1.00 to 2.49)[c]
Major coronary events[b]	**1.70 (1.19 to 2.41)**	**2.22 (1.10 to 4.48)**	0.84 (0.52 to 1.35)	**1.76 (1.31 to 2.37)**
Heart failure (hospitalisation)	**1.85 (1.17 to 2.94)**	**2.59 (1.19 to 5.20)**	**1.87 (1.10 to 3.16)**	**2.28 (1.62 to 3.20)**

CI confidence interval; NSAID nonsteroidal anti-inflammatory drug; RR risk ratio
a Non-fatal myocardial infarction, coronary death, myocardial infarction or chronic heart failure death, non-fatal stroke, stroke death, any stroke, other vascular death
b Non-fatal myocardial infarction, coronary death, myocardial infarction or coronary heart disease death
c 99% CI calculated due to multiple comparisons

bold values: 95% certainty that the true RR is not 1.0 and we conclude that the observed RR is statistically significantly different from 1.0 at the 0.05 level.

Reproduced with permission from McDonagh MS, Selph SS, Buckley DI, Holmes RS, Mauer K, Ramirez S, et al. Nonopioid Pharmacologic Treatments for Chronic Pain. Rockville (MD): Agency for Healthcare Research and Quality; 2020 Apr. Report No. 20-EHC010

Authors of the AHRQ systematic review report that, in the intermediate term, three RCTs compared the risk for cardiovascular events with celecoxib and non-selective NSAIDs, with none finding a significant difference.[49]

In the long term, one large good-quality RCT (7,297 participants) randomised patients with osteoarthritis or rheumatoid arthritis who were under the age of 60 years, had no known cardiovascular disease, and who were currently taking a non-selective NSAID, to celecoxib or to continue their non-selective NSAID. At follow-up (median three years), there was no significant difference in the incidence of hospitalisation for non-fatal myocardial infarction or other biomarker positive acute coronary syndrome, non-fatal stroke, or cardiovascular death (hazard ratio (HR) 1.12, 95% CI 0.81 to 1.55). The results demonstrate non-inferiority between celecoxib and non-selective NSAIDs for these outcomes.[49] 1++

Serious upper gastrointestinal (GI) events (largely bleeding). In the short term, the AHRQ systematic review found increased risk of serious GI events with NSAIDs, with the size of risk varying by specific drug. The systematic review cited within this review, described above, which analysed data on risks associated with coxibs and traditional NSAIDs using individual patient data meta-analysis, found moderate increased risk of serious upper GI harms for coxibs compared with placebo (RR 1.81, 95% CI 1.17 to 2.81: no evidence certainty rating), and for diclonefac compared with placebo (RR 1.89, 95% CI 1.16 to 3.09). A large increase in risk of serious GI harms was reported for ibuprofen (RR 3.97, 95% CI 2.22 to 7.10) and for naproxen (RR 4.22, 95% CI 2.71 to 6.56). The evidence certainty was not reported for these analyses. The authors reported no evidence of a difference in effect according to the specific coxib used. Most of the harms were GI bleeds and the findings were not affected by lower or higher baseline risk for GI events. The risk was greater in the first six months for coxibs (RR 2.55, 99% CI 1.49 to 4.35), diclofenac (RR 3.93, 99% CI 2.16 to 7.13), ibuprofen (RR 5.73, 99% CI 3.24 to 10.14), and naproxen (RR 6.31, 99% CI 3.81 to 10.44).[49] The systematic review noted mixed evidence for the harms associated with coxibs compared with non-selective NSAIDs. The authors cite a Cochrane review which directly compared GI harms in people with osteoarthritis who used celecoxib with those using any non-selective NSAID. Their analysis found no difference between celecoxib and non-selective NSAIDs or placebo (odds ratio (OR) 0.61, 95% CI 0.15 to 2.43; four RCTs, 1,755 participants: very low-certainty evidence). In the short term, the AHRQ meta-analysis reported no significant difference in risk of serious GI events between celecoxib and placebo (7.5% vs 6.7%, RR 1.04, 95% CI 0.67 to 1.54; four RCTs, 4,399 participants: low certainty evidence). In contrast, a pooled analysis of diclofenac, ibuprofen, naproxen, and meloxicam found a large increased risk of serious GI events compared with placebo (13% vs 3%, RR 4.29, 95% CI 2.75 to 6.93; nine RCTs, 4,448 participants: low certainty evidence). The authors noted that the evidence was inconsistent and imprecise and insufficient to draw conclusions. In the intermediate term, based on a single study comparing celecoxib with any non-selective NSAID in people with osteoarthritis over six months, non-selective NSAIDs had a moderately greater risk of clinically important GI events than celecoxib (OR 1.82, 95% CI 1.31 to 2.55; one RCT, 8,067 participants: low certainty evidence).[49]	1++
Hepatic events The AHRQ review[49] cited one fair-quality systematic review which evaluated the hepatic harms of NSAIDs (specifically diclofenac, naproxen, ibuprofen, meloxicam, celecoxib, rofecoxib, and valdecoxib) in people with osteoarthritis or rheumatoid arthritis. This systematic review included 64 RCTs most of which were six months or longer in duration.[53] Diclofenac was found to have a large increased incidence of elevated liver enzymes (aminotransferases more than three times the upper limit of normal) than placebo (3.55%, 95% CI 3.12 to 4.03 vs 0.29%, 95% CI 0.17 to 0.51: low	1++

certainty evidence). Diclofenac also resulted in a larger increase in liver-related discontinuations from treatment (2.17%, 95% CI 1.78 to 2.64) than placebo (0.08%, 95% CI 0.02 to 0.29: low certainty evidence). Liver enzyme elevations and liver-related discontinuations with diclofenac were elevated more with greater dose (>100 mg daily) and duration of treatment (>13 weeks). Liver-related serious adverse events were infrequent, but naproxen resulted the highest incidence (0.06%, 95% CI 0.02 to 0.15) compared with placebo (0.00%, 95% CI 0.00 to 0.08: low certainty evidence). One liver-related hospitalisation and one liver-related death occurred, both with naproxen.

The AHRQ review also cited a further systematic review which investigated liver injury associated with NSAIDs although with no limit to population or study duration. The authors note that this reached similar conclusions.[54]

Renal events

No evidence was identified meeting the inclusion criteria which reported events of renal dysfunction or renal failure in people with chronic pain. Authors of the AHRQ systematic review cite adverse event findings from other sources to address missing evidence.

They identified two systematic reviews on NSAIDs and acute kidney injury (published in 2015-2017) from wider populations not directly related to NSAIDs use in the management of chronic pain. Those studies showed a moderate to large increased risk of renal harm associated with NSAID use which was higher in older patients and in those with chronic kidney disease (CKD) (evidence from observational studies, includes short-term use) and with no difference found between NSAIDs.[49] 1++

3.3.2 Paracetamol

In people with chronic pain due to osteoarthritis, the AHRQ review included two short-term and one intermediate-term RCTs which reported on adverse events from paracetamol compared with placebo.[49]

Serious Adverse Events (SAEs)

At short-term follow-up, meta-analysis found no statistically significant difference in SAEs between people receiving paracetamol compared with those receiving placebo (2.4% vs 0.9%, RR 2.57, 95% CI 0.60 to 10.8; two RCTs, 1,023 participants: low certainty evidence). A single study found no meaningful difference in SAEs between people who received 1,950 mg daily versus 3,900 mg daily of paracetamol (1.9% vs 1.9%, RR 1.01, 95% CI 0.21 to 4.94; one RCT, 318 participants: low certainty evidence). There was also no meaningful difference in SAEs between paracetamol and placebo at intermediate-term follow-up (4.6% vs 4.8%, RR 0.96, 95% CI 0.29 to 3.23; one RCT, 212 participants: low certainty evidence).[49] 1++

Withdrawals Due to Adverse Events (WAEs)

Paracetamol did not result in an increase in WAEs compared with placebo in the short or intermediate term. At short-term follow-up, meta-analysis found no meaningful difference in WAEs between paracetamol and placebo (7.4% vs 7.1%, RR 1.14, 95% CI 0.67 to 1.95; two RCTs, 1,023 1++

participants: low certainty evidence)). A single study found no meaningful difference in WAEs between people who received 1,950 mg and 3,900 mg daily of paracetamol (6.3% vs 5.0%, RR 1.27, 95% CI 0.51 to 3.12; one RCT, 318 participants: low certainty evidence). At intermediate-term follow-up in a single trial, there was no statistically significant difference in WAEs between people who received paracetamol compared with placebo (11.1% vs 8.7%, RR 1.28, 95% CI 0.56 to 2.92; one RCT, 212 participants: low certainty evidence).[49]

3.4 Summary of benefits and harms of simple analgesics for chronic pain

Evidence shows that oral NSAIDs slightly reduce pain and improve function in people with osteoarthritis in the short term, with these effects maintained in the intermediate term with celecoxib (based on a single RCT). There is no evidence of benefit over placebo in the long term (>12 months) for NSAIDs or paracetamol in people with knee osteoarthritis.

Oral NSAIDs result in small improvements in pain severity and function, and moderate improvement in pain response compared with placebo for people with inflammatory arthritis.

There were no significant differences in effect between different doses of oral NSAIDs.

Evidence on QoL is inconsistent, with studies finding different effects although none were clearly clinically significant.

Evidence suggests that NSAIDs do not significantly increase the risk of serious adverse effects but lead to a small increase in WAEs, with ibuprofen, diclofenac, and naproxen each having moderately-increased risk in the short term.

There was no increased risk of any cardiovascular adverse event for NSAIDs as a class compared with placebo, although there was a small increase in risk with diclofenac. There was a moderate increased risk of major coronary events with both diclofenac and celecoxib, and a large increased risk with ibuprofen. In the intermediate and long term there was no difference in cardiovascular events between non-selective NSAIDs and celecoxib.

Non-selective NSAIDs, led to a moderate to large increase in GI events (largely bleeding) in the short term, particularly in the first six months of treatment. Evidence on non-selective NSAIDs versus celecoxib was mixed and inconclusive in the short term, while in the intermediate term non-selective NSAIDs had a moderately increased risk of serious GI events.

Evidence showed hepatic harms (eg liver enzyme elevations) with both diclofenac and naproxen in the intermediate term.

Based on the wider population using these drugs, studies show a moderate to large increased risk of renal harms with NSAID use, particularly in older populations and patients with CKD. There was no difference in the risk between different NSAIDs.

In contrast paracetamol did not significantly improve pain or function in the

short, intermediate or long term, across all doses. The use of paracetamol (in the short or intermediate term) had no statistically significant adverse events compared with placebo.

3.5 Other factors

When choosing and prescribing medication for chronic pain management it is good practice to follow the 5As of analgesic prescribing:

- analgesia (improvement in pain)
- activities of daily living (function and QoL)
- adverse effects
- affect
- aberrant drug behaviours.

The recommendations in this guideline should be used in conjunction with the Quality Prescribing for Chronic Pain 2026–2029 Guide (see section 2.10). This provides practical advice to clinicians regarding applying SIGN guideline recommendations to individual patients.

Oral medication is easily obtainable and straightforward from a patient or carer perspective, therefore an acceptable intervention. Medication options for chronic pain are limited, and so patients are willing to accept risk of harm, with risk of benefit. Potential adverse events caused by the medication ceases if the patient stops medication, thus not long term.

The BRAN approach can be used to aid discussion regarding treatment options and reach shared decision making with patients:

- Benefits
- Risks
- Alternatives
- do Nothing.

Patients with chronic pain commonly purchase over the counter medicines and remedies to manage their condition. It is prudent to check what (if any) medication patients are purchasing over the counter before making any prescribing decisions.

Paracetamol has a high tablet burden if being taken regularly at full dose.

Nefopam is included in the items of limited clinical value listed in the document released December 2024 Achieving Value and Sustainability in Prescribing (Achieving Value and Sustainability in Prescribing) Recommendation:

- prescribe only if the item is for an exception named in this guidance or no other item or intervention is clinically appropriate or available
- consider deprescribing where safe and appropriate in individuals currently prescribed this item. Continued prescribing of these medicines should be subject to regular review.
- Exceptions: nefopam may be considered for specific individuals, when choice of alternative analgesia is limited due to other

comorbidities eg patients with renal failure.

- particular caution should be used in adults who would be at elevated risk of anticholinergic side effects, eg older adults or in cognitive impairment.

A NMA which explored the long-term outcomes (≥12 months) of medications for people with knee osteoarthritis and included 47 RCTs in total, reported that diclofenac was the most frequently studied NSAID (five RCTs), followed by naproxen and celecoxib (four RCTs), rofecoxib and etoricoxib (two RCTs) and remaining NSAIDs in one RCT each.[50] Rofecoxib is not available for prescribing in Scotland and has been withdrawn from the worldwide market after a study showing that long-term use significantly increased risk of heart attack compared with patients receiving placebo. Phase III trials using licofelone for osteoarthritis were conducted in the early 2000s, but results were mixed and the drug has never been submitted for regulatory approval. The European Medicines Agency has completed a review of the safety and effectiveness of systemic medicines containing nimesulide. The Agency's Committee for Medicinal Products for Human Use concluded that the benefits of nimesulide, when used systemically, continue to outweigh its risks but that its use should be restricted to the treatment of acute pain and primary dysmenorrhoea. It has issued a recommendation that nimesulide should no longer be used for the treatment of painful osteoarthritis.

3.6 Recommendations

R **NSAIDs (non-selective and selective) should be considered for short-term (less than six months) or intermittent use in patients with osteoarthritis and inflammatory arthritis.**

✓ The use of NSAIDs (non-selective and selective) increases the risk of GI bleeding and may increase the risk of cardiovascular issues (diclenofac and celecoxib) and this should be considered carefully before initiation. Patients often have comorbidities or other medication that would increase their individual risk of harm (eg elderly population, CKD, cardiac conditions, previous gastric ulcer or bleed, other nephrotoxic medication or medication increasing the risk of adverse GI effects such as SSRIs - this list is not exhaustive).

✓ There was no significant difference between different doses of NSAIDs studied and therefore they should be used at the lowest effective dose for the individual patient to minimise the risk of harms.

4 Antiepileptics

4.1 Introduction

Chronic pain is a common condition which can be difficult to manage with medicines. Chronic neuropathic pain can be particularly challenging to manage and often does not respond to simple analgesics or opioids. Antiepileptic medicines are commonly prescribed for neuropathic pain, with mixed evidence of benefit for pain reduction, improved function and/or improved QoL. Antiepileptic medicines are also associated with several potential harms.

Antiepileptics are often prescribed for neuropathic pain associated with conditions such as fibromyalgia, diabetic neuropathy and postherpetic neuralgia. They are also sometimes used in patients with other conditions such as lower back pain and pelvic pain. It is important that people living with chronic pain and the clinicians guiding their treatment can identify medicines that may be beneficial for the individual patient, and medication that is unlikely to bring benefit. This will avoid patients taking ineffective medication and thus avoid unnecessary polypharmacy.

There are increasing concerns regarding potential harms from antiepileptics with long-term use, such as dependency on or addiction to gabapentinoids. It is important for patients and clinicians to be aware of the potential harms from medication, the likelihood of these harms occurring and any scenarios where the risk of harm is increased (for example, use alongside other medicines and individual patient risk factors). This will allow for appropriate assessment of the balance of risks and benefits of using antiepileptics in individual patients for chronic pain management.

The analgesic action of antiepileptic drugs is thought to be a result of limiting neuronal excitation and enhancing inhibition.[55] Gabapentinoids (gabapentin, pregabalin, and mirogabalin) share a similar structure and mechanism of action. They target α-2-δ subunit of voltage-gated calcium (Ca^{2+}) channels leading to decreasing Ca^{2+} influx, subsequent neurotransmitter release (eg glutamate) that affects pain sensation, and results in a reduction of neuropathic pain.[56] In Scotland, gabapentin and pregabalin are commonly used to manage neuropathic pain associated with a broad range of conditions. Mirogabalin does not have a marketing authorisation for use in the United Kingdom (UK) therefore evidence on this drug has not been included.

Carbamazepine is commonly prescribed for the management of trigeminal neuralgia. Oxcarbazepine is rarely prescribed in Scotland for neuropathic pain. The mechanism of action of both oxcarbazepine and carbamazepine is a modulation of voltage-gated sodium channels, leading to a decrease in neuronal activity.[57] Topiramate, sodium valproate, lamotrigine, lacosamide and levetiracetam are not commonly prescribed for chronic pain.

4.2 Evidence of benefit

Nine systematic reviews were identified which evaluated the effectiveness of antiepileptic drugs in adults living with chronic non-malignant pain. Four of the reviews were rated as acceptable quality[55,56,58,59] and five as high quality.[49,60-63] The number of trials included in the reviews ranged from three to 313, and the overall number of participants in the reviews ranged from 624 to 48,789. All trials were short or intermediate term with durations of six months or less.

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4.2.1 Diabetic peripheral neuropathic pain

A Cochrane systematic review reported that pregabalin provided a small but statistically significant reduction in pain intensity in people with diabetic peripheral neuropathic pain compared with placebo, with 600 mg daily dose providing slightly more benefit than 300 mg daily dose (≥50% reduction in pain intensity, (600 mg daily dose): RR 1.6, 95% CI 1.4 to 1.9; seven RCTs, 1,360 participants: moderate certainty evidence, (300 mg daily dose): RR 1.3, 95% CI 1.2 to 1.5; 11 RCTs, 2,931 participants: moderate certainty evidence).[5] In contrast, 150 mg daily dose of pregabalin did not provide more reduction in pain intensity compared with placebo (RR 1.14, 95% CI 0.8 to 1.63; two RCTs, 359 participants: low certainty evidence).[60] The results measured using PGIC showed a similar pattern. A further systematic review which investigated the effects of anticonvulsants on chronic pain reported no difference in quality of life between people using pregabalin or placebo (EuroQol five-dimensional questionnaire (EQ-5D) SMD 0.24, 95% CI -0.07 to 0.54; three RCTs, 1,015 participants: low certainty evidence).[49]

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Based on two trials where daily doses of oxcarbazepine varied from 300 mg to 1,800 mg, oxcarbazepine provided a small but statistically significant reduction in pain compared with placebo (MD -0.89 measured on 0–10 scale, 95% CI -1.50 to -0.37; two RCTs, 493 participants: no evidence certainty rating). These trials reported mixed results for changes in quality of life and sleep disruption.[49]

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One systematic review focused on the comparison of gabapentin (at doses of 300 mg to 3,600 mg daily) and duloxetine (at doses of 60 mg to 120 mg daily) in people with diabetic peripheral neuropathic pain and found no difference in pain intensity (SMD -0.26 on a 0–100-point VAS, 95% CI -0.53 to 0.02; seven RCTs, 624 participants: no evidence certainty rating), PGIC score (MD 0.07, 95% CI -0.20 to 0.35; two RCTs, 204 participants: no evidence certainty rating), or response rate (RR 1.05, 95% CI 0.92 to 1.20; three RCTs, 236 participants: no evidence certainty rating).[61]

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4.2.2 Neuropathic pain (not otherwise specified)

A systematic review and meta-analysis analysed head-to-head trials of gabapentinoids (pregabalin or gabapentin) compared with other drug classes used in the management of chronic pain. The review included 30 RCTs which included a range of neuropathic pain types, including one trial

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of cancer neuropathic pain. As results pooled data from these trials, it was not possible to discriminate effects on individual pain types, or exclude data from the cancer trial.[59] The review reported no evidence of a difference between gabapentinoids and tricyclic antidepressants (TCAs) in pain severity (MD 0.1, 95% CI -0.13 to 0.32; 10 RCTs, 920 participants), QoL (SMD -0.05, 95% CI -0.25 to 0.15; three RCTs, 372 participants), sleep scores (SMD -0.06, 95% CI -0.14 to 0.27; five RCTs, 570 participants) or symptoms of depression (SMD -0.09, 95% CI -0.31 to 0.13; two RCTs, 317 participants). The certainty of evidence was moderate for all comparisons. The review also reported a small effect of higher pain reduction for serotonin-noradrenaline reuptake inhibitors (SNRIs) compared with gabapentinoids (MD 0.36, 95% CI 0.01 to 0.70; five RCTs, 1,495 participants), but no evidence of a difference in QoL (SMD 0.06, 95% CI -0.11 to 0.22; three RCTs, 565 participants), sleep scores (SMD 0.33, 95% CI -0.30 to 0.95; three RCTs, 565 participants) or symptoms of depression (SMD 0.06, 95% CI -0.14 to 0.25; three RCTs, 1,314 participants). The certainty of evidence was low for all comparisons.	
A systematic review and meta-analysis completed by the Neuropathic Pain Special Interest Group of IASP evaluated the effects of a wide range of pharmacological therapies on people with neuropathic pain. The authors suggest that a result with number needed to treat (NNT) of 10 or below is clinically significant. The review reported evidence of a small difference in 50% pain reduction between gabapentinoids (gabapentin, mirogabalin and pregabalin) compared with placebo (risk difference 0.11 (no scale described), 95% CI 0.09 to 0.13, 46 RCTs, 14,192 participants: moderate quality evidence). There was a similar difference in 30% pain reduction between gabapentinoids compared with placebo (risk difference 0.13 (no scale described), 95% CI 0.06 to 0.21, four RCTs, 860 participants: moderate quality evidence). The combined NNT across 56 studies was 8.9 (95% CI 7.4 to 11.1).[63] Evidence for carbamazepine/oxcarbazepine, lacosamide, lamotrigine and topiramate was assessed to be inconclusive (all low or very low-certainty evidence) and the authors did not make recommendations for or against their use.[63] A recommendation was made against use of sodium valproate (pooled effect estimate not available, authors noted teratogenicity and other adverse effects) and against use of levetiracetam (risk difference for 50% pain reduction or moderate pain relief 0.03, 95% CI -0.03 to 0.09, four RCTs, 130 participants: low certainty evidence).[63]	1++
Two further systematic reviews investigated the benefits of pregabalin or gabapentin for neuropathic pain without further specifying the type of neuropathic pain.[49,56] Pregabalin or gabapentin provided significantly better pain relief compared with placebo when measured in percentage change in pain intensity or PGIC.[56] The level of pain relief provided by these drugs was very similar (≥50% reduction in pain intensity by pregabalin risk ratio (RR) 1.72, 95% CI 1.37 to 2.16; 15 RCTs, 4,247 participants: and ≥50% reduction in pain intensity by gabapentin RR 1.76, 95% CI 1.34 to 2.32; six RCTs, 1,851 participants: no evidence certainty rating).[56] A meta-analysis	1+ 1++

pooling data from 15 trials reported a small but statistically significant reduction in pain in people using either pregabalin or gabapentin compared with placebo (MD -0.61 on a 0–10 scale, 95% CI -0.87 to -0.36; 15 RCTs, 4,832 participants: moderate certainty evidence).[49] Based on three small head-to-head trials, there was no difference in pain reduction between pregabalin or gabapentin (effect size not reported; three RCTs, 433 participants: low certainty evidence). Pregabalin or gabapentin compared with placebo also provided a small but significant improvement in sleep (MD -0.65 measured on a 0–10 scale, 95% CI -0.89 to -0.41; 15 RCTs, participants not reported: no evidence certainty rating) but not anxiety or depression measured with the Hospital Anxiety and Depression Scale (Anxiety: SMD -0.11, 95% CI -0.25 to 0.03; eight RCTs, participants not reported: no evidence certainty rating. Depression: SMD -0.01, 95% CI -0.14 to 0.11; eight RCTs, participants not reported: no evidence certainty rating).[49]

4.2.3 Postherpetic neuralgia

The Cochrane systematic review of pregabalin for neuropathic pain reported that pregabalin provided a significant dose-dependent reduction in pain intensity compared with placebo in people with postherpetic neuralgia (≥50% reduction in pain intensity by 150 mg daily dose: RR 1.96, 95% CI 1.41 to 2.74; four RCTs, 360 participants: low certainty evidence, by 300 mg daily dose: RR 2.52, 95% CI 1.86 to 3.42; four RCTs, 713 participants: moderate certainty evidence, by 600 mg daily dose: RR 2.66, 95% CI 2.04 to 3.48; four RCTs, 365 participants: moderate certainty evidence). Similar results were also found with the PGIC.[60] However, in a further systematic review, there was no difference in function measured using the brief Pain Inventory Interference scale between groups receiving gabapentin or placebo (MD -0.23, 95% CI -0.70 to 0.23; one RCT, 371 participants: low certainty evidence).[49] 1++

4.2.4 HIV neuropathy, central neuropathic pain, and mixed neuropathic pain

One systematic review described trials comparing 600 mg daily pregabalin with placebo in people with human immunodeficiency virus (HIV) neuropathy, central neuropathic pain, or mixed neuropathic pain. Pregabalin provided significant reduction in pain intensity for people with central neuropathic pain (≥50% reduction in pain intensity RR 1.62, 95% CI 1.28 to 2.03; three RCTs, 562 participants: low certainty evidence), or mixed neuropathic pain (≥50% reduction in pain intensity RR 1.51, 95% CI 1.23 to 1.85; four RCTs, 1,367 participants: moderate certainty evidence) but not HIV neuropathy (≥50% reduction in pain intensity RR 0.86, 95% CI 0.70 to 1.06; two RCTs, 674 participants: moderate certainty evidence).[60] 1++

4.2.5 Lumbar radicular pain and lower back pain with or without radiating leg pain

A systematic review of the effects of anticonvulsants for the treatment of non-specific lower back pain, with or without radiating leg pain, or lumbar radicular pain (sciatica or neurogenic claudication secondary to lumbar spinal stenosis) included trials of gabapentin use at doses from 15 mg/kg/day to 3,600 mg/day. The review found that in people with low back pain with or without radiating leg pain gabapentin was not better than

placebo in reducing pain (MD 0.0 on a 0–10 Numerical Pain Rating Scale (NPRS), 95% CI -0.8 to 0.7; three RCTs, 195 participants: high certainty evidence) or disability (MD -0.2 on a 100-point ODI, 95% CI -5.9 to 5.5; one RCT, 71 participants) in the short term. In contrast, a trial comparing 300 mg/day topiramate and placebo in people with lower back pain with or without radiating leg pain found topiramate effective in reducing pain (MD -11.4 on a 78-point scale, 95% CI -16.7 to -6.1), although not disability (MD -4.9 on a 100-point ODI, 95% CI -19.4 to 9.6; one RCT, 89 participants: moderate certainty evidence) in the short term.[55]

In people with lumbar radicular pain, there was no evidence of any effect of antiepileptics on pain compared with placebo in the immediate term (≤2 weeks after randomisation) (MD -0.1 on a 0–10-point NPRS, 95% CI -0.7 to 0.5; two RCTs, 255 participants: high certainty evidence). The effects of antiepileptics on pain in the short term were inconsistent. One trial reported a statistically significant reduction in pain compared with placebo in people using up to 3,600 mg/day gabapentin (MD -0.8 on a 0–3-point NPRS, 95% CI -1.2 to -0.5; one RCT, 43 participants), but a further and larger trial reported no evidence of an effect of up to 600 mg/day pregabalin on pain compared with placebo (MD 0.6 on a 0- to 10-point NPRS, 95% CI -0.2 to 1.4; one RCT, 207 participants). There was no effect of antiepileptics on pain compared with placebo in the intermediate-term (MD -0.1 on a 0- to 10-point NPRS, 95% CI -0.9 to 0.7, one RCT, 184 participants: high certainty evidence) or long-term (MD 0.4 on a 0- to 10-point NPRS, 95% CI, -0.5 to 1.3; one RCT, 178 participants: moderate certainty evidence).[55] 1++

There was no effect of antiepileptics on disability over any follow-up period, including immediate-term (pooled SMD -0.1, 95% CI -0.3 to 0.2; two RCTs, 249 participants: high certainty evidence); short-term (MD 0.6 on a 23-point RMDQ, 95% CI -1.5 to 2.7; one RCT, 182 participants: moderate certainty evidence); intermediate-term (MD -1.4 on a 23-point RMDQ, 95% CI -3.6 to 0.8; one RCT, 172 participants: moderate certainty evidence) and long-term (MD 0.8 on a 23-point RMDQ, 95% CI -1.5 to 3.1; one RCT, 162 participants: moderate certainty evidence) durations.[55]

Similarly, 400 mg/day of topiramate did not reduce pain (MD -0.7, 95% CI -2.1 to 0.6 on a 0- to 10-point NPRS; one RCT, 58 participants: very low-certainty evidence) or disability (MD -2.0 on a 100-point ODI, 95% CI -10.0 to 6.0; one RCT, 58 participants: low certainty evidence) in the intermediate term compared with placebo.[55]

4.2.6 Pelvic pain

Mixed results were identified on the effectiveness of gabapentin compared with placebo in reducing pelvic pain. One systematic review found a significant reduction in pain at three months (MD -0.79, 95% CI -1.23 to -0.35; two RCTs, 76 participants) and six months (MD -1.68, 95% CI -2.30 to -1.05, two RCTs, 59 participants) when measured using VAS, but only at three months (MD -0.2, 95% CI -0.25 to -0.15; two RCTs, 256 participants) and not at six months (MD -0.27, 95% CI -0.80 to 0.26; two RCTs, 256 participants) when measured using a Numerical Rating Scale.[62] The certainty of evidence was not reported.

