



The British Pain Society's

Opioids for persistent pain:
Good practice

A consensus statement prepared on behalf of the British Pain Society, the Faculty of Pain Medicine of the Royal College of Anaesthetists, the Royal College of General Practitioners and the Faculty of Addictions of the Royal College of Psychiatrists

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Introduction

This guidance has been written for all healthcare professionals who manage patients with persistent pain, to help their understanding of the role of opioids in pain management. The document outlines good practice regarding decision making in relation to opioid therapy, ongoing monitoring of treatment and identification and management of problems related to opioid use. The document may be used in conjunction with existing local guidance on good practice in opioid prescribing. The recommendations are accompanied by an information leaflet for patients to support them and their carers in making informed choices about management of persistent pain.

Persistent pain is common, affecting around five million people in the UK. For many sufferers, pain can be frustrating and disabling, resulting in functional impairment physically, emotionally and vocationally. Medications and other treatments that aim to reduce pain intensity play a role in the management of symptoms, but should be provided as part of a wider management plan focused on reducing disability and improving overall quality of life.

Opioids are increasingly being used to treat persistent pain. Opioid drugs have a well established role in the management of acute pain following trauma (including surgery) and in the management of pain associated with terminal illness. There is evidence from clinical trials that opioids can be effective, in the short and medium term, in providing symptomatic improvement in a variety of non-cancer pain conditions. However, the safety and efficacy of opioids in the long term is uncertain as is the propensity for these drugs to cause problems of tolerance, dependence and addiction. The benefits of opioid treatment for the patient must be balanced against burdens of long term use as therapy for persistent pain may need to be continued for months or years. The position of opioid treatment must also be considered within a wider social context and issues such as diversion must be addressed.

Process of preparation

Guidance on appropriate opioid prescribing for pain was produced by the Pain Society, The Royal College of Anaesthetists, The Royal College of General Practitioners and The Faculty of Addictions of the Royal College of Psychiatrists in 2004. The current document updates the existing guidance and represents a reappraisal of the role of opioids in long term pain management based on contemporary evidence. Recommendations in this document have been supported by published clinical evidence (particularly in relation to opioid efficacy and adverse events) where this is available and reflect a consensus of expert international opinion where evidence is lacking. Key information resources are listed at the end of the document.

The guidance was produced by a core group of representatives from stakeholder professional organisations. The development of the document included a period of public consultation with relevant organizations and professional and service-user groups.

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Competing Interests

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Douglas Justins, Amanda Williams and Judy Myles have no competing interests.

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1 Executive summary

- This document provides guidance on the prescription of opioids for persistent pain.
- The guidance applies to all opioids available in the UK.
- The guidance does not include recommendations on the use of spinally delivered opioids.
- Opioids are traditionally classified as strong or weak. This guidance does not apply to patients who use weak opioids within the BNF dose range, but supports prescribing for patients who use weak opioids outside the BNF range and for patients who might benefit from using strong opioids.
- Opioids are prescribed to reduce pain intensity. Data demonstrating sustained analgesic efficacy in the long term are lacking.
- Complete relief of pain is rarely achieved with opioids. The goal of therapy should be to reduce symptoms sufficiently to support improvement in physical, social and emotional functioning.
- 80% of patients taking opioids will experience at least one adverse effect. These should be discussed with the patient before treatment begins.
- Patients taking appropriate doses of prescribed opioids are permitted by law to drive in the UK if they are using no more than the prescribed dose and feel fit to drive. Patients should be advised to avoid driving at the start of opioid therapy and following dose changes. Patients should be informed that it is their responsibility to advise the DVLA that they are taking opioid medication.
- Patients must be aware of uncertainty regarding the long term effects of opioids, particularly in relation to endocrine and immune function.
- Opioids should not be used as first line pain therapy if other evidence-based interventions are available for the condition being treated.
- The decision to start long term opioid therapy should be considered carefully by the prescriber, the patient and his/her carers and other members of the healthcare team. Arrangements for long-term monitoring and follow-up must be in place.

