Chronic pain: opiates and dependence-forming medications

The role of opiates in the management of cancer pain and acute pain is well established. From this evidence base, use and benefit has been extrapolated for chronic pain.

The balance of evidence is that in chronic pain, opiates and gabapentinoids are neither as effective nor safe as we previously thought. There are **no** drug treatments that work consistently well for persistent pain.

This is now enshrined in the NICE guidance on chronic pain (2021). Primary care needs a plan to support the majority of people experiencing harms but minimal benefits from these drugs.

If you are planning to work with people with chronic pain in adjusting their medications and potentially deprescribing, we strongly recommend reading the article on *Chronic pain: communication skills and self-management* first.

How big is the problem?

Big….

The 2019 Public Health England report on prescribed medications (https://www.gov.uk/government/publications/prescribed-medicines-review-report) looked at prescribing data for drugs that can cause dependence and/or have withdrawal reactions. This was an update of an earlier report first commissioned in 2017. (Note that the report stressed that antidepressants were NOT addictive but can be associated with *withdrawal reactions*).

….But not as big as in the USA (yet):

Between December 2019 and December 2020, 93 000 Americans died from drug overdoses, an increase of 29.4% on the 2018–2019 figures and representing around 255 overdose deaths per day (Lancet 2021;398:277).

The report identified that in the UK:

- **1 in 4** adults are taking potentially dependence-forming medications – this has increased over the past 10 years. People are also often taking them for longer.
- If we take the whole adult population of the UK, the following percentages are prescribed each of these drugs (also incudes prescribing trend since 2017):
  - 17% antidepressants (increasing).
  - 13% opioids (decreasing).
  - 3% gabapentinoids (increasing).
  - 3% benzodiazepines (decreasing).
  - 2% Z-drugs (decreasing).
- Rates of prescribing vary substantially between and within different CCGs, and there is a strong association between opioid and gabapentinoid prescribing and socioeconomic deprivation. There was a weaker association with antidepressant prescribing.

The bottom line is that, in the majority of cases, the harms of opioids, gabapentinoids, benzodiazepines and Z-drugs outweigh the benefits, and the national guidance (including NICE chronic pain, NICE back pain and sciatica, NICE neuropathic pain, and campaigns like Opioids Aware from the Royal College of Anaesthetists) encourages us to think again and adopt a more holistic approach. We hope that clearer funded care pathways will emerge as a result of this consensus.

Critics point out that guidelines are written using evidence from the average response of a population to a treatment, and do not take into account that opiates are effective for some people, even if, statistically, they are the outliers (BJGP 2021 https://doi.org/10.3399/bjgp21X715457).

In this article, we are mostly considering opiates, but similar principles apply to gabapentinoids and benzodiazepines/Z-drugs.

Can we do anything about this?

Yes…but it isn't easy.

A BJGP editorial asked the important questions, 'Should we, can we, halt the rise of prescribing for pain and distress?' (BJGP 2020;70(698):432–433). Without a doubt, socioeconomic deprivation, traumatic early life events (adverse childhood experiences – ACES), distress and pain are associated with higher levels of prescribing. The psychoactive drugs that are prescribed then alter neuronal pathways, and bring the risk of adverse effects and scant benefits for most. There is a second imbalancing of neurochemistry when the drugs are reduced and stopped.

This may feel like a mountain to climb, particularly for those of us working in areas of high socioeconomic deprivation. GPs and clinical pharmacists cannot do this on their own, and comprehensive recommissioning of services will be required. But this does not mean there is nothing we can do.

The editorial reminds us that we can learn from our own history. Primary care ***has*** successfully reduced prescribing of amphetamines, benzodiazipines and, more recently, antipsychotics in dementia and inappropriate use of antibiotics. It requires a shift in approach to the primary care consultation – away from routine prescribing of 'psychoactive drugs for short-term solace'.

This will not be easy but we have the skills to do *some of* this – think Balint and 'the drug doctor', well worth a read (see link in useful resources).

Working as practice and/or PCN team, and building the support of our multi-professional teams of clinical and community pharmacists, social prescribing link workers and third-sector organisations, will be essential.

In the remainder of this article, we will look at what we **<u>can</u>** do.

