Healthcare Improvement Scotland | SIGN Makes sense of evidence

SIGN 173 Management of chronic pain

(Part 1)

A national clinical guideline

December 2025

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 pain management service delivery

framework[16] includes approaches to help increase knowledge in the non-specialist setting, through a Chronic Pain Knowledge Hub for health and social care professionals.

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 Scottish Government 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.

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.

In section 8, evidence for comprehensive pain management programmes, which are generally delivered in secondary care, is reviewed. While pain management programmes can be delivered in primary care and therefore should not be defined as an intervention limited to secondary care only, at present, this model is not delivered widely in Scotland, where most pain management programmes involve input from multidisciplinary teams in secondary care settings.

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 14.1) 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 first part of the guideline and contains information on:

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

The second part of the guideline will be published when available 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.

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.[22] 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.[23,24] 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.[25]

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

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'.[26] 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.[27] 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.[28,29] 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.[30]

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.[28]

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.[31]

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.[32-34]

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.[35-37]

To allow comparison between studies, a standardised approach to outcome measures is recommended by IMMPACT.[35] 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.[38,39]

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. 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.[37]

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 14.2).

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."[40] 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.[41] 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 to 100-point Oswestry Disability Index (ODI), 1 to 2 points on the 0 to 24-point Roland-Morris Disability Questionnaire (RDQ), 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 RDQ, 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.[42]

"Prescribing medicines outside the conditions of their marketing authorisation alters (and probably increases) the prescribers' professional responsibility and potential liability".[42]

The General Medical Council (GMC) recommends that when prescribing a medicine 'off label', doctors should:[43]

- 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.[44]

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.[45]

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 13.4.

2 Key recommendations

The following recommendations were highlighted by the guideline development group as the key clinical recommendations that should be prioritised for implementation.

2.1 Opioids

R **Opioids should not be considered routinely for people with chronic non-malignant pain.**

R **In carefully selected individuals, and only when other pain therapies have been fully explored, opioids can be considered for short-term treatment (up to 3 months), if it is considered that the potential benefits outweigh the risks of serious harms such as addiction, overdose and death.**

R **If prescribing opioids, undertake early and frequent review to identify any benefits and potential or actual adverse events/drug reactions. If necessary, the dose should be adjusted or treatment stopped.**

R **All people receiving opioid doses of >50 mg MED/day should be reviewed regularly (at least annually and preferably more often) to detect emerging harms and consider ongoing effectiveness.**

R **Pain specialist advice or review should be sought at doses >90 mg MED/day.**

2.2 Medicinal cannabis

R **Medicinal cannabis-based products are not recommended for use in the management of chronic pain outside of the context of a clinical trial.**

2.3 Pain management programmes

R **Following appropriate assessment, consider comprehensive pain management programmes for people with chronic pain.**

3 Key principles in managing chronic pain

3.1 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.[26]

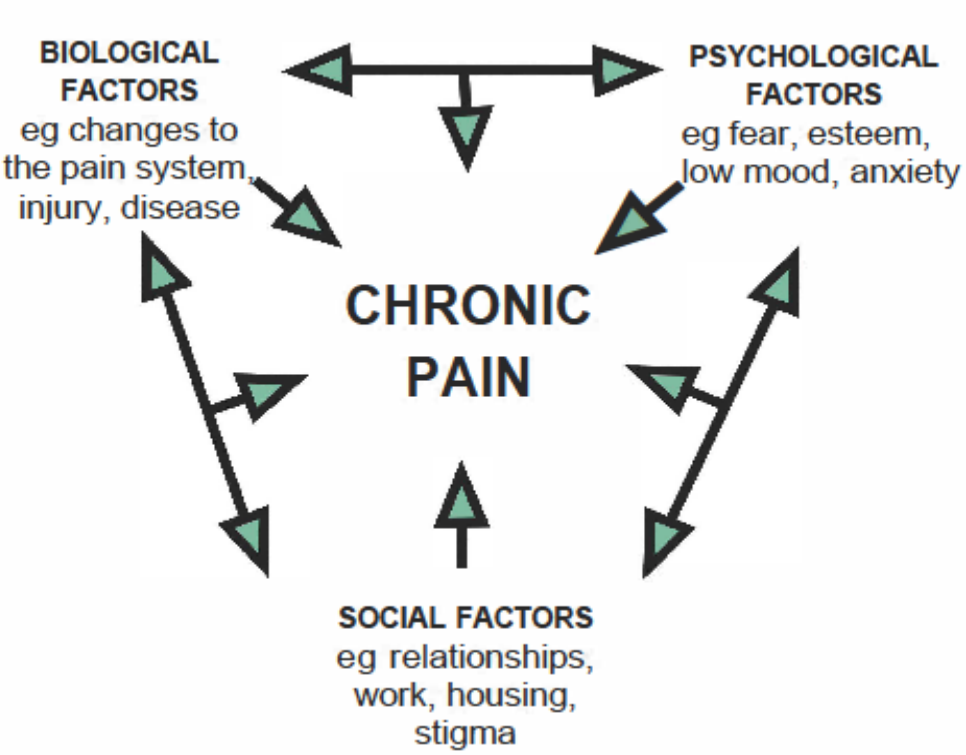
Scottish Government's Realistic Medicine aligns closely with this approach and encourages open discussion between people and healthcare professionals, shared decision making and care that is guided by each person's values.

3.2 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.[26] 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[27] 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.[46]

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.

3.3 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.

3.4 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.

3.5 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.

3.6 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.

3.7 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 section 8) and selected specialist interventions can be accessed, where appropriate.[47]

3.8 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 12.2).

3.9 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 CBT or ACT, when appropriate (see section 9).

3.10 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.

The Quality Prescribing guide provides 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.

4 Opioids

4.1 Introduction

In recent decades, there has been a significant increase in opioid prescribing for people living with chronic pain, despite limited evidence for long-term efficacy. There is international concern around the rise in opioid prescribing and opioid-associated mortality rates in the United States, Australia and Europe.[48-50] Between 2012 and 2016 Scotland and England saw similar increases.[51,52] Meanwhile, there has been growing awareness and concern about the harms caused by long-term use of opioids and their adverse effects.[53,54] As a result, monitoring of National Therapeutic Indicators has been able to demonstrate a fall of 10% in opioid prescribing rates between 2017 and 2024 (excluding a slight increase during the coronavirus disease (COVID-19) pandemic.[55,56]

These concerns prompted the Faculty of Pain Medicine (Royal College of Anaesthetists) 'Opioids Aware' campaign, which provides evidence-based resources and advice for clinicians and patients on the use of opioids for pain (including chronic pain). In 2018 the IASP produced a statement on the use of opioids in people with chronic pain, which concluded that, "There may be a role for medium-term, low-dose opioid therapy in carefully selected patients with chronic pain who can be managed in a monitored setting. However, with continuous longer-term use, tolerance, dependence and other adaptations compromise both efficacy and safety".[57] (The IASP did not define 'medium-term', 'low-dose' or 'longer-term' in this statement.) Evidence from the United States of America (USA) indicates that opioid use around the time of surgery (peri-operative opioid use) may have contributed to the large increase in prolonged opioid use.[58]

Opioids have been used for their analgesic effects for centuries. For the majority of clinically used opioids, this effect is predominantly, although not exclusively, via the mu opioid receptor (MOR). The potency of different opioids at this receptor varies. Some opioids, such as codeine, dihydrocodeine, tramadol and tapentadol, have defined upper dose limits in the British National Formulary (BNF). Among these, the BNF classifies codeine and dihydrocodeine as 'weak opioids', with the other commonly used opioids being classed as 'strong opioids'.[59] Tramadol and tapentadol have additional actions on pain systems through noradrenergic mechanisms; tramadol also acts through serotoninergic reuptake inhibition. These additional actions on pain systems may have advantages in some chronic pain conditions, such as neuropathic or mixed pains, but they can also limit upward dose titration and increase the range of adverse effects. Strong opioids listed in the BNF include morphine, diamorphine, hydromorphone, oxycodone, tramadol, fentanyl, buprenorphine and methadone.[59]

4.2 Evidence of benefit

High-quality evidence was identified comparing the clinical effectiveness of

opioids with placebo or non-opioids, including a systematic review published in 2020 pooling data from 74 RCTs (20,502 participants),[60] with additional studies providing surveillance from August 2019 to March 2022,[61-63] and a systematic review and network meta-analysis (NMA) pooling data from 82 RCTs (22,619 participants).[64]

There were no RCTs comparing opioids with placebo for longer than six months' follow-up, and only one that compared opioids with non-opioids for up to one year's follow-up.[65]

4.2.1 Opioids versus placebo

Comparing opioids with placebo in the short term (1 to <6 months) opioids were associated with a slightly lower pain intensity score (mean difference (MD) -0.79 on a scale from 0 to 10, 95% confidence interval (CI) -0.93 to -0.67; 71 RCTs, 19,616 participants: high-certainty evidence).[60] This difference of less than one point on an 11-point scale is unlikely to be clinically significant. When only trials with three to six months' follow-up were included, there was no difference in pain intensity between opioids and placebo (MD -0.30, 95% CI -0.83 to 0.23; eight RCTs, 2,243 participants: no evidence quality rating). When considering all studies regardless of follow-up duration, there was evidence of a pain response (typically defined as a 30% or great pain reduction, though definitions across studies varied) for opioids when compared with placebo (risk ratio (RR) 1.35, 95% CI 1.24 to 1.48; 44 RCTs, 12,481 participants: high-certainty evidence). When restricted to studies with follow-up periods between 3 and 6 months, there was no significant difference in the likelihood of pain response from opioids compared with placebo (RR 1.19, 95% CI 0.68 to 2.17; five RCTs, 1,503 participants: no evidence quality rating). There was evidence of better function and physical health status for people who received opioids in the short term (1 to <6 months). Greater improvement in physical health status was seen with opioids (1.64/100, 95% CI 1.10 to 2.17; 23 RCTs, 8,005 participants: high-certainty evidence) compared with placebo, although this improvement was small and not clinically significant, and there was no difference in mental health status (-0.48/100, 95% CI -1.39 to 0.44; 21 RCTs, 7,586 participants: high-certainty evidence). No studies had longer than six months' follow-up.	1++
Greater short-term benefit from opioids (versus placebo) has been reported for people with neuropathic pain (-1.15 points on an 11-point scale, 95% CI -1.43 to -0.91; 20 RCTs, 2,568 participants: no evidence quality rating) compared with those with musculoskeletal pain (-0.67 points on an 11-point scale, 95% CI -0.81 to -0.54; 50 RCTs, 16,979 participants: no evidence quality rating).[60] The difference of 0.48 points is statistically significant (p=0.009), although of uncertain clinical importance (see section 1.4.1). Although the difference in pain intensity reduction with enriched enrolment RCTs (which ensure that only responders who experience considerable pain relief and no or acceptable side effects on a predefined or titrated dose during a selection phase are included in the randomised double-blind experimental phase) compared with non-enriched enrolment RCTs was non-significant (-0.86 vs -0.75), with enriched enrolment	

resulting in a significantly lower relative risk of discontinuation due to adverse events (RR 1.35, 95% CI 1.02 to 1.78; 25 RCTs, 8,011 participants: no evidence quality rating) compared with non-enriched RCT designs (RR 3.06, 95% CI 2.50 to 3.81; 36 RCTs, 11,983 participants: no evidence quality rating).

A well-conducted systematic review with NMA evaluated 14 opioids either against placebo or against each other.[64] Seventy-eight trials that included 21,906 participants reported on pain relief. Using the surface under the cumulative ranking curve (SUCRA) rankings suggested that modified-release (MR) codeine, MR oxymorphone, and immediate-release (IR) oxycodone were the best opioids for pain relief with reduction in pain scores ranging from 0.99 to 2.03 cm on a 10 cm scale but these findings were supported by evidence rated by the authors as low to very low certainty.

Sufficient relevance, sufficient credibility

There was high to moderate-certainty evidence that IR tramadol, MR morphine, sublingual buprenorphine, MR tapentadol, and MR tramadol were superior to placebo, with pain reduction ranging from 0.80 to 1.09 cm on a 10 cm scale.

For physical function, the evidence (39 studies, 13,134 participants) was rated low to very low quality and according to the SUCRA rankings the most effective opioids for improving function were MR codeine and MR hydromorphone.

4.2.2 Opioids versus non-opioid medication

Comparing opioids with non-opioids (medications used across trials included non-steroidal anti-inflammatory drugs (NSAIDs), antiarrhythmic drugs, anticonvulsants and antidepressants), no significant difference was reported in pain reduction (MD -0.29 on a 0 to 10 scale, 95% CI -0.61 to 0.03) at short-term follow-up (1 to <6 months; 14 RCTs, 2,195 participants: moderate-certainty evidence), nor for likelihood of a pain response (RR 1.28, 95% CI 0.90 to 1.85; 12 RCTs, 2,886 participants; moderate-certainty evidence).[60]

Pooled analysis of 11 RCTs, that included 2,010 participants, found that there was no difference in functional ability between opioids and non-opioids (SMD 0.00, 95% CI -0.14 to 0.12: high-certainty evidence).

1++

Only one study which followed participants up for longer than six months, the Strategies for Prescribing Analgesics Comparative Effectiveness (SPACE) trial,[65] was identified in a meta-analysis.[60] The trial compared outcomes in 106 people with chronic musculoskeletal pain who received opioids with 115 receiving non-opioid medicines and found no difference in function between the groups, but a greater reduction in pain severity among those receiving opioids (4.0/10 vs 3.5/10) at 12 months. The size of this effect did not meet the minimum clinically important difference established by the trial authors (see section 1.4.1).

No data were reported on quality of life in studies comparing opioid and non-opioid use.

4.2.3 Specific chronic pain conditions

It is not possible to draw conclusions about opioid effectiveness in different chronic pain conditions. Analysis of studies of specific pain types in one systematic review compared the effects of opioids in participants with neuropathic pain and those with musculoskeletal pain.[60] They found that, compared with placebo, opioids were associated with a slightly larger improvement in neuropathic pain compared with those with musculoskeletal pain, (low back pain and osteoarthritis). There was only one RCT identified in participants with fibromyalgia where no effect was demonstrated. The most frequently assessed neuropathic pain conditions were diabetic neuropathy and postherpetic neuralgia. There were no interactions between pain type and risk of discontinuation due to adverse events or of serious adverse events. | 1++

4.2.4 Summary of effectiveness

Evidence based on high-quality systematic reviews consistently found little or no reduction in pain severity among people with chronic pain who were treated with opioids, compared with placebo or non-opioid medications. Where improvements in pain severity and function were seen with opioids, these were small and not clinically significant, and there was no evidence of opioid efficacy when treatment was given beyond three months.

The low certainty of evidence and the calculated rankings of relative efficacy from the NMA shows that individual opioids are similarly ineffective with no opioid showing superior short-term effectiveness.