- There is no right or wrong sort of patient for opioid therapy. Assessment of the patient in pain should include a history of the patient's mental health, in particular screening questions for depression and substance misuse disorders. This is especially important when prescribing opioids for persistent pain.
- Where possible, modified release opioids administered at regular intervals should be used in the management of patients with persistent pain. Use of more flexible dosing regimens using immediate release preparations (alone or in combination with modified release preparations) may be justified in some circumstances.
- Injectable opioids should not be used for the management of persistent pain.
- Patients being considered for long term treatment with opioids should have a carefully supervised trial of opioid therapy with evaluation of analgesic efficacy and adverse effects.
- If patients do not achieve useful relief of pain when titrated to doses between 120-180 mg morphine equivalent per 24 hours, referral to a specialist in pain medicine is strongly recommended.
- The prescription of opioids can result in problem drug use. The likelihood of this occurring might be influenced by a number of social, psychological and health related factors.
- Concerns about problem drug use should prompt referral to specialised pain and addiction services.
- Patients with a current or past history of substance misuse or with a comorbid non-substance misuse psychiatric diagnosis may be more likely to develop problems with opioid use. Opioid treatment for these patients should be closely and collaboratively monitored by specialists in pain management and/or addiction medicine.

2 Opioid pharmacology

Opioids are drugs that exert their activity by acting as agonists at endogenous receptors (opioid receptors), and that elicit the characteristic stereospecific actions of natural morphine-like ligands. These receptors are widespread throughout the central and peripheral nervous systems. A number of opioid receptors have been described. Some opioids display differential receptor activity; the clinical relevance of this is not clear.

For prescribing information and approximate potency ratios in adults, refer to the BNF sections on "Opioid analgesics" and "Prescribing in palliative care". For information about prescribing for children, refer to the Children's BNF.

The clinical response to opioids is variable. Switching patients to different opioids may be worthwhile. Dose ratios vary, and therapy should always be individualised after specialist advice (e.g. specialist pain management or drug information services).

Opioids are classified as either strong or weak (see table 1). The distinction between these groups is not always clear and might depend on the dose. The term "weak opioid" should not encourage lack of caution in prescribing.

Low dose strong opioid preparations are available that represent a similar opioid load to maximum dose weak opioids. It is important when using transdermal opioid preparations to be aware of opioid load in terms of equivalent daily morphine dose. Table 2 shows approximate equivalent potencies of commonly used transdermal opioids. Conversion ratios are a guide only and depend on the dose of opioid to be converted.

NB This guidance does not apply to patients who use weak opioids within the BNF dose range, but supports prescribing for patients who use weak opioids outside the BNF range and for patients who might benefit from using strong opioids.

The guidance does not include recommendations on the use of spinally delivered opioids.

Drugs that are considered dangerous to individuals or society are controlled and regulated by law. Many opioids used for pain relief are classified as controlled drugs. This classification mandates specific requirements in relation to prescription writing and safe custody arrangements. Prescription writing guidance can be found in: *British National Formulary 2007 Guidance on prescribing: Controlled drugs prescribing* BMJ Publishing Group and RPS Publishing.

Table 1 Examples of non-injectable opioids currently available on prescription in the UK. - Strong and weak opioids		
	Approved name (some proprietary names)	Formulations available
Strong Opioid	Buprenorphine (Temgesic, Transtec, BuTrans, Subutex)	Sublingual, Transdermal
	Diamorphine	Parenteral
	Dipipanone (Diconal)	Oral
	Fentanyl (Durogesic, Matrifen, Effentora, Abstral)	Transdermal, oral transmucosal, sublingual
	Hydromorphone (Palladone, Palladone SR)	Oral
	Methadone	Oral
	Morphine (Oramorph, Sevredol, MST Continus, MXL, Zomorph)	Oral
	Oxycodone (OxyNorm, OxyContin)	Oral
	Pentazocine	Oral
	Pethidine	Oral
	Tramadol (Zydol, Zamadol)	Oral
Weak Opioid	Codeine	Oral
	Dextropropoxyphene	Oral
	Dihydrocodeine (DF118 Forte, DHC Continus)	Oral
	Meptazinol (Meptid)	Oral

Oral formulations can be immediate or modified release.

Table 2 Transdermal opioids: Approximate equivalence with oral morphine

Oral morphine equivalent (mg/24 hours)	10	15	30	45	60	90	120	180	270	360
Transdermal Buprenorphine (µg/hr)	5	10	20		35	52.5	70			
Transdermal Fentanyl (µg/hr)				12		25		50	75	100

NB Published conversion ratios vary and these figures are a guide only. Morphine equivalences for transdermal opioid preparations have been approximated to allow comparison with available preparations of oral morphine.