Reducing the prescribing of opiate and other dependence-forming drugs in practice

We have used a number of sources, combined with the pragmatic experience of the chronic pain clinicians in our team, to provide practical hints and tips about deprescribing opiates and other dependence-forming drugs:

- CDC guidelines for prescribing opiates in chronic pain from the USA (JAMA 2016;315:1624).
- The UK resource, Opioids Aware, developed by the Royal College of Anaesthetists (there is a link in the useful resources section).
- NICE NG215 (2022): *Medicines associated with dependence or withdrawal symptoms: safe prescribing and withdrawal management for adults.* This guidance is summarised below.
    - If we're honest, we're a little underwhelmed by the long-awaited 2022 NICE guideline. There's far less practical detail than we were expecting when compared with resources such as Opioids Aware from the Faculty of Pain Management, e.g. there was no detail on opiate conversion and proposed rates of tapering. NICE didn't give such advice because it concluded that "the evidence comparing different speeds of dose reduction was inconclusive".
    - Is there anything new and practice-changing in this guidance? Yes: NICE tells us to produce written management plans and share them with our patients taking, starting or tapering medications associated with tolerance or withdrawal AND *all antidepressant medication (regardless of indication)*. This represents a significant workload for the primary healthcare team. (Antidepressants are included because of the withdrawal effects possible with them, not because people develop dependence/tolerance.)

Please note, **this does not apply to prescribing for cancer pain, palliative care or in the last days of life.**

An interesting piece in JAMA found that mindfulness was more effective for reducing chronic pain and opioid misuse than psychotherapy. 250 patients with chronic pain who were misusing opioids were randomised to receive mindfulness or a group-based psychotherapy programme over an 8-week period (JAMA Intern Med. 2022;182(4):407-417).

Top tips

- **Work together as a practice**: if there is variation between clinicians in their approach to this, it will make all our lives, and those of our patients, more difficult. You can find out how your practice is doing compared with other practices in similar socioeconomic areas by using Open Prescribing (link below).
- **Connection before conflict**: it is essential that the person does not feel we are dismissing their experience of suffering and distress. This is why we focused on communication skills in the separate article on *Chronic pain: communication skills and self-management.* We need to do this FIRST. Hear the pain story, create a shared understanding, explore impact on life and function – then talk about medication.
- **Start with quick wins and celebrate them**, e.g. reduce new initiations of opiates and gabapentinoids, institute a prescribing checklist as part of QIPP.

- **Take it slow**: this will not all happen in a single consultation, but in most situations, we are seeing these people anyway, what we are doing is changing the **emphasis** of the consultation. In those prescribed long-term, higher-dose opioid therapy, tapering is associated with increased risk of overdose and mental health crisis (JAMA 2021;326:411). These patients likely warrant an even slower taper and closer monitoring (JAMA 2021;326:388).
- **Redefine success**: not all people who are taking dependence-forming drugs for chronic pain will be ready to make a change. Not escalating may be a success for some individuals, or even forming a consistent collaborative relationship.

NICE on dependence-forming medicines and antidepressants

Here, we summarise NICE's first guideline on dependence-forming medicines, first published in 2022 (NG215). NICE includes antidepressant medications in the guideline but maintains a clear distinction between antidepressants and the drugs likely to cause dependence or withdrawal symptoms. The inclusion of antidepressant prescribing appears to cover all prescribing, regardless of indication, e.g. mental health, migraine prophylaxis, neuropathic pain.

For clarity: despite their inclusion in this guideline, NICE does not imply that antidepressants cause physical dependence and tolerance in the same way as opiates, but there is increasing recognition that withdrawal symptoms from antidepressants can be severe and long-lasting in some patients (DTB 2022;60:7-12).

We include this guideline on dependence-forming medications in this article on pain because the core of the guideline deals with drugs which we're likely to encounter when managing our patients living with chronic pain, e.g. opiates and benzodiazepines.

NICE on starting a dependence-forming medication

Before prescribing

- **Consider alternative strategies before prescribing these medicines.**
- **Consider the risk of dependence in the individual** (although do not withhold medication solely because of increased risk because of these factors). Factors that increase the risk include:
  - Comorbid mental health diagnosis.
  - History of drug or alcohol misuse.
  - Absence of a clear diagnosis.
  - Taking an opioid together with a benzodiazepine.
- **Provide information to help the patient balance the risks and benefits of treatment;** however, recognise that patient distress can make decision-making difficult.
- **The decision to start such medication may be difficult for the clinician;** additional time may be needed to consider alternative options and consult with colleagues.
- **If you do not think that the medication is in the patient's best interest:**
  - Do not prescribe the medication.
  - Explain the reason and document the discussion, giving a copy to the patient.
  - Offer the patient a second opinion. (NICE refers us to the section in the GMC guidance on good practice in prescribing that covers "handling patient requests for medicines you don't think will benefit them", which it has basically summarised here. But the GMC guidance first reminds us to understand the patient's perspective on why they want a particularly medication and what they think it will achieve.)
- **For those for whom communication is difficult** (e.g. if they have a learning disability or cognitive impairment), take special care to ensure the patient's needs have been fully understood, and (if appropriate) involve family/carers.
- **For those with a learning disability or mental health problem,** ensure a full assessment is undertaken before prescribing dependence-forming medications or antidepressants to ensure they do not have other unmet needs for which prescribing may not be the most appropriate answer. Consider involving the relevant teams.

