

Perioperative opioid use and misuse

Authors: Jane Quinlan,^A Sarah Rann,^B Ruth Bastable^C and Nicholas Levy^D

ABSTRACT

Prescribed opioid misuse in North America is a public health crisis, with huge social, medical and economic repercussions. Surgery is an identified driver for persistent opioid use and misuse. The UK has also seen a surge in opioid consumption per capita and it is now necessary for primary and secondary care to work together to mitigate the problem of perioperative prescribed opioid misuse.

This review discusses the identified drivers for persistent opioid use following surgery and discusses the remedial actions that must be taken by all stakeholders to mitigate the UK developing its own perioperative prescribed opioid crisis.

KEYWORDS: Opioid, prescription opioid misuse, opioid use disorder, chronic post-surgical pain

Introduction and background

Prescribed opioid misuse in the United States of America is a public health crisis, with an associated economic burden estimated at around US\$80 billion per year.¹ Data from 2015 suggest that 33,000 people died from opioid overdose, with approximately half of those deaths involving a prescription opioid. Prescribed opioid dependence is now a global phenomenon affecting Canada, Australasia and Europe.²

The opioid crisis has been underpinned by a fundamental lack of appreciation that acute or palliative pain – an appropriate physiological response to actual tissue damage – is physiologically different to chronic pain. Surgery and trauma produce acute pain, where inflammatory processes drive nociception (the sensory response to harmful stimuli), and pain subsides in tandem with healing, within days or weeks depending on the severity of the

insult. Cancer pain at the end of life reflects an ongoing disease process producing appropriate nociception. Opioids are effective in these short-lived situations where pain is due to tissue damage and has a predictable trajectory.³

In contrast, chronic post-surgical pain (CPSP) is defined as pain that persists beyond 3 months, when inflammatory processes would have resolved. Generally, CPSP has an incidence of 10%, but may occur up to 65% depending on the surgical procedure.⁴ CPSP betrays an abnormal and damaged pain system, which is not responsive to opioids, and which is commonly compounded by psychological cofactors such as anxiety and depression. The optimal management of CPSP uses a multidisciplinary approach to improving quality of life living with the pain, rather than reliance on opioids which may only exacerbate the pain through opioid-induced tolerance and hyperalgesia.⁵

A series of well-intended but misinterpreted initiatives created a perfect storm for opioid over-prescription and the resultant surge in prescribed opioid dependence and are summarised in Table 1.

The first was the World Health Organization (WHO) pain ladder, devised in 1982 to reduce the stigma of opioid prescribing for cancer patients. Its simplicity prompted its adoption as the basis for all pain management, irrespective of cause or duration, with the message that opioids should be introduced and increased as pain worsened: an intent appropriate for cancer patients at the end of life, but not for those with chronic pain and longevity.³

In the 2000s, the International Association for the Study of Pain, together with WHO, promoted pain relief as a human right: its primary aim to increase the availability of opioids in developing countries.⁶ A 2015 report identified that 75% of the world's population have poor to non-existent access to opioids, while 17% of the global population consume 92% of its supply.⁷

Around the same time, the American Pain Society promoted 'pain as the 5th vital sign' to improve postoperative pain management for hospital patients with a reliance on pain intensity scores, such as the numerical pain score, to guide opioid administration.⁸ The misdirected broader application spread to patients suffering with chronic pain. The focus on pain scores, pharmacological treatments and the goal of pain reduction, together with a patient's perceived 'right to pain relief', allowed unscrupulous pharmaceutical companies to exploit the lack of treatment options and promote opioids. Purdue Pharma, in particular, who had sponsored the 5th vital sign campaign, introduced OxyContin in 1996 with aggressive and disingenuous marketing for its use in chronic pain. In 2007, three of their company executives pleaded guilty to federal criminal charges that they had deliberately underplayed OxyContin's addictive potential.