3 Why prescribe opioids?

Opioids are prescribed to reduce the aversiveness of the experience of pain. Clinical trials of opioid efficacy suggest that the drugs can provide useful analgesia in the short and medium term. Data demonstrating sustained analgesic effectiveness in the longer term are lacking.

Opioids can be effective in the management of somatic, visceral and neuropathic pain.

Complete relief of pain is rarely achieved. The goal should be to reduce pain sufficiently to facilitate engagement with rehabilitation and the restoration of useful function.

The management of persistent pain focuses not only on reduction in pain intensity but also on improvement in sleep, mood, and physical, vocational, social and emotional wellbeing. Data demonstrating improvement in these domains with opioid therapy are lacking, although improvement in sleep has been demonstrated in those for whom opioids provide useful pain relief.

Opioids should not be used as primary hypnotics, anxiolytics, sedatives or antidepressants. In monitoring the effect of any opioid, clear identification of an analgesic effect is essential.

Improvements in quality of life are unlikely to be achieved unless opioids are prescribed as part of a broader approach to improve patient function.

4 Adverse effects of opioid therapy

General considerations

80% of patients taking opioids will experience at least one adverse effect.

Patients should be advised about side effects and the likelihood of their occurrence before starting opioid therapy. The commonest adverse effects are :

- constipation
- nausea
- somnolence
- itching
- dizziness
- vomiting

Tolerance to some side effects usually occurs within the first few days of initiating treatment; pruritis and constipation tend to persist. Patients using intermittent dosing schedules might not become tolerant to side effects.

Adverse effects should be managed actively with antiemetics, aperients and antihistamines as appropriate.

Respiratory depression is a much feared complication of the use of opioids for acute pain, but it is only likely to be a potential problem in persistent pain if there have been major changes in dose, formulation or route of administration. Accidental overdose is likely to be the commonest cause of respiratory depression. Particular caution is necessary for patients taking more than one class of sedative medication and in those with pre-existing disorders of respiratory control, such as obstructive sleep apnoea.

There is little evidence that, in equi-analgesic doses, commonly used opioids differ markedly in their side effects. However, because of genetically influenced inter-individual variability in pharmacodynamics and pharmacokinetics, a patient might respond more favourably to one opioid than to another. If a patient fails to achieve useful analgesia or develops intolerable side effects with their initial opioid regimen, it may be worth trying an alternative drug.

Clinical features of opioid toxicity are described in Figure 1. It is helpful to discuss these features with the patient's carer, particularly if there is concern regarding concordance with the prescribed regimen.

Figure 1 Clinical features of opioid toxicity

Pinpoint pupils
Sedation
Slow respiration
Visible cyanosis e.g. lips, ears, nose (in severe cases)
Myoclonic jerks
Snoring when asleep
Agitation
Confusion
Vivid dreams, nightmares or hallucinations
In more severe cases:
 Hypotension
 Coma
 Convulsions

NB The dose of opioids causing toxicity varies between individuals and depends on medical comorbidity (particularly renal or hepatic impairment) and concomitant medication therapy, including over the counter medications and illicit drug use.

Opioid withdrawal occurs when the drug is stopped suddenly, the dose tapered too rapidly or when an opioid antagonist is given. Signs of opioid withdrawal are described in Figure 2. Treatment of acute withdrawal includes administration of: intravenous fluids, glucose, alpha2-adrenoceptor agonist drugs (e.g. clonidine, lofexidine) and antispasmodic medicines for abdominal cramps. Small doses of opioids may also be given to improve symptoms.

Tramadol has effects within noradrenergic and serotonergic systems in addition to its μ -opioid receptor actions and can lead to significant withdrawal symptoms even after short periods of dosing. In many cases, Tramadol withdrawal occurs within 12-24 hours after the last dose; it can occur with modified release formulations.

Figure 2 Signs of opioid withdrawal

Sweating
Mydriasis
Piloerection
Yawning
Abdominal cramps/vomiting/diarrhoea
Bone and muscle pain
Increase in usual pain
Restlessness
Anxiety
Rhinorrhoea
Lacrimation
Tremor

Driving and working while on opioid therapy

UK laws allow patients who are taking prescribed opioids for pain relief to drive.