4.3 Evidence of harms

4.3.1 Opioids versus placebo

Opioids were associated with a greater risk (RR 2.25, 95% CI 1.86 to 2.73; 61 RCTs, n=19,994 participants: high-certainty evidence) of participant discontinuation due to adverse events compared with placebo. There were significantly greater risks of all recorded adverse events (nausea, vomiting, constipation, somnolence, dizziness, pruritus), except for headache which showed no difference at short-term follow-up.[60] | 1++

In the NMA, 53 studies (n=20,283) reported on vomiting. Modified-release oxycodone was found to result in greater risk of vomiting than placebo (odds ratio (OR) 7.12, 95% CI 5.42 to 9.35; nine RCTs, 3,091 participants: moderate-certainty evidence). Analysis of 67 trials with 22,681 participants found that MR oxycodone, MR tramadol and MR tapentadol resulted in increased nausea compared with placebo (high to moderate-certainty evidence). Analysis of 64 studies with 22,531 participants found that MR oxycodone, MR hydromorphone, and MR tramadol resulted in increased risk of constipation compared with placebo (high to moderate-certainty evidence).[64] | Sufficient relevance, sufficient credibility

4.3.2 Opioids versus non-opioid medication

Pooled analysis of 12 RCTs with 3,637 participants found that opioids were more likely than non-opioids to be associated with discontinuation due to | 1++

adverse events (RR 2.18, 95% CI 1.48 to 3.08; moderate certainty of evidence). The most common adverse events were vomiting, pruritis, constipation, nausea, drowsiness and headache. Risk of adverse events, drug reactions and discontinuation did not differ between low and high opioid doses. There were also associations between opioid use and fractures, falls, cardiovascular events, and endocrine outcomes, but not with self harm.[60]

4.3.3 Long-term adverse events

No systematic review of RCTs has identified studies that investigate the long-term (>12 months) adverse events of opioids. Observational studies identified in one systematic review found that, compared with people taking opioids, people not taking opioids were more likely to report lower pain intensity at one year,[60] and were less likely to experience severe pain-related interference with activities at two years.[66]

2++ (evidence level aligned to studies used in this analysis)

The SPACE trial, which followed participants up for 12 months, found that those receiving opioids experienced more (1.8 vs 0.9), and more frequent (p=0.03) medication-related symptoms than those receiving non-opioid medicines.[65]

4.3.4 Dose- and duration-related adverse events

A systematic review and its associated surveillance reports noted consistent evidence from observational studies on associations between increasing opioid dose and increasing risk of overdose and opioid-related mortality.[61] Similarly, observational studies report a dose-dependent association between opioid prescription and opioid use disorder (OUD), with both a higher daily dose, and, particularly, a longer duration of therapy associated with a greater risk of subsequent OUD. One case-control study reported that doses of opioids greater than 20 mg/day morphine-equivalent dose (MED) taken by drivers were associated with increased odds of injuries related to road trauma.[60]

2++ (evidence level aligned to studies used in this analysis)

A 10-year longitudinal study followed up over one million adults (mostly in the UK) who were prescribed opioids for non-cancer pain. They found that UK adults who were prescribed morphine had a 12-fold risk of all-cause mortality compared with those who had been prescribed codeine (hazard ratio (HR) 12.58, 95% CI 11.87 to 13.32). This risk was dose dependent, and rose with age. All-cause mortality risk was greater among those prescribed >50 mg/day MED, and in the presence of multimorbidity and/or a history of substance misuse.[67]

2+

4.3.5 Dependence and opioid use disorder

A systematic review of studies involving individuals treated with opioids for chronic non-malignant pain (148 studies, >4.3 million participants) reported that 9.3% experienced dependence and opioid use disorder (D&OUD), with a further 12.4% at risk of this, and a total of 29.6% showing signs and symptoms of D&OUD.[68]

The authors of a large systematic review with meta-analysis of opioid treatments for chronic pain noted that most trials excluded people with

2++ (evidence level limited to

studies used in this analysis)

substance use history or mental health disorders or did not describe these characteristics, meaning that differential effects according to comorbidities could not be assessed.[60] However, they identified a large UK cohort study estimating risk of overdose (98,140 participants), which reported a dose-dependent increase of hazard ratio for overdose (≥50 mg MED/day compared with no opioid (HR 3.81, 95% CI 2.50 to 5.80).[69]

Although screening tools exist to predict D&OUD, evidence for their effectiveness is weak, and their effect size has been modest at best. A systematic review identified no reliable evidence for the effectiveness for the use of urine drug screening, pill counts or prescription drug monitoring programmes to predict subsequent misuse.[70]

There is, therefore, consistent evidence of adverse events associated with opioid treatment, and this association appears to be dose dependent.

4.4 Summary of benefits and harms of opioids for chronic pain

There may be limited short-term benefits associated with short-term use of opioids in terms of pain intensity and some aspects of function. These benefits appear to be small and to reduce or disappear with longer-term use (beyond three months). The possibility that some people who use opioids may experience greater short-term benefits cannot be excluded. This suggests that individualised treatment may be considered. There is no evidence suggesting that opioids may be more effective than a placebo after six months, and some evidence suggesting that pain-related and functional outcomes may be worse with long-term (>12 months) opioid use, compared with not taking opioids.

There are strong associations between opioid therapy and adverse events (minor and serious) irrespective of dose, with approximately two- to threefold greater relative risk of specific adverse events (gastrointestinal symptoms, drowsiness, dizziness, and itching) versus placebo. Observational evidence consistently shows dose-dependent associations between opioid therapy and subsequent OUD, overdose and death, as well as evidence that taking opioids for longer duration is associated with OUD. The risk of harm increases substantially at doses above an oral morphine equivalent of 50 mg/day.

Although most of the evidence includes studies undertaken in the UK, many studies were conducted elsewhere, particularly North America. Factors such as access to healthcare and prescribing regulations may affect the availability of opioids but are less likely to affect the evidence relating to benefits and harms.

4.5 Other factors

4.5.1 Prescribing opioids

The evidence suggests that for most people with chronic non-cancer pain, opioid treatment provides minimal-to-no benefit and is likely outweighed by adverse events, especially after three months, in terms of both pain intensity and overall function. In most people presenting with chronic non-

malignant pain, therefore, opioids are unlikely to be appropriate.

If a trial of an opioid is considered, then measurable treatment goals should be agreed between clinician and person with chronic pain before opioids are started and a strategy for deprescribing put in place if these goals are not achieved.[71] This can be achieved through a comprehensive biopsychosocial assessment, consideration of personal goals, knowledge, previous experience and preferences and shared decision-making, involving individuals, families and carers as well as the healthcare team. Resources, including information for patients, are available through Opioids Aware. The lack of good evidence for specific risk prediction tools means that clinical judgement, based on assessment, discussion and information, is important from the outset.

4.5.2 Risk of opioid dependence

A systematic review and meta-analysis found that those who were younger, were male, and/or reported a history of, or current substance use or mental health diagnosis were at a greater risk of developing opioid misuse.[72] A National Institute for Health and Care Excellence (NICE) Clinical Knowledge Summary describes a number of risk factors for opioid dependence, including:[73]

- availability of drugs
- peer substance use
- adverse childhood experiences
- history of mental illness
- social disadvantage
- genetic predisposition, and
- younger age and male gender.

The National Institute for Health and Care Excellence has published guidance on safe prescribing and withdrawal of medicines associated with dependence or withdrawal symptoms.[74]

4.5.3 Reviewing opioid use

Clinicians should work with patients to incorporate strategies to mitigate risk in management plans. This should include regular (<3-months) review of their medication, and consideration given to changes in their status (for example, infection, or changing comorbidities) which may increase the risk of opioid toxicity, including confusion, respiratory depression and overdose.

People who are already being prescribed long-term opioids also need regular review, and assessment of benefits (pain reduction, function, quality of life) and harms, potentially with a view to safe reduction and withdrawal of treatment, if appropriate.[75] It is important to consider the possibility of stigmatising people who have been taking opioids on long-term prescription, and to avoid this. The Scottish Government Quality Prescribing for Chronic Pain Guide (in development) contains information

on medication review and opioid management including practical steps to reduce high-dose opioids, deprescribing tips and advice on addressing challenges during reduction. Prescribers should note the additional risks from facilitating the dispensing of opioids in the community, where their potential illicit use may lead to more widespread harms.

4.6 Recommendations

The following recommendations are based on high-level evidence (for limited clinical effectiveness and risk of adverse events or drug reaction) during the first six months, and on low-level evidence for benefits and harms after six months and the risk of overdose and other adverse events. These recommendations cover both IR and MR opioids.

R **Opioids should not be considered routinely for people with chronic non-malignant pain.**

R **In carefully selected individuals, and only when other pain therapies have been fully explored, opioids can be considered for short-term treatment (up to 3 months), if it is considered that the potential benefits outweigh the risks of serious harms such as addiction, overdose and death.**

R **If prescribing opioids, undertake early and frequent review to identify any benefits and potential or actual adverse events/drug reactions. If necessary, the dose should be adjusted or treatment stopped.**

R **All people receiving opioid doses of >50 mg MED/day should be reviewed regularly (at least annually and preferably more often) to detect emerging harms and consider ongoing effectiveness.**

R **Pain specialist advice or review should be sought at doses >90 mg MED/day.**

✓ For people who are already on long-term opioids, clinicians should consider a review to assess the benefits and potential or actual harms, with a view to reducing or stopping the prescription.

✓ If an individual has pain that remains severe despite opioid treatment consider stopping opioids, with appropriate support, even if no other pharmacological treatment is available as the risks of continuation are likely to outweigh the benefits.

✓ At initiation of opioid prescribing, and at subsequent reviews, patients should be informed about the risks and potential harms of taking opioids. Any opioid prescribing must be based on the patient's fully informed understanding and agreement to the potential risks and benefits.

5 Naloxone

5.1 Introduction

Naloxone is an opioid antagonist that can be used to temporarily reverse the central nervous system (CNS) and respiratory depressant effects of an opioid overdose. Naloxone is licensed for lay administration in the event of a suspected opioid overdose; legislation allows for anyone to administer naloxone for the purpose of saving a life.

Naloxone is a prescription-only medicine, however specific legislation is in place in the UK that allows the supply of intramuscular and intranasal formulations to people at risk of an opioid overdose without the need for a prescription, under certain circumstances.

A national naloxone programme was established in Scotland in 2011 in response to increasing numbers of drug-related deaths. After training, naloxone kits suitable for community administration are supplied to people at risk of opioid overdose, their friends, family and service workers to help reduce drug-related deaths in Scotland. From October to December 2023 7,589 naloxone kits were issued across Scotland.

While the supply of naloxone has been successfully established in Scotland, the focus of the programme is to target those at increased risk of opioid overdose due to substance misuse. Current practice in Scotland does not proactively identify people who are prescribed opioids for chronic pain who may be at an increased risk of opioid overdose (see section 4.3.4–5).

5.2 Evidence of benefit

There is limited evidence around coprescribing naloxone when opioids are indicated for chronic pain. One systematic review was identified which included evidence on risk mitigation strategies for people who are prescribed opioids.[60]

The review identified one observational study that assessed the association between coprescribing of intranasal naloxone for people taking daily opioids for chronic pain and the use of emergency departments (ED) in a safety-net healthcare setting in the USA.[76] Safety-net hospitals provide healthcare for individuals regardless of their insurance status or ability to pay. These hospitals typically serve a proportionately higher number of uninsured, low-income, and other vulnerable individuals. While in Scotland, the risk of being prescribed an opioid is higher in areas of high deprivation,[52] differences in the healthcare systems and other sociodemographic factors may make this study population less representative of the Scottish target population. 2+

The mean age of the study participants was 56.7 years (± 10.8), 58.6% were male, and the majority of patients were Black. The most commonly prescribed opioid was oxycodone and the median dose was 53 mg MED/day. The study does not provide any information about comorbidities or polypharmacy within this population. Notably, they were unable to

determine whether the patients included in the analysis had any history of substance use, however, people taking opioids for OUD at the time of the study were excluded.

The study suggested benefit from coprescribing naloxone when opioids are indicated for chronic pain. The study found that, on average, coprescribing naloxone was associated with 6% fewer ED visits per month (incidence rate ratio (IRR) 0.94, 95% CI 0.89 to 0.998, p=0.044), a 47% reduction in ED visits per month after six months (IRR 0.53, 95% CI 0.34 to 0.83, p=0.005) and 63% reduction after one year (IRR 0.37, 95% CI 0.22 to 0.64, p<0.001).

When advised to offer naloxone to all people receiving long-term opioids, clinicians were found to be more likely to prescribe naloxone to those whom they considered to be at higher risk of opioid overdose, including individuals receiving higher doses of opioids and those who had previously had an opioid-related ED admission. There is no information about whether naloxone prescribed was actually dispensed, and no investigation of outcomes other than ED attendance.

5.3 Evidence of harms

The study hypothesises that prescribing naloxone may change patient behaviour with respect to opioids. However, the authors also caution that there may be hazards to risk stratifying users of opioids to be offered naloxone, including stigma and concerns about identifying an individual's elevated risk for overdose.

Further information about harms associated with coprescription of opioids with medications which have a depressant effect on the CNS is included in a section of the draft guideline which will be consulted on at a later date.

5.4 Summary of benefits and harms of naloxone coprescription with opioids for chronic pain

There is limited evidence to support widespread coprescribing of naloxone to people prescribed opioids for chronic pain. However, learning from other at-risk groups may be applied and where additional risk factors for opioid overdose are identified, clinicians should consider offering naloxone in a suitable formulation intended for lay person administration, ie provided in a ready-to-use kit with needles for intramuscular administration or an appropriate nasal spray.

The supply of naloxone to those at higher risk of opioid overdose does not negate the need for safe prescribing of opioids. Clinicians should work with patients to incorporate strategies to mitigate risk in management plans, this should include regular (<3-months) review of their medication, and consideration given to changes in patient status, which may increase the risk of overdose.

5.5 Other factors

Public Health Scotland has reported that the supply of naloxone for use in the community is feasible in the Scottish context as it is already

established for other at-risk groups, such as those receiving opiate substitution treatment.

When considering overdose risk among people who misuse drugs, additional risk factors include a history of opioid-related hospital admissions, previous near-fatal overdoses, a history of substance use (including alcohol), coprescribing of depressant medicines (for example, gabapentinoids, benzodiazepines), high-dose opioid prescribing, and multimorbidity that increases the risk of opioid toxicity (see section 4.5.2).[77,78]

It is recognised as good practice to offer training to people who are prescribed opioids for chronic pain and their significant others to recognise the signs of an opioid overdose and about appropriate interventions, including naloxone administration.[71]

Further information on naloxone coprescription with opioids is included in the Scottish Government Quality Prescribing for Chronic Pain Guide (in development). Details on accessing and using naloxone appropriately can be found in section 12.2.

5.6 Recommendations

R **Consider prescribing naloxone for people with chronic pain who are prescribed opioids and who may be at risk of an opioid overdose.**

✓ Offer a naloxone product that is suitable for use in the community, for example, an intranasal formulation or prefilled syringe.