Authors: ^Aconsultant in anaesthesia and pain management, Oxford University Hospitals NHS Foundation Trust, Oxford, UK; ^Bassistant medical director, NHS East of England, Fulbourn, UK and controlled drugs accountable officer, NHS East of England, Fulbourn, UK and Royal College of General Practitioners representative for dependence forming medications, NHS East of England, Fulbourn, UK; ^CRoyal College of General Practitioners representative for dependence forming medications, NHS East of England, Fulbourn, UK; ^Dconsultant in anaesthesia and perioperative medicine, West Suffolk NHS Foundation Trust, Bury St Edmunds, UK

Table 1. Identified risk factors for opioid dependence following surgery

Pharmaceutical properties of drugs	Addictive properties of drugs. Modified release preparations. Compound analgesics.
Personal	Surgery and exposure to opioids. Past medical history of drug/alcohol dependence. Past medical history of psychological issues. Past medical history of chronic pain. Personality traits eg catastrophising personality.
Physician/ prescribing	Poor knowledge surrounding safe opioid stewardship. Poor knowledge concerning acute and chronic pain prescribing. Use of repeat opioid prescriptions. The dispensing of long duration opioid prescriptions. Use of 'weak' opioids. Mistaken belief that dependence to prescribed opioids is rare. Failure to promote opioid deprescribing. Failure to educate patients on the importance of safe opioid stewardship.
Society	Opioid diversion. Lack of safe opioid disposal. Acceptability of 'weak' opioids. Deprivation.
Pharmaceutical industry	Aggressive marketing. Misbranding. False marketing claims about addiction to new longer-acting opioids. Sponsoring drug trials that are designed to demonstrate superiority of their products. Corporate greed. Involvement with researchers who are subsequently penalised for fabricating data.
Healthcare initiatives	Pain as the 5th vital sign campaign. Titration of opioids to numerical pain scores. Incentivisation eg payment by results and payment by patient reported outcome measures.
Under-provision of services	Lack of alternative resources/services to support people with chronic pain. Lack of recognition of chronic pain as a long-term condition.

One of the most interesting reported drivers for the prescribed opioid crisis was the publication in 1980 in the *New England Journal of Medicine* of a five-sentence letter that created the

myth that addiction to prescribed opioids was rare.⁹ This letter has been cited over 600 times and, while the letter cannot in isolation be seen as the cause of the prescribed opioid crisis, it has been inappropriately used by the pharmaceutical industry to provide reassurance that their products are safe.¹⁰

The initiation of opioids for acute postoperative pain can lead to persistent opioid use. This may either reflect suboptimal management of CPSP, or the development of opioid substance use disorder, or a combination of both. Evidence from North America suggests that the risk of opioid use at 90 days after surgery in previously opioid naive individuals may be as high as 6.5%.¹¹ Risk factors included patients with preoperative substance abuse disorders (including tobacco and alcohol), mood disorders including anxiety, and pre-existing pain states.

It is this perioperative opioid prescribing that primary and secondary care must influence to stop patients transitioning to long-term use.

Opioid prescribing in the UK

The UK has seen a huge rise in opioid prescribing over the last 2 decades. A review of primary care prescribing of all general practices in England by the Oxford Datalab group reveals a consistent rise in opioid prescriptions between 1998 and 2017, with a 34% increase in number of opioid items dispensed dwarfed by the far greater rise of 127% in the oral morphine equivalent dose (OME); 190,000 mg to 431,000 mg OME per 1,000 population over the same time period.¹²

Opioids Aware, a website launched in 2015 by the Royal College of Anaesthetists' Faculty of Pain Medicine, the British Pain Society, several medical colleges and Public Health England was established to guide safe prescribing of opioids.¹³ It clarifies that opioid doses greater than 120 mg/day OME for chronic pain provide no improved benefit but carry significant risks of harm. Unfortunately, it appears that it is this high dose prescribing that has proliferated. The Datalab results show a 580% increase in prescribing of high-dose, long-acting opioids, with fentanyl, morphine and oxycodone accounting for over 90% of the drugs dispensed, with significant regional variation.¹² The team have developed OpenPrescribing, a free, open access website, where individual practices can scrutinise their own prescribing data, with local, regional and national comparators.¹⁴

A report commissioned by the Public Health Research Consortium found similar escalations in other dependence forming medicines (DFMs) such as gabapentinoids and Z-drugs over the last 20 years, although benzodiazepines fell in that time.¹⁵ They also identified longer continuous prescribing periods, with opioid durations increasing from 64 days in 2000 to 102 days in 2014.