4.2.7 Fibromyalgia

Trials comparing pregabalin or gabapentin to placebo in people with fibromyalgia found a small but statistically significant reduction in pain (MD -0.59 on a 0–10-point scale, 95% CI -0.75 to -0.43; nine RCTs, 5,081 participants: moderate certainty evidence), improvement in function (SMD -0.21 on Fibromyalgia Impact Questionnaire 0 to 80 or 0–100, 95% CI -0.28 to -0.15, eight RCTs, 5,074 participants: moderate certainty evidence), and sleep (various measures used: SMD -0.33, 95% CI -0.40 to -0.25; seven RCTs, participants and evidence certainty not reported). Although, improvements were also seen in the Hospital Anxiety and Depression Scale for depression (SMD -0.11, 95% CI -0.18 to -0.03; five RCTs, participants and evidence certainty not reported) and anxiety (SMD -0.11, 95% CI -0.25 to -0.02; five RCTs, participants and evidence certainty not reported), these results fell below the threshold for a small effect and are unlikely to be clinically important.[49]

4.3 Evidence of harms

4.3.1 Pregabalin / gabapentin

In a systematic review of head-to-head trials of medication used in the management of chronic pain, there was no statistically significant difference between groups receiving gabapentanoids or TCAs in number of withdrawals during active treatment (risk difference 0.02, 95% CI -0.03 to 0.07, nine RCTs, 953 participants: moderate certainty evidence) or number of trial dropouts because of adverse events (risk difference -0.02, 95% CI -0.06 to 0.02, nine RCTs, 953 participants: moderate certainty evidence). The most frequent adverse events for people receiving tricylic antidepressants were dry mouth and dizziness. People receiving gabapentinoids most frequently reported somnolence and dizziness.[59]	1+
A meta-analysis pooling results from trials investigating pregabalin or gabapentin compared with placebo found no significant increase in the risk of having a serious adverse event (RR 0.94, 95% CI 0.63 to 1.40; 21 RCTs, 8,622 participants: low certainty evidence). Subgroup analyses by pain condition, specific drug, dose and study quality did not alter these results. However, there was a moderate increase in withdrawals due to adverse events (RR 1.74, 95% CI 1.51 to 2.03; 28 RCTs, 10,148 participants: moderate certainty evidence).[49] Similar findings were reported in other systematic reviews.[55,56,60,63]	1++
Specific adverse events in which significant increases were noted included sedation, dizziness, cognitive effects, weight gain, and peripheral oedema (RR ranged from 2.32 for peripheral oedema to 3.57 for weight gain).[49] A further systematic review reported a variety of specific adverse events, with the highest risk being for inco-ordination in pregabalin trials (RR 7.21, 95% CI 1.36 to 38.25; three RCTs, 1,294 participants: evidence certainty not reported) and weight gain in gabapentin trials (RR 5.61, 95% CI 1.04 to 30.22; two RCTs, 504 participants: evidence certainty not reported). Trials did not report the incidence of gabapentinoid misuse disorder.[56]	

4.3.2 Oxcarbazepine

In one systematic review, oxcarbazepine did not significantly increase the risk of serious adverse events compared with placebo (RR 1.82, 95% CI 0.74 to 5.05; two RCTs, 493 participants: low certainty evidence), but led to a large increase in withdrawals due to adverse events (RR 3.64, 95% CI 1.86 to 7.12; two RCTs, 493 participants: low certainty evidence). Participants receiving oxcarbazepine reported more sedation (RR 3.13, 95% CI 0.74 to 16.08; two RCTs, 490 participants: low certainty evidence) and/or hyponatremia (RR 5.93, 95% CI 0.55 to 63.8; two RCTs, 490 participants: low certainty evidence) compared with participants receiving placebo, but the difference was not statistically significant.[49]

In a further systematic review and meta-analysis which evaluated pooled effects of medications compared with placebo in people with neuropathic pain, risk difference for study withdrawal was statistically significantly higher in groups using oxcarbazepine or carbamazepine than placebo (risk difference 0.18, 95% CI 0.13 to 0.23, five RCTs, 709 participants: very low-certainty evidence).[63]	1++

4.3.3 Topiramate

One systematic review of antiepileptics used in people with low back pain identified two RCTs where effects of topiramate were reported. One RCT comparing 400 mg/day topiramate with placebo found no significant increase in the number of participants reporting adverse events (RR 1.2, 95% CI 0.9 to 1.6, one RCT, 58 participants: very low-certainty evidence). A further RCT where topiramate was titrated from 50 mg to 300 mg per day found differences in the number of adverse events reported between topiramate (21 events among 48 participants) and placebo groups (10 events among 48 participants) however effects were not calculated as the total number of participants who experienced an event was not reported.[55]	1++
In a further systematic review and meta-analysis which evaluated pooled effects of medications compared with placebo in people with neuropathic pain, risk difference for study withdrawal was statistically significantly higher in groups using topiramate than placebo (risk difference 0.16, 95% CI 0.13 to 0.20, three RCTs, 1,668 participants: very low-certainty evidence).[63]	1++

4.4 Summary of benefits and harms of antiepileptics for chronic pain

Gabapentinoids are associated with statistically significant reductions in pain intensity compared with placebo in people with unspecified neuropathic pain, and specific types of neuropathic pain (due to diabetic neuropathy, postherpetic neuralgia and central neuropathic pain) with risk ratio for ≥50% reduction in pain intensity ranging from 1.3 (treatment of diabetic peripheral neuropathic pain with 150 mg/day pregabalin) to 2.2 (treatment of postherpetic neuralgia with 600 mg/day pregabalin). There is evidence of higher efficacy at higher doses of gabapentinoids in people with diabetic neuropathic pain and postherpetic neuralgia. Reductions in pain severity, as well as secondary measures including quality of life, are

likely similar for patients treated with gabapentinoids compared with patients treated with TCAs. There is some evidence of a beneficial effect on sleep in unspecified neuropathic pain. Gabapentinoids were not effective in pain relief in trials of HIV-related neuropathy.

Gabapentin and pregabalin are not more effective in reducing lumbar/radicular pain or improving function than placebo. In women with chronic pelvic pain, there is limited evidence of efficacy of gabapentin, with differing results in different studies using different measures of efficacy and at different timepoints. In people with fibromyalgia, there is evidence of a small statistically significant reduction in pain severity, although these effect sizes may not be clinically significant.

There is limited and inconsistent evidence of efficacy of non-gabapentinoid antiepileptic medications in people with low back pain. One study of people with low back pain with or without radiating leg pain reported topiramate reduced pain intensity in the short term while a further study reported no effects of topiramate on pain in the intermediate term in people with lumbar radicular pain. Oxcarbazepine is associated with a small reduction in pain in people with diabetic neuropathy which is statistically significant but not clinically significant.

Gabapentin, pregabalin and oxcarbazepine were associated with study withdrawal due to adverse events. However, the rate of serious adverse events was not elevated compared with placebo. There was mixed evidence of harms associated with topiramate with one systematic review reporting increased risk of study withdrawal in people using topiramate compared with placebo, but a further review included a trial of topiramate which reported no increase in adverse events compared with placebo. In clinical practice, oxcarbazepine commonly causes sedation, unsteadiness, irritability and weight changes. These may not have been observed due to the small sample size of the trials. No study reported risk of gabapentinoid misuse, or risks of use in combination with opioid medications.

4.5 Other factors

Specific antiepileptic drugs (currently sodium valproate and topiramate) may only be prescribed subject to restrictions, including a pregnancy prevention programme. Restrictions apply to both females and males. Prescribers should review current safety and educational information provided by UK Government. Versions current at the time of writing are available on use of valproate in men and women under 55 years of age, use of valproate in men (additional fertility advice) and topiramate. Some patients may prefer not to enrol in a pregnancy prevention programme or agree to other restrictions, which may affect the range of medications available to them.

Only one trial of long-term treatment was included in any systematic review used as evidence within this guideline section and therefore there is insufficient evidence on the long-term efficacy and harms of antiepileptic drugs for the management of chronic pain to support recommendations beyond six months' duration.

The guideline development group (GDG) notes that it is common practice for people with chronic pain to remain on these medicines long term and advises that patients should be reviewed appropriately to monitor efficacy and adherence. Scottish Government has published Manage My Meds – for patients and carers to help support people to manage medical therapy and prepare for a medicines review.

Not all antiepileptic medications are licensed for use in the management of chronic pain. This does not preclude their use, however clinicians should consider this when prescribing and appropriately consent the patient to use.

This guideline did not review the evidence for using carbamazepine for trigeminal neuralgia. Trigeminal neuralgia appears in the International Classification of Headache Disorders, and as headache is an exclusion criterion for the literature review, is omitted from the scope of this guideline. Carbamazepine remains the only licenced treatment for trigeminal neuralgia and is commonly used in this indication.

The GDG notes that the potential for gabapentinoid misuse remains poorly characterised, and that none of the reviewed literature reported the risk of gabapentinoid misuse. Therefore, the potential for misuse should be subject to clinical judgement on an individual basis.

In January 2026, the Medicines and Healthcare Products Regulatory Agency (MHRA) updated and strengthened the warnings regarding addiction, dependence, withdrawal and tolerance for gabapentin, pregabalin, benzodiazepines, and z-drugs. Strengthened warnings have been included in the SmPc, patient information leaflets and outer packaging of these medications. Full details, including current advice and information for communication with patients are available from the MHRA.

Gabapentinoids, both illicitly sourced and legally prescribed, are increasingly being implicated in drug-related deaths, especially when co-prescribed with opioids.[64] Gabapentinoids can be abused in the community and particularly within the prison service. Consequently, caution should be exercised and alternatives considered when prescribing to patients with a history of substance misuse or who are detained within the prison service.

It is common for people with chronic pain to use more than one medication to manage their pain and/or to manage other comorbidities. Careful consideration needs to be given to the increased risk of harm when using antiepileptic drugs in combination with other medicines, such as opioids and benzodiazepines (see section 7).

4.6 Recommendations

R **Gabapentinoids (gabapentin and pregabalin) should be considered in patients with neuropathic pain, fibromyalgia or pelvic pain for up to six months. It is not possible to recommend one drug over the other.**

✓ Individuals who are prescribed pregabalin or gabapentin should be regularly reviewed to monitor for adverse effects and reduced efficacy. Following medication review, use of these medications should be weaned and potentially withdrawn based on shared decision making with the patient in the context of either of these situations.

R **Gabapentinoids should be titrated to maximum tolerated dose (pregabalin: up to 600 mg/day, gabapentin: up to 3,600 mg/day) before efficacy is ruled out.**

✓ Information about potential adverse effects of antiepileptic medications, including dose-dependent effects and their reversal on discontinuation, should be clearly explained to patients.

5 Muscle relaxants

5.1 Introduction

Muscle relaxants are a broad range of drugs that include benzodiazepines (BZD), non-BZD antispasmodics and antispasticity agents. Although frequently prescribed in the UK for conditions involving acute muscle spasm,[65] their role in the management of chronic pain is less well understood. Benzodiazepines are indicated for short-term use (two to four weeks only) to treat severe anxiety and severe insomnia, both of which can occur with acute and chronic painful conditions.

Use of BZDs in people who have been prescribed other medication to manage chronic pain is particularly dangerous as the benzodiazepine-opioid combination, for example, can lead to potentially life-threatening respiratory depression (see section 7.3).

5.2 Evidence of benefit

Two systematic reviews and one NMA were identified.

The first review assessed the efficacy of skeletal muscle relaxants for the treatment of fibromyalgia from 14 RCTs which included 1,851 participants. The systematic review included a range of skeletal muscle relaxants. Non-BZD muscle relaxants were the most frequently investigated type of muscle relaxant with cyclobenzaprine being the most widely used drug (10 RCTs). Carisoprodol and chlormezanone were the other two non-BZD muscle relaxant studied. The remaining studies focused on alprazolam (two RCTs). All studies compared muscle relaxants against a placebo, and one three-arm study compared cyclobenzaprine with amitriptyline or a placebo. Most of the study drugs used in the systematic review are not licensed for use in NHS Scotland. The only drug which is available is alprazolam which is only licensed for the short-term symptomatic treatment of severe anxiety, therefore the GDG did not consider this evidence any further.[66] 1++

Another high-quality systematic review and meta-analysis assessed the efficacy, acceptability, and safety of muscle relaxants for adults with non-specific low back pain.[65] Of the trials included in the meta-analysis, two involved people with chronic pain. Antispastic muscle relaxants did not reduce chronic back pain intensity (MD -5.4, 95% CI -13.7 to 2.9; one RCT, 80 participants: very low-certainty evidence) or disability (MD -3.2, 95% CI -8.3 to 1.8; one RCT, 80 participants: very low-certainty evidence) at 3–13 weeks compared with control. A single RCT reported benefit of adding the sedative eszoplicone (described as a “miscellaneous muscle relaxant“ by authors of this systematic review) as a treatment for insomnia to standard pain medication regimen (twice daily naproxen 500 mg). Participants receiving eszoplicone reported reduced chronic back pain intensity (MD -19.9 on a 0–100 point scale, 95% CI -31.5 to -8.3; one RCT, 52 participants: moderate certainty evidence) but not disability (MD -5.6, 95% CI -20.6 to 9.4; 1 RCT, 52 participants: low certainty evidence) at 3–13 weeks compared with control. 1++

A NMA identified 52 RCTs which compared two or more treatment modalities, including muscle relaxants, in patients with painful temporomandibular disorders of muscular origin. Muscle relaxants had no statistically significant effect on post-treatment pain (SMD -0.48, 95% CI -1.09 to 0.13, five RCTs, 161 participants: very low-certainty evidence). Based on short-term follow-up (less than five months), muscle relaxants had a small effect on pain (MD -0.73 (scale not reported), 95% CI -1.39 to -0.06; five RCTs, 161 participants: very low-certainty evidence).[67] | sufficient

5.3 Evidence of harms

The systematic review of muscle relaxants for adults with non-specific low back pain reported that no difference was found in the risk of experiencing an adverse event with miscellaneous muscle relaxants compared with control (RR 1.5, 95% CI 0.4 to 5.7; two RCTs, 95 participants: moderate certainty evidence). The authors note that whilst muscle relaxants are typically prescribed for short-term use, the effects of long-term use are not known. This is particularly important when considering that a risk of dependency and misuse associated with muscle relaxants has been observed from indirect evidence.[65] | 1++

5.4 Summary of benefits and harms of muscle relaxants for chronic pain

There is insufficient evidence to support the use of muscle relaxants which are available in the UK for treatment of chronic pain of any type. There is also an absence of long-term safety outcome data.

5.5 Other factors

Scottish Government has published a Quality Prescribing Guide on benzodiazepines and z-drugs which aims to improve the care of individuals receiving these medicines and promote a holistic approach to person-centred care.[68]

In January 2026, MHRA updated and strengthened the warnings regarding addiction, dependence, withdrawal and tolerance for gabapentin, pregabalin, benzodiazepines, and z-drugs. Strengthened warnings have been included in the SmPc, patient information leaflets and outer packaging of these medications. Full details, including current advice and information for communication with patients are available from the MHRA.

5.6 Recommendations

✓ Prescribers should be familiar with up-to-date advice on the safe use of benzodiazepines, and z-drugs.

6 Topical analgesia

6.1 Introduction

Topical analgesics are medications that are applied on or massaged into the skin to temporarily relieve superficial pain or pain of muscles or joints. Formulations include patches or plasters that are stuck directly to the skin surface and creams which are rubbed into the skin. Topical analgesics have the potential to benefit localised pain, while reducing the likelihood of systemic adverse effects. Some topical agents, such as NSAIDs and menthol can be obtained over the counter without prescription. Capsaicin cream (at 0.025% or 0.075% concentrations), on the other hand, is only available by prescription.

Topical analgesics, including NSAIDs and plant alkaloids, have been widely used in people with chronic pain, although there remains uncertainty about the supporting evidence for some agents. They often have to be applied frequently and may be inconvenient to apply, causing localised skin irritation.

6.2 Evidence of benefit

Three systematic reviews were identified which focused, respectively, on topical capsaicin for neuropathic pain,[69] capsaicin, diclofenac and lidocaine used generally in people with chronic pain,[49] and the use of topical diclofenac in the management of chronic musculoskeletal pain.[70] A further systematic review was identified on use of the vasodilator topical clonidine,[71] which is licensed only for prevention of migraine or recurrent headache or for the management of vasomotor conditions commonly associated with the menopause, therefore this evidence is not further considered in this guideline. All systematic reviews were of high quality, but the included RCTs varied from moderate to very low in the quality and certainty of evidence for outcomes of interest. 1++

6.2.1 Pain intensity

<u>Topical capsaicin</u>

One systematic review reported no statistically significant participant-reported clinically meaningful response in people with diabetic neuropathy, postherpetic neuralgia or trigeminal neuralgia who received topical capsaicin cream or patch compared with placebo at four weeks or less (RR 1.60, 95% CI 0.93 to 2.75; two RCTs, 175 participants: no evidence certainty rating).

The review reported a clinically meaningful response (at least 30% improvement in pain) in people who received topical capsaicin cream or patch compared with placebo over six to 52-weeks follow-up (RR 1.40, 95% CI 1.26 to 1.55; ten RCTs, 2,344 participants: low certainty evidence). Both low-dose capsaicin patches (at 0.625% or 1.25% by weight) or creams (at 0.075% by weight) which were applied frequently (RR 1.56, 95% CI 1.20 to 2.03; seven RCTs, 534 participants: no evidence certainty rating) and high-potency capsaicin patches (8% by weight) which were 1++

applied less frequently (RR 1.36, 95% CI 1.22 to 1.52; six RCTs, 1,810 participants: no evidence certainty rating) provided a significant reduction in pain.[69]	
A further systematic review reported that while 8% topical capsaicin patch reduced pain severity in the short term in people with HIV-related neuropathy or postherpetic neuralgia, the magnitude of benefit fell below the prespecified level for a small effect (MD -0.33 on a 0–10-point scale, 95% CI -0.60 to -0.00; three RCTs, 1,051 participants: moderate certainty evidence). There was no significant difference in pain response (≥30% reduction in pain) between people receiving topical capsaicin or controls (RR 1.17, 95% CI 0.98 to 1.37; three RCTs, 1,051 participants: moderate certainty evidence).[49]	1++
Topical diclofenac	
The same systematic review evaluated topical diclofenac for chronic pain in people with osteoarthritis of the knee. Diclofenac improved pain severity in the short term (MD -0.58, 95% CI -0.81 to -0.35; four RCTs, 1,451 participants: moderate certainty evidence). Meta-analysis of pain response (≥30% reduction in pain) also resulted in a small effect in favour of diclofenac (RR 1.20, CI 1.09 to 1.38; three RCTs, 1,232 participants: moderate certainty evidence).[49]	1++
A further systematic review investigated use of topical diclofenac to manage pain in people with a range of chronic musculoskeletal pain conditions, mainly osteoarthritis of the knee. Based on studies with follow-up over two to six weeks, topical diclofenac had a small effect on ≥50% pain reduction (number needed to treat (NNT) of five) compared with placebo (RR 1.86, 95% CI 1.50 to 2.31; five RCTs, 732 participants: moderate certainty evidence). A smaller effect on ≥50% pain reduction (NNT of 9.5) compared with placebo was sustained in studies which were followed up over six to 12 weeks (RR 1.22, 95% CI 1.13 to 1.30; five RCTs, 2,652 participants: moderate certainty evidence). There was no significant difference in pain reduction between topical diclofenac and an oral NSAID (diclofenac or ibuprofen) (RR 0.98, 95% CI 0.89 to 1.08; three RCTs, 1,230 participants: no evidence certainty rating).[70]	1++
Lidocaine patch	
A systematic review identified two studies on topical lidocaine, one in participants with knee osteoarthritis which was terminated early and one in people with diabetic peripheral neuropathic pain in which all participants received pretreatment with lidocaine cream in addition to the lidocaine patch, limiting applicability to this evidence review. There is insufficient evidence available to draw conclusions about the effectiveness or lidocaine patches for the management of chronic pain.[49]	1++

6.2.2 Function

Topical capsaicin

No evidence was identified which reported on function in people with chronic pain who were treated with topical capsaicin.

Topical diclofenac

One systematic review reported no effect on short-term function in people treatment with topical diclofenac compared with placebo (MD -0.51, 95% CI -1.06 to 0.04; four RCTs, 1,538 participants: moderate certainty evidence).[49] 1++

Lidocaine patch

No evidence was identified which reported on function in people with chronic pain who were treated with lidocaine patches.

6.2.3 Quality of life

None of the systematic reviews reported evidence on the effects of any topical analgesic on QoL outcomes.

6.3 Evidence of harms

6.3.1 Adverse events and study withdrawal

Topical capsaicin

A systematic review of studies including people with diabetic neuropathy, postherpetic neuralgia or trigeminal neuralgia reported greater of risk application site burning, stinging and/or erythema (RR 1.63, 95% CI 1.50 to 1.79) and application site pain (RR 2.38, CI 1.99 to 2.84) in people using topical capsaicin compared with placebo. The review reported withdrawals due to adverse events occurred in 6% of participants using topical capsaicin, compared with 2% using control (RR 3.31; CI 1.56 to 7.01; three RCTs, 1,027 participants: low certainty evidence).[69] 1++

A further systematic review in people with HIV-related neuropathy or postherpetic neuralgia reported a greater risk of both application site erythema (RR 1.46, 95% CI 1.29 to 1.66; three RCTs, 1,075 participants: moderate certainty evidence) and application site pain (RR 2.26, 95% CI 1.61 to 2.82; three RCTs, 1,075 participants: moderate certainty evidence). The review reported no statistically significant increase in the likelihood of study withdrawal due to adverse events (RR 2.20, 95% CI 0.37 to 12.91; three RCTs, 1,075 participants: moderate certainty evidence).[49] 1++

Topical diclofenac

The same systematic review also reported no evidence of increased risk of serious adverse events associated with use of topical diclofenac (RR 1.03, CI 0.29 to 27.01;two RCTs, 912 participants: low certainty evidence) or study withdrawal due to adverse events in studies involving people with osteoarthritis of the knee (RR 1.50, 95% CI 0.81 to 3.58; four RCTs, 1,549 participants: low certainty evidence).[49] 1++

A further systematic review which included studies of a range of chronic pain conditions, but mainly osteoarthritis of the knee, reported an increased risk of local adverse events, such as dry skin, redness or erythema and pruritis (RR 1.62, 95% CI 1.36 to 1.93; 12 RCTs, 3,774 participants: moderate certainty evidence) and withdrawal due to adverse events (RR 1.50, 95% CI 11 to 2.0; ten RCTs, 3,093 participants: 1++

moderate certainty evidence) associated with use of topical diclofenac compared with placebo.[70]

Lidocaine patches

No evidence was identified which reported on adverse events or study withdrawal in people with chronic pain who were treated with lidocaine patches.

6.4 Summary of benefits and harms of topical analgesia for chronic pain

Based on moderate-certainty evidence from two systematic reviews, there was a small effect of topical diclofenac on pain severity in the short term for people with musculoskeletal pain. There was no evidence of increased risk of serious adverse effects, and all reported harms are minor, self-resolving and limited to local effects.

There was evidence of benefit on pain reduction for topical capsaicin from two systematic reviews, however the clinical importance of the effects was unclear. While more people experienced a clinically meaningful response from treatment with capsaicin than placebo in one review (49% v 34%), this represented less than half of those in the treatment group.[69]

There is little evidence available on the effect of topical analgesics on function, and no evidence of benefit.

Despite absence of published evidence of benefit or harm compared with placebo, the guideline development group acknowledge that some individuals using lidocaine plasters experience pain relief and that it may be an option for people with neuropathic pain that has not responded to other treatments and where there are no further treatment options. There is no evidence or clinical rationale for the use of lidocaine plasters in musculoskeletal or non-superficial pain.

6.5 Other factors

In October 2014, the SMC advised that capsaicin (Qutenza®) is accepted for restricted use within NHS Scotland for the treatment of peripheral neuropathic pain in non-diabetic adults who have not achieved adequate pain relief from, or have not tolerated, conventional first and second line treatments.

However, in March 2016, the SMC advised that capsaicin (Qutenza®) is not recommended for use within NHS Scotland for the treatment of peripheral neuropathic pain in diabetic adults either alone or in combination with other medicinal products for pain (see section 14.4).

Scottish Government has published guidance to promote the effective use of medicines and minimise unwarranted variation in prescribing practice across NHS Scotland.[72] This guidance advises that rubefacients (with the exception of capsaicin and topical NSAIDs) are medications of low clinical effectiveness and should not be prescribed in primary or secondary care. This guidance also classifies lidocaine plasters as medications of limited clinical effectiveness where prescribing may be appropriate in some exceptional circumstances. Specifically, they may be prescribed to

individuals who have been treated in line with SMC guidance (see section 14.4) and are still experiencing neuropathic pain associated with previous herpes zoster infection (postherpetic neuralgia), or where the decision to prescribe is in line with the Scottish Palliative Care guideline, or where no other item or intervention is clinically appropriate or available. Consider deprescribing where safe and appropriate in individuals currently prescribed this item. Continued prescribing of these medicines should be subject to regular review.

There are a number of products available for topical pain relief over the counter. These may not necessarily be at the same concentrations or formulations as prescribed medications and individuals should consult with pharmacists or GPs for advice.

Topical diclofenac is commonly prescribed for musculoskeletal pain in Scotland and is also available over the counter.

Lidocaine patches are commonly prescribed and patients perceive benefits, however there is considerable variation in prescribing across Scotland and significant costs to health boards, while there is no conclusive evidence of an effect on pain or quality of life.

8% topical capsaicin patch is only available in secondary care and requires training for appropriate use.

6.6 Recommendations

R **Consider topical diclofenac in people with chronic musculoskeletal pain.**

R **Consider topical capsaicin cream 0.025% and 0.075% in people with chronic neuropathic pain. If tolerated, treatment should be maintained for at least six weeks.**

R **Consider referral to secondary care pain management for assessment for treatment with 8% capsaicin patch.**

✓ Consider a trial of lidocaine 5% medicated plasters in people who are experiencing superficial neuropathic pain associated with previous herpes zoster infection or superficial neuropathic pain in a postoperative scar, where extreme pain to light touch (allodynia) is present.

7 Combination pharmacological therapies

7.1 Introduction

Management of chronic pain is challenging due to the multifactorial influences which can modify pain responses, such as stress, sleep, diet, relaxation, relationships, etc. Therefore, pharmacological management is part of the many options available to support pain management.

In clinical trials, analgesics are considered effective if they demonstrate a reduction in pain intensity by 30% or 50%, and many are limited by adverse effects (see previous sections). Thus individuals may continue to have ongoing pain despite treatment. Many clinical conditions are managed by multiple medicines, eg hypertension, therefore it is reasonable to consider that the addition of a second, or even third, analgesic will reduce pain intensity whilst minimising adverse effects. Individuals are often commenced on a second or third analgesic, without the first being stopped at the time of initiation or after trial of the second, which can increase the risk of adverse effects, and many will continue the first analgesic even if ineffective.

The evidence of benefit and harms of monotherapy for simple analgesics (see section 3), antiepileptics (see section 4), muscle relaxants (see section 5) and topical analgesia (see section 6) are considered separately. Information on opioid, antidepressant and medicinal cannabis monotherapies is included in part 1 of SIGN 173.[22] This section considers the evidence for combination pharmacological therapies and the potential harms associated with these.

Combination pharmacological therapies are either a combination of analgesics, eg morphine and amitriptyline (ie an opioid and an antidepressant), or an analgesic and another therapy which may reduce pain perception/alter other factors affecting pain, eg amitriptyline and melatonin.

As with the initiation of any analgesic, efficacy should be regularly assessed and if there is no reduction in pain intensity, or improvement in function, then the therapy should be stopped or reduced to stop, to minimise adverse effects and medication interactions.

Non-pharmacological pain management options should always be considered in conjunction with analgesia.

7.2 Evidence of benefit

Three systematic reviews were identified which assessed the effectiveness of combination pharmacological therapies compared with single pharmacological therapies, on pain scores (30% reduction and 50% reduction), functional ability, quality of life, adverse events/drug reactions or dependency (physiological or psychological).

The reviews considered neuropathic pain,[73] fibromyalgia,[74] and low back pain and sciatica[75] in adults.

7.2.1 Pain intensity

Neuropathic pain

A systematic review and meta-analysis examining combination pharmacotherapy for treatment of neuropathic pain in adults included 40 RCTs.[73] Although the studies were of acceptable quality, they were downgraded due to incomplete outcome data, short duration of treatment (10 studies had durations less than three weeks), small sample sizes (nine studies had fewer than 30 participants), and high risk of bias (in 35 studies). Due to heterogeneity across many studies, meta-analysis was completed for only three combinations: between opioids and gabapentinoids, opioids and antidepressants, and gabapentinoids and antidepressants.	1+
Opioid and gabapentinoid combination Combination treatment with an opioid and gabapentinoid provided at least moderate/good pain relief (≥30% pain reduction) compared with gabapentin monotherapy (RR 1.27, 95% CI 1.01 to 1.59; two RCTs, 452 participants: no evidence certainty rating) but no statistically significant difference compared with opioid monotherapy (RR 1.06, 95% CI 0.80 to 1.40; three RCTs, 548 participants: no evidence certainty rating).[73]	1+
Opioid and antidepressant combination Combination treatment with an opioid and antidepressant provided at least moderate/good pain relief (≥30% pain reduction) compared with antidepressant monotherapy (RR 1.29, 95% CI 1.03 to 1.65; two RCTs, 214 participants: no evidence certainty rating), but no statistically significant difference compared with opioid monotherapy (RR 1.22, 95% CI 0.97 to 1.52; two RCTs, 214 participants: no evidence certainty rating).[73]	1+
Gabapentinoid and antidepressant combination Combination treatment with a gabapentinoid and antidepressant provided at least moderate/good pain relief (≥30% pain reduction) (RR 1.34, 95% CI 1.02 to 1.76; three RCTs, 502 participants: no evidence certainty rating) and (≥50% pain reduction) (RR 1.76, 95% CI 1.25 to 2.47; two RCTs, 390 participants: no evidence certainty rating) compared with antidepressant monotherapy. There was no significant difference between combination treatment with a gabapentinoid and antidepressant compared with gabapentinoid monotherapy for at least moderate/good pain relief (≥30%pain reduction) (RR 1.40, 95% CI 0.93 to 2.10; three RCTs, 527 participants: no evidence certainty rating), nor ≥50% pain reduction.[73] Authors of the systematic review concluded that there is no compelling evidence that combination therapies offer greater pain relief when compared with both constituent monotherapies. The studies compare different gabapentinoids (pregabalin and gabapentin) and different antidepressants (nortriptyline, imipiramine and duloxetine), thus there is the potential for further study to determine if	1+

there is a particular combination which may yield improved outcomes.

The GDG notes that where there was a benefit in combination therapy, the choice of second agent was important in relation to the first with addition of antidepressant having no benefit, but addition of opioid yielded greater intensity reductions than gabapentinoid. However, this should be balanced against the harms of these medicines (see sections 4.3 and 7.3 of SIGN 173[22] and section 7.3 of this guideline).