Patients taking opioids are banned from driving if their use constitutes drug misuse or dependency.

Use of drugs in greater than therapeutic doses constitutes misuse/dependency for licensing purposes. Dependency in this context does not include patients taking stable doses of prescribed opioids who would be expected to experience withdrawal symptoms on cessation of opioid therapy (see Section 7 for definitions).

Patients being treated with opioids should be advised to avoid driving when:

- the condition for which they are being treated has physical consequences that might impair their driving ability;
- they feel unfit to drive;
- they have just started opioid treatment;
- their dose of opioids has been recently adjusted upwards or downwards (as withdrawal may have an impact on capability); and
- they have consumed alcohol or other drugs that can produce an additive sedative effect.

The only body that can advise a patient about their legal right to hold a driving licence is the Driving and Vehicle Licensing Authority (DVLA).

Patients starting opioids should be advised to inform the DVLA that they are taking opioids. Prescribers should document that this advice has been given.

Patients might need to modify their domestic (e.g. child care) and work activities when starting opioid treatment. They might also need to discuss their treatment with their employers.

Long term effects of opioids

There are currently insufficient data to quantify the risks of long term opioid therapy. Concerns relate to the effects of opioids on the endocrine and immune systems and the risk of inducing a hyperalgesic syndrome.

Endocrine effects of opioids

Long term administration of opioids is associated with endocrine impairment in men and women. Influences on both the hypothalamic-pituitary-adrenal axis and the hypothalamic-pituitary-gonadal axis have been demonstrated in patients taking oral opioids with consequent hypogonadism and adrenal insufficiency in both sexes. These effects are probably dose related and can lead to amenorrhoea, reduced libido, infertility and depression in women and erectile dysfunction and diminished libido in men. Patients (particularly women of childbearing age) should be told about these effects before starting opioids. Endocrine function should be monitored regularly if symptomatically indicated and patients should be referred to an endocrinologist for advice regarding the benefits of hormonal replacement therapy.

Immunological effects of opioids

Both animal and human studies have demonstrated that opioids have an immunomodulating effect. These effects are mediated via opioid receptors both on immune effector cells and in the central nervous system. In animals, opioids have been demonstrated to have effects on antimicrobial response and anti-tumour surveillance. Opioids may differ in their propensity to cause immunosuppression. In animal studies, buprenorphine has been demonstrated to have no impact on

immune function. The relevance of these findings to the clinical use of opioids is not known.

Opioid induced hyperalgesia

Both animal and human studies have demonstrated that prolonged use of opioids might lead to a state of abnormal pain sensitivity. There is neurobiologic commonality between the hyperalgesia and allodynia that typify neuropathic pain, opioid induced hyperalgesia and opioid tolerance. This phenomenon has been demonstrated in patients being treated with opioids for addiction and for pain. Clinically, the patient on long term opioid therapy presents with increased pain. This might be qualitatively distinct from pain related to disease progression or to breakthrough pain resulting from development of opioid tolerance. Pain associated with hyperalgesia is more diffuse than the pre-existing pain and less defined in quality. The management of opioid induced hyperalgesia is opioid dose reduction or changing to an alternative opioid preparation.

Opioids and Pregnancy

Any woman taking opioids and planning pregnancy should seek pre-conception advice about potential problems from appropriate health care professionals (e.g. departments of fetal medicine or fetal toxicology). Alternative pain management might be needed during pregnancy. Patients and their partners should be warned of the effects of maternal opioid consumption on neonatal well being. Babies born to women taking opioids may show symptoms of drug withdrawal. Patients and their partners should be made aware of this possibility. With long acting drugs such as methadone, neonatal withdrawal symptoms can first manifest up to five days after birth. This should be taken into account when planning the mother and baby's length of hospital stay after delivery. The possibility of having to treat neonatal withdrawal syndrome should not, in itself, rule out the use of opioids in pregnancy, if these drugs confer significant benefits to the mother.

5 Practical aspects of prescribing

Patients

There is no right or wrong type of patient with pain who is suitable for opioid therapy. Patients with pain and psychological or psychiatric co-morbidity, including substance misuse disorders (see section 7), may be considered for therapy with opioids but will need additional support and monitoring.