It could be argued that this increase in opioid prescribing may reflect good practice in the care of patients at the end of life, but, in a 2014 study investigating the primary care prescribing of four strong opioids (morphine, oxycodone, fentanyl and buprenorphine), only 16% of patients had a cancer diagnosis.¹⁶

Chronic pain, including CPSP, is thus driving the increase in opioid prescribing which, in the majority of cases, is ineffective and exposes patients to significant risk. In a 2013 *BMJ* editorial, Cathy Stannard articulated that opioids are prescribed too often, for too long and at too high a dose.¹⁷ For all of the opioid prescribing measures investigated, this increasing trend has only appeared to have stabilised since 2015.¹² So why has it taken so long to see a plateauing of prescribing, let alone a decrease?

Opioid prescribing appears to be greatest in areas of high deprivation where there may be fewer resources to support people with chronic pain and its associated psychological comorbidities.^{12,15} It is known that adverse selection is a significant problem in opioid prescribing, whereby patients with mood disorders are more likely to use long-term opioids for pain, despite being at most risk of dependence.¹⁸ With the reduction in community mental health services across the UK, general practitioners (GPs) may be inadvertently fuelling this ‘chemical coping’.

In the UK, prescribed opioids can be accessed from multiple sources including the internet and the independent health sector. Independent healthcare prescribers are required to use the special form (FP10PCD) for only schedule 2 and 3 controlled drugs (CDs), such as strong opioids and, as of April 2019, gabapentinoids, but not for schedule 4 and 5 CDs (benzodiazepines, Z-drugs and weak opioids). Worse, internet prescribers and CD providers can often be based overseas and are therefore not subject to normal accountability. This makes it difficult to have a clear picture about all dispensing nationally, compounded by a paucity of information about over-the-counter opioid-containing compounds, such that NHS prescribers may not have accurate information about their patients’ use of DFMs.

Promoting safer postoperative opioid stewardship

Implications for hospital staff

Secondary care initiates much opioid prescribing for acute pain and must take that responsibility seriously.

The length of hospital stay for patients after surgery and trauma has decreased markedly over the last few years, with enhanced recovery protocols speeding patients through their postoperative stay. Patients are thus being discharged home with continuing pain, necessitating opioids as discharge medication, with an expectation that their use will cease within a few days or weeks.¹⁹

However, for those 6.5% of surgical patients still taking opioids beyond 3 months postoperatively, this prolonged use may indicate a transition to CPSP, the development of problem opioid use or reflect a continuation of preoperative chronic pain.¹¹ In all three groups, psychological factors play a major role, so identifying vulnerable patients preoperatively would allow interventions to reduce these risks. These strategies may include preoperative opioid reduction, individual counselling and creation of realistic expectations concerning the postoperative period, and the formulation of a postoperative analgesic plan including opioid, non-opioid and non-pharmacological elements, with clear discussion about post-discharge opioid weaning. For the most complex patients, this may involve consultation with a member of the hospital pain team and communication with the GP to ensure clarity for ongoing care.^{4,5}

Table 2 summarises some of the proposed strategies that should be adopted within UK surgical units to mitigate replicating the US’s prescribed opioid crisis.¹⁹

Good anaesthesia consists of both procedure specific analgesic strategies and multi-modal opioid sparing techniques, including the judicious use of regional anaesthetic techniques that promote return of function: drinking, eating and mobilisation.⁴ All patients should have regular, opioid-sparing, simple analgesics, such as paracetamol and (unless contraindicated) non-steroidal anti-inflammatory drugs (NSAIDs), with postoperative immediate