✓ Coprescribing of naloxone to those at higher risk of opioid overdose does not negate the need for safe prescribing of opioids. Clinicians should work with patients to incorporate strategies to mitigate risk in management plans, this should include regular (<3-months) review of their medication.

6 Medicinal cannabis

6.1 Introduction

There is a need for new, effective, safe pharmacotherapy for long-term management of chronic pain. Since the previous guideline was published in 2013, several medicinal cannabis products have become available for clinical use.

The hemp plant, *Cannabis sativa* (marijuana), produces up to 60 cannabinoid derivatives, of which delta-9 tetrahydrocannabinol (THC) and cannabidiol (CBD) are best known, with medicinal products available containing these compounds.[79] There is a potential neurobiological basis for analgesic effects of cannabinoids, with preclinical evidence of antinociception, through the endocannabinoid system, mediated by G-protein-coupled cannabinoid receptors (CB1 and CB2) in the peripheral and central nervous system (PNS, CNS). Both receptors may have a role in nociception, including in chronic pain.[80-82]

For new classes of analgesic drugs, such as cannabinoids, it is important to understand the evidence for analgesic use, and any related implications for clinical practice, particularly safety issues, with long-term use.

Currently in Scotland, there is no medicinal cannabis preparation licensed for treatment of chronic pain.

Delta-9-tetrahydrocannabinol and cannabidiol (Sativex®) is accepted for use within NHSScotland as treatment for symptom improvement in adults with moderate to severe spasticity due to multiple sclerosis, who have not responded adequately to other antispasticity medication and who demonstrate clinically significant improvement in spasticity-related symptoms during an initial trial of therapy.[83]

4

Any use for chronic pain would therefore be off label.

National Institute for Health and Care Excellence guideline 144 on cannabis-based medicinal products does not recommend the use of cannabinoids for the treatment of chronic pain, unless within the context of a clinical trial.[84] Subsequent to this, position statements from the Faculty of Pain Medicine (Royal College of Anaesthetists, London),[85] and the IASP (after a comprehensive evidence review for chronic pain)[86] did not recommend use for chronic pain due to the lack of high-quality evidence of efficacy and safety, particularly with long-term use. The need for robust clinical trials was highlighted by both organisations, as well as the importance of regulatory standards to ensure safety.

4

6.2 Evidence of benefit

Thirteen systematic reviews with meta-analyses, and one NMA, published between 2018 and 2023, were identified.[87-100] The number of included RCTs in the systematic reviews ranged from eight[91] to 65[87] (90 from the NMA comparing cannabinoids to opioids or placebo),[92] with six[88] to 57[97] observational studies. There was considerable overlap of included studies

1++
1+
Sufficient relevance, sufficient credibility

across the reviews. Four of the reviews focused specifically on chronic neuropathic pain. Most of the reviews (11/13) were rated as high quality, two acceptable quality, and the NMA was rated as sufficient. Overall, the quality of the studies included in the systematic reviews was mainly very low to low, with a high (or unclear) risk of bias, reducing our confidence in the conclusions.	
6.2.1 Pain severity	
In most reviews (10/13), small reductions in pain were reported compared with placebo, to a level unlikely to be of clinical significance according to the authors. Three reviews reported no statistically significant improvement in pain. In the NMA, cannabis reduced pain on a 0–10 cm scale compared with placebo (weighted mean difference (WMD) -0.60, 95% CI -0.87 to -0.33; 19 RCTs, 2,116 participants: low-certainty evidence). The authors note that the size of this effect fell below the 1 cm threshold for clinical significance using VAS, and was not significantly different to that seen with opioids (WMD 0.23, 95% CI -0.06 to 0.53; 82 RCTs, 19,693 participants: low-certainty evidence).[92] Although cannabinoids were compared with opioids in the NMA, most of these comparisons were indirect, with the only RCT directly comparing an opioid (dihydrocodeine) to a cannabinoid (nabilone) finding a statistically significant reduction in pain intensity for dihydrocodeine compared with nabilone in people with neuropathic pain.[101]	1++ Sufficient relevance, sufficient credibility
In a high-quality living systematic review and meta-analysis (minimum of one month of follow-up), a number of different preparations were included, with a reported MD in pain severity (0–10 scale) ranging from -0.54 (95% CI -0.95 to -0.19; seven RCTs, 702 participants: moderate-certainty evidence) to -1.97 (95% CI -5.91 to 1.21; two RCTs, 294 participants: insufficient certainty evidence) for cannabis products compared with placebo).[89]	1++
Meta-analysis of longer-term observational studies (up to 12 months) found that reductions in pain intensity did not meet predefined criteria of clinical significance with a WMD of pain intensity reduction of 1.75 (95% CI 0.72 to 2.78; six studies, 2,571 participants: very low-certainty evidence) on a 0–10 scale, compared with placebo,[88] with a further meta-analysis finding no evidence of sustained benefit in terms of reduced pain intensity, beyond six months.[89]	2++
None of the four systematic reviews that focused on chronic neuropathic pain, found a clinically significant reduction in pain severity, SMD -0.26, (95% CI -0.42 to -0.10; nine RCTs, 1,289 participants: low-certainty evidence),[90] SMD -0.44 (95% CI -0.69 to 0.19; eight RCTs, 893 participants: moderate-certainty evidence),[94] SMD -0.35 (95% CI -0.60 to -0.09; 14 RCTs, 1,837 participants: low-certainty evidence),[95] and MDs (0–100 scale) ranging from -6.62 (95% CI -9.15 to -4.09; five RCTs, 552 participants: moderate-certainty evidence) for THC/CBD to -8.68 (95% CI -10.97 to -6.38; seven RCTs, 332 participants: moderate-certainty evidence) for THC[96] with a calculated number needed to treat of 20 (11–100) for one person to benefit from a 50% reduction in pain intensity.[95]	1++ 1+

6.2.2 Function, quality of life and sleep

Seven systematic reviews[87-89,92,96-98] reported on the effect of cannabinoids on functional abilities (for example, physical, emotional, social), with three of those finding very small to small benefits to physical function from cannabinoids compared with placebo. For example, one review found a MD (0–10 scale) ranging from -0.42 (95% CI -0.73 to -0.16; 6 RCTs, 616 participants: moderate-certainty evidence) to 1.75 (95% CI -0.46 to 3.98; one RCT, 16 participants: low-certainty evidence) in function with cannabis-based products compared with placebo, depending on the formulation of the cannabinoid.[89] A further review found a WMD of 2.52 (95% CI 0.37 to 4.91; 44 RCTs, 12,727 participants: moderate-certainty evidence) with cannabis compared with placebo (0–100 scale on the 36-Item Short Form Health Survey (SF-36)).[92] A systematic review of observational studies found moderate benefits from cannabis to disability compared with placebo, with a SMD 0.45 (95% CI 0.05 to 0.88; five RCTs, 2,201 participants: very low-certainty evidence).[88] There was little effect from cannabis compared with opioids on physical functioning on a 0–100 scale (SF-36), with a WMD 0.47 (95% CI -1.97 to 2.99; 44 RCTs, 12,727 participants: moderate-certainty evidence).[92]	1++ 1+ 2++ Sufficient relevance, sufficient credibility
Evidence on quality of life (QoL) was inconsistent, with either minor benefits (one study)[88] or no benefit (six studies)[87,89,91,94-96] reported when compared with placebo, with low-certainty evidence.	1++ 1+ 2++
For people experiencing neuropathic pain, there was a small, but statistically significant improvement in sleep quality compared with placebo (SMD 0.40, 95% CI 0.19 to 0.61; six RCTs, 744 participants: moderate-certainty evidence) in the one review where sleep quality was a primary outcome. However, there were also increases in daytime somnolence (SMD 2.23, 95% CI 1.32 to 3.74), nausea (OR 1.66, 95% CI 1.22 to 2.27) and dizziness (OR 3.80, 95% CI 2.52 to 5.73). All comparisons included seven RCTs with 867 participants and were rated as high-certainty evidence.[94]	1++

6.3 Evidence of harms

An increase in adverse events from cannabinoids compared with placebo at levels likely to be of clinical significance was consistently reported. Adverse events described were extensive, and included sedation, daytime somnolence, anxiety, mood disorder, suicidal thoughts, and nausea and vomiting.	
One systematic review reported a relative risk (RR) of dizziness ranging from 2.52 (95% CI 1.20 to 4.82; three RCTs, 360 participants: moderate-certainty evidence) to 8.34 (95% CI 4.53 to 15.34; one RCT, 277 participants: low-certainty evidence); and of sedation from 1.60 (95% CI 1.01 to 2.95; four RCTs, 386 participants: low-certainty evidence) to 5.04 (95% CI 2.10 to 11.89; six RCTs, 866 participants: low-certainty evidence), for different cannabinoids compared with placebo.[89]	1++
In a further systematic review, pooled event rates for all-cause adverse	1++

events were 81.2% for cannabinoids compared with 66.2% for placebo, (OR 2.33, 95% CI 1.88 to 2.89) with a number needed to harm (NNTH) of 6 (95% CI 5 to 8; 10 RCTs, 1,959 participants: moderate-certainty evidence).[97] A Cochrane review of neuropathic pain found that nervous system adverse events were higher in people receiving cannabis-based medication compared with placebo (61% vs 29%, Risk Difference 0.38 (95% CI 0.18 to 0.58; nine RCTs, 1,304 participants: low-certainty evidence)).[95]	
One high-quality systematic review of 39 observational studies which included 12,143 participants with median duration of 24 weeks (interquartile range 12 to 33.8 weeks),[100] used long-term and serious harms from cannabinoids as the primary outcome. Prevalence of any adverse events was 26% (95% CI 13.2% to 41.2%) with a prevalence of psychiatric adverse events of 13.5% (95% CI 2.6% to 30.6%). Evidence was of low-certainty, with high risk of bias. Prevalence of serious adverse events was lower at 1.2% (95% CI 0.1 to 3.1) with very low-certainty evidence.	2++
Four systematic reviews specifically considered dependence or psychosis as secondary outcomes.[87,88,95,102] One review identified a single 32-week open-label extension study (n=124) where one participant displayed mild signs of cannabis dependence. There was no other evidence reported in any of the other studies on dependence. Many of the studies in the systematic reviews excluded people with dependence or substance use issues, or psychosis or severe mental health problems.	1++

6.4 Summary of benefits and harms of medicinal cannabis for chronic pain

In conclusion, although there were some statistically significant small reductions in pain severity, there was no strong evidence of clinically relevant pain reduction from cannabinoids. Overall, there was no improvement in QoL, or clinically significant improvement in function. While one review found a small improvement in sleep quality there was also an increase in daytime somnolence and other adverse events.

The evidence for increased adverse events or harms from cannabinoids compared with placebo was consistent (in all the reviews which reported on this, except one[90]), with generally much larger effect sizes than found for any benefits. A wide range of harms were reported, (even in short- to medium-duration studies) including sedation, anxiety, dizziness and nausea. There was insufficient evidence to comment on long-term dependence or mental health issues.

While the systematic reviews were mainly of high quality, the included studies had limitations in quality and risk of bias.

6.5 Other factors

While there are a considerable number of clinical studies on medicinal cannabis, from a broad geographical area (including Scotland/ the UK), and a range of research groups/ institutions, there are a number of major

limitations with these studies, including:

- Duration: The majority of the studies included in the reviews were of short duration, with only six observational studies identified that had follow-up for >6 months and the majority of RCTs having follow-up for <6 months. As chronic pain is a long-term condition, longer-term follow-up is needed to ensure studies reflect the clinical population.
- Comorbidities were not consistently reported, with many of the studies identified in the systematic reviews excluding people with a history of substance use, and major medical diseases, including mental health conditions. Reporting on dependency and substance use was limited, and often not specifically reported. 1++
- Risk of bias, where assessed, was moderate to high, and study quality was very low to low in the majority of studies included in the systematic reviews. All the authors of one systematic review on neuropathic pain declared links with the manufacturers of nabiximols.[90] Of the 16 studies included in the Cochrane review on cannabis in neuropathic pain, 12 declared potential conflicts or funding from the manufacturers of the studied drugs.[95] There was overlap of inclusion of these studies with other systematic reviews. 1+
- Only two of the reviews specifically mentioned input from people with lived experience, who were included on the guideline panels.[98,100]

6.6 Recommendations

R **Medicinal cannabis-based products are not recommended for use in the management of chronic pain outside of the context of a clinical trial.**

7 Antidepressants

7.1 Introduction

Depression and chronic pain are often interconnected, with pain symptoms worsening depression and depression causing pain and many symptoms overlapping within these clinical diagnoses (for example, fatigue and loss of motivation or pleasure in activities).[103]

Antidepressants, including tricyclic antidepressants (TCAs), serotonin-noradrenaline reuptake inhibitors (SNRIs) and selective serotonin reuptake inhibitors (SSRIs) are indicated for the treatment of depression and other mood disorders but some antidepressants also have limited indications for the treatment of neuropathic pain (*see Table 1*).

Table 1: Licensed indications of commonly used antidepressants

Drug (class)	Main indication for mood disorders	Additional indication for pain
amitriptyline (TCA)	major depressive disorder	neuropathic pain
clomipramime (TCA)	depressive illness	none
imipramine (TCA)	depressive illness	none
nortriptyline (TCA)	depressive illness	none*
trimipramime (TCA)	depressive illness	none
duloxetine (SNRI)	major depressive disorder	diabetic neuropathy
venlafaxine (SNRI)	major depression	none
escitalopram (SSRI)	depressive illness	none
fluoxetine (SSRI)	major depression	none
paroxetine (SSRI)	major depression	none
sertraline (SSRI)	depressive illness	none

Source: British National Formulary[104]

* while nortriptyline is listed in the BNF with an indication and dose for use in neuropathic pain, it is not licensed for this indication

NICE has published guidance on the safe prescribing and withdrawal of medicines associated with dependence or withdrawal symptoms.[74]

7.2 Evidence of benefit

A large Cochrane NMA assessed the effectiveness and safety of antidepressants compared with placebo or any active comparator for pain management and included 176 RCTs involving 28,644 adult participants (mean age 50.6 years, 68.3% were female) with fibromyalgia, neuropathic pain, musculoskeletal or other types of chronic pain. Study duration ranged from two weeks to nine months, with an average duration of 10 weeks.

Only six of the 176 trials included long-term follow-up data and the authors were unable to draw any conclusions on the long-term efficacy or safety of antidepressants. The NMA includes some studies of medications which are not available in the UK.[105]

The NMA considered the proportion of participants reporting substantial (at least 50%) reduction in pain, pain intensity, and mood as primary outcomes. Secondary outcomes were the proportion of participants reporting moderate (at least 30%) reduction in pain, physical function, sleep, QoL, Patient Global Impression of Change (PGIC), serious adverse events, and withdrawal.