Fibromyalgia

A systematic review evaluated combination pharmacotherapy for the treatment of fibromyalgia in adults. Most of the included studies are of low or very low quality due to methodological bias or poor design (eg limited comparisons to monotherapies, low numbers, short duration).[74]

Many combinations in the systematic review are not commonly used in clinical practice and were not considered relevant to the guideline target population, eg carisoprolol, paracetamol and caffeine (carisoprolol is not licensed in the UK), or NSAID and benzodiazepine (which are avoided due to known risks of long-term benzodiazepines). Heterogeneity of study outcomes and the specific drugs used in combination meant that meta-analysis was not possible. The authors note that none of the combinations of drugs provided sufficient data for analysis compared with placebo or other comparators for any outcome and they provide a narrative description of results. They note that three RCTs provide evidence of benefit for different drug combinations on pain outcomes compared with monotherapy. Evidence certainty was not reported as no pooled effects were calculated although the quality of these studies was low or very low. 1++

Melatonin and amitriptyline combination

One RCT (63 participants), which was assessed by the systematic review authors to be at moderate or low risk of bias for most aspects of methodology except size of study and similarities of baseline characteristics (high risk of bias), compared the combination of melatonin and amitriptyline with each drug as a monotherapy. There were no results reported for patient-reported pain relief of ≥30% or ≥50%. Participants receiving melatonin and amitriptyline in combination had significantly lower VAS pain scores compared with participants receiving amitriptyline monotherapy and significantly larger improvements in Fibromyalgia Impact Questionnaire (FIQ) score (which measures pain, fatigue, rest/sleep, stiffness, anxiety, and depression) compared with both monotherapies (effect sizes not reported).[74]

The GDG notes that pain is multifactorial and improved sleep quality can improve pain, therefore it is not unexpected that melatonin may reduce pain intensity via sleep improvement. This is supported by the study authors' conclusion that melatonin, alone or in combination, was effective in improving FIQ scores.

Amitriptyline and fluoxetine

One RCT (31 participants) compared the combination of amitriptyline and

fluoxetine with both monotherapies and placebo. There were no results reported for patient-reported pain relief of ≥30% or ≥50%. Considering secondary outcomes, combination therapy with amitriptyline and fluoxetine compared with both monotherapies produced significantly greater improvements in VAS scores of pain, sleep and global wellbeing and improved FIQ scores (effect sizes not reported).[74]

Pregabalin and duloxetine

One RCT (41 participants: very low-certainty evidence) compared the combination of pregabalin and duloxetine with both monotherapies and placebo. Combination therapy with pregabalin and duloxetine reduced pain scores from baseline (28%) statistically significantly more than pregabalin monotherapy (1.4%) or placebo (7.1%). Combination therapy participants experienced at least moderate pain relief (68%) significantly more than pregabalin monotherapy (42%), duloxetine monotherapy (39%) and placebo (18%) (effect sizes not reported).[74]

The authors of this systematic review concluded that there are too few high-quality trials evaluating the efficacy of combination pharmacological therapies in the management of fibromyalgia to support a recommendation for their use.

Chronic low back pain

One systematic review assessed the combination of two or more different drugs compared with constituent drug monotherapy or placebo for low back pain with or without sciatica.[75]

Of 27 RCTs, one small study reported a clinically significant benefit for combination pharmacotherapy (44 participants: low certainty evidence). The combination of transdermal buprenorphine (35 microgram/hour) and pregabalin (300 mg daily) in comparison to buprenorphine monotherapy showed a clinically important reduction in pain intensity measured by VAS for chronic back pain at immediate term, (two weeks or less) (MD -23.30 on a 0–100 mm scale, 95% CI -27.68 to -18.92; one RCT) and short term, (>two weeks but ≤12 weeks) (MD -27.60 on a 0–100 mm scale, 95% CI -31.70 to -23.50; one RCT) compared with buprenorphine monotherapy. 1+

Note that buprenorphine 35 micrograms/hour patch is the morphine equivalent daily dose of 84 mg, and recommendations regarding the prescribing of opioids should be considered.

The authors concluded that there was no clear evidence to support any combination drug therapy for the management of low back pain and sciatica, due to the limited number of studies and overall low quality of evidence.

7.3 Evidence of harms

Neuropathic pain

A systematic review and meta-analysis examining combination pharmacotherapy for treatment of neuropathic pain reported higher rates 1+

of adverse events in participants using combination therapy with an opioid and gabapentinoid (constipation, dry mouth, nausea, dizziness, fatigue, and somnolence) compared with groups using monotherapy (no effect size reported). A higher proportion of people using opioid and gabapentinoid combination (9.2%) dropped out of studies due to adverse events than those using opioid monotherapy (8.2%, no statistical comparison reported; four RCTs, 531 participants: no evidence certainty rating). A higher proportion of people using opioid and gabapentinoid combination (14.5%) also dropped out of studies due to adverse events than those using gabapentinoid monotherapy (4.6%, no statistical comparison reported; two RCTs, 395 participants: no evidence certainty rating).[73]

A lower proportion of people using opioid and antidepressant combination (8.4%) dropped out of studies due to adverse events than those using opioid monotherapy (12.1%, no statistical comparison reported; two RCTs, 107 participants: no evidence certainty rating). While a higher proportion of people using opioid and gabapentinoid combination (7.3%) dropped out of studies due to adverse events than those using antidepressant monotherapy (3.3%, no statistical comparison reported; three RCTs, 123 participants: no evidence certainty rating).

Study withdrawal due to adverse events was similar between those in gabapentinoid plus antidepressant (5.4%), antidepressant monotherapy (4.4%) and gabapentinoid monotherapy (5.7%) groups (no statistical comparison reported; three RCTs, 472 participants: no evidence certainty rating).

Fibromyalgia

One systematic review reported that adverse events were common in groups receiving combination therapies and controls, with no serious adverse events reported. Common adverse events were nausea, dizziness, somnolence, and headache.[74] 1++

Low back pain

The systematic review which focused on combination therapies for people with low back pain reported no serious adverse events in groups receiving the combination of transdermal buprenorphine (35 microgram/hour) and pregabalin (300 mg daily) compared with buprenorphine monotherapy. There was no statistically significant difference in incidence of any adverse event between groups receiving combination therapy and buprenorphine monotherapy (54.5% vs 63.6%, RR 0.86, 95% CI 0.52 to 1.41; one RCT; 44 participants: low certainty evidence), although in both groups over 50% of those receiving any pharmacological treatment experienced adverse events.[75]

Chronic pain in general

A further systematic review explored the safety issues around the use of gabapentinoids in the context of opioid use.[76] The review incorporated studies from a range of clinical settings including perioperative use, cancer pain and chronic non-cancer pain. As the review included two RCTs, four

case reports, three case-control studies, 14 cohort studies, and two cross-sectional studies, the data were analysed using narrative synthesis only.

All three case-control studies show evidence of an association between concurrent opioid and gabapentinoid use and opioid-related death. The first two studies reported, respectively, that concurrent prescribing of opioids and gabapentin (adjusted odds ratio (aOR) 1.49, 95% CI 1.18 to 1.88) or pregabalin (aOR 1.68, 95% CI 1.19 to 2.36) in the 120 days before death was associated with opioid-related death. Both studies noted that the highest doses of gabapentin (for ≥1800 mg gabapentin daily: aOR 1.58, 95% CI 1.09 to 1.27) and pregabalin (for >300 mg pregabalin daily: aOR 2.51, 95% CI 1.24 to 5.06) were linked to higher risks of drug-related death.

1+

The third nested case-control study was carried out in the UK and linked medical records from the Clinical Practice Research Database (CPRD) 1987–2015 for opioid analgesic users aged over 18 years with Office for National Statistics (ONS) death registrations 2000–2015 for opioid-related deaths.[77] The persistence of opioid utilisation (POU) was examined across three patient years. Persistent opioid use within one patient-year was defined as receiving an annual dose greater than or equal to oral morphine equivalent 4,500 mg covering three or more quarters in the year.

Individuals who were prescribed opioids persistently had a higher risk of opioid-related death compared with those who were not, and those who were also prescribed psychotropics concurrently had a greater risk (*see Table 2*).

Table 2: Association between persistent opioid prescribing and opioid-related deaths after adjusting for concurrent psychotropics

Use of medication	**Adjusted odds ratio of opioid-related death (95% CI)**
Persistent opioid prescribing (POU) and concurrent defined daily dose (DDD) >1 of benzodiazepines	6.5 (4.0 to 10.4), p<0.0001
POU and concurrent DDD >1 of gabapentinoids	6.2 (2.9 to 13.5), p<0.0001
POU and concurrent antipsychotics	4.3 (2.5 to 7.3), p<0.0001
POU and concurrent DDD 0 to ≤1 of benzodiazepines	3.6 (2.1 to 6.2), p<0.0001
POU and concurrent DDD >0.5 tricyclic antidepressants	2.0 (1.2 to 3.5), p=0.0342
POU in any of three patient-years	1.9 (1.2 to 2.9), p=0.0057

Note: for each comparison the accompanying reference value is an adjusted odds ratio of 1, representing no concurrent medication use, or, in the final row,

no persistent opioid prescribing.

Adapted with permission from Chen TC, Knaggs RD, Chen LC. Association between opioid-related deaths and persistent opioid prescribing in primary care in England: a nested case-control study. Br J Clin Pharmacol. 2022;88(2):798–809.[77]

These findings align with the evidence of harms in the opioid section of this guideline (see SIGN 173,[22] section 4.3), and the MHRA warnings issued in 2017 regarding the increased risk of respiratory depression with the combination of opioids and gabapentinoids.

7.4 Summary of benefits and harms of combination pharmacological therapies

Although commonly used in practice, there is limited evidence to support combination therapy over constituent monotherapies in the management of chronic pain. However, the GDG acknowledges that despite the lack of evidence, combination therapy is used, and it is common for people to be prescribed an antidepressant and gabapentinoid.

Clinicians should be aware that combination therapy may be used for outcomes other than chronic pain reduction, for example antidepressants may be required for the management of depression/anxiety, and therefore each person should be considered as an individual and any additions to existing treatments should consider the potential risks.

While some combinations did show benefit compared with some monotherapies in people with neuropathic pain (the addition of an opioid to a gabapentinoid or an antidepressant, or addition of a gabapentinoid to an antidepressant), in general, combinations with opioids were not more effective than opioid monotherapy and combination gabapentinoid plus antidepressant was not more effective than gabapentinoid alone.

There is insufficient high-quality evidence to determine the effectiveness and safety of combination therapies in the management of low back pain and/or sciatica, and the management of fibromyalgia.

Evidence for harms were poorly reported, inconsistent and it was not always reported whether differences in adverse events were statistically significant. Studies had small numbers of participants or were of low or very low quality. These studies should be used as the basis for further research.

Where combinations are used, clinicians should consider the potential harms of monotherapy and the potential for additive effects of combinations, and consult MHRA advice for any alerts.

7.5 Other factors

While the included evidence considers some people with chronic pain, there is an absence of information for populations with multimorbidity and the frail and/or elderly and conclusions may not be as applicable to these groups.

Clinicians should be aware of SMC restrictions and licensed indications of the combinations being prescribed, and any items of limited clinical value listed in the document released December 2024 Achieving Value and Sustainability in Prescribing (Achieving Value and Sustainability in Prescribing).

Individuals may choose to purchase analgesics over the counter including paracetamol, NSAIDs and codeine-containing products, which may confer increased risks of harm to the individual. The risk of divergence of medication, either to the individual or by the individual, should be considered, especially if there are unexpected adverse effects or lack of efficacy. A good therapeutic relationship between the clinician and individual is required to identify these.

7.6 Recommendations

R **In management of neuropathic pain, clinicians should carefully consider the addition of an opioid to gabapentinoid or antidepressant monotherapies, or addition of a gabapentinoid to an antidepressant, but not other combination therapies. Clinicians should note the limitations of evidence for long-term management of chronic pain for these medications.**

✓ Prescribing the combination of opioids and gabapentinoids should be carefully considered due limited evidence of benefit and the increased risk of respiratory depression and death.

8 Physical therapies (hands-off)

8.1 Introduction

This section of the guideline focuses on hands-off physical therapies including physical activity and mobility aids. The World Health Organization (WHO) defines physical activity as any bodily movement produced by skeletal muscles that results in energy expenditure. Physical activity can consist of a range of categories, such as occupational, sports, household or other activities.

Exercise is a subset of physical activity that is planned, structured and repetitive. It has a goal/objective in mind, for example building strength or increasing functional capacity.

Physical activity is regularly used to manage a number of health conditions, including chronic pain. Chronic pain can impact physical fitness, activity levels, energy levels and overall function, resulting in a significant impact on quality of life.[78,79]

People in Scotland living with chronic pain may access support from various healthcare professionals, across all sectors of health and social care, where conversations, referral, signposting and direct input to support physical activity is often a core part of their management. However, there remains uncertainty about the relative effectiveness of types of exercise and physical activity across a range of chronic pain conditions.

8.2 Evidence of benefit

Sixteen systematic reviews were selected that assessed the effectiveness of hands-off physical activity interventions for chronic non-cancer pain in adults aged 18 years or older. Twelve reviews used meta-analysis and four reviews used NMA.

Seven systematic reviews focused on chronic lower back pain,[80-86] five systematic reviews focused on fibromyalgia,[85,87-90] four systematic reviews focused on chronic neck pain,[85,91-93] one systematic review included evidence on osteoarthritis,[85] one systematic review focused on chronic pain secondary to temporomandibular joint disorders[94] and one review focused on a range of musculoskeletal pain disorders.[95]

The systematic reviews included a range of hands-off physical therapy interventions. These were aquatic aerobic and strengthening exercise,[88] dance,[90] flexibility,[89] targeted temporomandibular joint exercises and stretching,[94] Kinesio taping,[83] mind-body exercise,[84,92] mixed exercise (eg including two or more types of exercise (aerobic, resistance or flexibility),[87] multiple types of exercise (eg aerobic exercise, high-intensity interval training, Pilates, resistance exercises, stretching, swimming, tai chi and yoga),[81,82,85,91,94] neck and shoulder exercise,[93] water-based exercise,[80,95] and structured exercise programmes.[86] No evidence was identified on the effect of mobility aids on chronic pain.

Nine systematic reviews were rated high quality.[81,84-90,93] Three systematic reviews were rated acceptable quality.[80,83,95] All four NMAs were rated as sufficient quality.[82,91,92,94]	1++, 1+, sufficient

8.2.1 Pain intensity

EXERCISE

Chronic lower back pain

A Cochrane systematic review evaluated the effect of exercise interventions on pain and function in people with chronic lower back pain. Exercise was statistically significantly more effective than no treatment, placebo or usual care at the earliest follow-up point, at short-term follow-up (6–12 weeks), at medium-term follow-up (around 6 months) and at long-term follow-up (greater than 12 months). The review authors note that the effect met the definition of a clinically important difference in outcome, which was a difference in pain of 15 points on a 100-point scale, at earliest follow-up (MD -15.22, 95% CI -18.26 to -12.18; 35 RCTs, 2,746 participants: moderate certainty evidence) and short-term follow-up (MD -16.36, 95% CI -20.32 to -12.40; 26 RCTs, 2,247 participants: no evidence certainty rating).[81]	1++
The same researchers also published a NMA which evaluated the relative effectiveness of different exercise treatments planned or prescribed by a healthcare professional for people with chronic lower back pain. The review found that most exercise types were more effective than minimal treatment for reducing pain outcomes. Within the network of effects measured using 0–100-point VAS, Pilates (MD -18.7, 95% CI -24.4 to -13.1; 17 RCTs, 719 participants: moderate certainty evidence), McKenzie therapy (MD -14.8, 95% CI -21.4 to -8.2; eight RCTs, 428 participants: moderate certainty evidence), and functional restoration (-14.7, 95% CI -21.3 to -8.1; 9 RCTs, 459 participants: moderate certainty evidence) were most likely to be compatible with a clinically important effect on pain. The authors note that the confidence in results was limited by quality of the evidence, and specifically highlighted incomplete reporting of trial and population characteristics, differing opinions about treatment type classifications, and potential misclassification of exercise types and population characteristics as potential concerns. They also note that "the interventions that appeared to be the most effective were also interventions that are costly to deliver and to 'purchase' for patients. It is possible that our results were conflated with other factors related to higher socioeconomic status in these patient groups (eg, physical labour, other healthcare access and health status)."[82]	sufficient
A further meta-analysis evaluated the effects of exercise or yoga on chronic lower back pain. Compared with usual care, an attention control or a placebo intervention exercise provided a moderate effect on pain at short (MD -1.05 in 0–10-point VAS, 95% CI -1.58 to -0.51; 13 RCTs, 1,131 participants: low certainty evidence) and long-term follow-up timepoints (MD -1.55, 95% CI -2.76 to -0.34; one RCT, 64 participants: no evidence certainty rating) and a small effect at intermediate term (MD -0.84, 95% CI	1++

-1.49 to -0.22; six RCTs, 712 participants: low certainty evidence). Yoga resulted in a small effect on pain compared with an attention or waiting list control in the short term (pooled difference -0.87 on a 0–10 scale, 95% CI -1.49 to -0.24; seven RCTs, 710 participants: low certainty evidence) and a moderate effect at intermediate term (pooled difference -1.16, 95% CI -2.16 to -0.27; two RCTs, 268 participants: moderate certainty evidence).[85]	
A systematic review investigating the benefits and harms of structured exercise programmes was commissioned by WHO to support a clinical guideline on the management of chronic primary low back pain. This reported that while the quality and volume of evidence to support individual exercise types was low, based on pooled data, exercise (including aerobic, motor control, Pilates, yoga, core strengthening, and mixed exercise) probably reduces pain in the immediate term (SMD -0.33, 95% CI -0.58 to -0.08; eight RCTs, 619 participants: moderate certainty evidence). Exercise probably makes little or no difference to pain in the short term (MD -0.68 on a 0–10-point scale, 95% CI -1.82 to 0.46; two RCTs, 97 participants: very low-certainty evidence), or long term (between-group MD 8.88 on a 0–100-point scale, 95% CI -0.36 to 18.13; one RCT; 119 participants: very low-certainty evidence).[86]	1++
A systematic review investigated the effects of the mind-body practice tai chi on pain in people with chronic lower back pain. Six RCTs evaluated tai chi alone, three RCTs evaluated tai chi as an add-on therapy in combination with other treatments (such as massage, acupuncture and other conventional physical therapy), and one RCT with ai chi (water-based intervention). Pooling evidence from these trials, tai chi had a large effect to reduce pain compared with controls (weighted mean difference (WMD) -1.09, 95% CI -1.26 to -0.92; ten RCTs, 886 participants: medium certainty evidence).[84]	1++
One systematic review, which included evidence from randomised and non-randomised studies, compared the effects of water-based exercise training with land-based exercise and non-active controls in people with chronic lower back pain. A very large effect on pain was reported in favour of water-based exercise compared with non-active controls (effect size -3.61, 95% CI -4.89 to -2.32; nine studies, 338 participants: very low to low certainty evidence) but there was no difference in effect between water-based and land-based exercise groups (effect size -0.14, 95% CI -0.42 to 0.15; five studies, 177 participants: very low to low certainty evidence).[80]	1+
<u>Chronic neck pain</u>	
A NMA evaluated the relative effectiveness of different physical exercise interventions for people with chronic non-specific neck pain. Studies included interventions with durations and follow-up assessments ranging from three weeks to 12 months but it was not possible to analyse results within this category due to insufficient data in the network nodes. Compared with no treatment, very low-certainty evidence indicated several	sufficient

types of exercise reduced pain intensity, including proprioceptive exercise (SMD -1.47, 95% CI -2.76 to -0.18), strengthening and motor control exercise (SMD -1.44, 95% CI -2.42 to -0.47), motor control exercise (SMD -1.32, 95% CI -1.99 to -0.65), yoga/Pilates/tai chi/qigong (SMD -1.25, 95% CI -1.85 to -0.65), stretching exercise (SMD -1.23, 95% CI -2.23 to -0.24), strengthening exercise (SMD -1.21, 95% CI -1.63 to -0.78) and prescribed physical activity (SMD -0.84, 95% CI -1.47 to -0.20; all effects based on a network of 38 RCTs, 3,151 participants: very low-certainty evidence).[91]	
A further NMA investigated the relative effectiveness of nine mind-body exercise interventions in people with chronic neck pain. Yoga plus hot sand fomentation (HSF - a traditional Ayurvedic practice that involves applying heated sand to specific areas of the body: the treatment aims to reduce pain, inflammation, and stiffness by stimulating nerve endings, relaxing muscles, and increasing blood flow to the affected area) (MD -62.52 on a 0–100-point scale, 95% CI -85.76 to -39.27), yoga (MD -26.12, 95% CI -35.87 to -16.36), Pilates (MD -22.35, 95% CI -32.36 to -12.35) and qigong (MD -12.92, 95% CI -21.96 to -3.89; all based on a network of 18 RCTs, 1,442 participants: no evidence certainty rating) each resulted in statistically significant reductions in pain compared with usual care.[92]	sufficient
One systematic review reported that exercise had no significant effect on pain compared with no treatment, waiting list or an attention control in the short term (MD -0.70, 95% CI -1.62 to 0.15; three RCTs, 444 participants: low certainty evidence), intermediate term (MD -0.25, 95% CI -0.81 to 0.31; three RCTs, 353 participants: low certainty evidence) and long term (MD 0.07, 95% CI -0.51 to 0.88; three RCTs, 349 participants: low certainty evidence). There was insufficient evidence available on mind-body practices to draw a conclusion.[85]	1++
One systematic review evaluated the effect of home-based or workplace neck and shoulder exercises on office workers with non-specific chronic neck pain. Neck and shoulder exercises reduced pain intensity compared with no training (pooled effect size 7.31, 95% CI 4.95 to 9.67; four RCTs, 296 participants: very low-certainty evidence).[93]	1++
<u>Fibromyalgia</u> Five systematic reviews were identified which provided evidence on the effect of exercise on pain in people with fibromyalgia. In general, results suggest exercise, dance and mind-body practices in their different forms, but not flexibility exercise, provide small reductions in pain.	
One systematic review evaluated the benefits and harms of mixed exercise training protocols that include two or more types of exercise (for example aerobic, resistance or flexibility) for adults with fibromyalgia against control (treatment as usual, waiting list control), non-exercise interventions (for example biofeedback), or other exercise (for example mixed versus flexibility) interventions. Mixed exercise reduced pain postintervention compared with control, but not in the longer term (MD -7.01 on a 0–100-	1++

point scale, 95% CI -10.64 to -3.38; 10 RCTs, 487 participants: moderate certainty evidence). The authors note that this small effect did not meet the threshold for clinical relevance (a between-group difference of 15 points on a 100-point scale).[87]	
A further systematic review evaluated the effect of aquatic training based on aerobic and strengthening exercises compared with no intervention or land-based exercise in women with fibromyalgia. Aquatic combined aerobic and strengthening exercise improved pain postintervention only compared with no intervention or land-based exercise (MD -1.16 on a 0–10-point scale, 95% CI -1.75 to -0.57; four RCTs, 171 participants: very low-certainty evidence). This improvement may be small and clinically unimportant as the authors assumed a minimum clinically important difference of 2 points on a 0–10 scale. The authors also note that several of the included studies had insufficient sample sizes which could lead to inaccuracies in effect estimates and that several studies were published by the same research group, limiting the generalisability of findings.[88]	1++
Another systematic review investigated the effects of flexibility exercise on pain in adults with fibromyalgia compared with either land-based aerobic training, resistance training or a no treatment control. There was no evidence of any effect of flexibility exercise on pain postintervention compared with aerobic exercise (MD 2.48 on a 0–100-point scale, 95% CI -6.29 to 11.85; four RCTs, 131 participants: very low-certainty evidence), resistance exercise (MD 1.84, 95% CI -4.15 to 7.83; three RCTs, 152 participants: very low-certainty evidence) or untreated control (MD -18.0, 95% CI -37.63 to 1.63; one RCT, 28 participants: low certainty evidence).[89]	1++
One systematic review considered the effects of dance on pain associated with fibromyalgia. The review separately evaluated creative dance interventions, which use the five basic elements of dance (body, range of movement, space, time, and energy) to create original movements or ideas, and repetitive dance interventions, which consist of the repetition of movements provided by an instructor instead of creating their original movements against them. Both creative dance (SMD -1.43, 95% CI -1.72 to -1.13; five RCTs, 268 participants: moderate certainty evidence) and repetitive dance interventions (SMD -0.34, 95% CI -0.69 to -0.10; four RCTs, 259 participants: moderate certainty evidence) reduced pain postintervention compared with controls which included any other intervention.[90]	1++
A fifth systematic review evaluated the effect of exercise or mind-body practices (yoga, tai chi or qigong) on pain intensity compared with usual care, an attention control, a placebo intervention or waiting list in people with a range of chronic pain conditions, including fibromyalgia. Compared with control, exercise resulted in a small reduction in pain intensity in the short term (MD -0.84 on a 0–10-point scale, 95% CI -1.24 to -0.30; seven RCTs, 406 participants: moderate certainty evidence) and intermediate term (MD -0.51, 95% CI -0.92 to -0.06; eight RCTs, 382 participants: moderate certainty evidence). There was no significant effect of exercise in the long term (MD -0.18, 95% CI -0.77 to 0.42; four RCTs, 241	1++

participants: moderate certainty evidence). The authors note that a moderate treatment effect (>1 to 2 points on a 10-point scale) roughly corresponds to reported the minimum clinically important difference for the measure, suggesting that these effects may not be clinically relevant.[85]	
Osteoarthritis	
One systematic review evaluated the effect of exercise or mind-body practices (yoga, tai chi or qigong) compared with usual care, no treatment or an attention control in people with chronic osteoarthritic pain of the hand, knee or hip. For people with knee osteoarthritis, exercise resulted in a small reduction in pain compared with controls in the short term (MD -0.50 on a 0–10-point scale, 95% CI -0.84 to -0.16; nine RCTs, 832 participants: moderate certainty evidence) and long term (MD -0.26, 95% CI -0.43 to -0.01; six RCTs, 1,538 participants: low certainty evidence) and a moderate reduction in the intermediate term (MD -1.21, 95% CI -1.96 to -0.44; 12 RCTs, 1,141 participants: low certainty evidence). For people with hip osteoarthritis, exercise resulted in a small reduction in pain compared with controls in the short term (MD -0.30 on a 0–10-point scale, 95% CI -0.70 to -0.02; three RCTs, 371 participants: low certainty evidence) but not in the intermediate term (MD -0.14, 95% CI -0.40 to 0.12; two RCTs, 307 participants: low certainty evidence) or long term (MD -0.25, 95% CI -0.62 to 0.11; one RCT, 118 participants: insufficient certainty evidence). There was insufficient evidence from one poor-quality RCT of exercise in people with hand osteoarthritis to determine effectiveness.	1++
Mind-body practices consisting of tai chi or qigong resulted in a moderate improvement in pain in people with knee osteoarthritis compared with usual care, attention control or placebo (SMD -0.75, 95% CI -1.05 to -0.42; two RCTs, 306 participants: low certainty evidence). There was insufficient evidence to determine the effect of yoga.[85]	
Chronic pain secondary to temporomandibular disorder	
A NMA evaluated all available interventions for the management of chronic temporomandibular disorder (TMD) pain. Network estimates for pain reduction indicated that supervised jaw exercise plus mobilisation (MD -2.86 on a 0–10-point scale, 95% -3.21 to -2.52; modelled risk difference (RD) for achieving the minimally important difference in pain relief of 1 cm on a 10 cm scale 36%, 95% CI 33 to 39: low certainty evidence), supervised postural exercise (MD -1.56, 95% CI -2.33 to -0.79; RD 26%, 95% CI 14 to 34: medium certainty evidence), supervised jaw exercise plus stretching (MD -1.55, 95% CI -1.99 to -1.11; RD 26%, 95% CI 20 to 31: high certainty evidence), supervised jaw exercise plus stretching plus trigger point therapy (MD -1.31, 95% CI -1.99 to -0.62; RD 23%, 95% CI 11 to 31: medium certainty evidence) each reduce pain significantly more than placebo (all estimates are based on a network of 153 RCTs with 8,713 participants).[94]	sufficient
Chronic musculoskeletal disorders	
One systematic review evaluated the effects of aquatic exercise on a	1+

range of outcomes in the treatment of people with chronic musculoskeletal disorders. Included studies had treatment durations ranging from three to 32 weeks. Aquatic exercise reduced participants' pain compared with no exercise (SMD -0.64, 95% CI -0.87 to -0.41; 22 RCTs, 1,551 participants: no evidence certainty rating). Subgroup analysis showed that aquatic exercise significantly reduced pain in people with osteoarthritis (SMD -0.36, 95% CI -0.59 to -0.13; 12 RCTs, 995 participants), fibromyalgia (SMD -0.64, 95% CI -0.85 to -0.43; seven RCTs, 367 participants) and low back pain (SMD -1.68, 95% CI -2.29 to -1.07; three RCTs, 189 participants). Aquatic exercise also relieved pain compared with land-based exercise (SMD -0.35, 95% CI -0.67 to -0.03; 11 RCTs, 578 participants).[95]	
KINESIO TAPING <u>Chronic lower back pain</u>	
One systematic review evaluated the effects of Kinesio Taping® (adhesive acrylic medical tape used to relax or compress muscles, aiming to reduce pressure and inflammation and improve symptom relief) on pain in people with chronic lower back pain. Kinesio taping compared with addition of Kinesio taping to another intervention, no intervention or placebo had no statistically significant effect on pain at any follow-up point.[83]	1+