Table 2. Surgical unit strategies to mitigate postoperative opioid dependence

Preoperative screening	<ul style="list-style-type: none"> Identification of patients at risk of developing CPSP. Identification of patients developing opioid substance use disorder. Identification of patients on pre-existing opioids.
Preoperative interventions	<ul style="list-style-type: none"> Preoperative opioid weaning. Individual counselling and creation of realistic expectations concerning the risk and benefits of surgery. Discussion about the need for post-discharge opioid weaning.
Operative interventions	<ul style="list-style-type: none"> Administration of both paracetamol and NSAIDs where safe. Procedure specific analgesic strategies ie appropriate regional analgesic techniques that promote return of function. Low-dose ketamine. Other atypical analgesics eg lidocaine, magnesium and the gabapentinoids. Opioid ‘light’ anaesthesia and avoidance of remifentanyl.
Postoperative interventions	<ul style="list-style-type: none"> Use of functional pain scores to guide subsequent analgesia administration. Use of numerical pain scores to identify patients at risk of developing CPSP or a surgical catastrophe. Use of sedation scores to identify patients at risk of OIVI. Reduced reliance on WHO analgesic ladder. Avoidance of compound analgesics. Avoidance of modified release opioid preparations. Avoidance of more addictive opioids.
Preparation for discharge interventions	<ul style="list-style-type: none"> Avoidance of compound analgesics. Avoidance of modified release opioid preparations. Avoidance of more addictive opioids. Limit duration of opioid prescription. Regular simple analgesics.
Patient discharge education	<ul style="list-style-type: none"> Promote opioid weaning. Set realistic expectations regarding analgesia. Promote regular administration of simple analgesics. Promote use of non-pharmacological analgesic strategies. Avoid repeat opioid prescriptions. Promote safe opioid disposal. Avoid opioid diversion.

CPSP = chronic post-surgical pain; NSAIDs = non-steroidal anti-inflammatory drugs; OIVI = opioid-induced ventilatory impairment; WHO = World Health Organization.

release opioids titrated to function rather than just to pain score.⁴ Acute pain is intermittent and often movement related, so the use of modified release opioids, including transdermal preparations, is no longer recommended due to the increased risks of opioid induced ventilatory impairment and subsequent dependence.²⁰ Patients with more complex pain may be given low-dose ketamine and other atypical analgesics such as lidocaine, magnesium and the gabapentinoids in the immediate perioperative period.⁴

At discharge, patients should be given advice on non-pharmacological analgesic techniques as well as instruction on how to taper their analgesics: wean and stop opioids first and simple analgesics last. In the US (and likely in the UK too), there is huge variation in the amount of discharge opioid given to patients with, in one study, laparoscopic cholecystectomy patients receiving between 0 and 50 oxycodone tablets to take home.²¹ There should be procedure specific guidelines for quantity and duration of opioids dispensed for discharge, which should also reflect opioid consumption in the 24 hours preceding discharge.^{19,22} Patients should receive no more than 5 days' worth of opioids on discharge and must be given explicit instructions on safe opioid storage and disposal to protect the patient, household and community, and warned of the perils of repeat opioid prescription.

Implications for primary care

There is little specific UK data on the impact of postoperative analgesia and how this relates to general practice and other primary care prescribers, but opioids and other DFMs (ie benzodiazepines, Z-drugs and gabapentinoids) prescribed in the postoperative period can cause significant challenges in primary care, whether initiated by the GP or continued from secondary care.¹⁵ Co-prescribing of opioids with other DFMs has well-recognised dangers, including a heightened risk of opioid induced ventilatory impairment.^{22,23}

GPs and other primary care prescribers may find themselves challenged by poor flow of information due to delayed or incomplete discharge summaries. However, the General Medical Council states that

You are responsible for any prescription you sign, including repeat prescriptions for medicines initiated by colleagues, so you must make sure that any repeat prescription you sign is safe and appropriate.²⁴

Thus, primary care prescribers should not continue prescriptions initiated by others which they feel are unsafe or inappropriate. Indeed, GPs may be better placed to recognise patients who are higher risk of developing problem opioid use, particularly where there are existing mental health issues or substance misuse problems which have not been declared to the surgical team. Caution and restraint in opioid prescribing are paramount for these patients and particular care is needed to monitor postoperative use in the community, specifically avoiding repeat or prolonged prescribing.