NB Assessment of patients in pain should include evaluation of their current psychological state, with particular regard to depression, substance misuse, post-traumatic stress symptoms or any significant history of these, since they may complicate pain management if left untreated. This is especially important when prescribing opioids for persistent pain.

Patients or their carers must be competent to administer the prescribed regimen safely and recognise problems when they occur.

Uncertainty about long term effects of opioid therapy should prompt caution when prescribing analgesics for children and adolescents. If a child suffers from a painful, often progressive, debilitating condition, he/she might be suitable for treatment with opioids. It is advisable to discuss opioid prescribing in children with a specialist, multi-professional, children's pain management team that includes the child's family doctor.

Prescribing opioids for elderly patients should take account of relevant age-related changes in pharmacokinetics and pharmacodynamics. Starting doses should be cautious with frequent reassessment and dose adjustment as appropriate.

Types of pain that might benefit from opioids

Pain of both nociceptive and neuropathic origin (including pain related to nervous system injury or disease) might respond to opioid therapy. Good evidence for efficacy or otherwise of therapeutic interventions for a variety of pain syndromes is now available. For some conditions, evidence based guidelines suggest that interventions other than medications are likely to be more successful. There are no conditions under which opioid

therapy is contraindicated, but prescribers must be aware of the likely efficacy of a range of interventions for a given condition and use this information to guide management.

In most situations, for most patients and most pains, opioids should not be considered as the first choice treatment. To understand where opioids fit into the treatment pathway, refer to validated, evidence-based guidance such as Cochrane Reviews or the Map of Medicine. Discussion with a specialist in pain medicine may be helpful if a prescriber has concerns about starting a patient on opioid treatment.

When to prescribe opioids

Drugs with demonstrated efficacy for persistent pain syndromes (e.g. tricyclic antidepressants and antiepileptic drugs for neuropathic pain) should always be prescribed before starting opioids. These drugs may be co-prescribed with opioids if useful benefit is not achieved with opioids alone.

The context in which opioids should be prescribed

It is important that patients are adequately informed of the risks and benefits of opioid therapy. It is helpful to supplement discussions regarding treatment with written information (see further reading). A patient should be given adequate time to make a decision whether to start opioids and may wish to discuss treatment with his/her family, carers and other healthcare professionals involved in his/her care.

Patients presenting to secondary care services with either acute exacerbations of chronic pain or those with persistent painful symptoms following pain relieving operations are frequently started on opioids to facilitate their discharge from hospital. It is important that these individuals have their pain assessed fully by an experienced professional and that the pain management plan be in accordance with best practice. If opioids are considered the most appropriate therapy, arrangements must be made to monitor and follow-up treatment appropriately. The patient's general practitioner must be involved in the formulation of these plans.

Choice of drug

Where possible, modified release opioids administered at regular intervals should be used in the management of patients with persistent pain. Clinical experience suggests that immediate release preparations are more associated with tolerance and problem drug use. Use of flexible dosing regimens using immediate release preparations (alone or in

combination with modified release preparations) can, in some circumstances, provide effective symptomatic relief and allow an overall reduction in opioid dose. Use of such regimens may be justified when :

- the pain is intermittent and short-lived;
- pain intensity has significant diurnal variation; and
- background pain is well controlled with modified release preparations but the patient has infrequent, short-lived episodes of increased pain.

The need to use immediate release opioids for persistent pain should prompt specialist review.

Opioid drugs may be administered orally or transdermally.

Injectable opioids should not be used in the management of patients with persistent non-cancer pain except in extraordinary circumstances and then only after consultation with a specialised multidisciplinary pain management service.

Choice of drug depends on clinical circumstance, local experience and expertise. There are no high quality randomised trials that compare different opioids in the management of persistent non-cancer pain. Clinical experience suggests that pethidine is particularly unsuitable for patients with persistent pain. Its high lipid solubility and rapid onset/offset may predispose patients to problem drug use. Its active metabolite norpethidine can lead to serious side effects. It does not produce less smooth muscle spasm than equipotent doses of other opioids and so confers no advantage for patients with visceral pain.

Serotonin syndrome can occur as a consequence of excess serotonergic activity at central nervous system and peripheral serotonin receptors. This can produce specific symptoms, including cognitive, autonomic and somatic effects. The symptoms may be barely perceptible but can be more serious. Numerous drugs and drug combinations have been reported to produce serotonin syndrome; for example tramadol should be used with care in patients who are co-prescribed tricyclic antidepressants and selective serotonin reuptake inhibitors.