8.2.2 Function

EXERCISE <u>Chronic lower back pain</u>	
A Cochrane systematic review evaluated the effects of exercise interventions in people with chronic lower back pain. Exercise was more effective for reducing functional limitations compared with no treatment, placebo or usual care at the earliest follow-up timepoint (MD -6.81 on a 0–100-point scale, 95% CI -8.32 to -5.31; 38 RCTs, 2,942 participants: moderate certainty evidence). The authors note that this effect does not meet the prespecified threshold for minimal clinically important difference (a difference in function of ten points).[81]	1++
The same researchers also published a NMA which evaluated the relative effectiveness of different exercise treatments planned or prescribed by a healthcare professional for people with chronic lower back pain. Within the network of effects measured using 0–100-point scale, McKenzie therapy (MD -11.7, 95% CI -16.7 to -6.7; seven RCTs, 419 participants: high to moderate certainty evidence), flexibility exercise (MD -11.0, 95% CI -17.2 to -4.8; four RCTs, 151 participants: high to moderate certainty evidence) and Pilates (MD -10.2, 95% CI -13.8 to -6.6; 15 RCTs, 667 participants: high to moderate certainty evidence) all had a clinically significant positive effect on function (≥10 points) compared with controls.[82]	sufficient
A further meta-analysis evaluated the effects of exercise or yoga on function in people with chronic lower back pain. Exercise improved function compared with usual care, an attention control or a placebo intervention in the short term (SMD -0.33, 95% CI -0.51 to -0.16; 13 RCTs, 1,126	1++

participants: moderate certainty evidence) and intermediate term (SMD -0.20, 95% CI -0.41 to -0.03; six RCTs, 712 participants: low certainty evidence) but not in the long term. Yoga had moderate effects on function compared with an attention or waiting list control in the short term (SMD -0.45, 95% CI -0.69 to -0.28; eight RCTs, 982 participants: moderate certainty evidence) and small effects in the intermediate term (SMD -0.29, 95% CI -0.47 to -0.11; three RCTs, 540 participants: low certainty evidence).[85]	
A systematic review investigating the benefits and harms of structured exercise programmes in people with chronic primary lower back pain reported that exercise improved function compared with no intervention, placebo or sham interventions in the immediate term (around two weeks postintervention) (MD -1.32, 95% CI -1.80 to -0.85; 41 RCTs, 2,068 participants: low certainty evidence) and short term (around three months postintervention) (MD -0.54, 95% CI -0.88 to -0.20; five RCTs, 347 participants: very low-certainty evidence) but not in the long term (around 12 months postintervention) (MD -0.10, 95% CI -1.32 to 1.12: one RCT, 70 participants: very low-certainty evidence).[86]	1++
A systematic review investigated the effects of the mind body practice tai chi on pain in people with chronic lower back pain either alone or in combination with other treatments. Tai chi significantly improved disability compared with controls (routine care or other interventions) (SMD -1.75, 95% CI -2.02 to -1.48; four RCTs, 296 participants: low certainty evidence).[84]	1++
One systematic review compared the effects of water-based exercise training with land-based exercise and non-active controls in people with chronic lower back pain. A very large effect on disability was reported in favour of water-based exercise compared with non-active controls (effect size 2.15, 95% CI 1.12 to 3.19; nine studies, 395 participants: very low to low certainty evidence).[80]	1+
<u>Chronic neck pain</u>	
A NMA evaluated the relative effectiveness of different physical exercise interventions for people with chronic non-specific neck pain. Based on a network of 29 RCTs with 2,336 participants, several types of exercise reduced pain-related disability compared with no treatment, including yoga/Pilates/tai chi/qigong (SMD -1.16, 95% CI -1.75 to -0.57: very low-certainty evidence), strengthening exercise (SMD -0.75, 95% CI -1.28 to -0.22:very low-certainty evidence) and motor control exercise (SMD -0.87, 95% CI -1.45 to -0.29: very low-certainty evidence).[91]	sufficient
A further NMA investigated the relative effectiveness of nine mind-body exercise interventions in people with chronic neck pain. Based on a network of 15 RCTs with 1,165 participants, yoga plus HSF (see section 9.2.1) (MD -19.13 on a 0–100-point scale, 95% CI -27.90 to -10.37), tai chi (MD -14.90, 95% CI -22.76 to -7.04), yoga (MD -6.93, 95% CI -11.01 to -2.86) and Pilates (MD -5.61, 95% CI -9.27 to -1.96) each resulted in statistically significant reductions in functional disability compared with	sufficient

usual care.[92]	
One systematic review in people with chronic neck pain reported that exercise had no significant effect on function compared with no treatment, waiting list or an attention control in the short term (SMD -0.42, 95% CI -1.03 to 0.09; four RCTs, 487 participants: low certainty evidence) or in the intermediate term (SMD 0.14, 95% CI -0.12 to 0.40; one RCT, 230 participants: low certainty evidence) but may improve function in the long term (SMD -0.39, 95% CI -0.74 to -0.03; one RCT, 125 participants: low certainty evidence). Alexander Technique resulted in a small improvement in function in the short term (difference -5.56 on a 0–100% scale, 95% CI -8.33 to -2.78; one RCT, 344 participants: low certainty evidence) and intermediate term (difference -3.92, 95% CI -6.87 to -0.97 one RCT, 344 participants: low certainty evidence) compared with usual care alone. There was insufficient evidence available to determine the effect of qigong on function in people with chronic neck pain.[85]	1++
One systematic review evaluated the effect of home-based or workplace neck and shoulder exercises on office workers with non-specific chronic neck pain. Neck and shoulder exercises reduced pain-related disability compared with no training (pooled effect size 13.75, 95% CI 2.69 to 24.83; three RCTs, 249 participants: very low-certainty evidence).[93]	1++
<u>Fibromyalgia</u>	
One systematic review evaluated the benefits and harms of mixed exercise training protocols for adults with fibromyalgia against control (treatment as usual, waiting list control), non-exercise interventions or other exercise interventions. Mixed exercise improved physical function compared with control (MD -12.77 on a 0–100 scale, 95% CI -17.63 to -7.9; six RCTs, 311 participants: no evidence certainty rating). The authors note that the minimum clinically important difference for this outcome was a relative difference of 15%, therefore the confidence intervals of this estimate include effects which are both clinically important and not important.[87]	1++
A further systematic review considered aquatic training (hydrotherapy) compared with no intervention or land-based exercise in women with fibromyalgia. Aquatic combined aerobic and strengthening exercise improved physical function compared with no intervention immediately postintervention (MD 14.82 on a 0–100 scale, 95% CI 7.97 to 21.28; three RCTs, 118 participants: low certainty evidence) and up to 16 weeks postintervention (MD 9.80, 95% CI 2.38 to 17.22; two RCTs, 88 participants: very low-certainty evidence). The authors note that no MCIDs have been prespecified for physical function.[88]	1++
One systematic review investigated the effects of flexibility exercise on pain in adults with fibromyalgia. The review identified a single small RCT which reported no significant difference in physical function between people receiving flexibility exercise and untreated controls (MD -3.33 on a 0–100-point scale, 95% CI -16.29 to 9.63; one RCT, 28 participants: low certainty evidence).[89]	1++

In a further systematic review which evaluated the effect of exercise or mind-body practices (yoga, tai chi or qigong) on physical function in people with a range of chronic pain conditions, including fibromyalgia, exercise significantly improved physical function compared with usual care, an attention control or a placebo intervention in the short term (MD -8.39, 95% CI -12.87 to -3.61; nine RCTs, 545 participants: low certainty evidence) and intermediate term (MD -6.04, 95% CI -9.25 to -3.01; eight RCTs, 461 participants: moderate certainty evidence) but not in the long term (MD -4.33, 95% CI -10.46 to 1.97; three RCTs, 178 participants: low certainty evidence). Mind-body practices did not significantly improve function compared with waiting list or attention control (MD -15.44, 95% CI -31.11 to 0.23; two RCTs, 154 participants: low certainty evidence).[85]	1++
Osteoarthritis	
One systematic review evaluated the effect of exercise or mind-body practices (yoga, tai chi or qigong) compared with usual care, no treatment or an attention control in people with chronic osteoarthritic pain of the hand, knee or hip. In people with knee osteoarthritis and in people with hip osteoarthritis, exercise improved function in the short, medium and long term with standardised mean differences ranging from 0.18, which represents a result below the threshold of a small effect, to 0.57, which represent a moderate effect. Analysis of evidence for mind-body therapies in people with chronic knee osteoarthritis showed a large effect favouring treatment compared with controls (pooled SMD -0.92, 95% CI -1.74 to -0.15; three RCTs, 398 participants: low certainty evidence) but heterogeneity was substantial. Excluding the poor-quality outlier RCT substantially reduced the heterogeneity and resulted in a small improvement in function (pooled SMD -0.48, 95% CI -1.03 to -0.18; two RCTs, 304 participants: low certainty evidence).[85]	1++
Chronic pain secondary to temporomandibular disorder	
A NMA evaluated all available interventions for the management of chronic TMD pain. Based on a network of 33 RCTs with 1,910 participants, compared with placebo supervised jaw exercise with stretching (MD on a 0–100 scale, 16.23, 95% CI 11.58 to 20.88; RD for achieving the minimally important difference of 5 points on the 100 point short form-36 physical component summary score 43% (95% CI 33 to 51)), manipulation (MD 16.30, 95% CI 7.77 to 24.83; RD 43% (95% CI 25 to 56)) and supervised jaw exercise with mobilisation (MD 13.11, 95% CI 5.42 to 20.81; RD 36% (95% CI 19 to 51)) all probably improved physical functioning.[94]	sufficient
Chronic musculoskeletal disorders	
One systematic review evaluated the effects of aquatic exercise on a range of outcomes in the treatment of people with chronic musculoskeletal disorders. Aquatic exercise improved participants' physical function compared with no exercise (SMD 0.62, 95% CI 0.32 to 0.91; 14 RCTs, 739 participants: no evidence certainty rating) but there was no evidence of a difference compared with land-based exercise (SMD 0.13, 95% CI -0.20 to	1+

0.46; seven RCTs, 369 participants: no evidence certainty rating).[95]	
KINESIO TAPING	
Chronic lower back pain	
One systematic review evaluated the effects of Kinesio Taping® on disability in people with chronic lower back pain. Kinesio Taping® was not better than placebo for managing disability in the short (SMD -0.14, 95% CI -0.72 to 0.45; four RCTs, 287 participants: low certainty evidence) or intermediate term (SMD -0.34, 95% CI -1.42 to 0.75; two RCTs, 168 participants: very low-certainty evidence). When combined with physical activity, Kinesio Taping® did not improve disability more than physical activity alone (SMD 0.14, 95% CI -0.33 to 0.61; four RCTs, 254 participants: very low-certainty evidence).[83]	1+

8.2.3 Quality of life

EXERCISE	
Chronic lower back pain	
No evidence was identified that reported on quality of life outcomes for hands-off physical therapy interventions in people with chronic lower back pain.	
Chronic neck pain	
In the NMA which investigated the relative effectiveness of nine mind-body exercise interventions in people with chronic neck pain, based on a network of eight RCTs with 855 participants, yoga plus HSF (MD 16.22 on a 0–100-point scale, 95% CI 0.67 to 31.77) and qigong (MD 6.52, 95% CI 1.40 to 11.64) significantly improved SF-36 physical component scores.[92]	sufficient
Fibromyalgia	
One systematic review of mixed exercise interventions reported that individuals undertaking mixed exercise programmes which involved at least two of the three categories of aerobic/cardiorespiratory exercise, resistance/muscle training exercise or flexibility exercise, had improved health-related quality of life (HRQL) compared with controls (MD -8.38 on a 0–100 scale (high scores indicate worse HRQL), 95% CI -13.00 to -3.75; nine RCTs, 412 participants: moderate certainty evidence). Statistically significant effects of benefit were reported at short-term (6-12 weeks) and intermediate-term (13-26 weeks) but not longer term (27 to 52 weeks) follow-up points. The authors note that “For fatigue, physical function, HRQL, and stiffness, we cannot rule in or out a clinically relevant change, as the confidence intervals include both clinically important and unimportant effects”.[87]	1++
One systematic review reported that flexibility exercise training was not more effective than aerobic exercise (MD 4.41, 95% CI -5.77 to 14.05; two RCTs, 193 participants: very low-certainty evidence) or resistance exercise (MD 5.55, 95% CI -1.8 to 12.9; one RCT, 56 participants: low certainty evidence) in improving HRQL in adults with fibromyalgia postintervention.[89]	1++
A systematic review which evaluated the effects of creative or repetitive	1++

dance-based interventions in women with fibromyalgia reported that repetitive dance interventions improved HRQL compared with controls (SMD 0.43, 95% CI 0.09 to 0.76; two RCTs, 138 participants: moderate certainty evidence). No studies were identified which reported on the effects of creative dance interventions on HRQL, however the authors note that these were associated with larger effects on pain and fibromyalgia impact than repetitive dance interventions (see section 9.2.1).[90]	
Chronic musculoskeletal disorders	
One systematic review evaluated the effects of aquatic exercise on a range of outcomes in the treatment of people with chronic musculoskeletal disorders. aquatic exercise improved quality of life for participants compared with no exercise (SMD -0.64, 95% CI -0.94 to -0.34; 18 RCTs, 1,387 participants: no evidence certainty rating) but there was no evidence of effect for the comparison with land-based exercise (SMD -0.18, 95% CI -0.51 to 0.16; six RCTs, 277 participants: no evidence certainty rating).[95]	1+
Sections 8.2.4 to 8.2.6 have been reproduced from SIGN guideline 136: Management of chronic pain.	
8.2.4 Advice	
The addition of interventions based on cognitive behavioural therapy (CBT) to physiotherapy programmes may be effective for people with whiplash-associated disorder.[96]	1++
A systematic review of advice for the management of chronic low back pain found strong evidence to suggest that advice as an adjunct to exercise was more effective for improving pain, back specific function and work disability as opposed to advice alone. Advice in this sense was to stay active, along with specific advice regarding exercise and/or functional activities.[97]	1++
8.2.5 Exercise delivery	
Supervised exercise was found to be more effective for improving weekly training frequency than unsupervised exercise. Supplementing a home exercise programme with group exercise may increase overall physical activity levels.[96]	1++
Performance accuracy is improved by refresher sessions or by providing audiotapes or videotapes of exercises.[96]	1++
A systematic review of therapeutic interventions for patients with whiplash-associated disorder, including chronic whiplash of more than 12 weeks duration, indicated that an exercise programme was effective in relieving chronic whiplash-related pain in the short term although these gains were not maintained in the long term. The relative effectiveness of different exercise regimens was not determined.[98]	2+
8.2.6 Exercise adherence	
A Cochrane review considering adherence to exercise in patients with chronic musculoskeletal conditions identified moderate-certainty evidence that:[96]	1++

- Individual-specific exercises are more effective than generic group exercise for improving attendance at exercise classes.
- Therapeutic programmes that specifically address adherence are effective in improving the frequency/duration of exercise, and attendance at sessions.
- Graded activity is effective in improving adherence to a home exercise programme.
- Adding CBT-based approaches to physiotherapy programmes is not effective in improving exercise adherence.

8.3 Evidence of harms

EXERCISE

Chronic back pain

Systematic reviews reported that adverse events of exercise interventions were generally not reported in the included trials and that it was not possible to draw conclusions about safety or harms associated with exercise in people with chronic back pain. The small number of trials where adverse events were recorded report these to be few and minor in nature, for example temporary muscle pain.[81,82,84-86]	1++, sufficient
Systematic reviews reported no clear difference between mind body exercises (tai chi, yoga and qigong) and controls in risk of any adverse event.[84,85]	1++

Chronic neck pain

Three systematic reviews did not report the effect of exercise on adverse events.[91-93] A further systematic review noted that no serious adverse events were reported in the four RCTs which included data on harms.[85]	1++, sufficient

Fibromyalgia

One systematic review described that mixed exercise interventions appeared to be well tolerated in people with fibromyalgia but there was insufficient data on adverse events available to calculate an effect estimate. There was no difference in all-cause study withdrawal between those undertaking exercise interventions and controls (RR 1.02, 95% CI 0.69 to 1.15; 19 RCTs, 1,065 participants: moderate certainty evidence).[87]	1++
Similarly, a further systematic review reported flexibility exercise training to be well tolerated in people with fibromyalgia but there was insufficient data on adverse events available to calculate an effect estimate. There was no difference in study withdrawal between those undertaking flexibility exercise training compared with aerobic exercise (RR 0.97, 95% CI 0.61 to 1.55; five RCTs, 301 participants: very low-certainty evidence), or with resistance exercise (RR 1.43, 95% CI 0.77 to 2.67; three RCTs, 159 participants: low certainty evidence) or with untreated controls (RR 1.78, 95% CI 0.37 to 8.44; one RCT, 34 participants: low certainty evidence).[89]	1++
One systematic review noted that adverse events were poorly reported,	1++

and recorded no serious adverse events in any trial of exercise for people with fibromyalgia.[85]	
Two systematic reviews did not report on adverse events of exercise in people with fibromyalgia.[88,90]	1++
Osteoarthritis	
One systematic review of exercise in people with knee, hip or hand osteoarthritis noted that most trials did not report harms. One of the 18 RCTs that provided data on knee osteoarthritis reported a larger, but temporary, increase in minor pain in people completing exercise interventions compared with sham interventions, however the authors note the wide confidence interval (RR 14.7, 95% CI 2.0 to 107.7; one RCT, 150 participants: no evidence certainty rating). Four RCTs found no difference between exercise and comparators in worsening of pain symptoms and two RCTs reported no difference between exercise and standard analgesics in any adverse event. For hip osteoarthritis, two RCTs included data on harms and neither reported any adverse events in groups receiving exercise or usual care.[85]	1++
Chronic pain secondary to temporomandibular disorder	
A NMA of interventions to manage TMD reported that no intervention was associated with significantly increased adverse events compared with placebo or sham procedures.[94]	sufficient
Chronic musculoskeletal disorders	
No evidence was identified on adverse effects of interventions for people with chronic musculoskeletal disorders specifically.	
KINESIO TAPING	
Chronic lower back pain	
No evidence was identified on adverse effects of Kinesio taping for people with chronic back pain.	

8.4 Summary of benefits and harms of hands-off physical therapies for chronic pain

There is evidence of benefit for a wide range of exercise interventions across all pain types.

In people with chronic low back pain various exercise interventions can reduce pain in the short, intermediate and long term and can improve function in the short and intermediate term. In people with chronic neck pain various exercise interventions can reduce pain and improve function, although the effects were more inconsistent and based on low certainty evidence. In people with fibromyalgia, exercise in different forms can provide small improvements in pain, although these may not be clinically significant. Effects on function were inconsistent and, where positive effects were reported, it was unclear whether these were clinically significant. There is evidence of short-term reduction in pain with mind-body exercises (yoga, tai chi or qigong) in people with osteoarthritis of the

knee or hip which was sustained in the intermediate and long term for people with knee osteoarthritis. Similar effects were reported on function although effect sizes varied from less than small to moderate. In people with TMD exercise combined with a range of structured physical therapies can reduce pain and improve function. No evidence was identified on the effects of exercise alone in people with chronic TMD pain. In people with mixed musculoskeletal pain types, one systematic review reported that aquatic exercise can reduce pain and that this effect may be greater than land-based exercise therapies. Aquatic exercise may also improve physical function compared with no exercise, but there was no evidence for an improvement compared with land-based exercise. Where reported, exercise interventions generally improved health-related quality of life.

Kinesio taping did not improve pain or function compared with placebo in people with chronic low back pain.

No evidence was identified on the effect of mobility aids on chronic pain.

8.5 Other factors

The GDG acknowledged that while effects of individual physical activity interventions described in systematic reviews were limited to specific pain conditions, this does not always reflect the routine delivery of care to people with chronic pain, where exercise interventions are tailored to the individual's needs and may involve a range of activities.

Clinicians noted that there was restricted access to aquatic therapy / hydrotherapy facilities in NHS Scotland which may limit the implementation of this intervention.

Physical activities and exercise are widely available to people with chronic pain both within NHS Scotland and in self-led approaches. Members with lived experience of chronic pain in the guideline development group reflected on the fears and concerns experienced by the chronic pain community when considering and initiating physical activity. They acknowledged that many people were worried about further exacerbating existing pain. A realistic and achievable approach to initiating and maintaining physical activity based on shared understanding between individuals and professionals is vital. It is the responsibility of healthcare professionals to ensure a shared decision-making approach.

The following recommendations have been adopted and adapted from SIGN 136.

8.6 Recommendations

R **Physical activity (including exercise and exercise therapies), regardless of form, is recommended in the management of patients with chronic pain.**

R **Advice to stay active should be given alongside exercise therapy for patients with chronic low back pain to improve disability in the long term. Advice alone is insufficient.**

R **The following approaches should be used to improve adherence to exercise:**

- **supervised exercise sessions**
- **individualised exercises in group settings**
- **addition of supplementary material**
- **provision of a combined group and home exercise programme.**

✓ Any person-centred exercise and exercise therapies chosen should be based on shared decision making. It is pertinent that any recommendation is based on an individual's needs, capabilities and unique circumstances to help reduce barriers and facilitate a positive and meaningful experience.

9 Physical therapies (hands-on)

9.1 Introduction

Hands-on physical therapies are physical manipulation and/or manual contact using the hands to treat an injury, disability, condition or musculoskeletal pain. The main components are manual therapies (manipulation and mobilisation) and massage therapy. Manual therapy is a term encompassing mobilisation, or slow passive movements performed by a therapist within the physiological range of movement, while manipulation refers to application of manual thrust to a joint, at or near the end of the physiological range of motion by a physiotherapist, osteopath or chiropractor. Massage therapy is another form of passive treatment encompassing deep tissue massage, myofascial release, reflexology, sports massage and trigger point therapy.

9.2 Evidence of benefit

Nine systematic reviews which were rated at high, acceptable or sufficient quality, were included. Seven employed meta-analysis[85,99-104] one used NMA,[67] and one conducted a narrative synthesis due to study heterogeneity.[105] Most reviews focused on chronic pain related to specific conditions (eg, low back pain, multiple sclerosis, myogenous temporomandibular disorder, neck pain, and pelvic pain), with two reviews covering multiple pain conditions. The certainty of evidence varied significantly across the outcomes of interest. While some evidence was rated as high quality, most of the evidence was rated as low to very low quality, affecting the reliability of their findings. Reasons identified for the lower certainty evidence rating included methodological flaws, inconsistent study designs, and limited sample sizes, leading to uncertainty about the conclusions drawn from those studies.

1++, 1+, sufficient

The study populations are representative of the chronic pain population in Scotland. The current picture across Scotland is that most local clinical pathways for the management of these conditions have a strong focus on supported self-management approaches and active treatments. Realistic medicine has also become an integral approach to care. Therefore, whilst passive treatments such as manual therapy are considered an option in the management of certain chronic pain conditions along with other interventions such as exercise, there is uncertainty with regards to the availability and feasibility of delivering these treatments to patients with chronic pain within Scotland.

9.2.1 Pain intensity

MANUAL THERAPY

Chronic lower back pain

Three systematic reviews provide inconsistent evidence that manual therapy (manipulation and mobilisation) may reduce chronic low back pain[85,99,104] when compared with different comparators such as exercise or usual care in the short term, but the effect sizes are generally small, and the

1+
1++

clinical significance of these reductions varies and is often unclear.	
One systematic review reported that manipulation or mobilisation compared with an active comparator (exercise or physical therapy) resulted in a reduction in chronic lower back pain measured postintervention closest to one-month from baseline (SMD -0.28, 95% CI -0.47 to -0.09; nine RCTs, 1,176 participants: moderate certainty evidence). Manipulation compared with other active comparators showed reduced pain at three-months follow-up (SMD -0.68, 95% CI -1.14 to -0.23; three RCTs, 370 participants: moderate certainty evidence) and six-months follow-up (SMD -0.72, 95% CI -0.99 to -0.45; three RCTs, 223 participants: moderate certainty evidence). Effects of mobilisation at both three- and six-months follow-up did not significantly change from post-treatment.[99]	1+
In contrast, a systematic review of spinal manipulative therapies, including manipulation and mobilisation manual therapies, for chronic low back pain reported no clinically important benefits in pain reduction. Comparators included recommended pharmacological (eg NSAIDs or analgesics) and non-pharmacological (eg exercise) active treatments, non-recommended treatments (eg light tissue massage, waiting list control or no treatment) and sham procedures.[104]	
Spinal manipulative therapy was not statistically better than recommended comparators at one month (WMD -3.17, 95% CI -7.85 to 1.51; 17 RCTs, 3,155 participants: moderate certainty evidence) and 12 months (WMD -1.86, 95% CI -4.79 to 1.07; 10 RCTs, 2,502 participants: moderate certainty evidence), although the difference was statistically significant at six months (WMD -3.09, 95% CI -5.42 to -0.77; 11 RCTs, 2,462 participants: moderate certainty evidence). The size of the effect at six months was reported by the review authors as not clinically important.	
Spinal manipulative therapy did not reduce pain at one-month follow-up (MD -7.55, 95% CI -19.86 to 4.76; eight RCTs, 831 participants: low certainty evidence), at six-months follow-up (MD 0.96, 95% CI -6.34 to 8.26; two RCTs, 114 participants: very low-certainty evidence) or at 12-months follow-up (MD 0.20, 95% CI -5.33 to 5.73; one RCT, 63 participants: very low-certainty evidence).	1++
Spinal manipulative therapy employed as an adjuvant therapy resulted in a small, statistically significant, but not clinically important reduction in pain at one-month (MD -6.93, 95% CI -10.36 to -3.49; six RCTs, 1,046 participants: moderate certainty evidence) and 12 months (MD -3.31, 95% CI -6.60 to -0.02; two RCTs, 1,000 participants: moderate certainty evidence). Spinal manipulative therapy did not result in a statistically better effect as an adjuvant therapy at six months (MD -6.77, 95% CI -14.07 to -0.53; two RCTs, 143 participants: low certainty evidence).	
The systematic review reported no significant difference in pain reduction between studies using manipulation and mobilisation techniques at one-month follow-up (MD 0.32, 95% CI -3.05 to 3.69; four RCTs, 509 participants: moderate certainty evidence).[104] (Rubenstein 2019)	
A third systematic review reported no difference in the short term between	1++

spinal manipulation therapy and sham manipulation, usual care, an attention control, or a placebo intervention for people with chronic lower back pain (MD -0.32 on a 0–10 VAS, 95% CI -0.55 to 0.10; four RCTs, 683 participants: low certainty evidence). There was a small improvement in pain in those receiving spinal manipulation therapy at intermediate-term follow-up (MD -0.64, 95% CI -0.93 to -0.35; three RCTs, 978 participants: low certainty evidence). Comparing manipulation with exercise, there were no differences in short-term pain (MD 0.31, 95% CI -0.42 to 1.06; three RCTs, 636 participants: low certainty evidence) or intermediate-term pain (MD 0.23, 95% CI -0.14 to 0.59; four RCTs, 1,093 participants: low certainty evidence).[85]	
Chronic neck pain	
Spinal manipulation was associated with a large improvement in pain (difference -3.05 on a 0–10 scale, 95% CI -3.30 to -2.80; one RCT, 42 participants: low certainty evidence) over the short term compared with sham manipulation in people with chronic neck pain but when compared with exercise therapy, there were no differences between groups (data not reported).[85]	1++
Another systematic review evaluated the effect of manipulation and mobilisation manual therapy techniques on chronic non-specific neck pain. Manipulation combined with an exercise programme did not result in a statistically significant reduction in postintervention pain compared with exercise alone closest to one month from baseline (SMD -0.37, 95% CI -0.77 to 0.03; five RCTs, 535 participants: moderate to low certainty evidence), closest to three-months follow-up (SMD -0.27, 95% CI -0.60 to 0.06; five RCTs, 481 participants: moderate to low certainty evidence) or closest to six-months follow-up (SMD -0.20, 95% CI -0.54 to 0.14; four RCTs, 473 participants: moderate to low certainty evidence).[100]	1+
Fibromyalgia pain	
Spinal manipulation did not reduce fibromyalgia pain compared with sham at short-term follow-up (adjusted difference (AD) on the 0–10 VAS -0.56, 95% CI -2.21 to 1.08; one RCT, 101 participants: low certainty evidence) or at intermediate-term follow-up (AD -0.50, 95% CI -2.48 to 1.47; one RCT, 101 participants; low certainty evidence).[85]	1++
Chronic pain associated with osteoarthritis of the hip	
One systematic review identified two RCTs that evaluated manual therapy compared with usual care or exercise therapy. The only study reporting a pain outcome showed that manual therapy provided a small improvement in short-term pain at rest and during walking compared with exercise (AD on the 0–10 VAS -0.72, 95% CI -1.38 to -0.05, and -1.21, 95% CI -2.29 to -0.25, respectively; one RCT, 53 participants: low certainty evidence). In the intermediate term, effects on pain were inconsistent compared with exercise. A moderate effect on pain during walking was reported following manual therapy compared with exercise (AD -1.27, 95% CI -2.40 to -0.19), but there was no difference for pain at rest (AD -0.70, 95% CI -2.03 to 0.59).[85]	1++