Starting a dependence-forming medicine

Before prescribing, provide verbal AND evidence-based written information about the medication. You most likely do this already by explaining common side-effects and telling your patient to read the leaflet that comes in the box with the medication. Explain/discuss the following:

- Side-effects may occur before any benefits are seen; they usually ease over time.
- Next steps if the medicine is ineffective.
- The issues around withdrawal:
  - Missing doses may lead to withdrawal symptoms.
  - There can be difficulty in stopping this medicine, and how this might be managed.
- Safe storage.

- If appropriate, issues relating to pregnancy/planning a pregnancy.
- The issues around dependence:
  - Dependence is to be expected and is not a reason to avoid the medicine.
  - Outline the symptoms that signal development of problems associated with dependence, and consider making those close to the patient aware of these symptoms as well.

Document the management plan in the clinical record **and give the patient a copy**. This should include:

- Indication and intended outcomes of treatment.
- Starting dose and intervals between adjustments (the aim will be to use the lowest effective dose).
- Time to onset of action.
- Who to contact if there are problems.
- Anticipated duration of therapy and duration of each prescription.
- Risks of taking more than the prescribed dose; symptoms and signs of an overdose (and what to do).
- Plans for reviewing the medication (where, when and by whom).

When prescribing:

- Start low and keep to the lowest effective dose. With gabapentinoids, benefits may be slow to come but side-effects come sooner.
- Avoid modified-release opioids (more likely to cause tolerance).

Taking over medication prescribed in secondary care

When taking over drugs prescribed in secondary care, NICE says:

- Take the same level of care as if you were initiating the medicine yourself.
- If you decline to prescribe, you should liaise with the secondary care team and explain the reason for any delay to the patient.
- If possible, ensure that one person has overall responsibility for a prescription.

Reviewing dependence-forming medicines or antidepressants

- Review regularly (the actual frequency depends on a number of factors):
  - Patient preference.
  - Type(s) of medication.
  - Comorbidity, adverse effects, recent dose adjustments, pregnancy (or planning), polypharmacy, other care needs.
- Content of review:
  - Benefits vs. risks of continuation.
  - Consider reasonable dose adjustments (up or down).
  - Document effectiveness and adverse effects.
  - Are there signs that the patient is developing problems associated with dependence (early requests, lost prescriptions)?
- Update management plan and provide a copy to the patient.

NICE on withdrawing a dependence-forming medication

Shared decision-making

- Discuss withdrawal of the medication if:
  - Condition has resolved (medication no longer indicated).
  - Medication isn't effective.
  - Harms outweigh benefits.
  - Patient wants to stop.
  - Problems associated with dependence have developed.
- Explain the benefits of reducing, discuss differing views and aim to reach agreement using a shared decision-making approach.
- Understand that the person may be anxious or reluctant to reduce/stop.
- Avoid blame-apportioning language.
- Do not stop a medicine abruptly (unless exceptional circumstances, e.g. GI bleed from antidepressant or respiratory depression from an opioid).
- When planning withdrawal, consider:
  - Urgency of withdrawal.
  - Goal-setting (dose reduction or complete withdrawal).
  - Prioritisation (what to reduce first if there's more than one candidate).

- Factors that may make withdrawal challenging (long duration of use, high dose, previous withdrawal symptoms, history of dependence, an antidepressant with short half-life).
- Consider home circumstances and availability of support.

Information and support

- Before starting:
  - Explain and provide information about the process of withdrawal.
  - Provide details of support, e.g. support groups.
- Discuss withdrawal symptoms and explain:
  - It can be difficult and take a long time (months or longer).
  - Support will be available.
  - Withdrawal symptoms don't affect everyone, vary widely in severity and may occur at any time.
  - There are options for managing withdrawal symptoms (see below).
  - Sometimes, it can be hard to differentiate withdrawal symptoms from a relapse of the underlying medical condition or an entirely new problem.

Dose reduction

- Explain the risks of abrupt cessation.
- Tailor the rate of withdrawal against the risk of adverse effects from continued exposure to the drug, and ensure the planned rate is acceptable to the patient. Apply withdrawal schedules flexibly.
- Explain that the withdrawal rate can be modified should bothersome withdrawal symptoms occur; consider giving the patient control of the withdrawal rate.
- Agree regular intervals for review and dose adjustments.
- Ensure the patient knows who to contact if there are problems.
- Withdrawing from **opioids, benzodiazepines, Z-drugs or antidepressants**:
  - Slow, stepwise reduction proportional to the existing dose.
  - Decrements become smaller as the dose is lowered.
- Withdrawing from **gabapentinoids**:
  - Reduce the dose by a fixed amount at each decrement.
- Withdrawing from a **short half-life benzodiazepine**:
  - Consider switching to a benzodiazepine with a longer half-life.