Sufficient relevance, sufficient credibility

While study populations were similar to the target populations in Scotland, the authors note that most studies did not include people with anxiety or depression. All results and rankings were based on comparison of each antidepressant with placebo.

Duloxetine was consistently the highest-ranked antidepressant for pain relief, pain intensity, physical function and QoL outcomes (although not significantly different from placebo in terms of quality of life). Both standard and high-dose duloxetine were equally effective for most outcomes. Milnacipran was often ranked second among the antidepressants, although the certainty of evidence was lower than for duloxetine. There was insufficient evidence to draw conclusions about the effectiveness or safety of any other antidepressant.

Compared with placebo, standard-dose (60 mg) duloxetine showed a small-to-moderate effect on substantial pain relief (OR 1.91, 95% CI 1.69 to 2.17; 16 RCTs, 4,490 participants, moderate-certainty evidence) and pain intensity (SMD -0.31, 95% CI -0.39 to -0.24; 18 RCTs, 4,959 participants, moderate-certainty evidence). High-dose (>100 mg) milnacipran had a small effect on substantial pain relief (OR 1.72, 95% CI 1.13 to 2.62; one RCT, 384 participants, low-certainty evidence). Standard-dose (100 mg) milnacipran had a small effect on pain intensity (SMD -0.22, 95% CI -0.39 to 0.06; four RCTs, 1,866 participants, moderate-certainty evidence).

Duloxetine (OR 1.79, 95% CI 1.67 to 1.91; 24 RCTs, 7,833 participants, moderate-certainty evidence) and milnacipran (OR 1.70, 95% CI 1.48 to 1.92; seven RCTs, 3,056 participants, moderate-certainty evidence) had a small effect on moderate pain relief. Standard-dose duloxetine (SMD -0.24, 95% CI -0.32 to -0.18; 15 RCTs, 3,887 participants, high-certainty evidence), high-dose (>60 mg) duloxetine (SMD -0.23, 95% CI 0.30 to 0.16; 13 RCTs, 3,503 participants, moderate-certainty evidence) and standard-dose milnacipran (SMD -0.18, 95% CI -0.30 to -0.07; three RCTs, 1,840 participants, moderate-certainty evidence) had small effects on physical function. No antidepressant showed a significant effect on QoL (low- or very low-certainty evidence).

Due to small sample sizes and network sparseness the authors were unable to analyse results across different pain conditions but note that there is no high-quality or high-certainty evidence for the efficacy of amitriptyline, desipramine, desvenlafaxine, imipramine, mirtazapine,

nortriptyline, or venlafaxine for any of the included outcomes. They note that this aligns with previous systematic reviews in participants with neuropathic pain, which showed no high-quality evidence for the efficacy of amitriptyline, desipramine, imipramine, milnacipran, nortriptyline, or venlafaxine[106-111] but moderate-quality evidence that duloxetine is effective for people with diabetic peripheral neuropathy.[112] For people with fibromyalgia, systematic reviews have reported no unbiased evidence that amitriptyline, desvenlafaxine, venlafaxine, or SSRIs were better than placebo,[113,114] and low-certainty evidence that duloxetine, milnacipran, and mirtazapine may yield moderate pain relief.[114] The authors suggest that the previous literature is mixed on the efficacy of antidepressants for musculoskeletal pain.[105]

A further systematic review and meta-analysis examined the efficacy and safety of antidepressants for pain in older (over 65 years) adults. Data from 15 studies were included and all trials reported on chronic pain. Compared with placebo, 12–16 weeks of duloxetine treatment reduced pain (MD -9.07 on a 0 to 100 scale, 95% CI -11.77 to -6.38; three RCTs: 721 participants, high-certainty evidence) for older people with knee osteoarthritis. The authors note that this was considered a very small effect.[115]

Included trials on tricyclic antidepressants were not consistent in the dose, study duration or comparator medications and it was not possible to conduct pooled analyses. The effectiveness of amitriptyline for pain reduction in older people varied across six trials depending on the condition and comparator. In people with diabetic neuropathy, amitriptyline reduced pain from baseline but was less effective than gabapentin. For mixed pain conditions, it did not demonstrate a significant advantage over distigmine. However, in people with postherpetic neuralgia, amitriptyline consistently showed greater pain relief compared with placebo and lorazepam, and was comparable to other antidepressants such as desipramine and fluoxetine.

1++

7.3 Evidence of harms

7.3.1 Adverse events

Adverse events were recorded as a primary outcome of harm, while secondary outcomes included serious adverse events, and withdrawal.

The NMA was unable to draw any conclusions about the safety of antidepressants for treating chronic pain because adverse event data were sparse and studies were underpowered to detect them. All safety evidence had very low certainty. Adverse event rates for the highest-ranked antidepressants (those which had highest probability of being associated with few adverse events) – desvenlafaxine and mirtazapine – were not significantly different from placebo but were based on results from only two studies each. Standard- and high-dose duloxetine and standard-dose milnacipran were equally ranked.[105]

Sufficient relevance, sufficient credibility

Low-dose (<60 mg) duloxetine, high-dose milnacipran, standard-dose (25–75 mg) amitriptyline, and standard-dose (4–8 mg) esreboxetine were the

lowest-ranked antidepressants, and people taking each of these drugs had more than double the odds of reporting an adverse effect compared with people receiving placebo.

No antidepressants showed any significant difference for the outcome of serious adverse events when compared with placebo, and the confidence intervals were very wide.

Nortriptyline, mirtazapine, amitriptyline, desvenlafaxine, and venlafaxine all showed no significant difference compared with placebo for withdrawal. Duloxetine, milnacipran, esreboxetine, desipramine, and paroxetine all showed significant effects, ranging from small to moderate. The authors note that conclusions on the ranking of the individual drugs for this outcome were unreliable due to all antidepressants having wide and overlapping credible intervals.

Physiological or psychological drug dependency were not assessed in the NMA.

7.3.2 Adverse events in older people

In the systematic review of antidepressants for pain in older people, the authors noted that safety data were poorly reported across all antidepressants, but they reported an increased risk of discontinuation of treatment or withdrawal from trials associated with the use of SNRIs or TCAs.[115] The authors also note that previous studies have reported higher rates of harms in older people using antidepressants, including a significantly increased risk of falls. 1++

Further information on benefits and harms of combination pharmacological therapies in people with chronic pain is included in the second part of the draft guideline which will be consulted on at a later date.

7.3.3 Harms from polypharmacy

There is the potential for harm when individuals are prescribed multiple medications with anticholinergic properties. The Polypharmacy Guidance: Appropriate Prescribing - Making medicines safe, effective and sustainable 2025-2028 provides advice on measurement of anticholinergic burden (using the modified Anticholinergic Risk Scale (mARS)) and recommends caution when prescribing medicines with anticholinergic properties, prescribing only the minimum needed, especially for older adults, people with frailty, or people with complex multimorbidities. The guidance notes that TCAs are highly anticholinergic (mARS 2 and 3) while SSRIs have some anticholinergic properties (mARS 1). 4

The Quality Prescribing Guide for Antidepressants (2024–2027) supports healthcare professionals to facilitate the appropriate use of antidepressants and highlights potentially harmful scenarios that could be prevented by proactive medication review. These include: 4

- individuals receiving the same antidepressant continuously, long term (≥2 years)
- older adults (≥65 years) and/or frail adults receiving a SSRI plus

antiplatelet/non-steroidal anti-inflammatory drug/direct oral anticoagulant/warfarin without gastroprotection

- individuals receiving >1 defined daily dose per day of citalopram (>20 mg per day) or escitalopram (>10 mg per day)
- individuals receiving TCAs and other anticholinergics.

The guide also highlights combination pharmacological therapies that may be associated with particular harms, including:

- antidepressants plus long-term benzodiazepines (≥8 weeks) and/or z-drugs
- combination antidepressant treatments
- combinations which may increase risk of QTc prolongation (citalopram or escitalopram or TCAs plus: methadone, antipsychotics, quinine, some antinausea medicines, etc).

7.4 Summary of benefits and harms of antidepressants for chronic pain

The NMA results and rankings are limited to comparisons of each antidepressant with placebo. There are no head-to-head comparisons of antidepressants reported. This is probably because of the size and complexity of the network. In some analyses in the NMA, pharmacological interventions were split into dose categories (low, standard and high) to address between-study heterogeneity.

Duloxetine probably has a moderate effect on reducing pain and improving physical function in the short term, with no evidence of longer-term effects. Higher doses of duloxetine probably provide no more benefits than standard doses. Milnacipran may reduce pain but had a smaller effect and was supported by less evidence. It is not possible to draw conclusions about the effectiveness of any other antidepressant. There was very low-certainty evidence for all safety outcomes for all antidepressants and it is not possible to draw conclusions about the safety of any antidepressant prescribed for the management of chronic pain.

The SmPc notes that duloxetine has been associated with an increase in blood pressure and clinically significant hypertension in some patients. Therefore, in patients with known hypertension and/or other cardiac disease, blood pressure monitoring is recommended, especially during the first month of treatment. Duloxetine should be used with caution in patients whose conditions could be compromised by an increased heart rate or by an increase in blood pressure.

7.5 Other factors

In Scotland, antidepressants, particularly amitriptyline and other TCAs are frequently used in the treatment of chronic pain conditions, particularly neuropathic pain, fibromyalgia-type conditions and general chronic musculoskeletal type conditions. This practice is based on small, underpowered studies.

However, there is also a lack of evidence to suggest that antidepressants have no value as a treatment option for some people who continue to experience chronic pain symptoms and clinicians should consider each person in their individual circumstances and chronic pain experience.

Antidepressant medications may relieve both pain and depression through shared neurotransmitter pathways in the brain, hence there may be individuals with undiagnosed or unrecognised mood disorders where the beneficial effect on pain may be mediated by improvement in mood.

The Scottish Medicines Consortium (SMC) has accepted duloxetine for restricted use for the treatment of diabetic peripheral neuropathic pain in adults as second or third-line therapy (see section 13.4). However, the evidence from the NMA reported in this guideline includes RCTs which recruited people with a wide range of chronic pain types (fibromyalgia, low back pain, hip, knee or hand osteoarthritis, pain associated with Parkinson's disease or neuropathic pain associated with chemotherapy, multiple sclerosis, diabetes, spinal cord injury or stroke)[105] and the GDG took this into account, along with the older SMC advice for duloxetine which restricts use to people with painful diabetic neuropathy as second- or third-line therapy.

The NMA was not able to analyse efficacy of medicines by subtype of chronic pain but reported small-to-moderate effects for duloxetine on pain relief and pain intensity drawn from the pooled data of people with multiple pain types. The GDG considered that this increased the generalisability of the recommendation and concluded that it was appropriate for it to be considered in anyone with chronic pain, based on the evidence of clinical effectiveness and the likelihood of increased cost effectiveness as the medication is currently available as a generic drug. Prescribers should be aware of SMC advice for duloxetine in diabetic neuropathy and that use in people with chronic pain types other than diabetic neuropathy is off label.

Milnacipram is not licensed for use in the UK.

7.6 Recommendations

R **Clinicians should consider a trial of 60 mg duloxetine in people with chronic pain.**

✓ Monitor blood pressure, especially during the first month of treatment, in people with chronic pain who are prescribed duloxetine and who have known hypertension and/or other cardiac disease.

Adopting a person-centred approach is critical. Pain is an individual experience, and certain medications may work for people at an individual level even while the research evidence at the population level is inconclusive or unavailable.

✓ Prescribers should engage in shared decision-making conversations and codevelop a management plan in partnership with the individual.

8 Pain management programmes

8.1 Introduction

Pain management programmes (PMPs) are a fundamental resource provided by secondary care pain services within NHSScotland. For selected people, they are an intervention of choice when there is significant impact on physical, psychological or social function associated with chronic pain.[116]

Pain management programmes involve multidisciplinary working between various professionals including psychologists, physiotherapists, occupational therapists, clinical nurse specialists, pharmacists and specialist doctors. Typically, these exist within secondary care settings and are deemed comprehensive pain management programmes (CPMPs). Integrated pain management programmes (IPMPs) may also exist when the service is provided within primary care.[117] These programmes do not represent a single model of care but provide a range services at different intensities to meet individual needs. This person-centred and graded approach acknowledges psychological and functional impairment alongside medical and pharmacological complexities while taking into account individuals' experience of previous interventions and characteristics of their pain.

There are examples of IPMPs in Scotland, but this is one form of service delivery which offers a qualitatively different (and more restricted) range of interventions compared with those offered in CPMPs. Many IPMPs do not meet the definition of a pain management programme described in section 8.2.

Pain management programmes consist of methods that promote long-term behavioural change, pain education and insight, including methods based on cognitive behavioural therapy (CBT), acceptance-based methods, mindfulness, skills training, physical exercise and education. This is highly person-centred and tailored to each participant's ability and social context and based on behavioural change theories. These skills are then taken home and integrated into individuals' daily routine. Normally, PMPs are provided in a group format.[117]

Training to support people to make changes to their behaviour that can have a positive impact on their physical and mental health and well-being is available to healthcare and third-sector staff from the Health Behaviour Change Learning Programme.

Currently in Scotland, the demand for pain management programmes is high.[118] They require significant resources given the number of healthcare professionals involved, and the time taken per patient.[119] It is therefore important to assess their effectiveness and ensure adequate value for users of services within NHSScotland.

In pain medicine literature, PMPs are often treated as simple, one-off interventions, and the outcome measures used are comparable to those used to evaluate the effect of pharmacological treatments. In practice,

PMPs are designed to improve QoL, understanding and self efficacy in the presence of persistent pain.[117] Benefits that patients report, or alternative outcomes following completion of a PMP, are not always reflected in changes in the outcome measures used in published research.

8.2 Definitions

While there is no universal definition of a pain management programme, for the purposes of a consistency, this guideline aligned with existing definitions developed by other groups. A range of definitions of PMPs have been considered.

The British Pain Society defines the aims, methods and delivery of pain management programmes within the UK. They consider a PMP to be a "group treatment which uses education and practice sessions to help people with chronic pain to manage their pain and everyday activities better… usually will have a psychologist and a physiotherapist providing most of the sessions and other staff such as occupational therapists, nurses and doctors are often involved".[120] They note that PMPs aim to improve the life experience, emotional well-being, activity levels, coping and self efficacy of those living with pain.

The IASP, while not using the term PMP, defines interdisciplinary treatment as "Multimodal treatment provided by a multidisciplinary team collaborating in assessment and treatment using a shared biopsychosocial model and goals. For example: the prescription of an antidepressant by a physician alongside exercise treatment from a physiotherapist, and cognitive behavioural treatment by a psychologist, all working closely together with regular team meetings (face to face or online), agreement on diagnosis, therapeutic aims and plans for treatment and review".[121]

NICE guideline NG193 on chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain defined a PMP as "any intervention that has two or more components including a physical and a psychological component delivered by trained people, with some interaction/co-ordination between the 2".[116]

Published research evidence uses a range of definitions for PMPs, for example a Cochrane systematic review of multidisciplinary biopsychosocial rehabilitation for chronic low back pain included multidisciplinary rehabilitation interventions if they "involved a physical component and one or both of a psychological component or a social/work targeted component. Furthermore, the different components had to be delivered by clinicians with different professional backgrounds, but no specific professional backgrounds were required".[119]

After reviewing the existing definitions and considering the most important requirements for PMPs in the Scottish context, the GDG agreed on the following definition of a PMP.