Postoperative prescribing of opioids should be short term only; the duration of prescribing relates directly to the development of dependence and should be limited.⁵ In a large US study, each repeat prescription increased the rate of opioid misuse by 40%, while each additional week of opioid use increased the rate by 20%.²⁵ Interestingly, the initial opioid dose had little predictive value of misuse. Patients should be prescribed a maximum 5 days of opioids postoperatively, if at all, with a need for formal review

if pain continues. Some operations, such as knee replacement, produce longer lasting pain than most, with the continued provision of analgesia necessary to facilitate physiotherapy to achieve the best surgical outcome. Other long-lasting pain may indicate a transition to CPSP, requiring swift referral to a specialist pain management centre or a switch from opioids to more appropriate anti-neuropathic agents.

All opioid prescriptions should be scrutinised to ensure there is no evidence of overuse, escalating use or evidence of diversion. Excessive repeat prescriptions, 'lost' prescriptions, medications obtained from multiple sources or a strong resistance to deprescribing are causes for concern. Medications which are unused and not needed should be taken to the community pharmacy for disposal. They are a potential safety hazard if put away 'in case they are needed' and can be a source of diversion.

Analgesic doses should be adjusted according to the patient's condition, with dose reductions of opioids or gabapentinoids made as needed for elderly patients or those with comorbidities. It is important in primary care to review polypharmacy and address overmedication once over the immediate postoperative period, and deprescribe accordingly.

Summary and recommendations

There is a global prescribed opioid crisis, and the UK has seen a surge in opioid use. Surgery is a risk factor and, to mitigate this, discussions with patients regarding analgesia should start preoperatively and expectations set with a postoperative deprescribing plan in place, typically using the reverse pain ladder (wean opioids first, then NSAIDs and finally paracetamol). Patients at risk of sustained opioid use should be identified preoperatively and may require multidisciplinary perioperative interventions.

GPs should avoid putting postoperative medications on the repeat prescribing screen and should review each request prior to issue. Requests for analgesics for more than a few weeks should be reviewed. Weak opioids themselves can initiate prolonged opioid use, with a significant number of patients transitioning to stronger opioids over time.²⁶

Patients with mental health or substance misuse disorders are at higher risk of developing opioid dependence so should be identified early and supervised closely.

All controlled drug incidents should be reported via reporting tools so that learning can be shared to reduce risk of harm.²⁷

Agreed care pathways between secondary and primary care would support professional practice and allow the development of realistic patient expectations. ■

References

- 1 Guy Jr GP, Zhang K, Bohm MK *et al*. Vital signs: changes in opioid prescribing in the United States, 2006–2015. *MMWR* 2017;66:697.
- 2 Humphreys K. Avoiding globalisation of the prescription opioid epidemic. *Lancet* 2017;390:437–9.
- 3 Ballantyne JC, Kalso E, Stannard C. WHO analgesic ladder: a good concept gone astray. *BMJ* 2016;352:i20.
- 4 Glare P, Aubrey KR, Myles PS. Transition from acute to chronic pain after surgery. *Lancet* 2019;393:1537–46.
- 5 Colvin LA, Bull F, Hales TG. Perioperative opioid analgesia – when is enough too much? A review of opioid-induced tolerance and hyperalgesia. *Lancet* 2019;393:1558–68.
- 6 Cousins MJ, Brennan F, Carr DB. Pain relief: a universal human right. *Pain* 2004;112:1–4.