Identify and manage withdrawal symptoms

- The following may indicate withdrawal symptoms rather than symptoms of an underlying condition:
  - Early onset after dose reduction/cessation of medicine.
  - Symptoms that are different and/or more severe than before.
  - New symptoms.
- Use clinical judgement: is this a new condition warranting investigation?
- If distressing symptoms occur, consider:
  - Delaying the next dose reduction.
  - Smaller dose reduction.
  - Reverting to the previous dose.

Interventions to support withdrawal

- Do not treat withdrawal symptoms with something that is associated with dependence or likely to produce its own withdrawal symptoms.
- Do not use valproate or buspirone to aid withdrawal from benzodiazepines.
- Consider group CBT when withdrawing from a benzodiazepine.

Strategies if withdrawal is unsuccessful

- More frequent review.
- Short-term use of medicines to treat physical symptoms of withdrawal.
- Avoid further escalation if dose reduction proves impossible.
- Plan to repeat the attempt at a later date.
- Make clear records in the management plan that potential harms have been explained.

What about antidepressants?

The NICE guidance on medicines associated with dependence or withdrawal also discusses antidepressants – not because they cause dependence but because they are associated with withdrawal reactions. This is discussed in our article on antidepressants.

How do we actually do this in practice?

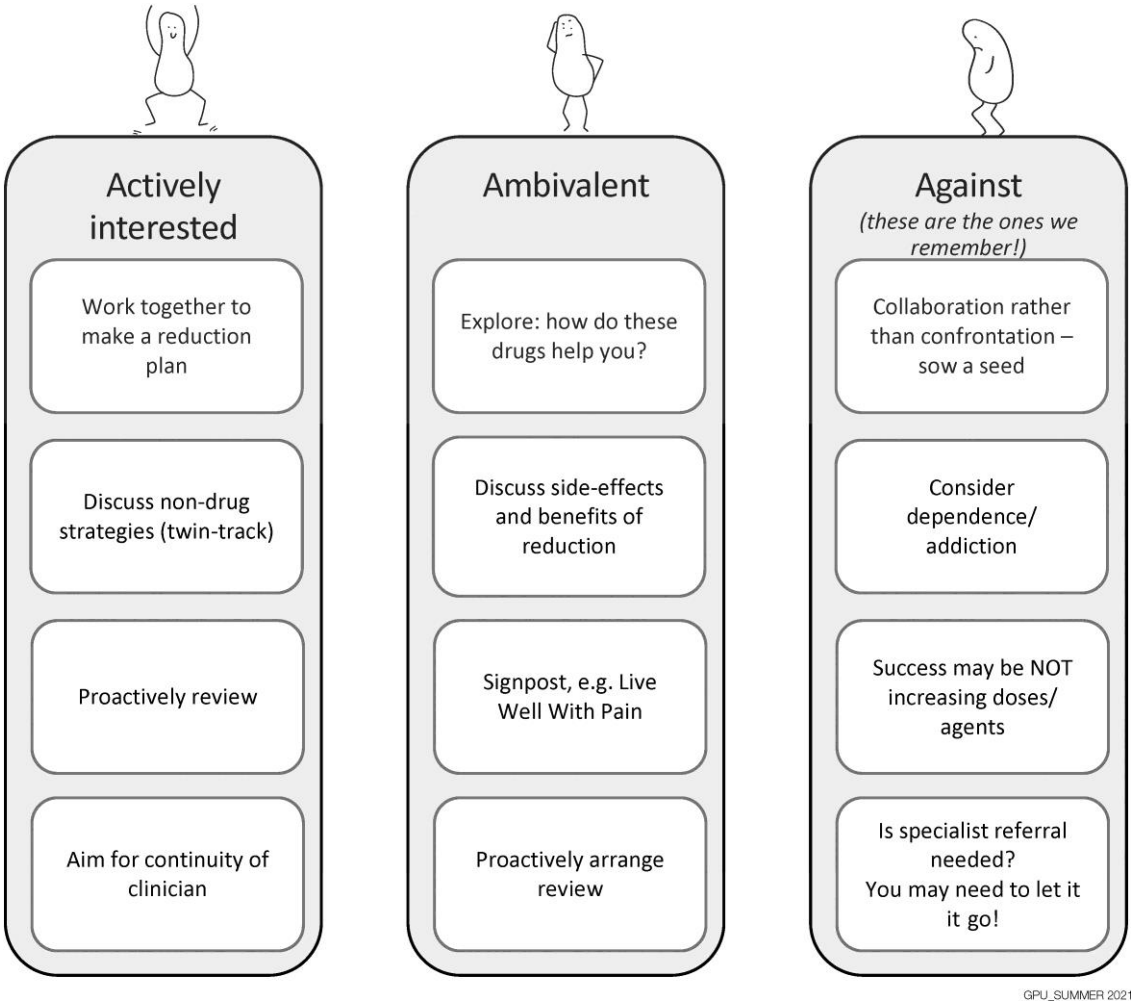
While the NICE guideline provides a framework, it isn't particularly detailed. For this, we should look at the Opioids Aware material which contains more detail and practical advice.