A pain management programme involves interventions that are:

- psychologically enhanced (eg, has components such as CBT, pain neuroscience education (PNE) and offer the ability for patients to reflect on their experiences, understand their pain better and develop insight into other factors which are involved in the distress and disability caused by pain. See sections 9.1 and 9.6 for further discussion on specialisation of psychological interventions).
- comprised of multiple interventions delivered concurrently (eg exercise or physical activity, CBT, PNE, medication review).
- delivered in a group setting, either face to face or remotely (eg online).
- typically run over several sessions or weeks.
- led by healthcare professionals from more than one professional group (eg psychologist, allied health professional, doctor).

8.3 Evidence of benefit

One high-quality systematic review with meta-analysis was selected to provide evidence on the effectiveness of PMPs.[122] This review included 57 RCTs (of low to moderate quality) that compared PMPs with a variety of alternatives (usual care, waiting list or attention control, physical therapy, psychological therapy and combinations of these). Eight studies examined IPMPs (based in primary care) and 49 studies examined CPMPs (not based in primary care). Concerns about bias were low. 1++

Some of the included RCTs investigated IPMPs delivered both in group and individual settings. There was limited evidence on different programme factors and their impact on outcomes. Many IPMPs do not meet the definition of a PMP (see section 8.2) and since services providing IPMPs do not exist widely in Scotland at this time, it was decided to limit the analysis to CPMPs (delivered in secondary care) only.

While evidence for a wide variety of musculoskeletal pain conditions was available (chronic low back pain, chronic neck pain, osteoarthritis of the knee, hip, or hand and fibromyalgia), and musculoskeletal pain is one of the most common pain symptoms, other pain conditions are not represented within this evidence base.

8.3.1 Comprehensive pain management programmes compared with usual care

Overall, taking part in CPMPs resulted in a small improvement in pain after the intervention (MD -0.53 on a 0 to 10 scale, 95% CI -0.80 to -0.25; 11 RCTs, 764 participants; moderate-certainty evidence). At short- (1 to <6 months), intermediate- (≥6 to <12 months) and long-term (≥12 months) follow-up, the difference was below the threshold for small effects (see section 1.4.2), was not statistically significant, or both.[122]

CPMPs resulted in moderate improvements in function compared with 1++

	usual care or waiting list at follow-up after the intervention (SMD -0.52, 95% CI -0.88 to -0.16; 13 RCTs, 981 participants: low-certainty evidence) and short-term follow-up (SMD -0.62, 95% CI -1.02 to -0.24; seven RCTs, 1,097 participants: low-certainty evidence). Heterogeneity was high with I^2 values over 80%. There was no evidence of a difference at intermediate and long-term follow-up timepoints. CPMPs had a small effect on depression compared with usual care at short-term follow-up (SMD -0.48, 95% CI -0.89 to -0.08; five RCTs, 543 participants: no evidence certainty rating). A statistically significant effect was not reported after the intervention, nor sustained at intermediate- or long-term follow-up. Based on two trials, there was no evidence that CPMPs affected health-related QoL as assessed by SF-36 physical component summary (PCS) or mental component summary (MCS) scores.	
8.3.2	Comprehensive pain management programmes compared with physical activity	
	There was no significant difference in reported pain intensity at any time point between participants undertaking CPMPs and those undertaking physical activity.[122] A small improvement in short-term function was identified in those participants taking part in a CPMP (SMD -0.37 95% CI -0.61 to -0.16; three RCTs, 459 participants: moderate-certainty evidence). There was no evidence of benefit after the intervention or at intermediate- or long-term follow-up. There were no statistically significant differences in the severity of depression between participants undertaking CPMPs and those undertaking physical activity after the intervention, at intermediate- or long-term follow-up timepoints. There were no statistically significant differences in health status between participants undertaking CPMPs and those undertaking physical activity measured by the SF-12 or SF-36 PCS and MCS after the intervention and at long-term follow-up timepoints.	1++
8.3.3	Comprehensive pain management programmes compared with pharmacological therapies	
	There was moderate improvement in pain scores in participants undertaking CPMPs compared with those on pharmacological therapy after the intervention (pooled MD -1.28, 95% CI -2.14 to -0.63; two RCTs, 204 participants: low-certainty evidence), and a small improvement at intermediate-term follow-up (pooled MD -0.84, 95% CI -1.64 to -0.15; two RCTs, 265 participants: low-certainty evidence). There was no difference seen at short- and long-term follow-up.[122] While there was no effect from CPMPs on function compared with pharmacological therapy after the intervention, small improvements were reported at short- (SMD -0.37, 95% CI -0.67 to -0.08; two RCTs, 342 participants: low-certainty evidence), intermediate- (SMD -0.44, 95%	1++

	CI -0.67 to -0.22; three RCTs, 453 participants: moderate-certainty evidence) and long-term (SMD -0.46, 95% CI -0.76 to -0.16; two RCTs, 301 participants: low-certainty evidence) timepoints. Evidence on the impact of CPMPs on health status and measures of psychological well-being compared with pharmacologic therapy alone are limited. Studies using different assessment measures report conflicting findings.	
8.3.4	Comprehensive pain management programmes compared with psychological therapies	
	There were no statistically significant differences between CPMPs and psychological therapies for the outcomes of pain, function, health-related QoL or depression at any timepoint.[122]	1++
8.3.5	Comprehensive pain management programmes compared with combined pharmacological and physical therapies	
	There was conflicting evidence from two RCTs about the effect of CPMPs on pain compared with combined pharmacological and physical therapies. In one fair-quality RCT involving 63 people with fibromyalgia, participating in a CPMP was associated with moderate improvements in Multidimensional Pain Inventory (MPI) pain intensity (differences -1.2 to -2.1 on a 0 to 6 scale) and MPI pain interference (differences -1.9 to -2.5 on 0 to 6 scale) at postintervention, intermediate-, and long-term timepoints. Only antidepressants were prescribed in this trial. In contrast, a poor-quality trial in 55 people with low back pain reported no difference in pain between groups after the intervention (difference 0.93 on a 0 to 10 scale, 95% CI -0.19 to 2.1). Medications in this trial included diclofenac, paracetamol, and omeprazole.[122]	
	There were no statistically significant differences in function between CPMPs and combined pharmacological and physical therapies reported in either of two RCTs.[122]	1++
	There was conflicting evidence about the effect on depression from the same two RCTs on CPMPs compared with combined pharmacological and physical therapies. Small improvements in MPI affective distress (0 to 6 scale) were seen in those undertaking CPMP after the intervention, and in the intermediate and long term (differences -1.9 to -2.3) in one trial. In contrast, no difference in emotional distress based on the Profile of Mood States Short Version (POMS-SV) was seen in the other trial after the intervention.[122]	
8.4	**Evidence of harms**	
	There were limited reports of adverse events from CPMPs (three RCTs reported increased pain due to the intervention, and one RCT reported an adverse event due to the intervention without further details). Reporting adverse events is inconsistent and lacks detail across the evidence.[122]	1++
	Since CPMPs encourage participants to carry out any movements or activities within a range that is safe and sustainable for them, harms	

directly related to participation would not be anticipated.

8.5 Summary of benefits and harms of pain management programmes

While the clinical significance in many of the reported outcomes is uncertain, the results demonstrated that CPMPs were either more effective or as effective as individual comparators and low levels of harms were reported. The reported benefits were small and mostly limited to people with musculoskeletal pain conditions which limits generalisability and lowers confidence in the strength of recommendation. Published evidence from the systematic review may not capture all key benefits of PMPs because of the emphasis on measures of pain and function, rather than self efficacy and agency.

Outcomes concerning acceptability or how suitable CPMPs are for most people with chronic pain in Scotland were not covered in this guideline and evidence of cost effectiveness was not reviewed.

8.6 Other factors

Scotland's population is geographically dispersed, with 17% living in rural areas, which makes providing PMPs challenging.[123]

Evidence on qualitative outcomes was not sought and there was limited perspective from people with lived experience available.

The guideline development group noted evidence of benefit for CPMPs, despite the limitations of the outcome measures for chronic pain interventions (such as pain scores), and the lack of evidence of harms and acknowledged the wider benefits of CPMPs to secondary care pain services, such as learning as part of the multidisciplinary team and innovation and research through interdisciplinary relationships. On this basis the GDG concluded that a conditional recommendation was justified.

8.7 Recommendations

R **Following appropriate assessment, consider comprehensive pain management programmes for people with chronic pain.**

9 Psychological interventions

9.1 Introduction

Psychological factors, alongside biological and social factors, are known to affect the experience of pain. People's beliefs, understanding and responses to living with pain may contribute to their experiences of distress and disability.[124,125] Hence, psychological treatment should always be considered as part of a holistic approach to pain management.

Psychological therapies or interventions may be useful in addressing the complexity of the pain experience. The Psychological Therapies standards published by Public Health Scotland defines psychological interventions as "a range of evidence-based therapies and interventions, based on psychological concepts and theory, which are designed to help people understand and make changes to their thinking, behaviour, and relationships in order to relieve distress and to improve functioning".[126]

Following this definition, this section focuses on psychological interventions categorised by the NHS Education for Scotland Matrix - a guide to delivering evidence based psychological therapies and interventions in Scotland as enhanced or specialist psychological practice. The benefits of psychological therapies are described in language and concepts that are considered active in terms of response and control, in contrast to passive and catastrophising behaviours and responses. Psychological therapies reflect Engel's biopsychosocial model, which is the gold standard model to understand chronic pain and which challenges the concept of mind-body dualism (which has the potential for stigmatisation of secondary pain experiences).[127,128]

However, mind-body dualistic thinking remains prevalent and people who live with pain may have to wait a long time to access pain services, which may lead to poor confidence in or mistrust of healthcare provision.[129] It is important that the benefits of psychological therapies are presented clearly with a strong person-centred focus.

Evidence-based national guidelines on management of chronic pain have recommended acceptance and commitment therapy (ACT) and/or CBT alongside pain management programmes, self-management programmes and mindfulness-based interventions.[116,130] While there is a large variety of psychological therapies available to manage chronic pain (including music therapy, pain reprocessing therapy, and emotional awareness and expression therapy), the inclusion of therapies is guided by, and overlaps greatly with, the psychological treatments covered by the Matrix. Further information is available in the Matrix - a guide to delivering evidence based psychological therapies and interventions in Scotland.

4

9.2 Definitions

Cognitive behavioural therapy is an approach to engaging with how people think and behave in response to pain. CBT is founded on core principles related to addressing unhelpful thoughts and behaviours that result from

living with pain.

Acceptance and commitment therapy, a third-wave cognitive therapy, is a form of psychotherapy that encourages people to accept their thoughts and feelings related living with pain, to identify what they cannot control and put their energy into positive actions that enrich their lives. The focus is on an increase in acceptance and in engagement with valued activities, rather than disability or distress.

Mindfulness-based stress reduction (MBSR) is a group intervention that seeks to reframe a person's relationship to pain through detached self-observation. It relies on training in mindfulness meditation to cope with stress, illness and pain.[131]

Biofeedback is a form of operant conditioning where people learn how to modify some of their behavioural responses to improve their health.

Relaxation therapy is a treatment that uses relaxation techniques to promote feelings of well-being and calmness.

9.3 Evidence of benefit

9.3.1 Cognitive behavioural therapy

A Cochrane systematic review with meta-analysis investigated the effectiveness of CBT and ACT delivered face to face for people with chronic pain.[132] The most frequently included pain conditions were fibromyalgia (19 studies), chronic lower back pain (16 studies), mixed chronic pain conditions (15 studies), rheumatoid arthritis (nine studies), osteoarthritis (five studies) and temporomandibular disorder (four studies). CBT was compared with either treatment as usual (TAU) which included participants being placed on a waiting list or an active control. Active comparators included exercise programmes, medical procedures, education or support group.

When compared with treatment as usual, CBT resulted in a small reduction in pain intensity (SMD -0.22, 95% CI -0.33 to -0.10; 29 RCTs, 2,572 participants: moderate-certainty evidence), disability (SMD -0.32, 95% CI -0.45 to -0.19; 28 RCTs, 2,524 participants: low-certainty evidence) and distress (SMD -0.34, 95% CI -0.44 to -0.24; 27 RCTs, 2,559 participants: moderate-certainty evidence) at the end of treatment.[132] 1++

When compared with an active comparator, CBT resulted in a very small reduction in pain (SMD -0.09, 95% CI -0.17 to -0.01; 23 RCTs, 3,235 participants: moderate-certainty evidence), disability (SMD -0.12, 95% CI -0.20 to -0.04; 19 RCTs, 2,543 participants: moderate-certainty evidence) and distress (SMD -0.09, 95% CI -0.18 to -0.00; 24 RCTs, 3,297 participants: moderate-certainty evidence) at the end of treatment for people with chronic pain. Benefits were statistically significant but owing to the range of measurement scales used it was not possible to assess clinical significance. Reductions in pain and disability at the end of treatment did not persist when outcomes were considered at follow-up of six months or more. There was evidence of a small reduction in distress at follow-up (SMD -0.13, 95% CI -0.25 to -0.01; 16 RCTs, 1,757 participants:

	moderate-certainty evidence).[132]	
	A further Cochrane systematic review with meta-analysis examined the effectiveness of remote psychological therapies for people with chronic pain.[133] The majority of studies were in people with chronic back pain, fibromyalgia or mixed chronic pain populations. Interventions were scalable to a large group of people with chronic pain, delivered primarily through technology (such as web-based and smartphone apps and virtual reality) and involved less than 30% contact time with a clinician.	
	Remote CBT resulted in small reductions in pain intensity (SMD -0.28, 95% CI -0.39 to -0.16; 20 RCTs, 3,206 participants, moderate-certainty evidence) and functional disability (SMD -0.38, 95% CI -0.53 to -0.22; 14 RCTs, 2,672 participants, low-certainty evidence) compared with TAU at the end of treatment. There was very low-certainty evidence of no benefit on QoL. The reduction in pain intensity did not persist at follow-up of three to 12 months. There were no statistically significant benefits to functional disability or QoL at follow-up.[133]	1++
	Remote CBT resulted in a small reduction in pain intensity (SMD -0.28, 95% CI -0.52 to -0.04; three RCTs, 261 participants, moderate-certainty evidence) compared with active control. There was no evidence of benefit to functional disability or QoL. Based on very low-certainty evidence there was no difference between interventions at follow-up.[133]	
9.3.2	Acceptance and commitment therapy	
	When compared with treatment as usual, ACT resulted in a large reduction in pain intensity at the end of treatment (SMD -0.83, 95% CI -1.57 to -0.09; two RCTs, 162 participants: very low-certainty evidence). No evidence was reported regarding the outcome of disability or distress. One small study (104 participants) assessed as being very low-certainty reported that ACT produced a large benefit in reducing pain intensity at six months follow-up, (MD -1.10, 95% CI -1.51 to -0.69).[132]	1++
	When compared with active comparators at the end of treatment there was no evidence of benefit to pain intensity (SMD -0.25, 95% CI -0.63 to 0.12; five RCTs, 385 participants: very low-certainty evidence) or distress (SMD -0.30, 95% CI -0.70 to 0.10; five RCTs, 385 participants: very low-certainty evidence). At follow-up, the finding was similar for pain intensity and for distress but for disability there was very low-certainty evidence of a large benefit from ACT (SMD -1.22, 95% CI -2.28 to -0.17; two RCTs, 156 participants).[132]	
	For remote ACT (remote delivery with no more than 30% contact time with a clinician) compared with TAU there was no evidence of benefit to outcomes of pain intensity (four RCTs) or functional disability (two RCTs). In both cases evidence was assessed as very low certainty. Findings were similar for follow-up at three to 12 months.[133]	
	For remote ACT compared with active comparator therapies only one study was identified providing very low-certainty evidence of likely no benefit to pain intensity at the end of treatment. Based on two RCTs there was very low-certainty evidence of likely no benefit to QoL at end of	1++

treatment. At follow-up only one small trial (50 participants) was identified which provided low-certainty evidence of no benefit to QoL.[133]

9.3.3 Mindfulness-based stress reduction

A network meta-analysis compared CBT with MBSR for the outcomes of pain intensity, physical functioning and depression in adults with chronic pain. The review identified 21 studies, which mostly involved participants with fibromyalgia and chronic low back pain.[134] Nine RCTs were rated as poor quality. The certainty of the evidence was not reported.