Drug dose

Pain treatment with opioids should start with a low dose that is titrated upwards according to analgesic effect and side effects. The patient must be warned that it may take some days to determine whether the drug is going to be effective.

The doses of opioid used for chronic non-cancer pain in well conducted controlled trials usually equate to less than 180mg morphine equivalent in 24 hours. There are no high quality data published that inform prescribers of the safety and efficacy of higher doses.

NB If patients do not achieve useful relief of pain symptoms at doses between 120-180mg morphine equivalent in 24 hours, referral to a specialist in pain medicine is strongly recommended.

Intravenous opioid testing

Intravenous testing with opioids provides little useful information about long term efficacy, although it may be used to screen out patients whose pain does not respond to opioids.

Trial of opioid therapy

A closely monitored trial of opioid therapy is recommended before deciding whether a patient is prescribed opioids for long term use.

It is good practice when assessing the patient in pain to elicit a mental health history, including screening questions relating to

- current or past history of depression or anxiety
- current or past history of substance misuse
- family history of substance misuse

A history of depression or anxiety, and substance misuse (by the patient or a family member) may be risk factors for problematic opioid use. This information is needed to determine the degree of monitoring and support needed to prescribe opioids safely.

Treatment should be started at a time when prescriber and therapist are able to meet or make contact at least monthly, although more frequent review is desirable.

The goals of therapy should be agreed before starting opioid treatment and assessed at each review. These goals should be clearly documented. A formal opioid 'contract' can provide a useful basis for further discussion if medication use becomes poorly controlled or the agreed outcomes of therapy are not achieved. It is helpful to plan for the

management of flare-ups in symptoms by means other than an increase in stable opioid dose.

Adverse effects should be documented at every assessment.

The patient may need two or three upwards adjustments of opioid dose (if tolerated) before effectiveness can be evaluated. If, after reasonable dose titration, useful pain relief is not achieved or intolerable side effects occur, the trial of opioid therapy should be considered unsuccessful. If opioid therapy is not to be continued, the dose of opioid should be stopped by gradual decrements.

Long term opioid prescribing

If the opioid trial is a success the patient may wish to continue taking opioids. Treatment may be continued until :

- the underlying painful condition resolves;
- the patient receives a definitive pain relieving intervention (e.g. joint replacement);
- the patient no longer derives benefit from opioid treatment (periodic dose tapering or cessation of therapy is recommended to confirm continued effectiveness of treatment);
- the patient develops intolerable side effects; or
- use of opioids becomes problematic (see section 7).

During long term opioid treatment, reviews should be conducted at least monthly in the first six months after stable dosing has been achieved. Frequency of review thereafter can be clinically determined by the complexity of the case, but should be at least biannually. If opioids have been started in secondary care, there should be agreement between the hospital and the patient's GP regarding where and by whom the patient will be assessed and who should provide the repeat prescriptions. In both primary and secondary care, arrangements must be made for the provision of prescriptions when the patient's principal prescriber is unavailable.

6 Non-medical prescribing of opioids

The law allows qualified Nurse and Pharmacist Independent Prescribers to prescribe any licensed medication for any medical condition, within their area of competence. There are restrictions on prescribing controlled drugs. Pharmacists cannot prescribe opioids, while Nurse Independent Prescribers are able to prescribe morphine and diamorphine for patients with acute pain, along with the following controlled drugs for palliative care:

- diamorphine, morphine, oxycodone, by oral, parenteral or rectal routes; and
- buprenorphine or fentanyl transdermal patches

The definition of what is meant by 'palliative care' is unclear and open to differing interpretations.

Nurses and pharmacists can prescribe any opioid as a supplementary prescriber, in partnership with a doctor. Management plans should be reviewed at least annually.

Independent prescribers are responsible and accountable for their actions, and prescribing should be supported by appropriate initial patient assessment, interpretation of findings and continued monitoring of the patient.

In March 2007 the Home Office and the Medicines and Healthcare Products Regulation Agency (MHRA) produced consultation document MLX338. It proposed that nurses and pharmacists should be able to prescribe controlled drugs for any medical condition within the practitioner's area of competence. The findings have yet to be published.