- 7 Global Commission on Drug Policy. *The negative impact of drug control on public health: The global crisis of avoidable pain*. Global Commission on Drug Policy, 2015. www.globalcommissionondrugs.org/wp-content/uploads/2012/03/GCOPD-THE-NEGATIVE-IMPACT-OF-DRUG-CONTROL-ON-PUBLIC-HEALTH-EN.pdf [Accessed 20 June 2019].
- 8 Levy N, Sturgess J, Mills P. 'Pain as the fifth vital sign' and dependence on the 'numerical pain scale' is being abandoned in the US: why? *Br J Anaesth* 2018;120:435e8.
- 9 Porter J, Jick H. Addiction rare in patients treated with narcotics. *New Engl J Med* 1980;302:123.
- 10 Leung PTM, Macdonald EMM, Stanbrook Dhalla IA, Juurlink DN. A 1980 letter on the risk of opioid addiction. *N Engl J Med* 2017;376:2194–5.
- 11 Brummett CM, Waljee JF, Goesling J *et al*. New persistent opioid use after minor and major surgical procedures in US adults. *JAMA Surg* 2017;152:e170504.
- 12 Curtis HJ, Croker R, Walker AJ *et al*. Opioid prescribing trends and geographical variation in England, 1998-2018: a retrospective database study. *Lancet Psychiatry* 2019;6:140–50.
- 13 Faculty of Pain Medicine. *Opioids Aware: A resource for patients and healthcare professionals to support prescribing of opioid medicines for pain*. London: RCoA, 2019. www.rcoa.ac.uk/faculty-of-pain-medicine/opioids-aware [Accessed 01 July 2019].
- 14 OpenPrescribing. *Explore England's prescribing data*. EBM DataLab, 2019. <https://openprescribing.net> [Accessed 01 July 2019].
- 15 Cartagena Farias J, Porter L, McManus S *et al* *Prescribing patterns in dependence forming medicines*. London: NatCen Social Research, 2017. http://phrc.lshtm.ac.uk/papers/PHRC_014_Final_Report.pdf [Accessed 01 July 2019].
- 16 Zin CS, Chen L-C, Knaggs RD. Changes in trends and pattern of strong opioid prescribing in primary care. *Eur J Pain* 2014;18:1343–51.
- 17 Stannard C. Opioids in the UK: what's the problem? *BMJ* 2013;347:f5108.
- 18 Halbert B, Davis R, Wee CC. Disproportionate longer-term opioid use among US adults with mood disorders. *Pain* 2016;157:2452–7.
- 19 Levy N, Mills P, Rockett M. Post-surgical pain management: time for a paradigm shift. *Br J Anaesth* 2019;123:e182–6.
- 20 Levy N, Mills P. Controlled-release opioids cause harm and should be avoided in management of postoperative pain in opioid naïve patients. *Br J Anaesth* 2019;122:e86–90.
- 21 Makary MA, Overton HN, Wang P. Overprescribing is major contributor to opioid crisis. *BMJ* 2017;359:j4792.
- 22 Macintyre PE, Huxtable CA, Flint SL, Dobbin MD. Costs and consequences: a review of discharge opioid prescribing for ongoing management of acute pain. *Anaesth Intensive Care* 2014;42:558–74.
- 23 National Institute for Health and Care Excellence, British National Formulary. *Controlled drugs and drug dependence*. NICE. <https://bnf.nice.org.uk/guidance/controlled-drugs-and-drug-dependence.html> [Accessed 05 July 2019].
- 24 General Medical Council. *Good practice in prescribing and managing medicines and devices*. Manchester: GMC, 2014. www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/prescribing-and-managing-medicines-and-devices [Accessed 05 July 2019].
- 25 Brat GA, Agniel D, Beam A *et al*. Postsurgical prescriptions for opioid naïve patients and association with overdose and misuse: retrospective cohort study. *BMJ* 2018;360:j5790.
- 26 Alam A, Gomes T, Zheng H *et al*. Long-term analgesic use after low-risk surgery: a retrospective cohort study. *Arch Intern Med* 2012;172:425–30.
- 27 General Pharmaceutical Council. *Guidance for registered pharmacies providing pharmacy services at a distance including on the internet*. London: GPhC, 2019. www.pharmacyregulation.org/sites/default/files/document/guidance_for_registered_pharmacies_providing_pharmacy_services_at_a_distance_including_on_the_internet_april_2019.pdf [Accessed 05 July 2019].

Address for correspondence: Dr Nicholas Levy, Department of Anaesthesia and Perioperative Medicine, West Suffolk NHS Foundation Trust, Hardwick Lane, Bury St Edmunds, Suffolk IP33 2QZ, UK.
Email: nicholas.levy@wsh.nhs.uk