Only one study in the network directly compared CBT with MBSR for pain intensity. Thirteen studies compared CBT with control and five studies compared MBSR with control. When the direct and indirect evidence (1,364 participants) was combined there was no evidence of a difference between the therapies (SMD 0.02, 95% Credible Interval (CrI) -0.43 to 0.48).

Sufficient relevance, sufficient credibility

Only one study in the network directly compared CBT with MBSR for function. Eleven studies compared CBT with control and five studies compared MBSR with control. When the direct and indirect evidence (1,320 participants) was combined there was no evidence of a difference between the therapies (SMD -0.02, 95% CrI -0.49 to 0.42).

Only one study in the network directly compared CBT with MBSR for depressive symptoms. Nine studies compared CBT with control and six studies compared MBSR with control. When the direct and indirect evidence (1,306 participants) was combined there was no evidence of a difference between the therapies (SMD -0.06, 95% CrI -1.08 to 0.47).

In one large systematic review and meta-analysis of non-pharmacological treatments for chronic pain, there was no evidence of benefit to pain from MBSR in the short term compared with usual care or attention control (where the control group completes some activities but they are not the same in intensity, time and/or contacts as the intervention activities; activities may or may not be similar to usual care) (MD -0.88 on a 0 to 10-point scale, 95% CI -1.82 to 0.08; five studies, 630 participants: moderate-certainty evidence).[135] When two poor-quality trials were excluded from the analysis there was a small statistically significant improvement in short-term pain (MD -0.68, 95% CI -1.29 to -0.28; three studies, 546 participants: moderate-certainty evidence). One study provided evidence of improved pain in the intermediate term (MD -0.75, 95% CI -1.16 to -0.34; 229 participants: low-certainty evidence).

1++

For short-term function there was low-certainty evidence that MBSR had no clear effect (SMD -0.14, 95% CI -0.51 to 0.02; four RCTs, 581 participants) when compared with usual care or attention control. Individual trials found no evidence of benefit from MBSR to intermediate or long-term function.

9.3.4 Biofeedback

The systematic review of non-pharmacological treatments for chronic pain identified insufficient and inconsistent evidence for biofeedback in people

1++

with fibromyalgia. Four small, poor-quality trials were identified.[135] Because of the wide range of function scales used, no meta-analysis could be conducted. Three of these studies reported no difference in function between people receiving biofeedback or attention control. The fourth trial (40 participants) compared biofeedback with escitalopram and reported improved mean Fibromyalgia Impact Questionnaire scores at 4–5 months follow-up and a statistically significant improvement in pain score of -2.7 on a VAS.

9.3.5 Relaxation

The systematic review of non-pharmacological treatments for chronic pain identified one poor-quality study on progressive relaxation therapy compared with usual care, which showed no evidence of benefit on pain or function in people with chronic lower back pain. A further fair-quality trial found no difference in pain or function in the short or intermediate term between relaxation training and no intervention or exercise for people with chronic neck pain.[135] 1++

9.4 Evidence of harms

9.4.1 Cognitive behavioural therapy

Cochrane reviews report that adverse event data for psychological therapies in chronic pain were only recorded in a few studies and were not collected in a consistent manner. Minor events such as temporary pain exacerbation were noted. In one study of remote CBT there was an increase in adverse events, including increased pain, in the intervention group (RR 6.00, 95% CI 2.2 to 16.40; 140 participants, very low-certainty evidence).[132,133] 1++

9.4.2 Acceptance and commitment therapy

Two studies reported that there were no adverse effects linked to ACT compared with active controls.[132] 1++

9.4.3 Mindfulness-based stress reduction

In the systematic review comparing MBSR with usual care or attention control one trial reported temporarily increased pain in 29% of people undergoing MBSR, and three trials reported no harms.[135] 1++

9.4.4 Biofeedback

No evidence of harm was reported.

9.4.5 Relaxation

No evidence of harm was reported.

9.5 Summary of benefits and harms of psychological interventions for chronic pain

CBT, delivered either in person or remotely, can yield small improvements in pain intensity in the short term which are not sustained over time. In-person CBT can also improve functional disability in the short term. ACT delivered in person may reduce pain compared with usual care but is no

more effective than active comparators.

MSBR may have similar short-term effects on pain and function to CBT. There is no evidence of benefit of biofeedback or relaxation interventions.

Few harms from psychological therapies were reported, and most interventions appear to be low risk, although there is a lack of clarity on what constitutes an adverse event for psychological therapies, which may persist long term. Many people with chronic pain are affected by mood disorder comorbidities and, although not the target of treatment, psychological interventions may also support individuals' mental health.

9.6 Other factors

Studies included in the systematic reviews used a wide range of controls or TAU conditions, such as waiting lists, standard care, active treatments and attention controls, which makes drawing conclusions difficult. The recommendations are mostly based on evidence for short-term outcomes, that is, effects that are measured immediately after treatment, as the evidence for long-term outcomes is lacking or of low certainty when available. The volume of evidence was limited and evidence for other outcomes, such as acceptance, self efficacy or psychological flexibility was not sought.

Information on the perspectives or preferences of people living with chronic pain was not sought in this guideline.

Management of chronic pain involves multidisciplinary healthcare teams that can include psychology, nursing, physiotherapy, occupational therapy, pharmacy, medical and administrative staff.[47] For the face-to-face interventions, all studies reported delivery of the intervention by a psychologist or trainee psychologist under supervision of a psychologist. Ideally, psychologists who are trained to a doctoral level in behavioural change techniques (for example, health psychologists or clinical psychologists) deliver psychological treatment for chronic pain, however this is often not feasible in practice due to a lack of psychologists in the workforce. In NHSScotland, healthcare professionals from other disciplines may deliver some psychological interventions in line with the competency-based approach described in the Matrix. The workforce competencies and skills framework categorises CBT and ACT within the specialist / enhanced types of psychological practices. Depending on local arrangements, further appropriate training may be required before delivering the interventions under supervision and within the structure of psychology-led local clinical governance.[126]

Given the difficulties accessing face-to-face psychological therapy (for example due to waiting times, rural living circumstances or reliance on patient transport), remote delivery should be considered and might be suitable for some circumstances and patients. The free online CBT platform Silvercloud is designed by clinical experts and supported by NHSScotland and Scottish Government. It provides secure and supportive access to online programmes to help mental well-being and is flexible, allowing users to work at their own pace. Importantly, remote delivery

would still involve contact with a trained health professional (typically around 30% contact time), to ensure person-centred delivered treatments rather than reflecting an online manualised intervention.

9.7 Recommendations

R **Offer CBT** (either face-to-face or remotely) **to adults experiencing chronic pain.**

R **Consider offering face-to-face ACT to manage chronic pain in people where there is a preference for an acceptance approach to pain.**

✓ CBT and ACT should be delivered either by healthcare staff with appropriate training or a trainee under supervision of a trained health professional.

R **Consider offering MBSR** (regardless of delivery mode) **to manage chronic pain in people where there is a preference for mindfulness approaches to pain.**

10 Self-help interventions

10.1 Introduction

Self management is seen as a cornerstone of chronic pain care.[116] Within the NHS, these skills are often imparted by physiotherapists in outpatient settings and by multidisciplinary pain management programs in secondary care. These programs typically involve a multidisciplinary team of pain consultants, specialist nurses, occupational therapists, pharmacists, physiotherapists, and psychologists.

There is no 'gold standard' definition of self management, but it may be broadly interpreted as the day-to-day tasks an individual may undertake to control or reduce the impact of a disease on physical or psychological health status. Self management describes the individual's ability to manage symptoms, treatment, physical and psychological consequences and lifestyle changes associated with a chronic condition.[136]

Barriers exist to people's engagement with secondary care pain management programs.[137] Logistical challenges, including transportation difficulties, reliance on public transport, the costs associated with private vehicle use and parking, the navigation of hospital grounds, poor mental health or dependence on family or friends may pose hurdles.[138]

The resources in specialised pain management healthcare services within the NHS may pose another challenge. Consequently, waiting times for pain management programs are often protracted.[118] These limitations suggest a need for innovative solutions to improve the accessibility and effectiveness of pain management support for individuals living with chronic pain.

Evidence was, therefore, sought on a range of interventions that involve no or minimal ongoing healthcare professional input and which are self led, with or without intermittent supportive contact. Evidence was only identified on peer support and digital self-management interventions.

10.2 Peer support interventions

Peer support has been defined as "the giving of assistance and encouragement by an individual considered 'equal' as part of a created network or intervention by 'peers' who are trained to deliver the intervention".[139]

In the context of chronic pain, the evidence base for peer support is weak, making it challenging to draw definitive conclusions about its benefits and harms. Recommendations are therefore based on the professional and lived experience of the GDG supported by a limited body of effectiveness evidence and considering wider qualitative data.

10.2.1 Evidence of benefit

One systematic review with meta-analysis was identified, which examined the effectiveness of peer support interventions for adults with chronic musculoskeletal pain.[139] Twenty-four RCTs were included, all of which

were rated at high or unclear risk of bias leading to all outcomes having low or very low-certainty of evidence.

When compared with usual care (nine RCTs) there was no evidence of benefit from peer support on pain intensity in the short term (up to three months) but, in the medium (four to nine months) and long term (longer than nine months), peer support resulted in small reductions in pain intensity. In the medium term this reduction was in the range of 0.35 to 6.61 points on a 100-point scale. There was no evidence of effect from peer support on pain intensity compared with waiting list control (eight RCTs) or active control (seven RCTs) at any follow-up timepoint.

When compared with usual care (nine RCTs) there was no evidence of benefit from peer support on function in the short or medium term. In the long term, peer support was superior to usual care; SMD -0.10 (95% CI -0.19 to 0.00; five RCTs, 1,730 participants: very low-certainty evidence). When this measure was converted to the function subscale of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) the degree of benefit (2.06 points) did not reach the minimal clinically important difference of nine points on a 0 to 68 scale. There was no evidence of effect from peer support on function compared with waiting list control (six RCTs) or active control (three to four RCTs) at any follow-up timepoint.

Four studies compared peer support with usual care and found no significant effect on QoL at any time point. Only one study compared peer support with waiting list and, while there were significant improvements in QoL at six weeks, these were not sustained at six months. Two studies compared the effect of peer support on QoL with active control. One reported significant improvement in QoL, while the other found no significant effects.

1++

10.2.2 Evidence of harm

The systematic review did not report outcome data on adverse effects. There is the potential for harm where people who may be managing chronic pain themselves attribute misinformation or provide unhelpful advice. Delivery of peer support interventions may place a burden on individuals, which could represent a harm over time, and there is no standardisation or governance of training for delivery of such interventions. It was suggested that providers should establish support mechanisms to avoid this.

10.2.3 Other factors

Peer support may offer a rewarding experience for both the individuals providing and receiving support, according to qualitative and non-randomised evidence supplied by Pain Concern and Pain Association Scotland and their representatives. Self efficacy (how able you feel you are to manage your condition), depression, anxiety and specific task-related outcomes were felt to be more relevant outcomes to this intervention than pain intensity and function.

Testimony from people with chronic pain on peer support interventions

includes:

- *This pain course has helped and given me such hope in such subtle ways. Amazed, such a big improvement in helping me to manage my pain better on a day-to-day basis.* (Person with lived experience after attending a Pain Association Scotland self-management course)
- *Proof you're not alone* (Feedback following sessions led by Pain Concern).

10.2.4 Summary of benefits and harms of peer support interventions for chronic pain

The evidence showed that peer support interventions for people with chronic musculoskeletal pain may provide a small benefit in reducing pain intensity in the medium and long term and on improving function in the long term compared with usual care. No evidence was identified for people with other pain types, such as neuropathic or visceral pain, which may have distinct underlying mechanisms and treatment responses, limiting the generalisability of these findings. There may be benefits from peer support interventions that have not been reported by using outcome measures such as pain scores. For example, both peer supporters and recipients may experience benefits such as increased self efficacy, a sense of agency, reassurance, access to information, and improved self-management skills.

No evidence was identified on adverse effects of these interventions, however, there is a burden of care on peer supporters. Because of the lack of governance or standardised training for delivery, there is a risk that peer supporters, who may themselves be managing the condition, could inadvertently offer unhelpful advice or misinformation in unsupervised settings while struggling with their own challenges.

10.2.5 Recommendations

R **Consider peer support interventions as part of the holistic and individualised management for people with chronic musculoskeletal pain.**

✓ Services providing peer support pain management interventions should establish mechanisms for monitoring and supporting individuals delivering peer support.

10.3 Digital self-management interventions

While evidence was sought on a wide range of self-management approaches, adequate evidence was only identified on digital self-management tools. These include technologies that support the individual to carry out activities to inform or assist management of their condition, for example smartphone and tablet apps to track symptoms rather than a paper diary, or wearable technology or web-based interventions to monitor activity rather than a written record.

Three systematic reviews were identified.[140-142] Intervention definitions varied across the reviews as did the populations of interest. The three reviews encompassed a total of 48 trials. Two trials were common to all three reviews. There was inconsistency across the reviews in the quality ratings assigned to the trials.