Opioids Aware: the 5Rs approach to deprescribing

The 5Rs approach can be found on the Opioids Aware website. It predates the NICE guideline but broadly mirrors its advice:

Refrain	Avoid prescribing these drugs in the first place where possible, and use a biopsychosocial approach from day 1.
Review	Create a relationship with the person; find out their perspective and understanding of chronic pain, and the role of their medication.
Reframe	Reframe their understanding if necessary, focusing on function and suffering/ distress just as much as pain (see the *Chronic pain: communication skills and self-management* article*).*
Reorganise	This is the nuts and bolts of restructuring to a single agent and creating a shared tapering plan.
(Refer)	We cannot manage all of this in primary care; some people will benefit from specialist input in the form of a multidisciplinary pain team, dependence and addictions services or psychological/psychiatry support. It is likely that services will evolve following the release of the NICE guideline – *do you know what you have available locally?*

- **In pain circles, it is estimated that 2/3 of this population are probably amenable to change**, but we remember the third who aren't! Roughly speaking, we can divide people into three groups, with a different strategy and approach for each:



Refrain: deciding whether to start dependence-forming drugs

This is, perhaps, the quickest win – avoiding or reducing initiation of opioids and gabapentinoids in the first place!

The key message from NICE 2021 is DON'T INITIATE OPIOIDS OR GABAPENTINOIDS for chronic primary pain (and many chronic secondary pain conditions – see *Chronic pain: NICE guideline* article for specific details).

We should broaden our approach to chronic pain – the drugs don't work *for most people*!

The CDC guideline recommends:

- Non-pharmacological and non-opiate options have a better evidence base and fewer harms. Use these first.
- Never use opiates as the only strategy for pain management.
- Think about pain AND function. Do the benefits for these outweigh the harms?
- Establish treatment goals together – what will success look like? Continue only if there is meaningful benefit.
- ***Explicitly*** discuss how therapy will be discontinued if goals are not achieved.
- ***Explicitly*** discuss the known harms and expected benefits, and continue to reassess this on an ongoing basis.

If, after this discussion, you still decide to try an opiate...

Review: patients already taking opiates or other dependence-forming drugs

Where do we start tackling this problem? This depends a lot on the demographics of the surgeries we work in and the availability of local resources.

We may need to prioritise by high-risk groups, high-risk doses and then readiness to change:

The CDC guidance identifies high-risk groups and high-risk doses of opiates. We might want to prioritise discussing tapering and withdrawal with these individuals.

High-risk groups

We should look for:

Absolute contraindications	**Increased risk of toxicity**	**Increased risk dependence/overdose**

Sleep disordered breathing, e.g. OSA Pregnancy	Renal impairment Hepatic impairment Age >65y Polypharmacy, e.g. benzodiazepines	Previous overdose Current or past substance misuse Alcohol misuse Prison population Mental health problems

High-risk doses

The CDC guidelines highlight high-risk cut-offs of 50mg of morphine/day or equivalent and 90mg of morphine/day or equivalent (**50 MMEs** and **90 MMEs)** because there is a marked step-up in the rates of harms and accidental overdose at each of these levels. *We will look at this more in a moment when we consider how to reorganise opiates.*

Remember to consider ALL opiates, including patches and prns.

Co-prescription of other dependence-forming drugs, e.g. gabapentinoids and benzodiazepines, also identifies a priority group. A paper in BMJ Open looked at the risks associated with concurrent use of opioids and benzodiazepines in Alberta (BMJ Open 2020;10:e038692):

- Co-prescription of opioids and benzodiazepines increases the risk of hospitalisation or A&E visit (OR 1.13, CI 1.10–1.17), more so in those aged over 65y (OR 1.5, CI 1.39–1.61). Morphine, oxycodone, hydromorphone and tramadol are riskier than codeine when used with benzodiazepines. Higher drug doses are associated with higher risk.
- Co-prescription increases the risk of death (OR 1.9, CI 1.76–2.05), with higher risk associated with higher doses of opioid (OR 3.13, CI 2.5–3.92).
- In March 2020, the MHRA issued a safety alert reminding us of the potentially fatal consequences of co-prescribing benzodiazepines and opiates (Drug Safety Update 2020;13:5).