Myogenous temporomandibular disorders	
Temporomandibular disorders (TMD) are common benign musculoskeletal disorders affecting up to 1 in 15 of the UK population.[106] Myogenous TMDs involve pain or dysfunction in the muscles used for chewing. One NMA evaluated interventions for the effects of manual therapies on pain intensity in people with chronic myogenous temporomandibular disorders. Manual therapy reduced pain intensity postintervention compared with placebo (SMD -1.10, 95% CI -1.69 to -0.51; based on network of 42 RCTs, 1,989 participants: low certainty evidence).[67]	sufficient
A further NMA evaluated the comparative effects of a wide range of interventions for TMDs on pain, including manual therapies. Trigger point therapy (MD -2.08, 95% CI -2.31 to -1.84; based on a network of 153 RCTs, 8,713 participants: moderate certainty evidence), jaw exercise plus stretching plus trigger point therapy (MD -1.31 on a 0–10-point scale, 95% CI -1.99 to -0.62: moderate certainty evidence) and jaw exercise plus mobilisation (MD -2.86, 95% CI -3.21 to -2.52: low certainty evidence) all reduced pain compared with placebo.[94]	sufficient
MASSAGE	
Chronic lower back pain	
One systematic review evaluated the effects of massage compared with attention control, sham or usual care on pain. A small short-term improvement in pain was reported for people receiving massage (MD -0.58 on a 0–10 scale, 95% CI -0.93 to -0.29; six RCTs, 703 participants: moderate certainty evidence). There was no difference between massage and controls in intermediate-term pain (MD -0.02, 95% CI -0.56 to 0.44; three RCTs, 680 participants: moderate certainty evidence).[85]	1++
Chronic neck pain	
A systematic review evaluating myofascial release for chronic mechanical neck pain reported no significant difference in pain between myofascial release and a wide range of conventional interventions (eg manual therapy, muscle energy technique, static stretching, suboccipital muscle inhibition technique, manual suboccipital inhibition technique, dry needling, post-isometric relaxation, ultrasound therapy, combined interferential therapy, transcutaneous electric nerve stimulation (TENS) and massage) (SMD -0.35, 95% CI -0.80 to 0.09; 12 RCTs, 539 participants: low certainty evidence).[103]	1+
A further systematic review identified two RCTs which evaluated the effects of massage (Swedish and Tuina) on pain compared with attention control (self-care education), exercise or waiting list. The review did not pool results for these RCTs as each used different comparators. In one small RCT, Tuina massage was associated with moderate improvement in pain intensity experienced during the previous seven days compared with waiting list controls (difference -1.8 on a 0–10 scale, 95% CI -2.7 to -0.9; one RCT; 64 participants: evidence certainty not reported). Another RCT reported no difference in intermediate-term pain comparing	1++

classical massage with neck co-ordination exercises (difference 0.2 on a 0–10 scale, 95% CI -0.82 to 1.22) or muscle performance exercises (no data given, p>0.05; one RCT, 108 participants: low certainty evidence).[85]	
Fibromyalgia pain	
One systematic review identified two RCTs (n=64 and 94 participants, rated at poor to fair quality) which evaluated myofascial release therapy compared with sham (eg electrotherapy or disconnected magnotherapy). The authors note that there was insufficient evidence to determine the effects of myofascial release therapy on short-term pain or intermediate-term pain compared with sham.[85]	1++
Chronic pain associated with osteoarthritis of the knee	
A systematic review included two RCTs which compared the effects of massage with usual care on pain. In the first RCT (125 participants) no significant effects were seen in WOMAC subscale or VAS at four months postmassage treatment versus usual care. The other RCT was poor-quality and reported a small improvement in short-term pain according to WOMAC pain score (difference -1.65 on a 0 to 20 scale, 95% CI -2.93 to -0.37; one RCT, 60 participants: insufficient certainty evidence).[85]	1++
Multiple sclerosis pain	
A Cochrane systematic review identified two RCTs evaluating reflexology for chronic pain associated with multiple sclerosis. A meta-analysis was not possible due to methodological, clinical and statistically heterogeneity of included studies. Both RCTs compared reflexology (ten 45-minute weekly sessions provided by an accredited reflexology specialist) with sham. The review authors reported that in one RCT with 71 participants, compared with baseline, there was a similar clinically and statistically significant decrease in median pain measured using the VAS score in both the reflexology (50% decrease at week 10) and sham (50% decrease at week 10) groups which was maintained up to 22 weeks, but no significant differences between groups. In the second RCT, 75 participants were randomised equally to either reflexology, relaxation or control groups. There were statistically and clinically significant differences in pain scores in the reflexology group (MD -2.56, confidence intervals not reported, p<0.001) and relaxation group (size of effect not reported p=0.01) pre- and post-treatment, whilst no significant changes were found in the control group (MD -0.28, confidence intervals not reported, p=0.34: very low-certainty evidence).[105]	1++
Chronic pelvic pain	
A further systematic review evaluated myofascial manual therapies for chronic pelvic pain syndrome compared with active interventions (eg general exercise, classic global massage, and anaesthetic injection) or usual care (eg oral medications and counselling). Myofascial manual therapies did not significantly reduce pain compared with control (SMD -0.54, 95% CI -1.16 to 0.08; four RCTs, 198 participants: very low-certainty evidence).[101]	1+

Multiple pain conditions

One systematic review evaluated the effect of trigger point manual therapy (TPMT) in people experiencing chronic pain at a range of sites (eg elbow, facial, foot, neck, pelvic, shoulder and wrist pain). The authors note that "trigger points are described as nodules in muscle, located within taut bands, that are painful to palpation, reproduce the patient's symptoms, and cause referred pain". Trigger point manual therapy is believed to reduce symptoms through ischaemic compression by digital pressure and positioning of the affected muscle to ablate the trigger points. The review reported that TPMT did not reduce pain postintervention (SMD -0.53, 95% CI -1.08 to 0.02; 11 RCTs, 535 participants: low certainty evidence).[102]	1+

9.2.2 Function

MANUAL THERAPY

Chronic lower back pain

Three systematic reviews reported data on the effects of manual therapies on functional ability in people with chronic lower back pain.[85,99,104]

The first systematic review compared manipulation and mobilisation interventions with an active comparator (exercise or physical activity). Pooled data from people receiving manual therapy showed a statistically significant reduction in disability (SMD -0.33, 95% CI -0.63 to -0.03; seven RCTs, 923 participants: moderate certainty evidence). Subgroup analysis showed a statistically significant larger effect in favour of manipulation (compared with other active comparators SMD -0.86, 95% CI -1.27 to -0.45; three RCTs, 225 participants: moderate certainty evidence). Mobilisation interventions did not show a statistically significantly larger reduction in disability after treatment compared with other active comparators (SMD -0.10, 95% CI -0.28 to 0.07; five RCTs, 698 participants: moderate certainty evidence). Data were available for six-months follow-up comparing manipulation with other active comparators. The pooled estimate was an SMD of -0.71 (95% CI -0.98 to -0.44; three RCTs, 223 patients: moderate certainty evidence). Mobilisation intervention effects at three and six-months follow-up did not significantly change from post-treatment.[99]	1+
Another systematic review evaluated spinal manipulative therapies including manipulation (thrust) and mobilisation (non-thrust) therapy techniques for chronic low back pain compared with recommended therapies, non-recommended therapies or sham spinal manipulation (see section 9.2.1). Spinal manipulative therapies resulted in a small improvement in function at one month compared with recommended therapies (SMD -0.25, 95% CI -0.41 to -0.09; 16 RCTs, 3,090 participants: moderate certainty evidence). There was no statistically significant improvement at six months (SMD -0.09, 95% CI -0.21 to 0.03; 12 RCTs, 2,762 participants: moderate certainty evidence) or at 12 months (SMD -0.09, 95% CI -0.23 to 0.04; 11 RCTs, 2,635 participants: moderate certainty evidence). Spinal manipulative therapies resulted in a small improvement in function at	1++

one month compared with non-recommended therapies (SMD -0.41, 95% CI -0.67 to -0.15; 7 RCTs, 835 participants: high certainty evidence), at six months (SMD -0.29, 95% CI -0.50 to -0.09; four RCTs, 373 participants: moderate certainty evidence) and at 12 months (SMD -0.42, 95% CI -0.72 to -0.11; one RCT, 169 participants: low certainty evidence). Spinal manipulative therapies resulted in a small improvement in function at one month compared with sham spinal manipulative therapy (SMD -0.73, 95% CI -1.35 to -0.11; six RCTs, 748 participants: low certainty evidence) but this was not maintained at six months (SMD -0.12, 95% CI -0.50 to 0.25; two RCTs, 114 participants: very low-certainty evidence) or at 12 months (SMD -0.19, 95% CI -0.69 to 0.31; one RCT, 63 participants: very low-certainty evidence). Where spinal manipulative therapy was used as adjuvant therapy, there were improvements in function at one month (SMD -0.29, 95% CI -0.55 to -0.03; four RCTs, 955 participants: moderate certainty evidence) and 12 months (SMD -0.21, 95% CI -0.34 to -0.09; one RCT, 994 participants: low certainty evidence) but not at six months (SMD -0.30, 95% CI -0.64 to 0.03; two RCTs, 142 participants: low certainty evidence). No significant differences were reported in function between groups receiving manipulation or mobilisation at one month (SMD 0.16, 95% CI -0.42 to 0.74; four RCTs, 520 participants: low certainty evidence) or six months (SMD 0.16, 95% CI -0.16 to 0.46; one RCT, 175 participants: low certainty evidence).[104]	
In the third systematic review, a small improvement in function was identified for manual therapies at short-term follow-up (SMD -0.24, 95% CI -0.61 to -0.09; four RCTs, 859 participants: low certainty evidence) and intermediate-term follow-up (SMD -0.40, 95% CI -0.85 to -0.05; three RCTs, 1,000 participants: low certainty evidence).[85]	1++
<u>Chronic neck pain</u> Two systematic reviews provided evidence on effects of manual therapies on function in people with chronic neck pain.	
The first systematic review provided separate analyses for studies involving unimodal and multimodal therapies. For unimodal studies, the review compared the effect of thrust interventions that included an exercise regimen to exercise alone on function at timepoints closest to one, three, and six-months follow-up. There was no significant difference in function between thrust interventions plus exercise and exercise only groups at any time point. Given the heterogeneity and varying combinations of interventions being used for each programme, the authors did not conduct a meta-analysis of multimodal studies (which included combination therapies, such as chiropractic care, manual and physical therapy combined with commonly-prescribed exercises, massage, ultrasound, education, or advice in which the effect of the thrust or non-thrust could not be distinguished from that of the programme). Of the eight multimodal RCTs measuring functional disability as an outcome, seven reported improved function using a	1+

multimodal approach although the size of effect and clinical significance was not stated.[100]	
A further systematic review identified a single RCT which evaluated spinal manipulation compared with sham manipulation and with exercise. Spinal manipulation resulted in a moderate improvement in function (difference -18.67 on the 0–100-point Neck Disability Index, 95% CI -26.04 to -11.30; one RCT, 42 participants: low certainty evidence) over the short term compared with sham manipulation but when compared with exercise therapy, there were no differences between groups (effects not reported).[85]	1++
Fibromyalgia pain	
The same systematic review identified one RCT which evaluated the effect of spinal manipulation compared with sham on function. There were no differences between groups on function measured by the Fibromyalgia Impact Questionnaire (0–100, higher score represents greater impact on fibromyalgia) in the short term (adjusted difference 1.2, 95% CI -4.9 to 7.3; one RCT, 101 participants: low certainty evidence) and intermediate term (adjusted difference -1.1, 95% CI -7.9 to 5.6; one RCT, 101 participants: low certainty evidence).[85]	1++
Chronic pain associated with osteoarthritis of the hip	
The same systematic review identified two RCTs which evaluated the effects of manual therapy compared with usual care (continued routine care from a general practitioner and other providers) and with combination exercise programmes on function. Compared with usual care, one RCT reported that manual therapy resulted in an improvement in function at intermediate term using the total WOMAC score (0 to 240) in the manual therapy group (mean change from baseline -22.9, 95% CI -43.3 to -2.6), but there was no significant change from baseline in the usual care group (mean change -7.9, 95% CI -30.9 to 15.3) or exercise group (mean change -12.4, 95% CI -27.1 to 2.3; one RCT, 69 participants: low certainty evidence). Review authors noted that a lack of data prevented calculation of effect size, and further results were not presented. Compared with exercise, one RCT showed that manual therapy resulted in a small improvement in short-term function (adjusted difference on the 0–100-point Harris Hip Score of 11.1, 95% CI 4.0 to 18.6; one RCT, 109 participants: low certainty evidence) and intermediate-term function (adjusted difference 9.7, 95% CI 1.5 to 17.9; one RCT, 109 participants: low certainty evidence) compared with exercise.[85]	1++
Chronic pain associated with osteoarthritis of the knee	
The same systematic review identified a single RCT which evaluated the effect of joint manipulation on function compared with usual care. The manipulation group showed a statistically significant improvement from baseline in function as measured by the WOMAC score (mean change -31.5 on a 0-240 scale, 95% CI -52.7 to -10.3), whereas the usual care group showed no significant improvement (mean change 1.6, 95% CI -10.5 to 13.7; one RCT, 58 participants: insufficient certainty evidence). The review authors note that insufficient data was provided to calculate an	1++

effect estimate.[85]	
Chronic pelvic pain syndrome	
A systematic review evaluated studies comparing myofascial manual therapies with various control procedures in people with chronic pelvic pain syndrome. Four RCTs of myofascial manual therapies which used osteopathic manipulative treatment or global therapeutic massage as comparators were combined in meta-analysis. Myofascial manual therapies did not significantly improve function compared with other procedures (effect size -0.37, 95% CI -0.87 to 0.13; four RCTs, 187 participants: very low-certainty evidence).[101]	1+
MASSAGE	
Chronic lower back pain	
A systematic review evaluated the effect of a range of massage techniques (such as acupressure, myofascial release, reflexology and Swedish massage) on function compared with sham or usual care in people with chronic lower back pain. A small improvement in short-term function was reported for people receiving massage compared with control (SMD -0.40, 95% CI -0.62 to -0.24; seven RCTs, 753 participants: moderate certainty evidence). This improvement was not maintained in the intermediate term (SMD -0.09, 95% CI -0.26 to 0.12; three RCTs, 676 participants: low certainty evidence).[85]	1++
Chronic neck pain	
The same systematic review evaluated the effect of massage (Swedish and Tuina) on function compared with attention control (self-care education), exercise or waiting list. There was no significant difference between Swedish massage and attention control on function (≥5 point improvement on the Neck Disability Index) in the short term (39% versus 17%, RR 2.7, 95% CI 0.99 to 7.5) or intermediate term (57% versus 31%, RR 1.8, 95% CI 0.97 to 3.5; one RCT, 64 participants: low certainty evidence). People receiving massage experienced a small improvement in short-term function compared with attention or waiting list control (pooled difference -3.66 on a 0-50 Neck Disability Index scale, 95% CI -6.58 to -0.56; two RCTs, 148 participants: low certainty evidence).[85]	1++
A further systematic review evaluated the effect of myofascial release therapy on function compared with various interventions including electrotherapy, physical therapy and traction in people with chronic mechanical neck pain. No improvement in function was reported for myofascial release therapy measured using the Neck Disability Index (SMD -0.21, 95% CI -0.58 to 0.16; eight RCTs, 379 participants: moderate certainty evidence).[103]	1+
Fibromyalgia pain	
A systematic review included two RCTs which evaluated myofascial release therapy compared with sham (eg electrotherapy) in people with chronic fibromyalgia pain. Myofascial release therapy resulted in a small improvement in intermediate-term function compared with sham as	1++

measured by the FIQ (0–100, higher score represents greater impact of fibromyalgia) (mean score 58.6, standard deviation, (SD) 6.3 versus mean score 64.1, SD 18.1, p=0.048) for the group in one fair-quality trial. The effect did not persist to the long term (mean score 62.8 (SD) 20.1 versus mean score 65.0 (SD) 19.8, p=0.329 at 12 months.(one RCT, 94 participants: low certainty evidence).[85]	
Chronic pain associated with osteoarthritis of the knee	
The same systematic review evaluated the effect of massage on function compared with usual care in people with chronic pain associated with osteoarthritis of the knee. Two RCTs were identified in which function was measured using the WOMAC total and physical function subscale scores. In one RCT, no significant effects were seen four months post-massage treatment compared with usual care (effect sizes not reported; one RCT, 125 participants: insufficient certainty evidence). In the other, poor-quality, RCT there was no difference between groups in short-term function according to the WOMAC physical function (difference -1.63 on a 0 to 68 scale, 95% CI -6.72 to 3.46; one RCT, 60 participants: insufficient certainty evidence).[85]	1++
Multiple sclerosis pain	
A Cochrane systematic review identified one RCT evaluating the effect of reflexology on function in people with chronic pain associated with multiple sclerosis. The RCT compared reflexology (ten 45-minute weekly sessions provided by an accredited reflexology specialist) with sham. Both intervention and sham groups showed significant decrease in disability at 10 weeks post-intervention on the RMDQ (effect size not reported; one RCT; 71 participants: very low-certainty evidence).[105]	1++
Multiple pain conditions	
One systematic review evaluated the effect of TPMT on function in people experiencing chronic pain at a range of sites (eg elbow, facial, foot, neck, pelvic, shoulder and wrist pain). Trigger point manual therapy improved function compared with control (eg dry needling, manual therapy and placebo) (SMD -0.81, 95% CI, -1.49 to -0.14; 15 RCTs, 802 participants: low certainty evidence).[102]	1+

9.2.3 Quality of life

MANUAL THERAPY

Chronic neck pain	
One systematic review compared the effect of manipulation plus exercise with exercise alone on quality of life in people with chronic neck pain. No statistically significant effects at one-month (SMD 0.19, 95% CI, -0.28 to 0.66; three RCTs, 405 participants), three-months (SMD 0.25, 95% CI, -0.30 to 0.80; three RCTs, 405 participants) and six-months follow-up (SMD 0.07, 95% CI, -0.46 to 0.59; three RCTs, 405 participants) were reported. The quality of the evidence was rated as moderate to low overall by review authors with no further categorisation.[100]	1+

MASSAGE

Two systematic reviews reported no statistically significant effect for massage interventions on quality of life in people with chronic pain (including musculoskeletal, pelvic and facial pain).[101,102] 1+

In the systematic review of reflexology for chronic pain associated with multiple sclerosis, the authors reported that one RCT measured significant improvements on the Multiple Sclerosis Impact Scale-29 psychological subscale in both intervention and sham groups by week 10. The intervention group demonstrated a greater reduction.[105] 1++

9.2.4 Adherence to intervention

No evidence was identified which reported data on this outcome.

9.2.5 Healthcare use or attendance

Three systematic reviews were identified which investigated healthcare utilisation associated with manual therapies in people with chronic pain.[85,102,105] The review authors were unable to identify any data. 1++, 1+

9.3 Evidence of harms

Seven out of the nine systematic reviews identified for hands-on physical therapies for chronic pain reported data on adverse events/reactions.[85,99-104] In general, few adverse events were reported and were not associated with significant effects.

9.3.1 Manual therapy

Four systematic reviews provided data on adverse events/reactions associated with manual therapies.[85,99,100,104] Information provided by the included RCTs was limited. The most common adverse event was an increase in pain following manual therapy. In one systematic review, one serious adverse event was judged by the Data Safety Monitoring Board as possibly being related to spinal manipulative therapy.[104] 1+ 1++

9.3.2 Massage

Four systematic reviews provided data on adverse events/reactions associated with massage.[85,101-103] Information provided by the included RCTs was limited. The most common adverse event was increase in pain following massage. However, this was mild in severity and temporary in nature. One systematic review investigating TPMT reported that most studies reported no adverse events. In the three RCTs which reported any adverse events, these included increased pain, infection, gastrointestinal disturbance and constitutional symptoms. Overall there was no significantly increased risk of adverse events in the treatment group (OR 2.04, 95% CI 0.88 to 4.73; three RCTs, 200 participants: low certainty evidence).[102] 1+ 1++

9.4 Summary of benefits and harms of hands-on physical therapies for chronic pain

Systematic reviews are largely consistent in suggesting that manual therapy (manipulation and mobilisation) offers modest pain reductions for certain

conditions, for example low back pain, but the effect sizes are generally small, and the clinical significance of these reductions is unclear in some cases. There is also variability in how different pain conditions respond to manual therapy, with conditions such as lower back pain showing better responses than chronic neck pain, where effects were inconsistent, and with fibromyalgia, where no beneficial effects of manipulation were reported. For all conditions, the certainty of evidence is often rated as moderate to low, which reduces confidence in these findings.

The evidence for massage therapy as a means of pain reduction is inconsistent. While some interventions show positive effects, in small, short-term studies, the overall certainty of the evidence is low or very low. This suggests that while there may be some potential benefits from reflexology, myofascial release, and massage therapies for chronic pain, these interventions are not consistently effective across all types of chronic pain, and more high-quality research is needed to provide reliable conclusions.

The evidence for the effects of manual therapies or massage on function is also inconsistent. While systematic reviews report modest short-term improvements in function for people with chronic back pain and in those with chronic hip osteoarthritis, manual therapy did not enhance function for people with chronic pelvic pain, fibromyalgia, or chronic neck pain. While certain manual therapies, such as reflexology, trigger point therapy and massage may provide small short-term improvements in function for specific chronic pain conditions, the evidence certainty is often low, and the effects may not be sustained in the long term.

No evidence of an effect of manual therapies on quality of life, adherence to therapies, healthcare use or attendance was identified.

The guideline development group considered the large volume of low-certainty evidence which described inconsistent effects on pain and function across different populations of people with chronic pain conditions. As no intervention appeared to be universally beneficial in all groups, the group decided that recommendations supporting manual therapies should not be applied universally to all people experiencing chronic pain and have made more specific recommendations in line with the strongest evidence of benefit.

9.5 Other factors

The guideline development group acknowledges that pain scores are not a standard outcome measure used by pain services across Scotland, with the focus being on function and quality of life measures, and has taken this into account in forming an appropriate recommendation.

9.6 Recommendations

R **Manual therapy may be considered for short-term improvement in function in people with chronic low back pain or hip osteoarthritis. If offered, it should be delivered alongside other active supported self-management approaches.**

10 Electrotherapy

10.1 Introduction

Electrotherapy is the therapeutic use of different forms of low- or medium-frequency electric currents to achieve physiological responses for clinical benefit. Therapeutic ultrasound is also considered an electrotherapy modality and uses high frequency sound waves to achieve similar physiological responses to other electrotherapy techniques. Electrotherapy modalities are considered a non-invasive, non-pharmacological treatment and are usually administered as part of physiotherapy management.

There is a broad range of contemporary electrotherapy modalities and, for many, the mechanism of action is currently unclear. Mechanisms of action are thought to include pain modulation via activation of pain gate mechanisms, delivery of mechanical forces to alter the physical properties of tissues and influence tissue healing, and repair by stimulation of cellular activity and reduction of inflammation.[107]

10.2 Evidence of benefit

A large volume of systematic reviews was identified. In order to limit the number of studies included as evidence, one large systematic review and meta-analysis of non-pharmacological treatment for chronic pain carried out by AHRQ which included evidence for a range of interventions in several pain types was considered the index review,[85] and other sources were considered against this and prioritised for inclusion accordingly. The prioritisation approach included comparing review objectives and overlap analysis of the included studies across reviews where similar interventions and/or chronic pain conditions were present. Studies were prioritised for inclusion where they reported on outcomes or populations which were not included in the index review.

Six systematic reviews were included as evidence for the topic of electrotherapy in people with chronic pain. Five systematic reviews employed meta-analysis[85,108-111] and one narratively reported the results, as pooling data for meta-analysis was not possible due to methodological, clinical and statistically heterogeneity of the included studies.[112] The latter review was included as it investigated non-pharmacological interventions for chronic pain associated with multiple sclerosis, a condition not included in the index review.[85]

Two systematic reviews focused on chronic prostatitis/chronic pelvic pain syndrome.[108,111] One review focused on burning mouth syndrome.[110] One review focused on multiple sclerosis.[112] One review focused pain irrespective of diagnosis, but analysed and reported chronic pain results separately.[109] One review focused on more than one chronic pain condition (eg chronic low back pain, chronic neck pain, fibromyalgia and osteoarthritis).[85] These represent conditions which are seen by specialist and non-specialist health services in NHS Scotland. The majority of participants in trials included within the systematic reviews were female, which is consistent with the context in Scotland where there is a higher

incidence of females reporting chronic pain.[113]

Whilst the methodological quality of the systematic reviews was acceptable or high quality, the evidence provided by RCTs underpinning the review conclusions was frequently low to very low certainty. This means confidence in the effect sizes reported across the reviews is reduced.

Relevant interventions included in the reviews were:

- extracorporeal shockwave therapy treatment (ESWT) including low-intensity shockwave therapy (LiST),
- high-level laser therapy (HLLT),
- interferential therapy (IT),
- low-level laser therapy (LLLT),
- shortwave diathermy (SDi),
- therapeutic ultrasound (TU) and
- transcutaneous electrical nerve stimulation (TENS).

10.2.1 Pain

Extracorporeal shockwave therapy treatment (ESWT) including low-intensity shockwave therapy (LiST)

One systematic review evaluated evidence for a range of interventions in men with chronic prostatitis/chronic pelvic pain syndrome. While the primary outcome was reduction in prostatitis symptoms measured by National Institutes of Health – Chronic Prostatitis Symptom Index (NIH-CPSI) score (0 to 43), the review also reported NIH-CPSI pain subscore (0 to 21). Compared with sham procedure, ESWT reduced pain in the short term (defined as up to 12 months) (MD -4.74 on a 0 to 21 scale), 95% CI -5.54 to -3.94; one RCT, 37 participants: no evidence certainty rating) but there was no evidence of effect in the long term (MD -0.01 on a 0 to 21 scale, 95% CI -1.26 to 1.24; one RCT, 37 participants: no evidence certainty rating). Compared with no treatment, ESWT reduced pain in the short term (MD -3.83 on a 0 to 21 scale, 95% CI -6.03 to -1.63; one RCT, 60 participants: no evidence certainty rating) and in the long term (over 12 months) (MD -4.27 on a 0 to 21 scale, 95% CI -6.15 to -2.39; one RCT, 60 participants: no evidence certainty rating). The authors note that caution must be taken when interpreting these findings, as the NIH-CPSI subscore has not been validated as a robust independent measure of pain in this population and a MCID has not been developed for the subscores.[108]	1++
A further systematic review explored low-intensity shockwave therapy (LiST) for the management of chronic prostatitis/chronic pelvic pain syndrome. Compared with sham intervention, LiST reduced pain measured by both NIH-CPSI pain subscore and NPRS immediately postintervention and at one and three-months follow-up after treatment, but not at six months (*see Table 3*). Certainty of evidence was low for all analyses. The authors note that the absolute improvement in the NIH-CPSI pain domain score, compared with baseline, was within 4–6 points which represents a clinically important difference.[111]	1+

Table 3: Effects of LiST on pain from baseline measured by NIH-CPSI and NPRS compared with sham intervention

Pain measure and timing	Effect (95% CI)	Number of RCTs (participants)
Pain on NPRS (0–10) (after the intervention)	WMD 1.43 (0.85 to 2.01)	2 (91)
Pain on NPRS (0–10) (one-month follow-up)	WMD 2.59 (1.92 to 3.27)	2 (105)
Pain on NPRS (0–10) (three-months follow-up)	WMD 2.64 (2.13 to 3.16)	3 (136)
Pain on NPRS (0–10) (six-months follow-up)	No data	
NIH-CPSI pain domain score (0 to 21) (after the intervention)	WMD 3.2 (0.88 to 5.52)	3 (151)
NIH-CPSI pain domain score (0 to 21) (one-month follow-up)	WMD 4.4 (2.84 to 5.95)	2 (125)
NIH-CPSI pain domain score (0 to 21) (three-months follow-up)	WMD 3.61 (1.49 to 5.74	4 (196)
NIH-CPSI pain domain score (0 to 21) (six-months follow-up)	WMD 0.86 (-2.18 to 3.9)	2 (85)

NIH-CPSI: National Institute of Health Chronic Prostatitis Symptom Index
NPRS: numerical pain rating scale

Transcutaneous electrical nerve stimulation

A systematic review evaluated the efficacy and safety of transcutaneous electrical nerve stimulation (TENS) for acute and chronic pain in adults. Based on pooled analysis of results from studies with any type of chronic pain, TENS reduced pain intensity after the intervention compared with a placebo intervention (SMD -0.87, 95% CI -1.19 to -0.55; 31 RCTs, 1,417 participants: no evidence certainty rating).[109] Pain was also reduced in people with chronic neuropathic pain who received TENS (SMD -1.68, 95% CI -2.58 to -0.78; seven RCTs, 169 participants: no evidence certainty rating) but there was no evidence of an effect in those with chronic secondary musculoskeletal pain (SMD -0.27, 95% CI -0.81 to 0.26; three RCTs, 164 participants: no evidence certainty rating) or chronic secondary visceral pain (SMD -1.31, 95% CI -2.79 to 0.17; four RCTs, 114 participants: no evidence certainty rating). The authors note that subgroup analyses on pain characteristics found no persuasive evidence that the effects of TENS were moderated by pain diagnosis or characteristics and concluded that TENS may alleviate the intensity of pain, irrespective of pain diagnosis. Treatment effects of TENS were not modified when pain was categorised by diagnoses according to RCT author. The direction subgroup effects were in favour of TENS but of different sizes, although substantial heterogeneity between results from the trials within each subgroup undermined confidence

1++

in the magnitude of treatment effect estimates. The authors also note that the primary outcome effect estimate (SMD -0.87) represents a large effect and judged there to be moderate-certainty evidence that the magnitude of the effect size estimate exceeds the prespecified threshold for clinical importance (SMD >0.5 or <-0.5).	
One systematic review of non-pharmacological interventions for men with chronic prostatitis identified two small, poor-quality RCTs involving TENS which could not be combined in meta-analysis due to differences in study design and small sample sizes.[108] One RCT reported that TENS reduced pain measured by NIH-CPSI pain domain subscore in the short term compared with sham procedure (MD -15.25 on a 0 to 21 scale, 95% CI -17.71 to -12.79; one RCT, 40 participants: no evidence certainty rating). The second RCT reported TENS reduced pain in the short term compared with no intervention (although review authors note that the baseline pain scores were not equal between treatment and control groups and categorise the RCT at high risk of bias) (MD -6.88 on a 0 to 21 scale, 95% CI -8.13 to -5.63; one RCT, 16 participants: no evidence certainty rating).	1++
The index review carried out by AHRQ evaluated a wide range of non-pharmacological treatments for people with chronic pain. In people with chronic back pain, there was no evidence of an effect for burst TENS (MD -0.80 on a 0–10 scale, 95% CI -2.24 to 0.64; one RCT, 73 participants: low certainty evidence) or conventional TENS (MD -1.30, on a 0–10 scale, 95% CI -2.74 to 0.14; one RCT, 73 participants: low certainty evidence) on pain compared with sham procedure in the short term. In people with knee osteoarthritis, there was no evidence of an effect for TENS compared with placebo (MD 0.90, 95% CI -11.7 to 13.4; one RCT, 70 participants: low certainty evidence) or compared with sham procedure (MD 0.09, 95% CI -0.41 to 0.59; one RCT, 220 participants: low certainty evidence) in the intermediate term.[85]	1++
A systematic review of people with chronic low back pain due to multiple sclerosis found no evidence of a clinically or statistically significant effect of TENS compared with sham on pain intensity (effect size not reported; one RCT, 90 participants: very low-certainty evidence).[112]	1++
<u>Low-level laser therapy</u>	
One systematic review evaluated evidence for the effect of low-level laser therapy (LLLT) on outcomes in people with burning mouth syndrome - a condition associated with chronic oral pain without an obvious cause, but which may have a neuropathic underpinning. In the short term, LLLT reduced pain compared with sham or placebo (SMD -0.92, 95% CI -1.38 to -0.46; seven RCTs, 321 participants: very low-certainty evidence) but there was no evidence of a difference in effect on pain compared with clonazepam (SMD -0.47, 95% CI -1.17 to 0.23; one RCT, 33 participants: very low-certainty evidence).[110]	1++
The index review carried out by AHRQ evaluated, separately, the effect of LLLT in people with chronic low back pain, chronic neck pain, chronic pain associated with hand osteoarthritis and chronic pain associated with knee	

osteoarthritis.[85] In people with chronic low back pain, one fair-quality RCT reported that LLLT reduced pain in the short term compared with sham laser (MD -16.0 on a 0–100 scale, 95% CI -28.3 to -3.7; one RCT, 59 participants: low certainty evidence). A second RCT, which was assessed to be poor quality and was funded by industry, reported a large improvement in pain in those using LLLT (MD -4.40 on a 0–10 scale, 95% CI -5.31 to -3.49; one RCT, 34 participants: low certainty evidence) compared with sham laser in the short term. A further poor-quality RCT reported an increased likelihood of having no pain at intermediate-term follow-up in those receiving LLLT compared with sham laser, (44.7% vs 15%, p<0.01; one RCT, 71 participants: low certainty evidence) but the analysis was restricted to patients who reported that laser therapy was effective at the end of a two-week course of treatment. In people with chronic low back pain, one fair-quality trial reported no clear differences in pain between people who received laser therapy compared with those receiving exercise plus sham laser (mean difference in change from baseline -0.9 on a 0–10 scale, 95% CI -2.5 to 0.7; one RCT, 53 participants: low certainty evidence) at short-term follow-up.[85] In people with chronic neck pain, LLLT reduced pain compared with sham laser (MD -1.89 on a 0–10 scale, 95% CI -3.34 to -0.06; three RCTs, 192 participants: moderate certainty evidence) at short term follow-up. [85] There was no evidence of a short-term effect of LLLT on pain compared with sham laser in people with chronic pain associated with hand osteoarthritis (MD 0.1 on a 0–10 scale, 95% CI -0.3 to 0.5; one RCT, 88 participants: low certainty evidence) or in people with chronic pain associated with knee osteoarthritis (MD -1.50 on a 0–10 scale, 95% CI -3.18 to 0.16; three RCTs, 160 participants: low certainty evidence). There was also no evidence of an effect of LLLT on pain in the intermediate term (MD -1.24 on a 0–10 scale, 95% CI -2.22 to 0.12; three RCTs, 193 participants: low certainty evidence). [85]	1++
<u>Therapeutic ultrasound</u> A systematic review evaluated evidence for the effect of therapeutic ultrasound (TU) on pain in men with chronic prostatitis/ chronic pelvic pain syndrome. One small, poor quality RCT was identified which assessed the effects of TU alone or in combination with westernised Chinese medical therapy compared with westernised Chinese medical therapy alone. There was no evidence of an effect of TU on prostatitis symptoms when delivered alone compared with westernised Chinese medical therapy (MD 0.37 on a 0–21 scale, 95% CI -0.18 to 0.92; one RCT, 70 participants: no evidence certainty rating). When added to westernised Chinese medical therapy, the combination therapy reduced pain more than westernised Chinese medical therapy alone (MD -1.87 on a 0–21 scale, 95% CI -2.59 to -1.15; one RCT, 70 participants: no evidence certainty rating).[108]	1++
The index AHRQ systematic review identified two RCTs on TU in people	

with chronic low back pain which were not combined in meta-analysis. These showed no evidence of an effect on pain in the short term compared with sham ultrasound (two RCTs, 505 participants: low certainty evidence).[85]

In people with chronic pain associated with knee osteoarthritis, there was no evidence of an effect on pain using pooled evidence from trials which compared continuous and pulsed TU with sham ultrasound (MD -1.07 on a 0–10 scale, 95% CI -2.81 to 0.67; four RCTs, 324 participants: low certainty evidence).[85]

1++

Interferential therapy

The AHRQ systematic review identified two RCTs on interferential therapy (IT), one each in people with chronic low back pain and chronic pain associated with knee osteoarthritis. In people with chronic back pain IT was associated with a small reduction in pain compared with placebo intervention. The review was unable to calculate statistics to support an effect size, due to reporting errors in the original study, although the review authors reported that the mean difference between treatment and control groups was below the threshold for a small effect.