7 Opioids and problem drug use

This section can be read in conjunction with "Pain and Substance Misuse: Improving the patient experience" (see Section 8)

The prescription of opioids may result in problem drug use. The likelihood of this occurring is influenced by a number of social, psychological and health related factors.

The possibility of substance misuse must be discussed with a patient when opioids are prescribed. If concerns arise they must be explored sensitively, and steps must be taken to minimise the risk of inappropriate medication use.

Controlled drugs prescribed for pain can be diverted to others for whom they are not prescribed or for non-medical use. Prescribers must be aware of this risk and take appropriate action if this occurs.

Definitions

Evaluation of problem drug use in relation to prescribed opioids for pain relief has been hampered by confusion regarding the terms tolerance, dependence and addiction.

Existing diagnostic criteria relating to substance dependence have poor applicability when prescribing opioids for pain relief, and have acted as a source of concern to both prescribers, and patients and their carers.

Terminology for patients in pain using opioids medicinally has been clarified by a consensus statement from the American Pain Society, the American Academy of Pain Medicine and the American Society of Addiction Medicine (figure 3). These definitions distinguish between expected sequelae of opioid therapy, including physical dependence and tolerance, and the more biologically and behaviourally complex syndrome of addiction.

The term **pseudoaddiction** has been coined to describe behaviours such as drug hoarding, attempts to obtain extra supplies and requests for early prescription or increased dose that might be mistaken as signs of addiction but are an attempt to obtain better pain relief. When pain is relieved, these behaviours cease.

Figure 3 Definitions related to the use of opioids for the treatment of pain. Adapted from American Academy of Pain Medicine, the American Pain Society and the American Society of Addiction Medicine (2001).

Addiction

Addiction is a primary, chronic, neurobiologic disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following:

- impaired control over drug use
- compulsive use
- continued use despite harm
- craving

Physical dependence

Physical dependence is a state of adaptation that is manifested by a drug class specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, or administration of an antagonist.

Tolerance

Tolerance is a state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug's effects over time.

Problem analgesic use

Problem analgesic use may be determined by eliciting the patient's thoughts regarding how they use analgesic substances and establishing their pattern of use, rather than the quantity used. If analgesics are being used to regulate mood, rather than control pain, this may indicate an established or developing problem.

Evidence of craving, increased salience, or other components of addiction are also likely to be indicative of problems.

Size of problem

The estimated risk of addiction to prescribed opioids is variably reported. Most data are derived from studies of analgesic efficacy that are usually of too short a duration to identify problems relating to aberrant drug use. Longer-term retrospective and prospective data are available, but these require caution in interpretation as the study populations are not consistent with respect to diagnosis and previous history, and because reported prevalence varies depending on the criteria used to define addiction. Rates of addiction in non-cancer pain patients are reported as occurring in 0-50% patients and in cancer pain in 0-7.7% of patients being prescribed opioids.

Risk factors

A number of factors are thought to indicate a risk of addiction to prescribed opioids. These include:

- current or past history of substance misuse, including alcohol
- family member with history of substance misuse
- poor social support
- co-morbid psychiatric disorders

Co-morbid psychiatric disorders may increase risk of addiction for a number of reasons, including high levels of mental health and substance abuse disorder co-morbidity and use of analgesic medications to alleviate symptoms of mental illness. Patients with pain may become depressed because of the impact of symptoms on their quality of life. If pain is successfully treated with opioids, mood might improve.

NB Presence of risk factors should not be a reason for denying a patient opioid therapy if opioids are the appropriate management of the painful condition. Identification of risk should help the prescriber determine the degree of monitoring and support needed to prescribe opioids safely.

Preventing, identifying and managing problems

Patients being considered for opioid therapy should understand that problem drug use might occur.

Assessment for opioid therapy must include screening for risk factors, which includes questions about depression and substance misuse. Patients should be asked to list all other medications they are taking, including over-the-counter preparations and illicit drugs. It is important to ask whether other members of the household and family might be misusing drugs.

Patients should understand that frequent monitoring minimises the risk of problems occurring.

Concerns regarding potential problem drug use should be discussed openly and sensitively with patients and their carers. Discussions should be clearly documented and communicated to other members of the patient's healthcare team.

If the clinician has concerns about how the patient is taking his/her medication, frequency of review should be increased.