Reframe

This is the subject of the *Chronic pain: communication skills and self-management* article.

Reorganise

This is all about identifying those on the highest doses who are at greatest risk, and tapering doses to reduce/minimise risk.

Calculating morphine milligram equivalents

This table is adapted from the UK guidelines Opioids Aware. There is also a great calculator spreadsheet you can use, particularly when people are on more than one opiate. This was developed by Oxford University Hospitals Trust; a link can be found here and in the resources box at the end of the article.

The conversion factors are only estimates. Individuals vary in how they metabolise these medications – we should always err on the side of caution, particularly in the frail elderly and when switching between opioids. In both of these situations, the dose equivalent should be reduced (by 25–50%) to ensure safety.

Opioid	Conversion factor*	50mg morphine per day equivalent (reassess if doses are escalating above these levels)	90mg morphine per day equivalent (do not escalate above these doses)
Morphine (oral)	1	50mg/d	90mg/d
Codeine (oral)	0.1	500mg/d	900mg/d
Tramadol (oral)	0.1	500mg/d	900mg/d
Oxycodone (oral)	1.5	33mg/d	60mg/d

**For those who find this muddling to calculate daily equivalent of morphine:*

- *Take current **daily** dose of opiate, e.g. 240mg codeine.*
- *Multiply by conversion factor, e.g. 240 x 0.1.*
- *This gives you the daily equivalent of morphine, e.g. 24mg.*

The Opioids Aware guideline (reviewed March 2021) also gives us equivalent doses for transdermal patches which reflect current BNF conversions:

Patch	Morphine milligram equivalent (MME) per 24h
Buprenorphine patch (changed every 7 days)	

5mcg/h	12mg
10mcg/h	24mg
20mcg/h	48mg
Buprenorphine patch (changed every 4 days)	
35mcg/h	84mg
52mcg/h	126mg
70mcg/h	168mg
Fentanyl patches (changed every 3 days)	
12mcg/h	30mg
25mcg/h	60mg
50mcg/h	120mg
75mcg/h	180mg
100mcg/h	240mg

Reorganise: tapering opiates

We don't know the best way to taper opiates; there is an absence of evidence as studies at high risk of bias predominate (BMJ 2018;362:k2990, BMJ 2022;377:e066375). We therefore have to use 'best practice' guidance. The BMJ article and Opioids Aware identified what we do know:

- Engagement (**reframing step**) is essential – finding a reason that is 'real' to the patient may help. Use resources such as Live Well With Pain (link below).
- Slow, monitored tapering by 5–10% per 1–2 weeks minimises withdrawal effects. This may lead to withdrawal or just lowering the dose. *Sometimes, a slower taper of 5% per 1–2 weeks may help those who are more anxious or psychologically (rather than physically) dependent; we may go faster for those with significant adverse effects.*
- Progress may not be linear, and we may need to allow a plateau at certain dose levels before trying again.
- Consider tapering long-acting opiates first and then gradually tapering short-acting opiates. When taking the lowest possible dose, increase the interval between doses; when taking once per day, they can be stopped.

Opioids Aware offers more details and resources as part of a toolkit. We have summarised it, here with a link to the whole resource. You'll notice that it is more detailed than the NICE guidance, providing more practical guidance such as suggested rates of withdrawal:

Tapering and stopping (Opioids Aware – Royal College of Anaesthetists)

When to taper or stop?

- The medication is not providing useful pain relief (use patient reports of pain and function to guide you).
- The underlying painful condition resolves/is 'fixed', e.g. joint replacement.
- Side-effects outweigh benefits.
- There is good evidence that the medication is being diverted/sold to others.

Preparing the patient to stop

This is the most important step, and will involve the reframing communication skills:

- Explain the rationale and the potential benefits of reduction (you may want to use the suggested videos below to help).
- Agree goals and timeframe for stopping.
- Address pain from a biopsychosocial perspective, particularly addressing mental health and physical health concerns, ideally before starting the taper.
- Discuss symptoms and signs of opiate withdrawal:
  - Sweating.
  - Yawning.
  - Abdominal cramps.
  - Restlessness.
  - Anxiety.
- Arrange regular review and support during the process.

How to taper

- Calculate total daily opioid dose (including any as-needed medication for breakthrough pain).
- Reduce dose by 10% every 1–2 weeks (if the patient is on more than one opiate, you may have to convert to a single oral drug – usually morphine, though specialist services may use buprenorphine or methadone).