10.3.1 Evidence of benefit

One systematic review examined the effectiveness of a wide range of digital self-care interventions for pain and function in people with spine musculoskeletal disorders (neck pain, back pain or low back pain). Most interventions were smartphone apps or websites, with smaller numbers of email-based tools, virtual reality, telemedicine and video games. In general, the interventions involved physical exercises, education and CBT. The physical exercises were provided in the form of videos, audios or image-based instructions. The certainty of evidence was not reported.[140]

In meta-analysis of ten out of 20 RCTs of people with chronic back pain, there was a small but statistically significant benefit from digital self-care interventions on pain intensity after the treatment; SMD -0.19 (95% CI -0.28 to -0.09; nine RCTs, 1,775 participants) and small-to-moderate benefits on pain intensity in the medium term; SMD -0.21 (95% CI -0.33 to -0.08; five RCTs, 940 participants) and in the long term; SMD -0.24 (95% CI -0.37 to -0.11; four RCTs, 908 participants) compared with usual care. For functional disability there were small benefits from the digital self-care interventions after the treatment SMD -0.18 (95% CI -0.26 to -0.10; nine RCTs, 2,513 participants) and in the medium term; SMD -0.13 (95% CI -0.24 to -0.02; four RCTs, 1,207 participants) and long term SMD -0.14 (95% CI -0.25 to -0.04; four RCTs, 1,452 participants). 1++

Meta-analysis of the three RCTs of neck pain was not undertaken due to high heterogeneity (I^2=89%). Of these, two studies had positive and statistically significant findings for pain and function (clinical significance not stated) and one reported no evidence of benefit to pain.

A second systematic review explored the effectiveness of mobile health (mHealth) interventions for pain, function and QoL in people with a range of chronic pain conditions.[141] mHealth interventions were diverse and apps included combinations of the following components:

- monitoring and tracking of physical activity and healthy lifestyle goals
- symptom monitoring
- treatment delivery (such as physical activity programmes, CBT and pain education). 1+

Meta-analysis was not undertaken because of the heterogeneity across the study interventions and outcome measures. The most frequent pain conditions were osteoarthritis, lower back pain and neck pain. Intervention duration ranged from four to 24 weeks and follow-up from none (measured at end of intervention) to six months.

Ten of the 17 studies assessing pain intensity and functional disability

separately reported statistically significant effects for mHealth interventions compared with controls. Two and one of these studies, respectively, were at high risk of bias. The extent and clinical significance of the benefits was not assessed. Six of 15 studies that assessed QoL found benefits from mHealth interventions. One of these was at high risk of bias.

A third systematic review with meta-analysis examined the effect of digital self-management interventions (either using a digital intervention accessible via smartphone, smartwatch, tablet, computer or internet browser, or using a guided or unguided self-management technique) on various aspects of pain (intensity, catastrophising and interference or disability) for people with chronic low back pain.[142]

In meta-analysis of 12 RCTs there was a small improvement in pain intensity after treatment as a result of the digital self-management intervention (SMD 0.24, 95% CI 0.09 to 0.40; 12 RCTs, 1,545 participants: high-certainty evidence). Pain interference (which encompassed pain disability) showed a small-to-moderate improvement as a result of the intervention (SMD 0.43, 95% CI 0.27 to 0.59; 11 RCTs, 930 participants: moderate-certainty evidence). There was no statistically significant benefit for pain catastrophising. When all three pain concepts were combined into one measure there was a small-to-moderate positive effect from the intervention (SMD 0.33, 95% CI 0.17 to 0.49; 12 RCTs, 1,545 participants: high-certainty evidence). Sensitivity analysis identified that this positive effect was lost when only studies at low risk of bias were included (SMD 0.08, 95% CI -0.18 to 0.34; six RCTs, number of participants not stated). 1++

10.3.2 Evidence of harm

The systematic reviews noted that most included trials did not present adverse event data, and one review did not evaluate harms.[142] Where events were reported, they were mainly related to increase in pain associated with increased physical activity.

10.3.3 Other factors

The widespread adoption of digital interventions may exacerbate existing health inequalities. Individuals with limited digital literacy, access to technology, or reliable internet connectivity may be excluded from these services, potentially widening the gap in healthcare access. This should be balanced with potential benefits in addressing certain aspects of health inequality, such as access in rural areas.

Concern was expressed by the GDG around the diversity of commercial interventions; ethical concerns were raised regarding the prioritisation of financial gain over optimal patient outcomes, complicated by factors including motivation, bias, evidence methodology and heterogeneity. The GDG also noted that it was not always clear how digital tools maintained the security of individual's data.

NHSScotland digital facilitators have an important role in transforming healthcare for those who lack access to technology. Facilitators:

- deliver support to clinical staff and service users to build their

confidence and ability to join virtual programmes and interventions.

- work with library service colleagues to support those without devices or connectivity, eg loan schemes.
- work with organisations who deliver digital interventions to help them reach those who lack access to technology.

While evidence on the optimal timing of communication about self-management options was not reviewed, NICE guideline NG193 recommends healthcare professionals to provide advice and information relevant to the person with chronic primary pain's individual preferences at all stages of care to help them make decisions about managing their condition, including self management.[116] Although this recommendation was based on a single qualitative study which described beliefs gathered in focus groups that discussions about self management often happen late in the care pathway, or not at all, the NICE guideline committee decided that this was particularly important to highlight as initiating this type of discussion early on and at subsequent consultations can make a difference to how people are able to manage their pain. The primary care consultation model in the Scottish Government Quality Prescribing for Chronic Pain Guide (in development) also describes providing introduction to self-management options at the first consultation and reinforcing them in consultation 3.

The feasibility of delivering digital self-management interventions as a prescribed treatment option has not been evaluated. While they may potentially reduce the need for certain healthcare resources, the initial costs of funding access to individuals and supporting their use must be considered.

Given the wide range of digital interventions reviewed, assessing their specific feasibility and economic impact in real-world Scottish settings is complex. Further research is needed to identify practical barriers and facilitators to implementation, as well as to evaluate the cost effectiveness of these interventions.

10.3.4 Summary of benefits and harms of self-management interventions for chronic pain

Digital self-management interventions have a small effect on reducing pain intensity and functional disability with little evidence of harms. As these interventions most commonly involve exercise and physical activity, education and CBT, potential benefits and harms are likely to be associated with the facilitation of these interventions (see section 9).

The effectiveness of digital interventions may vary across different chronic pain conditions and by the specific intervention offered. While promising collective results have been observed in people with musculoskeletal pain, further research is needed to evaluate their efficacy in groups with other chronic pain conditions, such as neuropathic pain or fibromyalgia and to clarify optimal delivery pathways.

10.3.5 Recommendations

✓ Provide advice about self management tools at the earliest opportunity in line with individuals' preferences and circumstances.

R **Consider digital self-management interventions as part of the holistic and individual management for people with chronic musculoskeletal pain.**

✓ As digital self-management tools can, in themselves, be a barrier to practising self care for people who do not have access to, or are not able to use, digital tools, hybrid models of care, whereby they receive support from a digital facilitator or healthcare professional that encourages them to self care, should be available.

Data security measures should be clearly explained to people in an easy-to-understand way, fostering trust and transparency. When recommending digital support interventions for chronic pain management, it is crucial to prioritise safety and trust in people with lived experience.

✓ Robust measures must be in place to ensure the confidentiality and security of all patient data.

11 Occupation-based interventions

11.1 Introduction

What constitutes a meaningful activity will vary from person to person, and might include hobbies, exercise, social activities or employment (paid and voluntary). Chronic pain can hinder people engaging in meaningful activities, affecting their self care, productivity and/or leisure occupations. Occupation-based interventions in the context of chronic pain support individuals to engage in meaningful activities even in the presence of pain. Occupation is defined by the World Federation of Occupational Therapists as 'the everyday activities that people do as individuals, in families and with communities to occupy time and bring meaning and purpose to life', meaning that the term occupation relates to all activities a person participates in and not restricted to only work and employment-based activities.

Reducing pain intensity is not an intended outcome of occupation-based interventions, although some may report changes in their pain experience. These interventions help individuals identify valued activities and align well with the ACT model of psychological flexibility. Engagement in meaningful activities can support improvements in areas such as mood, motivation, independence, routine and sense of purpose. Activity management interventions, informed by pain science, can improve a person's ability to do more over time despite ongoing pain.

Occupational-based interventions are often part of wider programmes of self management (in a secondary care pain service, and/or a tertiary level PMP) and it can be difficult to measure their impact as stand-alone interventions. They tend to be person-centred and vary in delivery, making objective comparison challenging.

11.2 Evidence of benefit

Three systematic reviews on the effectiveness of occupation-based interventions for chronic non-malignant pain were identified. These focused on pacing,[143] return to work (RTW)[144] and sleep hygiene.[145] After review of the evidence on sleep hygiene, the GDG noted that it aligns more closely with non-pharmacological sleep interventions for people with chronic pain which falls outside of the remit of this guideline.

After excluding sleep hygiene, the evidence base consisted of 18 RCTs across two intervention areas (RTW and pacing). The evidence was inconclusive due to variations in study design, RTW and pacing definitions, and intervention delivery formats, making it difficult to support any specific RTW or pacing approach for people with chronic pain. In addition, occupational performance and participation in meaningful activities were not an outcome focus for these trials.

A systematic review of 13 RCTs examined the effectiveness of RTW | 1+

interventions for people with chronic pain on sick leave.[144] The primary outcome was RTW, which was measured in a range of ways including, number of days per month without receipt of sickness benefit, self-reported return to occupation, early retirement rates and cessation of wage loss. Most of the studies involved multiple components and there was a wide range of control conditions. Duration of intervention and follow-up also varied and heterogeneity across the studies meant that meta-analysis was not possible.

Five of the 13 studies showed statistically significant improvements in RTW rates, however, three of these five studies were assessed at being at high risk of bias.

Pacing is a strategy for balancing physical, mental, and emotional activity with rest to avoid exacerbating pain and fatigue and improve function, and can involve activity planning as well as adjustment. A narrative systematic review of five RCTs examined the effectiveness of pacing as a learned strategy for people with chronic pain.[143] Meta-analysis was not possible due to heterogeneity in interventions and outcome measures. Based on three studies that reported pain outcomes, the review concluded that pacing as a learned strategy does not significantly reduce pain in people with chronic pain due to osteoarthritis or fibromyalgia. This finding is in line with expectations, as the aim of this intervention is improved function rather than pain reduction and none of the interventions used an occupation-based approach in which pacing was implemented practically within an occupation under the guidance of a therapist. 1+

Occupational therapists support people with chronic pain to regulate their activity, which aims to improve function by addressing an integrated range of approaches including, but not limited to, pacing alone.

No further RCTs were identified on other occupation-based interventions, including energy conservation strategies, postural and positional strategies, sensory integration strategies, therapeutic education and disease self-management training, advocacy skills development, community reintegration strategies, environmental adaptations/equipment provision, and engagement in meaningful daily activity or meaningful occupation.

11.3 Evidence of harms

There are limited reports of adverse events. One RTW trial focusing on CBT resulted in delayed RTW versus usual care. Findings highlight the need to consider RTW intervention effectiveness and the potential hinderance or delay to RTW.[144] 1+

Since occupation-based interventions encourage people to engage in self-identified movement and activities in a way that is within their capacity, it would not be anticipated for harm to be directly related to these interventions.

11.4 Other factors

The GDG discussed issues relating to the design and implementation of studies on RTW and pacing interventions. Focusing RTW interventions purely on the primary outcome of return to work is reductive and risks excluding other important benefits. They considered that returning to the same work, doing the same hours may not necessarily be a 'good' outcome for an individual, and that acceptance, considering values and QoL or returning to meaningful activities (such as caring for grandchildren or helping at a community club) can lead to people enacting changes in their work and personal lives. Linking people with employability services can aid career changes and training needs. Confidence and satisfaction in work roles can be more accurate indicators of occupational outcomes.

A UK government website acknowledges the link between employment and health and states ‘there is clear evidence that good work improves health and well-being across people’s lives, not only from an economic standpoint but also in terms of quality of life’. It defines good work as ‘having not only a work environment that is safe, but also having a sense of security, autonomy, good line management and communication within an organisation.’ Conversely a difficult work environment and unsupportive management can lead to increased stress and pressure and be unhelpful to an individual's pain management.

Pacing interventions delivered from a symptom reduction compensatory approach can lead to functional decline and increased activity avoidance. When pacing interventions are delivered in such a way, and interpreted as being limited to taking breaks, slowing down activities and spacing out tasks, this alone does not encompass the many facets involved in activity management occupation-based interventions. This may lead to clinicians unintentionally supporting activity restrictions and limitations that may then reduce function rather than improve function. There is value in occupation-based interventions being delivered by clinicians with experience in facilitating conversations around planning, grading, chunking, alternating and monitoring activity underpinned by acceptance, awareness and psychologically-informed methods.

The research reflects the diverse nature of occupation-based interventions, as well as the need for an individualised treatment approach. However, considering the current variability in access to these interventions across Scotland, best practice is informed by availability of resources in the first instance.

11.5 Summary of benefits and harms of occupation-based interventions for chronic pain

The low volume of evidence with inconsistent findings is insufficient to support recommendations. Variations in study designs, heterogeneity across studies, and differences in RTW and pacing definitions impact on generalisation to the wider chronic pain population. Even in the context of low volume evidence, expert clinicians acknowledge that work and activity

dysregulation issues are common amongst the chronic pain population and to not address these issues would mean disregarding needs identified by people with lived experience.[47]

The evidence base shows little to no evidence of harm related to occupation-based interventions. Expert clinicians highlight areas for consideration for measuring RTW interventions and for the delivery of pacing (activity management) interventions.[47]

11.6 Recommendations

✓ Clinicians should be aware that activity management (pacing) interventions focused on symptom reduction may inadvertently lead to greater activity avoidance. However, activity management interventions which are underpinned by a values-based approach, pain science education, and delivered by psychologically-informed clinicians may encourage greater activity engagement, improving both occupational performance and satisfaction.

✓ The term ‘pacing’ is too narrow to fully capture the scope of activity management interventions. Clinicians are encouraged to move away from exclusively using the label ‘pacing’ and instead adopt terms like ‘activity management’ or ‘activity regulation’. These terms better encompass the many facets involved in the intervention.

✓ Clinicians and people living with chronic pain should understand that occupation-based interventions are not intended to reduce pain. Instead, these interventions aim to increase occupational performance and satisfaction, participation in life roles, participation in social functioning, and engagement in personally meaningful occupations within the domains of self care, productivity and leisure.

✓ Clinicians delivering work-related occupational interventions to individuals with chronic pain should adopt a holistic approach, considering both performance and satisfaction in relation to employment and wider life roles. The intervention may include, but not be limited to addressing:

- quality of life
- satisfaction with work-life balance
- confidence and ability to communicate needs in the workplace
- support in negotiating reasonable adjustments
- the ability to regulate during and outside working hours
- confidence to manage flare ups and work absences, and
- balancing life roles alongside work and chronic pain management.