In people with chronic pain associated with knee osteoarthritis there was no evidence of an effect of IT on pain at rest compared with sham procedure in the short term (MD -0.87 on a 0–10 scale, 95% CI -2.01 to 0.26; one RCT, 84 participants: low certainty evidence) or intermediate term (MD -0.32 on a 0–10 scale, 95% CI -1.34 to 0.70 one RCT, 84 participants: low certainty evidence). There was also no evidence of an effect of IT on pain during activity in the short term (MD -0.42, 95% CI -1.65 to 0.80) or intermediate term (MD 0.49, 95% CI -1.63 to 0.64; one RCT, 84 participants: low certainty evidence).[85]

Shortwave diathermy

The AHRQ systematic review identified one RCT evaluating shortwave diathermy (SDi) in people with chronic back pain (68 participants) and three RCTs evaluating SDi in people with chronic pain associated with knee osteoarthritis (264 participants). The review authors reported that the evidence was insufficient to determine the effects of SDi over any time period.[85]

1++

10.2.2 Function

Extracorporeal shockwave therapy treatment (ESWT) including low-intensity shockwave therapy (LiST)

No evidence was identified on the effects of ESWT or LiST on function in people with chronic pain.

Transcutaneous electrical nerve stimulation

Effects of TENS on function in people with chronic pain were generally not reported in systematic reviews considered for this guideline. A systematic review of non-pharmacological interventions for chronic pain in people with low back pain due to multiple sclerosis identified a single RCT which reported no significant changes in disability between treatment and placebo groups and within groups (no effects reported; one RCT, 90 participants:

1++

very low-certainty evidence).[112]

The AHRQ systematic review reported no evidence of an effect on function for either burst TENS (MD -2.90 on a 0–50 scale, 95% CI -7.97 to 2.17; one RCT, 73 participants: low certainty evidence) or conventional TENS (MD -2.30 on a 0–50 scale, 95% CI -7.77 to 3.17; one RCT, 73 participants: low certainty evidence) compared with sham in people with chronic low back pain. [85]

In people with chronic pain associated with knee osteoarthritis, there was no evidence of an effect of TENS on function compared with placebo in the intermediate term (MD -1.9 on a 0–100 scale, 95% CI -9.7 to 5.9; one RCT, 70 participants: low certainty evidence) and no evidence of an effect of TENS on function compared with sham in the short term (MD 0.08 on a 0–63 scale, 95% CI -0.28 to 0.43; one RCT, 220 participants: low certainty evidence).[85] 1++

Low-level laser therapy

The AHRQ systematic review identified RCTs which reported on the effects of LLLT on function in people with chronic low back pain, chronic neck pain or chronic pain associated with knee or hand osteoarthritis.

In people with chronic low back pain, LLLT improved function in the short term compared with sham laser (MD -8.2 on a 0–100 scale, 95% CI -13.6 to -2.8; one RCT, 56 participants: low certainty evidence). Based on a further small, poor-quality trial, LLLT improved function compared with sham (MD -5.70 on a 0 to 24 scale, 95% CI -8.47 to -2.93; one RCT: 34 participants: low certainty evidence). One trial found no evidence of a difference between LLLT and exercise therapy in intermediate-term function (difference in change from baseline -4.4 on a 0–100 scale, 95% CI -11.4 to 2.5; one RCT, 53 participants: low certainty evidence).[85]

In people with chronic neck pain, LLLT resulted in a moderately greater effect on short-term function compared with sham (pooled difference -13.60 on a 0–100 scale, 95% CI -26.30 to -6.30; two RCTs, 144 participants: moderate certainty evidence).[85] 1++

There was no evidence of an effect of LLLT on short-term function compared with sham laser therapy in people with chronic pain associated with hand osteoarthritis (MD 0.2 on a 0–100 scale, 95% CI -0.2 to 0.6; one RCT 88 participants: low certainty evidence). There was no evidence of an effect of LLLT on function compared with sham laser therapy in people with chronic pain associated with knee osteoarthritis in the short term (SMD -0.39, 95% CI -0.80 to 0.00, two RCTs, 133 participants: low certainty evidence) or intermediate term (SMD -0.54, 95% -1.19 to 0.05; three RCTs, 193 participants: low certainty evidence).[85]

Therapeutic ultrasound

The AHRQ systematic review reported inconsistent effects of TU on function in people with chronic low back pain. One good quality RCT (455 participants) found no difference between TU and sham ultrasound in RMDQ score, which is a measure of function (median 3 vs 3). A further 1++

smaller trial (50 participants), TU was associated with better short-term function than sham ultrasound (MD 7.7 on a 0 to 40 scale, confidence intervals not reported).[85]	
There was no evidence of an effect of TU on function compared with sham ultrasound in the short term in people with chronic pain associated with knee osteoarthritis when measured by either Lequesne Index (MD -2.50 on a 0–24 scale, 95% CI -6.37 to 1.22; three RCTs, 249 participants: low certainty evidence) or WOMAC physical function scale (MD -2.50 on a 0–68 scale, 95% CI -8.11 to 3.12; one RCT, 75 participants: low certainty evidence).[85]	
Interferential therapy	
The AHRQ systematic review reported no evidence of any effect of IT on function in people with chronic low back pain or chronic pain associated with knee osteoarthritis. The authors include one trial in people with low back pain which reported that IT was associated with an effect on short-term function that was below the threshold for small (statistical significance uncertain) when compared with a placebo therapy.	1++
In people with chronic pain associated with knee osteoarthritis, there was no evidence of an effect for IT compared with sham procedure in the short term (MD 0.55 on a 0–96 scale, 95 % CI -24.31 to 7.05) or intermediate term (MD 1.42 on a 0–96 scale, 95 % CI -6.73 to 9.58; one RCT, 84 participants: low certainty evidence).[85]	
Shortwave diathermy	
The AHRQ systematic review identified one RCT evaluating SDi in people with chronic back pain (68 participants) and three RCTs evaluating SDi in people with chronic pain associated with knee osteoarthritis (264 participants). The review authors reported that the evidence was insufficient to determine the effects of SDi over any time period.[85]	1++

10.2.3 Quality of life

Extracorporeal shockwave therapy treatment (ESWT) including low-intensity shockwave therapy (LiST)	
A systematic review of non-pharmacological interventions for treating chronic prostatitis/chronic pelvic pain syndrome identified two small RCTs which reported on the effect of ESWT on QoL. Each study measured QoL in terms of prostatitis symptoms using NIH-CPSI quality of life subscore (0–12). One RCT found ESWT had a significant effect on QoL compared with sham procedure in the short term (MD -1.73 on a 0–12 scale, 95% CI -2.35 to -1.11; one RCT, 37 participants: no evidence certainty rating) but not in the intermediate term (MD -0.16 on a 0–12 scale, 95% CI -0.98 to 0.66; one RCT, 37 participants: no evidence certainty rating). A further RCT found ESWT had a significant effect on QoL compared with no intervention in the short term (MD -2.46 on a 0–12 scale, 95% CI -3.94 to -0.98; one RCT, 60 participants: no evidence certainty rating) and intermediate term (MD -2.03 on a 0–12 scale, 95% CI -3.62 to -0.44; one RCT, 60 participants: no evidence certainty rating).[108]	1++
A further systematic review evaluated the effects of LiST in men with	1+

prostatitis / chronic pelvic pain syndrome. The authors report LiST improved QoL compared with sham immediately postintervention (WMD 2.52 on a 0–12 scale, 95% CI 1.23 to 3.81; three RCTs, 151 participants), at one-month follow-up (WMD 3.93 on a 0–12 scale, 95% CI 1.40 to 6.47; two RCTs, 125 participants), at three-months' follow-up (WMD 2.81 on a 0–12 scale, 95% CI 0.83 to 4.80; four RCTs, 196 participants) but not at six months (WMD 1.43 on a 0–12 scale, 95% CI -1.22 to 4.07; two RCTs, 85 participants: no evidence certainty rating for any analysis).[111]

Transcutaneous electrical nerve stimulation

Effects of TENS on QoL in people with chronic pain were generally not reported in systematic reviews considered for this guideline.

One systematic review of people with chronic low back pain due to multiple sclerosis found no evidence of an effect of TENS compared with sham on QoL (no effects reported; one RCT, 90 participants: very low-certainty evidence).[112] 1++

Low-level laser therapy

A systematic review evaluated the effects of LLLT on pain and QoL in people with chronic burning mouth syndrome. Oral health-related QoL was assessed by the Oral Health Impact Profile-14. There was no evidence of an effect of LLLT on QoL in the short term (SMD 0.03, 95% CI -0.63 to 0.70: seven RCTs, 346 participants: very low-certainty evidence).[110] 1++

Therapeutic ultrasound

A systematic review evaluated evidence for the effect of therapeutic ultrasound (TU) on pain in men with chronic prostatitis / chronic pelvic pain syndrome. One small, poor quality RCT was identified which assessed the effects of TU alone or in combination with westernised Chinese medical therapy compared with westernised Chinese medical therapy alone. There was no evidence of an effect of TU on prostatitis symptoms QoL subscore when delivered alone compared with westernised Chinese medical therapy (MD -0.41 on a 0–12 scale, 95% CI (-1.35 to 0.53; one RCT, 70 participants: no evidence certainty rating). When added to westernised Chinese medical therapy, the combination therapy improved QoL more than westernised Chinese medical therapy alone (MD -2.63 on a 0–12 scale, 95% CI -3.60 to -1.66; one RCT, 70 participants: no evidence certainty rating).[108] 1++

Interferential therapy

No evidence was identified on the effects of IT on QoL in people with chronic pain.

Shortwave diathermy

No evidence was identified on the effects of SDi on QoL in people with chronic pain.

10.3 Evidence of harms

Adverse events were not consistently reported across interventions and pain conditions. Where reported, they appear infrequent and, most commonly, there was no evidence of an effect compared with controls.

Extracorporeal shockwave therapy treatment (ESWT) including low-intensity shockwave therapy (LiST)	
One systematic review in men with chronic prostatitis / chronic pelvic pain syndrome identified three RCTs which included information on adverse events of ESWT. In two RCTs, no adverse events were reported. In the third RCT, there was no evidence of a difference in adverse events between people receiving ESWT and those who did not receive ESWT (RR 1.22, 95% CI 0.59 to 2.51; one RCT, 60 participants: low certainty evidence).[108]	1++
A further systematic review in men with chronic prostatitis / chronic pelvic pain syndrome evaluated the benefits and harms of LiST. Five of the six included RCTs reported that LiST was well tolerated and no adverse events were reported. The remaining RCT reported four cases (out of 16) of transient haematuria and haematospermia in the treatment group.[111]	1+
Transcutaneous electrical nerve stimulation	
Where reported, adverse events of TENS were noted to be mild in severity, infrequent in occurrence and included skin irritation, tenderness and TENS discomfort.[85,109]	1++
Low-level laser therapy	
One systematic review reported no serious adverse events associated with LLLT in people with burning mouth syndrome.[110]	1++
The AHRQ index review reported no adverse events from three RCTs of LLLT in people with chronic low back pain. In people with chronic neck pain, adverse effects were reported with similar frequency in treatment and control groups. In people with chronic pain associated with hand osteoarthritis, no serious adverse events were reported in people receiving LLLT.[85]	1++
Therapeutic ultrasound	
A systematic review identified one RCT which evaluated TU alone compared with TU in combination with westernised Chinese medical therapy. The review authors reported that the study reported five cases of vertigo, six cases of gastrointestinal discomfort and three cases of sleepiness but indicated the RCT did not specify which group experienced them.[108]	1++
The AHRQ index review reported no evidence of an effect of TU compared with sham on any adverse events (RR 1.03, 95% CI 0.49 to 2.13; one RCT, 455 participants: low certainty evidence) or on serious adverse events (RR 0.48, 95% CI 0.12 to 1.88; one RCT, 455 participants: low certainty evidence) in people with chronic low back pain.	
In people with chronic pain associated with knee osteoarthritis, four RCTs reported no adverse events in people receiving TU and one RCT reported two study withdrawals in the sham group only.	
Interferential therapy	
The AHRQ index review reported no evidence of an effect of IT on adverse events compared with placebo in people with chronic low back pain (RR 1.0,	1++

95% CI 0.14 to 6.8; one RCT, 150 participants: no evidence certainty rating).

In people with chronic pain associated with knee osteoarthritis, one RCT reported no difference in withdrawal due to any adverse event between those receiving IT compared with controls.[85]

Shortwave diathermy

The AHRQ index review reported insufficient evidence available to determine the effects of SDi on adverse events in people with chronic pain.[85] 1++

10.4 Summary of benefits and harms of electrotherapy for chronic pain

There is inconsistent evidence to support any electrotherapy modality in people with chronic pain.

Shockwave therapy (ESWT or LiST) reduced pain and improved QoL in men with chronic prostatitis / chronic pelvic pain syndrome in the short term but the effects on function are not known.

There is inconsistent evidence that TENS may reduce pain in people with a range of pain conditions, although different systematic reviews include results which suggest clinically significant benefit or no evidence of any effect depending on the pain conditions included, volume and certainty of evidence. There was no evidence of any effect of TENS on function or QoL.

There is evidence that LLLT may reduce short-term pain in people with burning mouth syndrome to a greater degree than placebo, but not more than those receiving benzodiazepine treatment. There was moderate-certainty evidence of short-term improvements of chronic neck pain and function with LLLT. Low certainty evidence from small, poor to fair quality single studies suggests LLLT may reduce chronic low back pain in the short and intermediate term and may improve function in the short term compared with sham, but this effect may not be sustained when combined with exercise therapy. There was no evidence of any effect on pain or function in people with osteoarthritis and no evidence of any effect on QoL for any condition.

Generally, there was no evidence of an effect of TU on pain or QoL (except when combined with westernised Chinese medical therapy in one small, poor-quality study) and inconsistent evidence of an effect on function in people with chronic low back pain.

There was no clear evidence that IT reduced chronic pain in any group, except in one small study of people with low back pain, where the result was below the threshold for a small effect. There was no evidence of an effect on function or QoL.

Evidence on SDi was insufficient to determine potential effects.

Few harms were reported for any intervention and where noted, there was no evidence of a significant difference from groups receiving control procedures.

10.5 Other factors

While some electrotherapy modalities may be available within some physiotherapy departments across Scotland, their accessibility varies by locality and service. TENS devices, where available, are typically self administered, therefore healthcare professionals should assess individuals' ability to place electrode pads and manage the device. Access to loan or prescription of TENS is inconsistent.

Given the low risk of TENS and its accessibility, individuals could be signposted to access in the community setting.

Additionally, some Health board MSK best practice guidance suggests that there is insufficient evidence to support the routine use of electrotherapy for various MSK conditions. These factors have resulted in a consistent downturn in the use of electrotherapy within physiotherapy departments across NHS Scotland.

10.6 Recommendations

✓ Support individuals who wish to manage their pain with TENS and discuss how they might access the intervention.

11 Dietary interventions

11.1 Introduction

Individuals with chronic pain who use pharmacological therapies must balance the risks of adverse events or dependency with potential benefits in pain reduction. Clinicians should support all people with chronic pain to self manage their pain in ways which best meet their needs. Non-pharmacological approaches to pain management involve a wide range of lifestyle factors including activity, mental health, stress, sleep, social connection and nutrition (*See the Quality Prescribing for Chronic Pain 2026–2029 Guide and section 2*). Beyond general healthy eating principles, evidence was sought on the role of specific dietary interventions in the management of chronic pain.

There are many reasons diet could impact on chronic pain including pro- and anti-inflammatory effects, oxidative stress, health of the gut microbiome and impact on musculoskeletal health. Overall energy intake is also important as prevalence of chronic musculoskeletal pain increases as body mass index rises.[114]

11.2 Evidence of benefit

Eleven systematic reviews or NMAs were identified which provided evidence for a range of dietary interventions in people with a range of chronic pain types (*see Table 4*).

11.2.1 Pain and function

Anti-inflammatory diet

No systematic review evidence was identified.

Chondroitin sulphate

Chondroitin sulphate is a natural glycosaminoglycan and is found in all connective tissues, especially in the extracellular matrix of articular cartilage, where it plays a role in its resistance to compression.

One NMA reported that chondroitin sulphate had no significant effect on long-term (≥12 months) pain (SMD -0.06, 95% CI -0.17 to 0.05; 42 RCTs, participants not reported: no evidence quality rating) or function (SMD -0.03, 95% CI -0.20 to 0.14; 13 RCTs, participants not reported: no evidence quality rating) in people with chronic pain due to knee osteoarthritis.[50]

sufficient

Glucosamines

Glucosamine is a naturally occurring amino monosaccharide and is a precursor for a major component of joint cartilage and synovial fluid. It is available in over 50 preparations, most commonly as a hydrochloride or sulphate compound.

Glucosamine hydrochloride is the only preparation licensed for medical use in the UK and the license is restricted to the symptomatic relief of mild to moderate knee osteoarthritis. There is more evidence available for glucosamine sulphate, which does not have a product license but is sold

over the counter as a supplement. Neither product is recommended by SMC (see section 14.4).	
One NMA reported that glucosamine sulphate reduced pain (SMD -0.29, 95% Credible Interval (CrI) -0.49 to -0.09; two RCTs, 207 participants: no evidence quality rating) and improved function (SMD -0.32, 95% CrI -0.52 to -0.12; two RCTs, 207 participants: no evidence quality rating) in people with knee osteoarthritis compared with placebo.[50]	
The review also reported that other glucosamines (including glucosamine hydrochloride and other complexes involving any glucosamine other than glucosamine sulphate) had no significant effect on pain (SMD 0.11, 95% CI 0.26 to 0.04; three RCTs, 325 participants: no evidence quality rating) or function (SMD 0.04, 95% CI 0.20 to 0.12; three RCTs, 325 participants: no evidence quality rating) in people with knee osteoarthritis compared with placebo.	sufficient
A systematic review evaluated the use of any glucosamine in people with chronic back pain and signs of spinal osteoarthritis. Out of three RCTs, compared with placebo, two found no evidence of a difference and one (with high risk of bias) measured an improvement in pain intensity. There was no evidence of effect on function. The trial which reported a statistically significant effect was open-label design, did not use an intention to treat protocol, recruited older participants than the other studies and had unclear compliance.[115]	1+
A further systematic review, conducted as part of United States Special Operations Command's Preservation of the Force and Family Behavioural Health Programme, examined the effectiveness of a wide range of dietary supplements and ingredients for pain and pain-related outcomes in adults with chronic musculoskeletal pain. The review incorporated both primary and secondary evidence sources (RCTs and systematic reviews). The authors discussed the complexity of the evidence base for the commonly combined supplements glucosamine and chondroitin and outlined potential reasons for inconsistency in findings depending on patient groups, comparators and the various preparations employed in trials. They reported that glucosamine supplements vary substantially from the prescription formulation in their molecular formulation and dose regimens and that pooled results from studies of glucosamine supplements have failed to show an effect on pain, while high-quality studies have demonstrated efficacy of prescribed glucosamine sulphate with moderate effect size for osteoarthritis symptoms compared with placebo.[116]	1++

Table 4: Systematic review evidence for dietary interventions in people with chronic pain

Intervention	Pain type				
	Mixed pain types	Crohn's disease and inflammatory bowel disease	Ulcerative colitis	Chronic musculoskeletal pain	Chronic neuropathic pain
Anti-inflammatory diet					
Chondroitin					
FODMAP diet		Sinopoulou et al, 2021a (1++)	Sinopoulou et al, 2021b (1++)	Elma et al, 2020 (1+)	
Glucosamines				Crawford et al, 2019 (1++) Gregori et al, 2018 (sufficient) Sodha et al, 2013 (1+)	
High-fibre diet					
Magnesium					Frediani et al, 2024 (1+)
Mediterranean diet				Field et al, 2021 (1+)	
Polyunsaturated fatty acids (PUFA)	Crawford et al, (1++)				
Turmeric				Crawford et al, 2019 (1++)	
Vitamin D	Straube et al, 2015 (1++)	Chong et al, 2022 (1+)		Gregori et al, 2018 (sufficient) Lee, 2024 (1++)	

<u>High-fibre diet</u>

No systematic review evidence was identified.

<u>Low fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAP) diet</u>

The FODMAP diet is a temporary elimination diet used to help manage symptoms associated with diagnosed irritable bowel syndrome. It involves an elimination phase, a systematic reintroduction of foods to identify triggers then a personalised long-term diet to limit problematic foods while ensuring adequate nutrition. Removing these triggers can reduce pain and improve function for some people.

One systematic review reported that a low FODMAP diet reduced pain | 1++

intensity in people with chronic inflammatory bowel disease compared with sham diet (MD -8.46 on a 1–100 mm VAS scale, 95% CI -15.76 to -1.16, two RCTs, 82 participants; very low certainty evidence). There was no evidence of effect in people with Crohn's disease (MD 0.2 on a 1–100 mm VAS scale, 95% CI -8.67 to 9.07, one RCT, 52 participants; very low certainty evidence). Effects on function were not assessed in this review. Despite the statistically significant effect, the authors note that no conclusions on efficacy of FODMAP diet could be reached due to the low numbers of studies and participants in each comparison and clinical heterogeneity amongst the studies.[117]	
Another systematic review reported no evidence of effect for low FODMAP diet on pain intensity in people with ulcerative colitis compared with sham diet (MD -9.00 on a 1–100 mm VAS scale, 95% CI -20.07 to 2.07, one RCT, 26 participants; very low certainty evidence).[118]	1++
A further systematic review included one uncontrolled clinical trial which reported that VAS pain scores significantly decreased after an eight-week low FODMAP diet in 38 female participants living with fibromyalgia (week 0: 6.6, week 4: 4.9, week 8: 5.4; p<0.01 difference from baseline at four weeks, scale not described). The authors note that a FODMAP diet might alleviate pain severity in patients with fibromyalgia, but that more rigorous and high-quality clinical trials are needed on this topic.[119]	1+
<u>Magnesium</u>	
A systematic review with qualitative synthesis on the role of diet and non-pharmacologic supplements for the management of chronic neuropathic pain included one small RCT on magnesium supplementation. The review reported that magnesium supplementation "was not effective" for pain reduction compared with placebo (no effect reported; one RCT, 45 participants: low certainty evidence).[120]	1+
<u>Mediterranean diet</u>	
A systematic review with meta-analysis on dietary interventions for chronic pain included two studies (one RCT involving 56 participants and one case-control study involving 130 participants) evaluating Mediterranean diet in people living with rheumatoid arthritis.[121] The trial was classified as having medium risk of bias. The effect of Mediterranean diet was estimated as statistically significant when reported in this trial, however, when standardised within the meta-analysis, the confidence interval touches zero (SMD -0.56, 95% CI -1.12 to 0.0; one RCT, 56 participants: no evidence certainty rating).	1+
<u>Polyunsaturated fatty acids (PUFA)</u>	
One systematic review of dietary supplements and ingredients in adults with chronic musculoskeletal pain, published by the United States Preservation of the Force and Family Behavioral Health Program[116] used an older, published systematic review[122] as their main evidence base on PUFA, and based on this evidence, reported that PUFA supplementation reduced pain across a range of chronic pain conditions (SMD -0.40, 95% CI -0.58 to -0.22, 46 RCTs, 2,783 participants). This small to moderate effect remained when	1++

limited, in subgroup analysis, to participants with rheumatoid arthritis (SMD -0.36 95% CI -0.62 to -0.10; 29 RCTs, number of participants not stated) and eight other pain conditions (SMD -0.61, 95% CI -1.03 to -0.20; eight RCTs, number of participants not stated). The cited systematic review did not report evidence quality ratings, however authors of the Preservation of the Force and Family Behavioral Health Program systematic review have interpreted the evidence certainty as moderate.

Turmeric

One systematic review reported that, at two-months follow-up, turmeric significantly reduced pain intensity in people with chronic musculoskeletal pain (osteoarthritis or rheumatoid arthritis) compared with placebo (SMD -1.05, 95% CI -1.68 to -0.02; three RCTs, 133 participants: low certainty evidence). Translated into a 0–100-point scale, such as a VAS or WOMAC, pain intensity reduction was 26.25 points higher in the turmeric arm than in the placebo arm (95% CI -42.0 to -0.5).[116]

Based on the same three RCTs, turmeric also significantly improved global function compared with placebo (higher scores represent worse function) (SMD -0.87, 95% CI -1.54 to -0.19; three RCTs 133 participants: very low certainty evidence).

All studies were reported to involve turmeric delivered in capsule form, as dietary supplements, however the main report from this group made a conditional recommendation in favour of use of turmeric to support pain reduction only as a dietary ingredient, rather than as a supplement, for reasons which are unclear. Dosages ranged from 700 to 2,000 mg/day over durations from 42 days to 12 weeks.

Vitamin D

A NMA of RCTs in people with knee osteoarthritis reported that vitamin D supplementation did not reduce pain (SMD 0.12, 95% CI -0.29 to 0.05; two RCTs, 310 participants: no evidence quality rating) or improve function (SMD -0.16, 95% CI -0.33 to 0.02; two RCTs, 310 participants: no evidence quality rating).[50]

sufficient

A systematic review with meta-analysis in people with chronic low back pain reported that vitamin D supplementation did not reduce pain compared with control (SMD -0.13, 95% CI -0.26 to 0.00; ten RCTs, 1,008 participants: no evidence quality rating). In a subgroup analysis for the effectiveness of vitamin D in individuals with and without vitamin D deficiency the authors reported no evidence of an effect on pain in either the vitamin D deficient group (SMD -0.28, 95% CI -0.54 to -0.02)[sic] or the non-deficient group (SMD -0.08, 95% CI -0.23 to 0.07) compared with placebo. A further subgroup analysis revealed that neither short-term (SMD -0.19, 95% CI -0.40 to 0.01) nor long-term use of vitamin D (SMD -0.10, 95% CI 0.29 to -0.10) significantly reduced chronic low back pain. Long-term supplementation did not show a significant benefit over short-term supplementation in pain relief or functional improvement in people with chronic low back pain.