- When changing from one opiate to another, e.g. a patch to morphine, the new opiate should typically be dosed at a lower level than the calculated MME to avoid accidental overdose. The Royal College of Anaesthetists and the CDC guideline recommend a 25–50% reduction, particularly in the frail elderly.
- **The conversion from one opiate to another is a high-risk activity; seek specialist advice if there is any uncertainty.**
- Regular consistent review will be needed, especially after the first conversion.
- Remove opioids from repeat prescriptions. It is important that the whole practice works as a team, and that there is clear documentation of the current dose and tapering plan. Continuity of care is likely to be beneficial.

Who needs referral for tapering?

- Patients taking 300mg MMEs or more per day are likely to need specialist support in stopping. This will usually be through local addiction services – refer them.
- Patients where there is a strong indication of morphine dependence disorder (see below).
- Seek advice and support if you are uncertain.

Reorganise: tapering gabapentinoids

PHE 2014 and NICE CKS (accessed March 2021) state that while both gabapentin and pregabalin can be discontinued over one week, a more gradual dose reduction may be advisable to observe for 'emergent symptoms'. They recommend:

- Gabapentin: reduce daily dose at a maximum rate of 300mg every 4 days.
- Pregabalin: reduce daily dose at a maximum rate of 50–100mg per week.

Refer: identifying opiate dependence/misuse disorder

- Dependence refers to the development of:
  - Tolerance: the need for increased amounts to achieve the desired effect.
  - Withdrawal effects: symptom development with attempts to reduce or stop the drug.
- Dependency has been demonstrated at 1m of treatment in patients taking oxycodone.
- Over half of all patients taking opioids for 3m will still be taking them at 1y.
- Studies vary on the level of dependency due to different diagnostic criteria, but range between 5 and 30%.
- Urine testing of patients taking opioids tends to discover a 'surprise' in 1 in 5 cases (either no drug found (!), or higher levels than prescribed).

In primary care, our role will be identification and referral to specialist addiction services. Some GPwSI or practices working under Locally Enhanced Service provision of addiction services may take on more of the role themselves.

Identifying and managing prescription opioid dependence (Opioids Aware – Royal College of Anaesthetists)

When should we consider this?

Consider prescription opioid dependence in the following situations *(these won't come as a surprise)*:

- Long-term use for non-cancer pain.
- Current or past psychiatric illness or significant emotional trauma.
- History of other substance/prescription drug/alcohol misuse.
- Reports of losing prescriptions/early replacement requested/taking higher doses than prescribed.
- Family express concerns about opiate use.
- Refusal/failure to attend medication reviews or accept referral to addiction services.
- Dr-shopping or location-shopping (OOH/A&E/111) for opioid prescriptions.
- Deteriorating function, e.g. work, social interaction.
- Refusing specialist referral to tackle the underlying issue.

Assessment and referral

- Avoid judgement and confrontation.
- Work together to create a formulation of the whole pain experience, including all biopsychosocial factors (*you are going to need more than 10 minutes or a few appointments).*
- Document all dependence-forming drug use and routes of administrations (so, benzos, Z-drugs and gabapentinoids).
- Depending on complexity and our individual experience level:
  - In most cases, we will refer these patients to addiction services.
  - Some practices may be well set up to manage this in house.
- One doctor should take over prescribing of all dependence-forming drugs, and develop a treatment and reduction plan.
- This may involve maintenance on current dose of opiates, or opiate substitution treatment and detoxification.

Maintenance treatment

This involves maintaining the current dose of opiates – switch to a long-acting oral opiate, e.g. methadone or buprenorphine.

- Great care must be taken in dose conversion, and it should only be undertaken with support from a clinician experienced in the use of these drugs (*so, for most of us, this will require referral or discussion).*
- Supervised dosing should be considered, but patients will not be converted to their full dose immediately in case they have been non-compliant (i.e. diverting some of their prescribed dose to others).
- Discuss referral for group support to work towards motivation for detoxification, e.g. Narcotics Anonymous.
- Testing for prescribed opiates and elicited substances should occur regularly.

Detoxification treatment

- Ideally, this should take place through outpatient addiction support services.
- Opiates will be converted to a single long-acting oral opiate, e.g. methadone or buprenorphine, and gradually reduced in a plan made with the patient.
- Patients should be warned of the risk of overdose if they relapse and leap up to a higher dose.
- If detoxification is successful, specialists may consider prescribing naltrexone.

Naloxone prescribing

Dependent patients who are at risk of overdose may be prescribed naloxone, and training in how to use this should be offered to their family and carers.

How to do an opiate/analgesia trial

The Opioids Aware resource discusses how to do a trial of opiates. It reminds us that short-term success does not predict long-term efficacy. Many of these principles are applicable to trials of other analgesics and dependence-forming medications.