12 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.

12.1 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).

12.2 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.

Naloxone

naloxone.org.uk

This website provides information on access and use of naloxone in the UK. It also contains practical information about how to spot signs of opioid overdose and how to put an individual into the recovery position.

www.sdftraining.org.uk/e-learning

A free e-learning module is available from the Scottish Drugs Forum which includes how to administer naloxone.

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.

#StopTheDeaths

www.stopthedeaths.com

#StopTheDeaths encourages all members of the public, including people who use drugs, their families and communities as well as services, policymakers and wider Scottish society, to act to prevent overdose deaths. In addition to campaign information to raise awareness of drug harms, it includes information and advice on how to access and use naloxone.

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.

13 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.

13.1 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.

Use of naloxone - while anyone can use naloxone legally in an emergency, training is recommended to ensure correct administration. A range of training courses is provided for health and social care professionals in territorial boards, such as NHS Lothian, NHS Greater Glasgow & Clyde and NHS Tayside. The charity, Scottish Drugs Forum, has developed a range of training for people who may respond to opioid overdoses. An e-learning module on opiate overdose prevention, intervention and using naloxone is focused at members of the public seeking overdose response skills or health and social care professionals working in harm reduction services.

13.2 Resource implications of key recommendations

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

13.3 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 adults with chronic pain prescribed opioids who have a documented exploration of other therapeutic approaches for pain management before confirmation of opioid treatment.
- the proportion of adults with chronic pain prescribed opioids who receive an initial review of opioid medication within four weeks of starting treatment (in line with advice in the Scottish Government Quality Prescribing for Chronic Pain Guide (2026–2029)).
- the proportion of adults with chronic pain prescribed >50 mg/day MED who have received a review of opioid medication within the previous 12 months.
- the proportion of adults with chronic pain who are assessed for the risk of an opioid overdose in advance of being prescribed opioid therapy. (This helps to monitor implementation of the recommendation for the consideration of naloxone).
- the proportion of adults with chronic pain prescribed duloxetine who have known hypertension or other cardiac disease and who have blood pressure monitoring at baseline and during treatment with duloxetine.
- the proportion of adults with chronic pain who have been assessed by a multidisciplinary team and who have a documented consideration for a comprehensive pain management programme.
- the proportion of adults with chronic pain that seek psychological support who receive CBT or ACT from a healthcare professional with appropriate training.
- the proportion of adults with chronic pain who have been considered for a peer support intervention and who complete these.
- the proportion of adults with chronic pain who have been considered for digital self-management interventions and who complete these.

13.4 Health technology assessment advice for NHSScotland

In August 2006, the Scottish Medicines Consortium (SMC) advised that duloxetine (Cymbalta®) is accepted for restricted use for the treatment of diabetic peripheral neuropathic pain in adults. It is restricted to initiation by prescribers experienced in the management of diabetic peripheral neuropathic pain as second- or third-line therapy.

scottishmedicines.org.uk/media/1590/duloxetine__cymbalta_285_06.pdf

14 The evidence base

14.1 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.

14.1.1 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

14.2 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),[146] and individual variation in treatment response.[147] 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.[35] Furthermore, ensuring robust involvement of people with chronic pain throughout the research cycle has been recognised as important[148] 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).[149]

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).[35,37,150]

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:

14.2.1 Opioids

- Studies to quantify the risk of adverse events, including overdose and substance use disorder in people being prescribed opioids for pain management, and to develop accurate risk prediction tools. These should include assessment of risks associated with coprescribed medications.
- Studies of comparisons of benefits and harms experienced according to different personal and pain characteristics, and different types of opioids.
- Studies to determine effective risk mitigation strategies in people who are prescribed opioids.
- Studies to identify the efficacy and adverse events of long-term (>12 months) opioid use.
- Studies to identify optimal opioid tapering or deprescribing strategies, and the type of support and services, that also assess the benefits and harms associated with deprescribing.

14.2.2 Naloxone

- Studies to assess the impact of naloxone prescribing on the incidence of fatal and non-fatal overdose events in people prescribed opioids for chronic pain, with a particular focus on other factors that may increase an individual's risk of overdose (eg comorbidity, polypharmacy, demographics).
- Studies to evaluate the acceptability of naloxone use, including the willingness of this population and their families, and how this may change management of their chronic pain and use of opioids.
- Studies to assess the efficacy of naloxone in people using opioids for chronic pain with a range of comorbidities commonly seen in Scotland. A larger observational study could stratify results according to specific combinations of concurrent medications, which would give useful feedback on the relative efficacy of naloxone in the context of commonly used analgesia and medicines prescribed for comorbid conditions.

14.2.3 Antidepressants

- Studies to assess the safety and efficacy of antidepressants used for longer than three months in the treatment of chronic pain.
- Studies to assess the safety and efficacy of antidepressants in

people with chronic pain comparing effects between those with and without a diagnosis of clinical depression.

14.2.4 Medicinal cannabis

- High-quality UK-based RCTs with appropriate duration of follow-up are needed to identify clinically relevant harms and benefits of medicinal cannabis in the treatment of chronic pain, with outcome measures aligned to IMMPACT recommendations. Where standard RCT designs may be inappropriate to adequately address the question(s) other robust trial designs should be considered.
- Studies to assess effects in specific populations, eg those with neuropathic pain; older adults; those with multimorbidity; polypharmacy, recruited from populations that reflect the characteristics of people with chronic pain in Scotland.
- Longer-term studies to identify harms that may take time to develop such as dependence and mental health issues.
- Studies to assess potential interactions between different formulations of medicinal cannabis and medications commonly used by people living with chronic pain.

14.2.5 Pain management programmes

The GDG is aware of individual UK PMPs having presented outcome data at national meetings, but this valuable data is then not submitted or does not reach publication. We propose a collaborative research network of PMP providers within the UK. This pooled, multicentre and international approach may lead to better data for a wider variety of outcomes. A national audit is proposed using the audit points suggested in this guideline (see section 13.3).

- Studies to investigate how best to capture behavioural change following participation on a PMP. (In practice PMPs are designed to promote behavioural change in the service of improving QoL in the presence of persistent pain. Changes that individuals report following completion of a PMP are often not reflected in changes in the outcome measures used to quantify effects in the historical research evidence. Individual items on the outcome measures currently used can mean different things to people living with chronic pain and clinicians. The use of less relevant outcome measures makes it harder to properly evaluate the role of PMPs).
- Studies to assess long-term clinical and cost effectiveness of PMPs measured in terms of effects on mood, anxiety, QoL, medication usage, activity levels, fear of movement, disability, pain intensity, psychological flexibility and measures of primary and secondary healthcare utilisation, in addition to qualitative descriptions of change in activity, well-being and behaviour.
- Further information is required on qualitative outcomes associated with PMPs. Published evidence commonly doesn't reflect lived experience of change and there is a need for greater incorporation of the perspective of people living with chronic pain, including local

viewpoints which take into account cultural and societal differences.

- Further information is required on factors that affect the suitability of people for CPMPs, and how to target a population who are likely to benefit and systematically comparing individual vs group-based PMPs to better understand how different modes of delivery, intervention components and dose characteristics influence outcomes and subjective experiences.

14.2.6 Psychological interventions

In general, studies of psychological interventions should establish greater standardisation of control conditions.

- Any research on the impact of psychological interventions should actively involve people with lived experience of chronic pain.
- To establish the generalisability of interventions, high-quality RCTs which include adults with a wide variety of chronic pain conditions.
- Studies that include long-term follow-up periods of all outcomes (including acceptance, self efficacy, psychological flexibility and cost effectiveness, where appropriate).
- Studies using appropriate outcome measures that match the goals of the intervention (for example, daily functioning). More specifically, studies which assess acceptance and valued activity as outcome measures, as these better align with ACT focus.
- Studies to establish adverse events using clearer, consistent definitions and standardised reporting on adverse events (including long-term adverse events).
- Studies that compare intervention delivery modes directly with each other (ie, face-to-face versus remote delivery, and delivery by psychologists versus non-psychologists).

14.2.7 Self-help interventions

- Studies to quantify the impact of peer support on both peer supporters and recipients, including emotional well-being, social connectedness, and QoL, for both groups.
- Studies examining the qualities and skills that contribute to successful peer support, such as empathy, active listening, and problem-solving abilities.
- Research should focus on designing and implementing effective training programmes to equip peer supporters with the necessary knowledge and skills.
- Long-term follow-up studies to assess the sustainability of the effects of peer support interventions and to measure any potential long-term benefits or harms.
- Studies to evaluate the effectiveness of digital self-help interventions in people experiencing pain conditions other than musculoskeletal

pain.

- Research to improve the understanding of the acceptability, engagement, and adherence in digital support interventions.

14.2.8 Occupation-based interventions

- Studies to establish the effectiveness of the wide range of occupation-based interventions, including and not limited to, energy conservation strategies, postural and positional strategies, sensory integration, advocacy skills, community reintegration strategies, environmental adaptations or equipment provision, meaningful engagement in daily occupations.
- High-quality studies to establish the effectiveness of return-to-work interventions. Researchers should consider defining a core outcome set and/or comparative outcomes to be used in trials to enable comparability across multiple studies.
- Studies in people with chronic pain who are unemployed and want to return to work, and people who are struggling to manage their pain condition while in work.
- Studies to capture the impact of interventions on the person's satisfaction with their work-life balance and confidence to manage their pain condition in the workplace.
- Researchers should consider investigating activity management (activity regulation, activity pacing) beyond osteoarthritis or fibromyalgia, including the diagnosis of chronic pain itself, to improve the generalisability of evidence. Also, to use valid and reliable outcome measures and justification of sample size to improve qualities of studies.
- Studies of activity management interventions for people with chronic pain delivered using a psychologically-informed approach to investigate the effectiveness of this approach and how this intervention might be delivered in a consistent way.
- Additional research is indicated to investigate the effectiveness of activity management as a learned strategy in the activity and participation outcome domains in determining the impact this intervention can have on a person's ability to participate in daily occupational and life roles.

15 Development of the guideline

15.1 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, which was grouped into sets of four to six questions, known as waves. Each wave proceeded with systematic literature searching, screening and selection, critical appraisal and evidence synthesis. The draft recommendations and supporting text were circulated in two public consultations. This document contains waves one and two and is informed by the first consultation. Evidence and recommendations for topics contained in waves three and four will be published separately. The guideline is published online as a toolkit on the Right Decision Service, the 'Once for Scotland' source of digital tools. When combined, the recommendations and supporting text for all four waves will collectively represent the SIGN guideline on chronic pain.

15.2 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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15.2.1 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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15.3 Consultation and peer review

A report of the consultation and peer review comments and responses is available 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.

15.3.1 Specialist review

This guideline was also reviewed in draft form by the following independent expert referees, who were asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline. The guideline group addresses every comment made by an external reviewer, and must justify any disagreement with the reviewers' comments.

SIGN is very grateful to all of these experts for their contribution to the guideline.

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15.3.2 Public consultation

The draft guideline was also available on the SIGN website for a month to allow all interested parties to comment. Responses were received from 18 individuals and nine organisations.

15.3.3 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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Abbreviations

Acas	Advisory, Conciliation and Arbitration Service
ACT	acceptance and commitment therapy
AHRQ	Agency for Healthcare Research and Quality
BNF	British National Formulary
BRAN	benefits, risks, alternatives, and nothing
CBD	cannabidiol
CBT	cognitive behavioural therapy
CI	confidence interval
CNS	central nervous system
COVID-19	coronavirus disease 2019
CPMP	comprehensive pain management programme
CrI	credible interval
D&OUD	dependence and opioid use disorder
ED	emergency department
GDG	guideline development group
GDP	gross domestic product
GMC	General Medical Council
GP	general practitioner
HR	hazard ratio
IASP	International Association for the Study of Pain
ICD	International Classification of Diseases
IMMPACT	Initiative on Methods, Measurement and Pain Assessment in Clinical Trials
IPMP	integrated pain management programme
IQR	interquartile range
IR	immediate-release
IRR	incidence rate ratio
LOCF	last observation carried forward
MA	marketing authorisation
MAP	Motivation, Action and Prompts
mARS	modified Anticholinergic Risk Scale
MBSR	mindfulness-based stress reduction

MCID	minimum clinically important difference
MCS	mental component summary
MD	mean difference
MED	morphine-equivalent dose
mHealth	mobile health
MOR	mu opioid receptor
MPI	Multidimensional Pain Inventory
MR	modified-release
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NMA	network meta-analysis
NNTH	number needed to harm
NSAID	non-steroidal anti-inflammatory drug
ODI	Oswestry Disability Index
OR	odds ratio
OUD	opioid use disorder
PCS	physical component summary
PGIC	Patient Global Impression of Change
PMP	pain management programme
POMS-SV	Profile of Mood States Short Version
PNE	pain neuroscience education
PNS	peripheral nervous system
QoL	quality of life
RCT	randomised controlled trial
RDQ	Roland-Morris Disability Questionnaire
RR	relative risk or risk ratio
RTW	return to work
SF-36	36-item Short Form Health Survey
SIGN	Scottish Intercollegiate Guidelines Network
SMART	specific, measurable, achievable, relevant, and time bound
SMC	Scottish Medicines Consortium
SMD	standardised mean difference
SmPc	Summary of Product Characteristics
SNRI	serotonin-noradrenaline reuptake inhibitor

SPACE	Strategies for Prescribing Analgesics Comparative Effectiveness trial
SSRI	selective serotonin reuptake inhibitor
SUCRA	surface under the cumulative ranking curve
TAU	treatment as usual
TCA	tricyclic antidepressant
THC	tetrahydrocannabinol
USA	United States of America
VAS	visual analogue scale
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
4	In people with chronic non-malignant pain are opioids more likely than placebo or other interventions to improve pain scores (30% reduction and 50% reduction), functional ability, and/or quality of life, and/or to cause adverse events/drug reactions, or dependency (physiological or psychological)?
5	Should naloxone be coprescribed when opioids are used for chronic pain (or when long-term/high-dose opioids are prescribed)?
6	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)?
7	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)?
8	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?
9	In patients with chronic non-malignant pain what is the effectiveness 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?
10	In patients with chronic non-malignant 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.
11	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?

Information relating to the following questions will be made available in future consultations.

Not included in this document	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)?
Not included in this document	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)?
Not included in this document	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)?
Not included in this document	In patients with chronic non-malignant pain what is the effectiveness of anti-epileptic 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)?
Not included in this	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%

document	reduction), functional ability, quality of life, adverse events/drug reactions or dependency (physiological or psychological)?
Not included in this document	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?
Not included in this document	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 on pain scores (30% reduction and 50% reduction), functional ability, quality of life or adverse events?
Not included in this document	In patients with chronic non-malignant pain what is the effectiveness of electrotherapy-based interventions (transcutaneous electrical nerve stimulation, 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?
Not included in this document	In patients with chronic non-malignant pain what is the effectiveness of other or 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?
Not included in this document	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?

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