When starting opioid therapy, there must be clear agreement regarding responsibility for prescribing. Patients must be given prescriptions from one prescriber only. If concerns about addiction arise, the number of doses prescribed should be reduced.

Some of the behaviours that may indicate of problem drug use include:

- earlier prescription seeking
- claims of lost medication
- intoxication
- frequent missed appointments
- use of other scheduled drugs

Concerns about problem drug use should prompt referral to specialised pain and addiction services.

NB Need for increased dose of opioid is not always indicative of problem drug use. Dose escalation may result because of:

- increase in intensity of underlying pain condition (disease progression)
- development of an additional painful condition
- opioid tolerance
- opioid induced hyperalgesia

Prescribing for patients with a history of substance misuse

Individuals with a history of substance misuse are at risk of developing problems when prescribed opioids for pain relief. However, there are a number of reasons why substance misusers have greater than usual pain management needs. If opioids are the most appropriate therapy, they may be prescribed for patients as part of a multidisciplinary treatment plan. Comprehensive assessment of both pain and addiction is mandatory, and therapy should be closely monitored by professionals in both pain management and addiction medicine.

8 References/further reading

American Pain Society and American Academy of Pain Medicine 2009. Guideline for the use of chronic opioid therapy in non-cancer pain. Evidence Review. http://www.ampainsoc.org/pub/pdf/Opioid_Final_Evidence_Report.pdf

Ballantyne J and Mao J Opioid therapy for chronic pain *NEJM* 2003;349:1943-53

Ballantyne J Opioids for chronic pain taking stock *Pain* 125 (2006) 3-4

Ballantyne J and LaForge S Opioid dependence and addiction during opioid treatment of chronic pain *Pain* 129 (2007) 235-255

Butler S F et al Development and validation of the Current Opioid Misuse Measure *Pain* 130 (2007) 144-156

Chou R, Fanciullo GJ, Fine PG, et al. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain *J Pain* (2009) 10:113-30
http://www.ampainsoc.org/pub/cp_guidelines.htm

Edlund MJ et al Risk factors for clinically recognized opioid abuse and dependence among veterans using opioids for chronic non-cancer pain *Pain* 129 (2007) 355-362

Eriksen J et al Critical issues on opioids in chronic non-cancer pain: An epidemiological study *Pain* 125 (2006) 172-179

Højsted J and Sjøgren P Addiction to opioids in chronic pain patients: A literature review *European Journal of Pain* 11(2007) 490-518

Hutchinson K et al Exploring beliefs and practice of opioid prescribing for persistent non-cancer pain by general practitioners *European Journal of Pain* 11 (2007) 93-98

Jensen MK et al 10-year follow-up of chronic non-malignant pain patients: Opioid use, health related quality of life and health care utilization *European Journal of Pain* 10 (2006) 423-433

Kalso E et al Opioids in chronic non-cancer pain: Systematic review of efficacy and safety *Pain* 112 (2004) 372-380

Kamboj SJ et al The effects of immediate-release morphine on cognitive functioning in patients receiving chronic opioid therapy in palliative care *Pain* 117 (2005) 388-395

McCracken L, Vellerman SC, Eccleston C Patterns of prescription and concern about opioid analgesics for chronic non-malignant pain in general practice *Primary Health Care Research & Development* 9 (2008): 146–156

NHS Clinical Knowledge Summaries <http://cks.library.nhs.uk/home>

Sullivan MD et al Regular use of prescribed opioids: Association with common psychiatric disorders *Pain* 119 (2005) 95–103

The British Pain Society 2007 Pain and substance misuse: Improving the patient experience. Available from: www.britishpainsociety.org/pub_professional.htm#misuse

The British Pain Society 2007. Pain and problem drug use: Information for patients. Available from: www.britishpainsociety.org/pub_patient.htm#misuse_patient

The British Pain Society 2010. Opioids for persistent pain: Information for patients Available from: http://www.britishpainsociety.org/pub_patient.htm#opioidpatient

Von Korff M and Deyo R Potent opioids for chronic musculoskeletal pain: Flying blind? *Pain* 109 (2004) 207–209

Williams A C De C Psychological distress and opioid efficacy: More questions than answers *Pain* 117 (2005) 245–246

Wasan AD et al The association between negative affect and opioid analgesia in patients with discogenic low back pain *Pain* 117 (2005) 450–461



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