Starting the trial	• Agree assessable outcomes with the patient that relate to pain and function, e.g. ability to attend work, do exercise, pain intensity, sleep pattern.
Duration	• If pain is constant, 1–2w is sufficient. • If pain is intermittent, the trial should be long enough to allow for 2–3 episodes of pain.
Choice of opioid	• Prescribe a short (1–2w) supply of immediate-release morphine liquid or tablets. • Advise patient to explore a range of doses within a fixed limit, e.g. 5–10mg of oral morphine. • Determine this dose range based on age, weight, renal and liver function, etc. • **If a single dose of 20mg immediate-release morphine does not offer pain reduction, opiates are not likely to be beneficial in the longer term.**
Assessing success	• Patient diary: focus on agreed outcomes and side-effects, and record exact timings of doses. • If there is no or <30% improvement, long-term opioid therapy is not likely to be effective. • If there is an improvement in pain, this should be balanced against impact on function and side-effects.
Documentation	• Clearly document all of the above.
Ongoing prescribing	For the small number of patients where there is a benefit on pain and function: • Oral preparations will be best for most patients. • For intermittent/variable pain, short-acting oral opiates are likely to be most suitable. They allow most flexibility of dosing. • For persistent pain, modified-release morphine may be more appropriate. • We should not prescribe pethidine, oral fentanyl or injectable opiates for non-cancer persistent pain. **Review regularly:** Minimally review at 4w and then at least 6-monthly. Define a maximum dose ceiling. Opioids Aware states this should definitely not exceed 120mg/day. For many patients, this should be substantially less (*as a team, we would feel cautious going above 50 MME daily – see below).* **It recommends using acute prescriptions rather than repeat to encourage regular review.**

Opioids and driving

There are two issues:

Legal

Drug-driving legislation changed in England and Wales in 2015. A new offence refers to driving with specified amounts of controlled drugs in the body; morphine and methadone are included, but not other prescription opioids. The set levels are generally above the prescribed therapeutic ranges, and there is a statutory 'medical defence' if people are

found with levels in their blood stream in accordance with documented prescribed quantities (or quantities recommended by the patient information leaflet).

Safety

In addition to this legislation, it is the responsibility of all drivers to consider whether their driving may be impaired on ***every occasion they drive.***

Information you can share with patients:

- Drivers testing positive for morphine are 8–32 times more likely to have an accident than those with a negative test result.
- Doses of >200mg/day can result in impairment similar to that seen with driving above the alcohol limit.
- Impairment may occur at much lower doses if there is polypharmacy with sedatives or alcohol.

Discussion in relation to drugs and driving should be clearly documented in the notes and a copy given to patients (see useful resources below for a printable leaflet).

Chronic pain: opiates and dependence-forming drugs

- Consider and use all alternatives first.
- Prescribe the lowest effective dose of oral short-acting opiates.
- Think very carefully before prescribing more than 50mg morphine or the equivalent per day.
- Do not prescribe more than the equivalent of 90mg morphine per day.
- Reassess regularly based on pre-agreed treatment goals for pain and function.
- Be aware of high-risk groups and discuss tapering, especially if no impact on pain and function.
- Refer opioid addiction.
- Formulate a written management plan for prescribing, review and withdrawal of opiates and dependence-forming drugs.
- Discuss, document and print driving advice for all patients.
- Pregabalin and gabapentin are now Schedule 3 controlled drugs.

Consider auditing all repeat prescriptions of opiates. You could use Open Prescribing to compare your practice and CCG with other local practices:

https://openprescribing.net

Identify and flag notes of patients taking more than 50mg morphine/d or equivalent. Review and assess the appropriateness of the dose, and whether a strategy for reduction and a naloxone prescription is needed.

Discuss the CDC guidelines and Opioids Aware at your PHCT meeting – re-audit prescription levels 3m later to see if there has been a change in practice.

Could you write to all your patients on repeat opiates, offering them information about harms and an opportunity to taper and reduce?

Useful resources:

Websites (all resources are hyperlinked for ease of use in Red Whale Knowledge)

- Oxford University Hospitals – opioid calculator (want to calculate morphine milligram equivalent doses for complex regimens? Try this website)
- Clin Calc – opioids (useful clinical calculator to convert total daily opiate dose into a single oral morphine dose, including the 25% recommended reduction for transdermal preparation)
- Faculty of Pain Medicine – Opioids Aware (professional and patient resources available)
- Faculty of Pain Medicine – opioids and driving (a handy printable leaflet on opioids and the law on driving)
- Live Well With Pain (a whole range of resources for clinicians and patients around self-management)
- GMC – good practice in prescribing and managing medicines and devices

Videos

- YouTube – Brainman: understanding pain in less than 5 minutes (this is a great video to show or share with patients when talking about chronic pain)
- YouTube – Brainman: understanding pain: Brainman stops his opioids (Brainman video explaining simply why opiates may make things worse!)