1++

Neither supplementation with active forms of vitamin D (such as calcitriol or

alfacalcidol; SMD -0.32, 95% CI -0.67 to 0.03) nor non-active forms of vitamin D (SMD -0.10, 95% CI -0.24 to 0.04) significantly reduced pain scores in people with chronic low back pain compared with controls. This was consistent across various baseline levels of vitamin D among participants.[123]	
A systematic review of RCTs of vitamin D for treating pain, which included people with a range of painful conditions, noted that majority of included trials did not report proportion of participants experiencing ≥50% pain relief nor the effect of the intervention on pain improvement. There was high heterogeneity between the trials in terms of included participants, interventions (amount and schedule of administration of vitamin D, co-interventions), duration, and outcomes reported. Only two studies recruited individuals with vitamin D deficiency, and the review authors question the degree to which the trials had the sensitivity to be able to detect any effect of vitamin D on pain. Based on methodological limitations, and lack of consistent effects, the authors concluded there was no convincing evidence of effect for vitamin D on chronic pain.[124]	1++

11.2.2 Quality of life

Only one systematic review was identified which reported effects of dietary interventions on quality of life. The review measured QoL using the IBS-QoL questionnaire which has 34 items consisting of dysphoria, body image, health-oriented worries, sexual related worries, social behaviour, interference with everyday activity, and personal relationship domains. Results were converted to a 0–100-point scale. The review reported that people with irritable bowel syndrome who received vitamin D supplements did not experience a significant improvement in their IBS-QoL scores compared with placebo (SMD 0.54, 95% CI -0.34 to 1.41; four RCTs, 448 participants: no evidence quality rating).[125]	1++

11.3 Evidence of harms

No evidence was identified reporting adverse effects for anti-inflammatory diet, chondroitin, high-fibre diet, Mediterranean diet, magnesium supplementation or PUFA in people with chronic pain.

One systematic review noted that, in one of the three RCTs included, approximately 30% of participants experienced adverse events irrespective of whether they received glucosamine or placebo. Adverse events included gastrointestinal and dermatological symptoms. There were no adverse events reported in the other two trials.[115]	1+
In two systematic reviews, there was no evidence of a difference in withdrawal from studies due to adverse events between people receiving low FODMAP diet and sham diet among those with inflammatory bowel disease or ulcerative colitis (a single result was extracted from the same RCT and reported in both systematic reviews) (RR 1.85, 95% CI 95% CI 0.18 to 19.19; one RCT, 52 participants: very low certainty evidence).[117,118]	1++
A systematic review identified six RCTs evaluating the effects of turmeric when used alone, which reported on adverse events. One study reported	1++

that none occurred, and the others cited a variety of adverse events that mainly consisted of minor gastrointestinal complaints. A small number of studies which investigated turmeric in combination with another ingredient noted that adverse events were more common in participants using the combination.[116]

In the systematic review of vitamin D in people with a wide range of painful conditions, adverse events were infrequent, with no consistent difference between those receiving vitamin D and placebo.[124] 1++

11.4 Summary of benefits and harms of dietary interventions for chronic pain

No systematic review evidence was identified on the effects of anti-inflammatory diets or high-fibre diets on pain outcomes in people with chronic pain. There was mixed evidence of benefit of glucosamines with most studies showing no evidence of effect on pain.

One NMA reported that glucosamine sulphate, which is not licensed for pain reduction in the UK and not approved by SMC, may have a small effect on pain in people with knee osteoarthritis.

Evidence on low FODMAP diet was of very low certainty and based on systematic reviews containing one to two studies. Effects on pain were mixed, with one review suggesting a small reduction in pain for people with inflammatory bowel disease but no effect in people with Crohn's disease, while another review reported no effects in people with ulcerative colitis. It was not possible to reach a conclusion due to the quality and volume of evidence.

One systematic review reported that magnesium supplementation was not effective for pain reduction in people with neuropathic pain.

A systematic review which included one RCT and one case-control study reported no evidence of effect of Mediterranean diet on pain in people with rheumatoid arthritis.

Evidence from one systematic review suggests that PUFA supplementation (mostly attributed to omega-3) may have a small effect on pain reduction in people with a range of chronic pain conditions.

Based on low to very low certainty evidence, turmeric supplementation may have a large effect on pain reduction and improving function.

Several systematic reviews reported consistently that vitamin D supplementation did not result in pain reduction in people with chronic pain, irrespective of their vitamin D sufficiency.

Adverse events for all dietary interventions were poorly reported, and, where identified, were minor and infrequent.

11.5 Other factors

Dietary management is increasingly valued by people with chronic pain as a non-pharmacological option, especially in the context of deprescribing. The GDG acknowledge that some people with chronic pain report benefits

from reducing processed foods and sugars.

Scottish Government's Quality Prescribing Guide for Chronic Pain 2026–2029 highlights a number of ways in which pain and nutrition are connected, including:

- for people living with pain, nutrient-rich foods can support overall health and may also play a role in managing pain levels
- limited/reduced mobility and functional strength can affect a person's ability to shop, cook and prepare meals
- comfort eating and/or lack of meaning around mealtimes can lead to low quality diet
- lack of sleep can result in irregular eating habits.

The low FODMAP diet is an elimination therapy which requires specialist support from dietitians. It is labour intensive and requires commitment from those following it to maintain compliance. While not specifically measured in the evidence base, any diet which alters gastrointestinal microbiota, particularly among people who could have abnormal intestinal bacteria, may result in unintended harm. Furthermore, there is some evidence that people with gastrointestinal disorders who undergo dietary change may be at increased risk for disordered eating behaviours.[126]

Use of dietary supplements is not regulated to the same standards as licensed medications and may involve access to products which vary in intensity, formulation and effect.

The Eatwell Guide is a visual tool to help people achieve a healthy balanced diet and shows the recommended proportions of different food groups most people should be eating. It applies to people over the age of five regardless of weight, dietary restrictions/preferences or ethnic origin, although anyone with special dietary requirements or medical needs might want to check with a registered dietitian on how to adapt the Eatwell Guide to meet their individual needs. The Eatwell Guide also provides information on hydration, calorie guidelines and nutrition labelling.

11.6 Recommendations

✓ Discuss healthy eating with people with chronic pain in line with The Eatwell Guide and provide advice to:

- maintain healthy weight as recommended to the general population by following a healthy balanced diet
- base meals on wholegrain carbohydrate foods
- incorporate fruit and vegetables (fresh, dried, tinned or frozen)
- include omega-3 fatty acids, including two portions of fish every week, one of which should be oily, and/or plant-based sources like walnuts, chia seeds or flax seeds
- include beans and pulses (along with fruit, vegetables and wholegrain foods) to increase fibre intake. Fibre supports gut

health and helps to prevent constipation which is a common side effect of medicines commonly prescribed for pain

- choose unsaturated oils and spreads (eg olive oil, rapeseed oil)
- have foods and drinks which are high in fat, salt or sugar less often and in small amounts
- maintain adequate fluid consumption to prevent constipation.

✓ Advise individuals with special dietary requirements or medical needs that registered dietitians can provide support on how to adapt the Eatwell Guide to meet their individual needs.

✓ Advise that turmeric consumption may have a role in pain relief and very little harms, however it is not possible to specify target amounts.

12 Alternative therapies

12.1 Introduction

Chronic pain is a common condition that can be difficult to manage with available conventional medical therapies. Many people who experience chronic pain will try alternative therapies in an attempt to reduce their pain. A national survey of people with chronic pain in Scotland reported that 27% of respondents had used an osteopath, chiropractor or acupuncturist to help manage their pain, while 20.8% had used a homeopath or alternative medicine professional.[17] These therapies are often not provided by NHS Scotland, for example, several pain services in Scotland have moved away from providing acupuncture for chronic pain.

Evidence was sought on the effectiveness of alternative interventions (acupuncture, aromatherapy, homeopathy, herbal products, hypnotherapy, music therapy and reiki) on pain scores, functional ability, quality of life and adverse events.

12.2 Evidence of benefit

12.2.1 Pain intensity

ACUPUNCTURE AND DRY NEEDLING

Several systematic reviews report evidence that acupuncture produces small short-term improvements in both pain and function but only some may be clinically important.

Chronic low back pain

In one systematic review acupuncture reduced pain compared with control (sham, usual care, attention control or placebo) (MD -0.61 on a 0–10 scale, 95% CI -0.99 to -0.27; six RCTs, 2,207 participants: moderate certainty evidence). However, the improvement is less than one point on a 0–10 pain scale and therefore appears to be clinically insignificant.[85]	1++
In a further review, acupuncture reduced pain to a level where the difference did not meet predefined clinically relevant change when compared with sham (MD -9.22 points on 100-point VAS, 95% CI -13.82 to -4.61; seven RCTs, 1,403 participants: low certainty evidence) and when compared with usual care (MD -10.26, 95% CI -17.11 to -3.40; five RCTs, 1,054 participants: low certainty evidence). Acupuncture reduced pain compared with no intervention (MD -20.32, 95% CI -24.50 to -16.14; four RCTs, 366 participants: moderate certainty evidence).[127]	1++

Chronic neck pain

A comprehensive systematic review evaluated the effectiveness of acupuncture on functional disability against a range of comparators in people with chronic neck pain. When compared against sham acupuncture, there was no effect of acupuncture on pain intensity at three months (MD -0.12 cm on a 0–10 cm scale, 95% CI -0.06 to 0.36; one RCT, 178 participants: no evidence certainty rating), six months (MD: 0.01 on a 0–10 cm scale, 95% CI -1.16 to 1.18; one RCT, 60 participants: no evidence	1+

certainty rating) or 12 months (MD -0.42 on a 0–10 cm scale, 95% CI -1.55 to 0.71; one RCT, 58 participants: no evidence certainty rating).[128] When compared with active controls (such as TENS, traction treatment, exercise or massage), there were no significant differences in pain intensity between groups receiving acupuncture and controls in the short term (up to three months) (SMD -0.17, 95% CI -0.46 to 0.12; three RCTs, 188 participants: no evidence certainty rating) or six months (MD -1.27 on a 0–100-point scale, 95% CI -17.41 to 14.87; two RCTs, 70 participants: no evidence certainty rating).[128] The systematic review also included comparison of acupuncture with active control against active control alone. The combined intervention was more effective than active control in the short term (up to three months) (SMD -0.79, 95% CI -1.13 to -0.46; three RCTs, 150 participants: no evidence certainty rating) and intermediate term (up to six months) (MD -18.13 on a 0–100-point scale, 95% CI -30.18 to -6.07; three RCTs, 239 participants: no evidence certainty rating).[128]	
In one systematic review, acupuncture did not improve pain compared with placebo or sham in the short term (pooled difference -0.27 on a 0–10 scale, 95% CI -0.59 to 0.05; four RCTs, 490 participants: low certainty evidence), intermediate term (pooled difference 0.40, 95% CI -0.45 to 1.44; three RCTs, 354 participants: low certainty evidence), or long term (difference -0.35, 95% CI -1.34 to 0.64, one RCT, 107 participants: low certainty evidence).[85]	1++
A further review reported that dry needling was effective in reducing chronic neck pain postintervention (MD -0.45, 95% CI -0.90 to -0.01; 12 RCTs, 1,009 participants: no evidence certainty rating).[129]	1++
<u>Chronic pelvic pain in women</u>	
In one review, there was no evidence of a difference between groups receiving acupuncture compared with conventional treatment for chronic pelvic pain total effectiveness rate (an outcome measure used in China) (RR 1.00, 95% CI 0.66 to 1.53; two RCTs, 277 participants: no evidence certainty rating). There was a small difference in total effectiveness rate when acupuncture plus conventional treatment was compared to conventional treatment alone (RR 1.29, 95% CI 1.13 to 1.47; two RCTs, 197 participants: no evidence certainty rating).[130]	1+
A further systematic review of non-pharmacological therapies for chronic pelvic pain in women also reported no significant effect of acupuncture. There was no significant difference in pain intensity between groups receiving acupuncture and control (an inert or non-conservative intervention) immediately postintervention (SMD 1.08, 95% CI -1.38 to 3.54; five RCTs, 221 participants: insufficient certainty evidence).[131]	1++
<u>Chronic prostatitis/Chronic pelvic pain syndrome</u>	
One review of men with chronic prostatitis or chronic pelvic pain syndrome reported that acupuncture reduced pain compared with sham acupuncture (MD -0.93 in 100-point National Institutes of Health Chronic Prostatitis Symptom Index, 95% CI -1.18 to -0.70; six RCTs, 769 participants: moderate certainty evidence) and reduced pain compared with medication	1++

(MD -1.04, 95% CI -1.29 to -0.79; five RCTs, 282 participants: low certainty evidence).[132] These small effects may not be clinically significant.	
Fibromyalgia	
In one review of people with chronic fibromyalgia, acupuncture did not reduce chronic pain compared with control (sham, attention control or no intervention) (MD -1.04 on a 0–10 scale, 95% CI -2.27 to 0.16; six RCTs, 466 participants: low certainty evidence).[85]	1++
There was insufficient evidence to draw conclusions for acupuncture compared with exercise.[85]	
Osteoarthritis of the knee	
One review found that acupuncture did not improve pain in the short-term (SMD -0.25 on a 0–10 scale, 95% CI -0.58 to 0.07; seven RCTs, 1,148 participants: low certainty evidence) or intermediate term (SMD -0.16, 95% CI -0.32 to -0.01; four RCTs, 767 participants: moderate certainty evidence) compared with control (usual care, no intervention, waiting list or sham). There was insufficient evidence to draw conclusions for acupuncture compared with exercise.[85]	1++
Temporomandibular disorder	
One NMA reported that acupuncture did not significantly reduce pain (MD -2.04 on a 0–10 cm scale, 95% CI -2.38 to 1.71 cm; 148 RCTs, 7,867 participants: low certainty evidence).[94]	sufficient
A further NMA reported that dry needling reduced overall pain compared with placebo post-intervention (SMD -0.70, 95% CI -1.27 to -0.14; 42 RCTs, 1,989 participants: very low-certainty evidence). This improvement was maintained in the short term (equal to or less than five months) (SMD -0.87, 95% CI -1.48 to -0.27; 42 RCTs, 1,525 participants: low certainty evidence). It is worth noting that in the short term, dry needling was ranked lower than other therapies, ie manual therapy, ozone, counselling and appliances.[67]	sufficient
HERBAL PRODUCTS	
Chronic low back pain	
One systematic review evaluated the effects of several herbal products on pain intensity in people with chronic low back pain.[133] Meta-analysis of results was not possible due to insufficient data and clinical heterogeneity. Based on a single small study, individuals who received Brazilian arnica (10 participants) experienced reduced perception of pain compared with the baseline values recorded for the intervention group (10 participants) (effect size not reported; one RCT, 20 participants: very low-certainty evidence). The review authors reported it was unclear if the RCT included individuals with acute or chronic low back pain.	1+
Two RCTs were identified which evaluated the effects of Harpagophytum procumbens (devil's claw) at two different doses (standardised to 50 mg and 100 mg of the active natural ingredient harpagoside) in people with chronic non-specific low back pain. In both trials, a significant increase in the number of pain-free patients was reported in the group receiving 50 mg	

H. procumbens (9% to 17%) compared with those receiving placebo (2% to 5%). The Arhus score, which is a composite measure of pain and disability, improved equally in both intervention and control groups (pooled effect not reported; two RCTs, 315 participants: very low-certainty evidence). One trial also evaluated effects of 100 mg dose of H. procumbens compared with 50 mg or placebo. The review authors report that "the number of patients who were pain-free for at least five days in the fourth week of treatment [with 100 mg H. procumbens] was significantly higher (N=10) than in either the placebo (N=3) or lower dose (50 mg) groups (N=6). There was no significant difference in Arhus score between any group (one RCT, 197 participants: very low-certainty evidence).

Two RCTs were identified which evaluated the effects of Salix alba (white willow bark) at two different doses (standardised to 120 mg and 240 mg of the active ingredient salicin) in people with chronic low back pain compared with placebo. The authors report "The number of patients who were pain-free for at least five days in the fourth week of treatment increased from baseline in the placebo (N=4), 120 mg salicin group (N=15) and the 240 mg salicin group (N=27), with the trend for dose being significant." There was no change in Arhus scores in the placebo group, but improvement in those receiving 120 mg and 240 mg salicin with the trend for dose being significant (two RCTs, 261 participants: moderate certainty evidence).

One RCT compared the effects of Spiroflor SLR homeopathic gel (SLR) with Capsici Oleoresin gel (CCC) in a mixed group of patients with new acute low back pain or acute episodes of chronic low back pain. The review authors report that "both groups showed a significant reduction in pain on the [0–100-point] VAS scale, with a decrease of 38.2 mm in the SLR group and 36.6 mm in the CCC group" (one RCT, 161 participants: very low-certainty evidence).

Neuropathic pain

One systematic review identified two RCTs which evaluated benefits and harms of herbal products in people with neuropathic pain. The first trial included topical application of a compound containing mace oil 2%, nutmeg oil 14%, methyl salicylate 6%, menthol 6%, coconut oil and alcohol. The second trial involved St John's wort taken in capsule form at a dose of 2,700 mg/day for five weeks. Neither study reported substantial pain relief of 50% or greater. One study reported no significant participant-reported pain relief of 30% or above over baseline in response to nutmeg compared with placebo (RR 1.12, 95% CI 0.69 to 1.85; one RCT, 74 participants: very low-certainty evidence). The authors note that there was no observable reduction in the total pain score in response to either nutmeg or St John's wort.[134] 1++

HYPNOTHERAPY

Musculoskeletal and neuropathic pain

One systematic review reported that hypnosis reduced pain intensity postintervention (SMD 0.42, 95% CI 0.78 to 0.07; nine RCTs, 530 1++

participants: moderate certainty evidence) and pain interference (SMD 0.39, 95% CI 0.73 to 0.06; six RCTs, 239 participants: low certainty evidence) compared with control (no intervention, usual care or other interventions).[135]	
Chronic pelvic pain in women	
A systematic review of women with chronic pelvic pain reported no statistically significant effect for hypnotherapy on pain (SMD -0.80, 95% CI -2.12 to 0.52; three RCTs, 100 participants: no evidence certainty rating) compared with control (physical rest, NSAIDs or usual care).[136]	1+
Temporomandibular disorder	
One NMA evaluated the relative effectiveness of a range of interventions on pain intensity in people with temporomandibular disorders (TMD). The authors concluded that hypnosis did not reduce overall pain postintervention (SMD -0.67, 95% CI -1.59 to 0.24; based on a network of 42 RCTs with 1,989 participants: very low-certainty evidence) or at less than five-months follow-up (SMD -0.62, 95% CI -2.06 to 0.81; based on a network of 42 RCTs with 1,525 participants: very low-certainty evidence) compared with placebo.[67]	sufficient
Multiple pain types	
A systematic review which investigated effects of hypnosis adjunctive to other primary interventions (medical therapies, psychological therapies or educational interventions) reported that hypnosis adjunctive to usual care had a small effect on postintervention pain, which may not be clinically significant, in people with chronic pain (MD -8.2 on a 0–100-point scale, 95% CI -11.8 to -4.6; 15 RCTs, 929 participants: very low-certainty evidence). The effect was maintained in the short term (up to 3 months) (MD -8.5 on a 0–100-point scale, 95% CI -15.7 to -1.30; four RCTs, number of participants not reported) but not over the long term (at 12 months) (MD -6.4 on a 0–100-point scale, 95% CI -18.5 to 5.7; three RCTs, number of participants not reported).[137]	1+

12.2.2 Function

ACUPUNCTURE AND DRY NEEDLING

Chronic low back pain	
In one systematic review acupuncture improved function in the short term (SMD -0.27 95% CI -0.42 to -0.08; five RCTs, 2,164 participants: low certainty evidence).[85]	1++
Acupuncture did not improve back-specific function compared with sham (MD 3.33 points on a 100-point Hanover Functional Ability Questionnaire scale, 95% CI -1.25 to 7.90; five RCTs, 1,481 participants: very low-certainty evidence) and improved function to a level where the difference did not meet predefined clinically relevant change when compared with no intervention (MD 11.50, 95% CI 7.38 to 15.84; five RCTs, 2,960 participants: moderate certainty evidence) and when compared with usual care (MD 9.78, 95% CI 3.54 to 16.02; five RCTs, 1,381 participants: low certainty evidence).[127]	1++

Chronic neck pain	
A systematic review reported that acupuncture was associated with small improvements in short-term function (Pooled SMD -0.40, 95% CI -0.67 to -0.14; five RCTs, 919 participants: low certainty evidence) but not intermediate-term function (Pooled SMD -0.19, 95% CI -0.37 to 0.05, three RCTs, 563 participants: low certainty evidence) compared with sham acupuncture, a placebo (sham laser), or usual care. A single RCT cited in this review reported no difference in function in the long term (SMD -0.23, 95% CI -0.61 to 0.16; 107 participants: low certainty evidence).[85]	1++
A comprehensive systematic review evaluated the effectiveness of acupuncture on functional disability against a range of comparators in people with chronic neck pain. When compared with a sham procedure, acupuncture was associated with different effects depending on the measurement instrument used. Studies using the Neck Disability Index (NDI) reported no difference in the reduction of disability scores from baseline between people receiving dry needling or sham at six months (MD 2.40 on a 0–100-point scale, 95% CI -5.46 to 10.26; one RCT, 60 participants: no evidence certainty reported) or 12 months (MD -0.11, 95% CI -7.69 to 7.47; one RCT, 58 participants: no evidence certainty rating) following treatment. Studies using the Northwick Park Neck Pain Questionnaire (NPQ) which is a 0–36-point scale and can be converted to percentage reported a statistically significant improvement in function at three months following treatment (MD -6.06, 95% CI -8.20 to -3.92; two RCTs, 704 participants: no evidence certainty rating). The authors note that this effect did not meet the MCID of 25% reduction from baseline.[128]	1+
When compared with active control, individual studies using NDI reported no difference in disability scores at three months (MD -0.29, 95% CI -2.37 to 1.80; three RCTs, 175 participants: no evidence certainty rating) but a statistically and clinically significant effect at six months (MD -9.00, 95% CI -14.06 to -3.94; one RCT, 30 participants: no evidence certainty rating). Statistically and clinically significant effects were measured at all follow-up points in studies which used NPQ: at three months (MD -6.67, 95% CI -9.42 to -3.92; two RCTs, 335 participants: no evidence certainty rating), six months (MD -6.33, 95% CI -9.22 to -3.44; one RCT, 304 participants: no evidence certainty rating) and 12 months (MD -4.75, 95% CI -7.86 to -1.64; one RCT, 294 participants: no evidence certainty rating).[128]	1+
Acupuncture combined with active control interventions compared with active control alone did not significantly improve function at three months (MD -3.83, 95% CI -9.22 to 1.57; two RCTs, 190 participants: no evidence certainty rating) or six months after treatment (MD -9.00, 95% CI -19.22 to 1.22; four RCTs, 346 participants: no evidence certainty rating).[128]	
A further review reported no effect of dry needling on functional capacity in people with chronic neck pain postintervention (MD -0.20, 95% CI -0.61 to 0.22; nine RCTs, 651 participants: no evidence certainty rating).[129]	1++
Chronic pelvic pain in women	
No evidence was identified on the effectiveness of acupuncture on function	

in women with chronic pelvic pain.

Chronic prostatitis/Chronic pelvic pain syndrome

No evidence was identified on the effectiveness of acupuncture on function in men with chronic prostatitis.

Fibromyalgia

In one review of people with chronic fibromyalgia, acupuncture improved function in the short term when compared with sham or no intervention (MD -8.60 on a 0–100-point scale, 95% CI -12.00 to -5.42; four RCTs, 350 participants: moderate certainty evidence). Acupuncture also improved function in the short term compared with sham acupuncture alone (MD -9.21, 95% CI -13.65 to -5.78; three RCTs, 283 participants: moderate certainty evidence). There was insufficient evidence to draw conclusions for acupuncture compared with exercise.[85]	1++

Osteoarthritis of the knee

One systematic review found that acupuncture did not improve function in people with chronic pain due to osteoarthritis of the knee in the short term (SMD -0.11, 95% CI -0.27 to 0.22; four RCTs, 954 participants: low certainty evidence) and intermediate term (SMD -0.15, 95% CI -0.31 to 0.02; four RCTs, 767 participants: low certainty evidence). There was insufficient evidence to draw conclusions for acupuncture compared with exercise.[85]	1++

Temporomandibular disorder

One NMA reported that acupuncture improved physical function compared with placebo or sham procedures (MD 16.04 mm on a 1-100 mm scale, 95% CI 11.60 to 20.48 mm; 36 RCTs, 2,009 participants: moderate certainty evidence).[94]	sufficient

HERBAL PRODUCTS

No evidence was identified which reported on the effects of herbal products on function in people with chronic pain.

HYPNOTHERAPY

No evidence was identified which reported on the effects of hypnotherapy on function in people with chronic pain.

12.2.3 Quality of Life

ACUPUNCTURE AND DRY NEEDLING

Chronic low back pain

In one systematic review evaluating acupuncture in people with chronic low back pain, acupuncture improved quality of life to a level where the difference did not meet predefined clinically relevant change compared with sham (MD 2.33 on a 100-point SF-12 scale, 95% CI 0.29 to 4.37; three RCTs, 1,068 participants: low certainty evidence).[127]	1++

Chronic low back pain

One systematic review which evaluated the effects of acupuncture in	1+

people with chronic neck pain included a single study which reported on quality of life outcomes.

There was no statistically significant difference between groups receiving acupuncture and sham acupuncture in both mental component summary (MCS) scores (MD 5.36, 95% CI -1.53 to 12.25) and physical component summary (PCS) scores (MD 1.02, 95% CI -6.20 to 8.24; one RCT, 190 participants: no evidence certainty rating).[128]

HERBAL PRODUCTS

No evidence was identified on the effects of herbal products on quality of life in people with chronic pain.

HYPNOTHERAPY

Chronic pelvic pain

A systematic review which evaluated the effects of hypnotherapy in women with chronic pelvic pain reported no difference in quality of life between groups receiving hypnotherapy compared with controls (physical rest, NSAIDs or usual care) (SMD -0.11, 95% CI -0.56 to 0.35; two RCTs, 75 participants: no evidence certainty rating).[136] 1+

12.3 Evidence of harms

There are relatively few harms reported with any of the interventions, and in most cases these were described as mild and did not happen significantly more often than in groups receiving sham interventions or usual care.[85,129,130,133] Where harms were identified, most were reported in association with acupuncture or dry needling which can cause local bruising, worsening of pain and local swelling.[85,128]

Herbal products are not licensed for the treatment of chronic pain and are not regulated to the same degree as medicines. Although a systematic review reported no significant difference in adverse events between nutmeg or St John's wort and placebo (RR 1.00, 95% CI 0.55 to 1.81; two RCTs, 128 participants: very low-certainty evidence)[134] the GDG acknowledges that herbal products may cause adverse effects when taken in combination with prescribed medications or make these less effective. 1++

It is unclear if hypnotherapy may be associated with adverse events as systematic reviews on hypnotherapy in people with chronic pain did not report on this outcome.[67,135,136] sufficient, 1+, 1++

12.4 Summary of benefits and harms of alternative therapies for chronic pain

There is a lack of evidence of long-term benefit of alternative therapies on pain or function.

Acupuncture is associated with small, short-term improvements in pain in people with chronic low back pain and prostatitis which may not be clinically significant. Dry needling produced a small, short-term reduction in neck pain and pain associated with temporomandibular joint dysfunction in one systematic review for each condition, while further reviews reported no

evidence of effect. Effects were not sustained beyond the short term.

Evidence of a small benefit on function of acupuncture in the short term was reported in people with chronic low back pain, chronic neck pain, fibromyalgia and temporomandibular joint dysfunction.

There was insufficient evidence to draw a conclusion about the use of herbal products for chronic pain.

There was inconsistent evidence for the effectiveness of hypnotherapy, with systematic reviews reporting a small benefit in people with musculoskeletal and neuropathic pain and when used as an adjunctive therapy in people with a range of pain types, but no effect in people with chronic pelvic pain or TMD.

No evidence was identified on the effectiveness of aromatherapy, music therapy or reiki in people with chronic pain.

Available evidence is insufficient to recommend the use of herbal products and hypnotherapy for chronic pain.

12.5 Other factors

There is widespread use of alternative therapies by people in Scotland for many conditions, including long-term pain, with some individuals reporting benefit. Those using alternative therapies perceive a low risk of harm. The biopsychosocial approach to pain reflects that pain is a complex subjective experience influenced by biological, psychological and social factors and it is acknowledged that it is difficult to design studies which objectively measure the effects of alternative therapies as experienced by individuals.

Over recent years, pain services in some areas of Scotland have withdrawn the provision of acupuncture. Many alternative therapies are not provided by the NHS.

There is some evidence for short-term improvement in pain and function in certain conditions with acupuncture, with a low risk of harm. There was insufficient evidence available to determine the most appropriate setting to deliver acupuncture in NHS Scotland, ie as a privately operated service, in the community, in primary care or as an NHS specialist service.

Experience from many healthcare professionals within pain services is that interventions (not just acupuncture) performed in isolation, with the hope of producing short-term pain reduction, can foster a reliance on healthcare. It is the view of the GDG that interventions, if thought appropriate for an individual based on shared decision making, should be part of a long-term self-management plan.

The GDG acknowledges that delivery of acupuncture requires resources, including administration, staffing, equipment and facilities. The cost effectiveness of providing acupuncture was not investigated in this guideline.

12.6 Recommendations

R **Acupuncture may be considered for short-term relief of pain and improvement in function in patients with chronic low back pain, chronic neck pain, chronic pelvic pain, temporomandibular disorder and fibromyalgia. Acupuncture should only be delivered alongside other active supported self-management approaches.**

13 Provision of information

This section reflects the issues likely to be of most concern to patients and their carers. These points are provided for use by health professionals when discussing chronic pain with patients and carers and in guiding the development of locally produced information materials.

13.1 Publications from SIGN

SIGN presents recommendations and rationales, created for health and social care professionals, in plain language to be easily understood and used by the public. This information aims to:

- help people understand the latest evidence around diagnosis, treatment, and self care
- empower people to actively participate in decisions about managing their condition in discussions with health and social care professionals
- highlight areas of uncertainty for people, making them aware of where more information or research is needed.

A copy of the plain language version of this guideline is available from www.sign.ac.uk/patient-publications.html

Patients may also find the following booklet helpful: Migraine: a booklet for patients and carers (2023).

13.2 Sources of further information

Information for people with chronic pain

Flippin' Pain®

www.flippinpain.co.uk

Flippin' pain is a public health campaign that aims to change the way we think about, talk about and treat persistent pain. It includes information on chronic pain, real life stories and resources to help understand pain and move towards recovery.

Healthtalk

healthtalk.org/introduction/chronic-pain

Healthtalk provides written and filmed personal health stories about what it's really like to live with a health condition. The website is run by the Dipex Charity and includes views on pain management approaches, medical treatments and the impact of living with chronic pain.

Live Well with Pain

livewellwithpain.co.uk/resources-for-people-with-pain

Live Well with Pain provides knowledge about and support for self managing persistent pain. The website offers a range of materials and a step-by-step online guide to living well with pain, including videos, tips and

tools and links to trusted resources.

Manage my meds

rightdecisions.scot.nhs.uk/manage-my-meds-for-patients-and-carers

This online toolkit helps people to build knowledge and understanding of their medicines, manage medicines more confidently and prepare for a medication review with a healthcare professional.

NHS Greater Glasgow and Clyde: Information and resources for people living with chronic pain

live.nhsggc.scot/hospitals-services/services-a-to-z/chronic-pain/information-and-resources-for-patients

A large collection of resources developed for people with chronic pain includes information about the NHS Greater Glasgow and Clyde Pain Service, More Harm Than Good leaflets (information about opioids), a library of mindfulness resources and links to further online information.

NHS Highland Chronic Pain Management Service

www.nhshighland.scot.nhs.uk/your-services/all-services-a-z/chronic-pain-management/how-you-can-help-yourself-with-your-pain

NHS Highland has developed a collection of resources to help people living with chronic pain to manage their condition. The set includes videos, booklets and links to further resources and information.

NHS Inform

www.nhsinform.scot/illnesses-and-conditions/brain-nerves-and-spinal-cord/chronic-pain

This resource provides information about chronic pain symptoms, pain management strategies to live better with chronic pain, how to cope with a flare up of chronic pain and a self-help guide.

Pain Association Scotland

painassociation.co.uk/online-self-management-wellbeing-videos

Pain Association Scotland is a national charity that aims to improve the quality of life for chronic pain sufferers by supporting and empowering them to live independently in the community. It promotes a reduced reliance on clinical services through collaborative working with health and social care professionals and encourages access to self management at an early stage of the clinical journey. The charity has developed a range of videos on topics such as stress management, pacing, relaxation and flare ups.

Pain concern

painconcern.org.uk/product-category/leaflets

Pain concern is a national charity that provides information and support to people with pain and those who care for them, and raises awareness and campaigns to improve the provision of pain management services. It has developed a range of information booklets on general topics such as

stress, pain and relaxation, managing emotions with chronic pain and managing healthcare appointments, alongside booklets for specific pain conditions, such as neuropathic pain, bladder pain syndrome and vulval pain.

Scottish Families Affected by Alcohol and Drugs

www.sfad.org.uk

Scottish Families Affected by Alcohol and Drugs is a national charity that supports anyone affected by someone else's alcohol or drug use in Scotland, whether they are still actively using substances, are in recovery, or are bereaved. The charity provides both national and local support services, befriending, bereavement support, a learning hub, listening and advice. They offer access to injectable or nasal naloxone via a click and deliver service from www.sfad.org.uk/naloxone.

The Pain Toolkit

www.paintoolkit.org

The Pain Toolkit is an interactive and simple information booklet, that provides readers or listeners with handy tips and skills to support people self managing their pain or long-term health condition. It offers a tailored set of 12 tools to help and aid in pain self management, plus a suite of tailored resources for both healthcare professionals and people living with persistent pain.

West of Scotland Chronic Pain Education Group

www.paindata.org

The Chronic Pain Education Group is a multidisciplinary group of NHS pain specialists working in the West of Scotland. It includes doctors, physiotherapists, nurses, pharmacists, psychologists, and a patient representative. The website includes a wide range of resources for patients with chronic pain, including information about commonly prescribed medications, non-pharmacological treatments and practical guidance to support self management.

Women's Health Concern

www.womens-health-concern.org

Women's Health Concern is the patient arm of the British Menopause Society and provides independent advice to inform and reassure women about their gynaecological, sexual and postreproductive health. They provide evidence-based factsheets on a wide range of topics, including endometriosis.

Occupational health support

Access to Work

www.gov.uk/access-to-work

Access to Work can help individuals to get or stay in work if they have a physical or mental health condition or disability. It can support some adjustments being made when costs are a barrier to providing these.

The support that is available will depend on the individual's needs. Through Access to Work, people can apply for:

- a grant to help pay for practical support with work
- support with managing mental health at work
- money to pay for communication support at job interviews.

Advisory, Conciliation and Arbitration Service (Acas)

www.acas.org.uk/advice
Helpline: 0300 123 1100

Acas is an independent public body that receives funding from the UK Government to provide free and impartial advice to employers, employees and their representatives on:

- employment rights
- best practice and policies
- resolving workplace conflict.

The website includes advice about equality, health and well-being at work and access to a free telephone helpline.

Citizens Advice Scotland

www.citizensadvice.org.uk/scotland/law-and-courts/discrimination/check-what-type-of-discrimination-youve-experienced/asking-for-reasonable-adjustments-if-youre-disabled

Citizens Advice Scotland is the largest independent advice network in Scotland. It is a network of independent charities that offers impartial and confidential advice about justice, human rights, debt and money, digital inclusion, energy, housing, social security and many other topics.

It supports individuals with access to benefits and employment rights, including asking for reasonable adjustments if they're disabled.

Equality Advisory Support Service

www.gov.uk/equality-advisory-support-service

The Equality Advisory Support Service provides information about disability discrimination and the Equality Act.

Arthritis UK

www.arthritis-uk.org/information-and-support/living-with-arthritis/work-benefits-and-finances/work-and-arthritis

Arthritis UK is a charity that provides information, supports research and healthcare and influences decision makers to understand and take account of arthritis and musculoskeletal conditions. It offers information and advice on managing musculoskeletal chronic pain in the workplace and making appropriate decisions about work, education, careers and benefits that are focused on individuals' needs.

Information for healthcare professionals

Quality Prescribing for Chronic Pain (2026–2029): A Guide for Improvement

Pending publication – link to be added

This guide promotes the importance of good communication between individuals living with chronic pain and the clinician, to enable an understanding of 'what matters to them' in line with the 7-Steps medication review process. It acknowledges that the medical model of treating pain is insufficient to meet all needs of patients and staff and highlights that even when effective pharmacological analgesia can be achieved, risks of adverse events and harm may promote non-pharmacological approaches to best support and empower what matters to individuals.

Grampian Pain Management

www.gpm.scot.nhs.uk/

The Pain Management Service in Grampian is made up of a multidisciplinary team, offering a range of services to help people living with persistent pain to improve their quality of life. Their website offers information leaflets and videos for people living with chronic pain, referral information and useful links to further resources.

Live Well with Pain

livewellwithpain.co.uk/professional-tools

Live Well with Pain has produced self-management tools and techniques for use by clinicians and other practitioners working with people with pain. These include videos, tools and guidance on skills and knowledge for practitioners, medicines management and written information for sharing with people with chronic pain.

National Trauma Transformation Programme

www.traumatransformation.scot

The National Trauma Transformation Programme is a multiagency training and implementation resource to support services to respond in ways that prevent further harm, support recovery, address inequalities and improve life chances for people affected by trauma and adversity. It includes a wide range of learning resources, guidance and implementation support for all sectors of the workforce, including leaders, to develop staff to the appropriate level of trauma-informed and responsive practice and to embed and sustain this model of working.

National Wellbeing Hub

wellbeinghub.scot/resource/supporting-your-wellbeing-free-apps-and-online-programmes

The National Wellbeing Hub is an evidence-led resource to promote, enhance and support the psychosocial well-being of everyone working in health, social care, and social work in Scotland, as well as unpaid carers. It provides access to free online apps and programmes which support good mental health, relaxation, anxiety improvement and sleep quality.

NHS Education for Scotland Motivation, Action and Prompts (MAP): Health Behaviour Change Learning Programme

www.nes.scot.nhs.uk/our-work/behaviour-change-for-health

The MAP Learning Programme aims to equip health, care and third sector staff with the knowledge, skills and confidence to talk to people about behaviour change and to deliver theory-based interventions which are person centred and will promote positive health and well-being outcomes.

NHS Education for Scotland: Chronic Pain Knowledge Hub

learn.nes.nhs.scot/74191

The Chronic Pain Knowledge Hub developed by NHS Education for Scotland provides an interactive chronic pain learning toolkit for all health and social care professionals providing support and management for people living with pain. The toolkit consists of four practice levels capturing what health and social care workers in different service contexts can do to make a positive difference to people with chronic pain.

(Access to this resource requires a Turas Learn account).

Primary Care Chronic Pain Management Multidisciplinary Team sway

sway.cloud.microsoft/szyeuKXg7Z8Jv0Is?

This sway for primary care staff includes a multidisciplinary flowchart and example letters for medication reviews.

The Institute of Psychosexual Medicine

www.ipm.org.uk

The Institute of Psychosexual Medicine is a professional organisation, registered as a charity, which provides education, training and research in psychosexual medicine for qualified registered practitioners. It focuses on training for a type of brief therapy, based on psychoanalytic skills and which can be applied in primary care, secondary care or community settings.

The Matrix - A Guide to Delivering Evidence-Based Psychological Therapies and Interventions in Scotland

www.matrix.nhs.scot/evidence-summaries/populations-requiring-special-considerations-and-adjustments/chronic-pain

The Matrix is a resource developed by NHS Education for Scotland and the Scottish Government to guide NHS boards in planning and providing effective psychological therapies. The Matrix provides information on the current evidence base for various therapeutic approaches, guidance on well-functioning psychological therapies services, and advice on governance issues.

The Pain Toolkit

www.paintoolkit.org

The Pain Toolkit is an interactive and simple information booklet, that provides readers or listeners with handy tips and skills to support people to self manage their pain or long-term health condition. It offers a tailored set of 12 tools to help and aid in pain self management, plus a suite of tailored resources for both healthcare professionals and people living with persistent pain.

West of Scotland Chronic Pain Education Group

www.paindata.org

The Chronic Pain Education Group is a multidisciplinary group of NHS pain specialists working in the West of Scotland. It includes doctors, physiotherapists, nurses, pharmacists, psychologists, and a patient representative. The website includes a wide range of resources for healthcare professionals supporting people with chronic pain, including an opioid converter, opioid tapering calculator, videos, training modules, guidelines, audits and links to further information.

14 Implementing the guideline

This section provides advice on the resource implications associated with implementing the key clinical recommendations, and advice on audit as a tool to aid implementation.

14.1 Implementation strategy

Implementation of national clinical guidelines is the responsibility of each NHS board, including health and social care partnerships, and is an essential part of clinical governance. Mechanisms should be in place to review care provided against the guideline recommendations. The reasons for any differences should be assessed and addressed where appropriate. Local arrangements should then be made to implement the national guideline in individual hospitals, units and practices.

Quality improvement methodologies can be used locally to implement the guidelines. The Quality Improvement Journey contains generic advice and tools to use quality improvement methods to support local implementation. NHS Education for Scotland also delivers the Scottish Improvement Leaders programme and Scottish Quality and Safety Fellowship programme to develop individuals to lead local implementation projects to improve the quality of care.

Implementation of this guideline will be encouraged and supported by SIGN. The implementation strategy for this guideline encompasses the following tools and activities.

14.2 Resource implications of key recommendations

No recommendations are considered likely to reach the £5 million threshold which warrants resource impact analysis.

14.3 Auditing current practice

A first step in implementing a clinical practice guideline is to gain an understanding of current clinical practice. Audit tools designed around guideline recommendations can assist in this process. Audit tools should be comprehensive but not time consuming to use. Successful implementation and audit of guideline recommendations requires good communication between staff and multidisciplinary team working.

The guideline development group has identified the following as key points to audit to assist with the implementation of this guideline:

- the proportion of people who are prescribed oral NSAIDs for chronic pain and who have an increased risk of harm (for example, chronic kidney disease or previous gastric bleed).
- the proportion of antiepileptic drug prescriptions for adults with chronic pain where prescription is in line with current Government prescription guidance or restrictions.
- the proportion of people who are prescribed a gabapentinoid for

chronic pain for longer than six months and who have not had a medication review.

- the proportion of people with chronic pain who have received information about possible use of TENS.

14.4 Health technology assessment advice for NHSScotland

In October 2014, the SMC advised that capsaicin (Qutenza®) is accepted for restricted use within NHS Scotland for the treatment of peripheral neuropathic pain in non-diabetic adults who have not achieved adequate pain relief from, or have not tolerated, conventional first and second line treatments.

In March 2016, the SMC advised that capsaicin (Qutenza®) is not recommended for use within NHS Scotland for the treatment of peripheral neuropathic pain in diabetic adults either alone or in combination with other medicinal products for pain.

In August 2008, the SMC advised that lidocaine 5% medicated plaster (Versatis®) is accepted for restricted use within NHS Scotland for the treatment of neuropathic pain associated with previous herpes zoster infection (postherpetic neuralgia).

In June 2008, the SMC advised that glucosamine (as hydrochloride) (Alateris) is not recommended for use within NHS Scotland for relief of symptoms in mild to moderate osteoarthritis of the knee.

In August 2011, the SMC advised that glucosamine sulphate (Glusartel®) is not recommended for use within NHS Scotland for relief of symptoms in mild to moderate osteoarthritis of the knee.

15 The evidence base

15.1 Systematic literature review

The evidence base for this guideline was synthesised in accordance with SIGN methodology. A systematic review of the literature was carried out using an explicit search strategy devised by a Healthcare Improvement Scotland Information Scientist. Databases searched include Medline, Embase, PsycINFO and the Cochrane Library. The year range covered was 2018–2025. Internet searches were carried out on various websites for relevant guidelines. The main searches were supplemented by material identified by individual members of the development group. Critical appraisal of relevant evidence was carried out by Healthcare Improvement Scotland Health Service Researchers or NHS Research Scotland Pain researchers. Each of the selected papers was evaluated by two reviewers using standard SIGN methodological checklists before conclusions were considered as evidence by the guideline development group.

The search strategies and further details of the methodology used will be available on the SIGN website, www.sign.ac.uk when this guideline is published.

15.1.1 Literature search for lived-experience issues

At the start of the guideline development process, a Healthcare Improvement Scotland Information Scientist conducted a literature search for qualitative and quantitative studies that addressed issues on the management of chronic pain relevant to people with lived experience of chronic pain. Databases searched include Medline, Embase, Cinahl and PsycINFO, and the results were summarised by the SIGN Patient Involvement Advisor and presented to the guideline development group. Group members were also made aware of a report published by the ALLIANCE.[17] Key points are summarised in section 1.1.1

15.2 Recommendations for research

There are significant limitations in the design, quality and certainty of evidence supported by many studies in the pain medicine literature.

Innovative approaches to the methodology of clinical pain trials are needed, taking into consideration a number of factors, including entry criteria (eg baseline pain scores),[138] and individual variation in treatment response.[139] Pragmatic clinical trials which bridge the translational gap between tightly controlled explanatory clinical trials and real-world clinical effectiveness may be one approach to be considered.[36] Furthermore, ensuring robust involvement of people with chronic pain throughout the research cycle has been recognised as important[140] to ensure relevance of study questions, appropriate study design and meaningful outcome measures, including consideration of composite measures (that reflect not just pain intensity but its wider impact).[141]

A number of factors need to be considered to optimise the design of trials studying chronic pain. These include patient selection (pain diagnosis,

duration, intensity) and sample size, different phases within the trial (eg enriched enrolment) and duration of study, treatment groups (including active versus inactive placebo comparator), dosing strategies (fixed versus flexible) and type of trial (eg parallel, crossover).[36,38,142]

The guideline development group was not able to identify sufficient evidence to answer all of the key questions asked in this guideline (see Annex 1). The following areas for further research have been identified:

15.2.1 Simple analgesics

- Further evidence on intermediate-term and long-term safety and effectiveness of NSAIDs for the treatment of people with chronic pain
- Further evidence on the safety and effectiveness of oral NSAIDs for the treatment of people with chronic lower back pain
- Further evidence on the head-to-head comparison between oral NSAIDs for the treatment of people with chronic pain

15.2.2 Antiepileptics

- Further evidence on the intermediate-term and long-term safety and effectiveness of AEDs for the treatment of people with chronic pain
- Further evidence on the effectiveness of carbamazepine for pain relief in people with trigeminal neuralgia.
- Further evidence on the effectiveness of topiramate for lower back pain and lumbar radicular pain.
- Studies to quantify the risk of overdose and substance use disorder in patients prescribed AEDs for chronic pain management.

15.2.3 Muscle relaxants

- Further evidence on the intermediate-term and long-term safety and effectiveness of muscle relaxants for the treatment of people with chronic pain.

15.2.4 Topical analgesia

- Further evidence on the safety and effectiveness of all topical analgesics, including analysis of effects on pain reduction and function.
- Establishment of the clinical significance of the pain reduction associated with topical capsaicin.

15.2.5 Combination pharmacological therapies

- Further evidence on effectiveness and safety (including appropriate dosage) of combination therapies in pain conditions other than neuropathic pain.
- Further evidence on effectiveness and safety (including appropriate dosage) of combination therapies other than opioid plus gabapentinoid, opioid plus antidepressant or gabapentinoid plus

antidepressant.

- Further evidence on effectiveness and safety (including appropriate dosage) of combination therapies in people with multimorbidities.

15.2.6 Physical therapies (hands-off)

- Further evidence to identify which types of hands-off physical therapies and at what intensity / duration are effective for the treatment of people with chronic pain.
- Further evidence on the effects of hands-off physical therapies on quality of life in people with chronic pain.
- Further evidence on the effect of mobility aids on chronic pain.
- Further evidence to identify barriers to exercise interventions for the treatment of people with chronic pain and how best to mitigate these.

15.2.7 Physical therapies (hands-on)

- Further evidence on the intermediate-term and long-term safety and effectiveness of physical therapies for the treatment of people with chronic pain.
- Further evidence on effects of physical therapies on quality of life and healthcare utilisation outcomes for the treatment of people with chronic pain.

15.2.8 Electrotherapy

- Further evidence on the role of ESWT/LiST in NHS Scotland, including the cost effectiveness of the intervention, service delivery factors (including training, knowledge and workforce specialisation) required to support it).
- Further evidence on the safety and effectiveness of electrotherapies, with particular attention to function, quality of life and healthcare utilisation outcomes for the treatment of people with chronic pain.

15.2.9 Dietary interventions

- Further evidence on the safety and effectiveness of anti-inflammatory diets, high-fibre diets, Mediterranean diets and FODMAP diets
- Further evidence on the effects of turmeric on chronic pain, investigating its role on pain reduction and functional improvement as a dietary component, or as a supplement. Studies should investigate possible dose effects.
- Further evidence on the effects of different doses of PUFA on pain intensity and function in people with chronic pain. Studies should carefully control comparators to avoid interference from other oils which may impact inflammation.

15.2.10 Alternative therapies

- Further evidence, including reporting of longer-term outcomes, on the safety and effectiveness of all alternative interventions in people with chronic pain.
- Further evidence on the safety and effectiveness of herbal products on pain intensity and function in people with chronic pain. Studies should aim to recruit larger samples, and include a wider range of herbal products.
- Further evidence on the effectiveness of acupuncture, herbal products and hypnotherapy on function in people with chronic pelvic pain.

16 Development of the guideline

16.1 Introduction

SIGN is a collaborative network of clinicians, other healthcare professionals and patient organisations and is part of Healthcare Improvement Scotland. SIGN guidelines are developed by multidisciplinary groups of practising healthcare professionals using a standard methodology based on a systematic review of the evidence. Further details about SIGN and the guideline development methodology are contained in 'SIGN 50: A Guideline Developer's Handbook', available at **www.sign.ac.uk**

This guideline was developed according to the 2019 edition of SIGN 50 with the following adaptations. In their first meeting, the guideline development group agreed a set of key questions for review which was later packaged into smaller work programmes of 4-6 questions each, known as waves. Each wave proceeded with dedicated systematic literature searching, screening and selection, critical appraisal and evidence synthesis. For each wave, the guideline development group developed draft recommendations and guideline text which has been consulted on separately. This document contains information relating to waves three and four. The guideline development group will incorporate revisions based on feedback received at consultation and from editorial reviewers and the final version of each wave will be published online as a toolkit within the Right Decision Service, the 'Once for Scotland' source of digital tools that enable people to make safe decisions quickly, based on validated evidence. When combined, the recommendations and supporting text for all four waves will collectively represent the SIGN guideline on chronic pain.

16.2 The Guideline Development Group

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The membership of the guideline development group was confirmed following consultation with the member organisations of SIGN. All

members of the guideline development group made declarations of interest. A register of interests is available in the supporting material section for this guideline at **www.sign.ac.uk**

Guideline development and literature review expertise, support and facilitation were provided by SIGN Executive and Healthcare Improvement Scotland staff. All members of the SIGN Executive make yearly declarations of interest. A register of interests is available on request from the SIGN Executive.

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Domenico Romano	Publications Designer
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16.2.1 Acknowledgements

SIGN is grateful to the following former members of the guideline development group and others who have contributed to the development of the guideline.

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16.3 Consultation and peer review

A report of the consultation and peer review comments and responses will be published in the supporting material section for this guideline on the SIGN website. All expert referees and other contributors made declarations of interest and further details of these are summarised on the report.

16.3.1 Specialist reviewers invited to comment on this draft

Ms Thora Allan	*Lived experience representative*
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16.3.2 Public consultation

The draft guideline was also available on the SIGN website for a month to allow all interested parties to comment.

16.3.3 SIGN editorial group

As a final quality control check, the guideline is reviewed by an editorial group comprising the relevant specialty representatives on SIGN Council to ensure that the specialist reviewers' comments have been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised. The editorial group for this guideline was as follows. All members of SIGN Council make yearly declarations of interest. A register of interests is available on the SIGN Council page on the SIGN website **www.sign.ac.uk**

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Dr Babar Akbar	Royal College of General Practitioners
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Abbreviations

ACT	acceptance and commitment therapy
AD	adjusted difference
AHRQ	Agency for Healthcare Research and Quality
aOR	adjusted odds ratio
aRR	adjusted relative risk or risk ratio
BNF	British National Formulary
BRAN	Benefits, Risks, Alternatives, doing Nothing
BZD	benzodiazepine
CBT	cognitive behavioural therapy
CI	confidence interval
CKD	chronic kidney disease
COX	cyclo-oxygenase
CPRD	Clinical Practice Research Database
CrI	credible interval
DDD	defined daily dose
ESWT	extracorporeal shockwave therapy treatment
EQ-5D	EuroQol five-dimensional questionnaire
FIQ	Fibromyalgia Impact Questionnaire
GDG	guideline development group
GDP	gross domestic product
GI	gastrointestinal
GMC	General Medical Council
GP	general practitioner
HIV	human immunodeficiency virus
HLLT	high-level laser therapy
HR	hazard ratio
HRQL	health-related quality of life
HSF	hot sand fomentation
IASP	International Association for the Study of Pain
ICD	International Classification of Diseases
IMMPACT	Initiative on Methods, Measurement and Pain Assessment in Clinical Trials

IT	interferential therapy
LiST	low-intensity shockwave therapy
LLLT	low-level laser therapy
LOCF	last observation carried forward
MA	marketing authorisation
MCID	minimum clinically-important difference
MD	mean difference
MHRA	Medicines and Healthcare Products Regulatory Agency
NICE	National Institute for Health and Care Excellence
NIH-CPSI	National Institutes of Health – Chronic Prostatitis Symptom Index
NMA	network meta-analysis
NNT	number needed to treat
NPQ	Northwick Park Neck Pain Questionnaire
NPRS	Numerical Pain Rating Scale
NSAID	non-steroidal anti-inflammatory drug
ODI	Oswestry Disability Index
ONS	Office for National Statistics
OR	odds ratio
PGIC	Patient Global Impression of Change
POU	persistence of opioid utilisation
QoL	quality of life
RCT	randomised controlled trial
RD	risk difference
RMDQ	Roland-Morris Disability Questionnaire
RR	relative risk or risk ratio
SAE	serious adverse event
SD	standard deviation
SDi	shortwave diathermy
SIGN	Scottish Intercollegiate Guidelines Network
SMC	Scottish Medicines Consortium
SMD	standardised mean difference
SmPc	summary of product characteristics
SNRI	serotonin-noradrenaline reuptake inhibitor

SSRI	selective serotonin reuptake inhibitor
TCA	tricyclic antidepressant
TENS	transcutaneous electric nerve stimulation
TMD	temporomandibular disorder
TU	therapeutic ultrasound
UK	United Kingdom
VAS	visual analog scale
WAE	withdrawal due to adverse events
WHO	World Health Organization
WMD	weighted mean difference
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

Annex 1
Key questions addressed in this update

This guideline is based on a series of structured key questions that define the target population, the intervention, diagnostic test, or exposure under investigation, the comparison(s) used and the outcomes used to measure efficacy, effectiveness, or risk. These questions form the basis of the systematic literature search.

Guideline section	Key question	
2	1.	In patients with chronic non-malignant pain what is the effectiveness of simple analgesics compared with placebo or other interventions on pain scores (30% reduction and 50% reduction), functional ability, quality of life, adverse events/drug reactions or dependency (physiological or psychological)?
3	2.	In patients with chronic non-malignant pain what is the effectiveness of anti-epilepsy drugs compared with placebo or other interventions on pain scores (30% reduction and 50% reduction), functional ability, quality of life, adverse drug reactions or dependency (physiological or psychological)?
4	3.	In patients with chronic non-malignant pain what is the effectiveness of muscle relaxants compared with placebo or other interventions on pain scores (30% reduction and 50% reduction), functional ability, quality of life, adverse drug reactions or dependency (physiological or psychological)?
5	4.	In patients with chronic non-malignant pain what is the effectiveness of topical analgesics compared with placebo or other interventions on pain scores (30% reduction and 50% reduction), functional ability, quality of life, adverse events/drug reactions or dependency (physiological or psychological)?
6	5.	In patients with chronic non-malignant pain what is the effectiveness of combination pharmacological therapies compared with single pharmacological therapies on pain scores (30% reduction and 50% reduction), functional ability, quality of life, adverse events/drug reactions or dependency (physiological or psychological)?
7	6.	In patients with chronic non-malignant pain what is the effectiveness of hands-on based interventions (manual therapies or massage) compared with comparator on pain scores (30% reduction and 50% reduction), functional ability, quality of life or adverse events?
8	7.	In patients with chronic non-malignant pain what is the effectiveness of hands-off based interventions (exercise, physical activity or mobility aids) compared with comparator

		(see table) on pain scores (30% reduction and 50% reduction), functional ability, quality of life or adverse events?
9	8.	In patients with chronic non-malignant pain what is the effectiveness of electrotherapy-based interventions (TENS, interferential, laser therapy, pulsed-shortwave diathermy, ultrasound, microcurrent therapy, or shockwave therapy) compared with comparator on pain scores (30% reduction and 50% reduction), functional ability, quality of life or adverse events?
10	9.	In patients with chronic non-malignant pain is there any evidence for the effectiveness of dietary interventions compared with usual care on pain scores (30% reduction and 50% reduction), functional ability, quality of life or adverse events?
11	10.	In patients with chronic non-malignant pain what is the effectiveness of other/alternative interventions (acupuncture, aromatherapy, homeopathy, herbal medicine, hypnotherapy, music therapy or Reiki) compared with comparator on pain scores (30% reduction and 50% reduction), functional ability, quality of life or adverse events?

Information relating to the following questions was made available in a previous consultation

Not available in this draft	11.	In people with chronic non-malignant pain are opioids more likely than placebo or other interventions to improve pain severity, functional ability, and/or quality of life, and/or to cause adverse events/drug reactions, or dependency (physiological or psychological)?
Not available in this draft	12.	Should naloxone be coprescribed when opioids are used for chronic pain (or when long-term/high-dose opioids are prescribed)?
Not available in this draft	13.	In patients with chronic non-malignant pain what is the effectiveness of medicinal cannabis compared with placebo or other interventions on pain scores (30% reduction and 50% reduction), functional ability, quality of life, adverse drug reactions or dependency (physiological or psychological)?
Not available in this draft	14.	In patients with chronic non-malignant pain what is the effectiveness of antidepressants compared with placebo or other interventions on pain scores (30% reduction and 50% reduction), functional ability, quality of life, adverse events/drug reactions or dependency (physiological or psychological)?
Not available in this draft	15.	In patients with chronic non-malignant pain, what is the effectiveness of pain management programmes (as defined in the guideline) compared with no treatment or other interventions on pain scores, functional ability, mood, quality of life and adverse events?
Not available	16.	In patients with chronic non-malignant pain what is the effectiveness

in this draft		of psychological interventions (cognitive behavioural therapy, acceptance and commitment therapy, mindfulness-based interventions, biofeedback or relaxation) compared with no treatment or other interventions on pain scores (30% reduction and 50% reduction), functional ability, mood, quality of life or adverse events?
Not available in this draft	17.	In patients with non-malignant chronic pain what is the effectiveness of patient and lay self-help advice compared with no treatment or other interventions on pain scores (30% reduction and 50% reduction), functional ability, quality of life or adverse events? Interventions were considered which had no or minimal ongoing healthcare professional input (which can potentially reach large numbers of patients) and which are generally self-led, with or without intermittent supportive contact, including • apps (mobile and web-based/mhealth, ehealth), • computer-based programmes • monitoring devices eg exercise trackers • automated reminders/ brief telephone support to follow programme or take actions • bibliotherapy/advice booklets/manuals • lay self-help or support groups, eg third-sector groups • mentoring/support by peers.
Not available in this draft	18.	In patients with chronic non-malignant pain what is the effectiveness of occupation-based interventions on pain scores (30% reduction and 50% reduction), occupational performance, engagement in personally meaningful occupations, return to work rates, quality of life or adverse events?

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