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Pain and pain prescribing: what is in a number?

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The international opioid painkiller conversation is well into its second decade, with no loss of momentum and indeed a recent acceleration of interest. Health journalists in the UK have absorbed the grave consequences of the very real ‘epidemic’ of painkiller misuse, overdose, and deaths in North America. The idea that we, in the UK, are about to see communities laid waste to the scourge of prescription opioid addiction makes good copy, and the purveyors of opioid formulations that are difficult to misuse (e.g. opioids formulated with opioid antagonists) are keen to keep the stories going. The primary-care data-linkage study by Torrance and colleagues¹ in this issue of the *British Journal of Anaesthesia* is thus timely and important, as it allows us to paint a more nuanced picture of how opioid painkillers are prescribed in the UK.

This highly respected and authoritative group of investigators have used sophisticated and robust analyses to describe changes in prescribing patterns of opioid analgesics in Scotland over a 10 yr period. They provide depth to these statistics by linking to patient-characteristic data, including postcode, to explore associations between opioid prescribing and deprivation. The link between deprivation and prescribing of opioids is robustly demonstrated and complements recent similar findings in the UK.² The next challenge in trying to unpack the as yet sketchily illuminated puzzle of prescriber behaviour (or rather the behaviours of prescriber and patients together that result in a prescription) is to understand this link. The paper also explores the relationship between prescribing and pain intensity through an analysis of population-based cohort data from the Generation Scotland: Scottish Family Health Study, promoting the idea that prescribing for severe pain is clinically appropriate. The third strand of this study examines the co-prescribing of opioids and benzodiazepines, a common but potentially hazardous practice.

So, what are the clinically important underpinnings of these three aims in relation to opioid prescribing in the UK, and do the findings in this study help us understand what we need to know?

Prescribing trends: clinical and public health significance

We prescribe many drug classes more than we used to, and the reasons are complex: ageing and more co-morbid populations, societal expectations of a cure for everything, service users

who are well informed regarding what is available, and the significant impact of marketing of products to clinicians who too often do not sufficiently question the appealing yet statistically sketchy clinical ‘evidence’ presented to them. Trends in prescribing painkillers have also been influenced by the attrition of some of the old mainstays of pain treatment, including the removal of co-proxamol from the market; the falling out of favour of first the coxibs, and then the nonsteroidal anti-inflammatory drugs more generally; and more recently, the realisation that, for persistent pain, paracetamol is less effective and more harmful than we thought.³ There has not been much left to fill this pharmacotherapeutic void other than opioids.

So, does this increase in opioid prescribing matter? The public health concern is that escalating opioid prescribing in the US and Canada has been paralleled by an increase in opioid-related deaths, overdoses, and treatment admissions.^{4–6} We do not collect prescription opioid harms data in the same systemised way in the UK and the rest of Europe, but the sources of data we have on serious adverse events suggest that the use of prescription medicines by those for whom they are not prescribed, addiction-treatment attendances, and prescription opioid deaths do occur, but not at all on the scale of that seen in the US (but devastating for those affected).^{7,8} About 40% of drug-related deaths in the US are related to prescription opioids compared with these drugs being mentioned on 8.2% of death certificates in the UK and Wales, often in combination with illicit substances (not including opioids used for the treatment of addiction and not including heroin cut with illicitly manufactured fentanyl and its high-potency analogues).^{8,9} The figure in Scotland is higher at about 14% (again not including drugs for opioid substitution treatment).¹⁰ These differences between North America and Europe have been well described and include structure of the healthcare system, predominance of prescribing in primary care in the UK, societal expectations, and availability of treatments for addiction.^{11,12}

Medicines cost money, and clinicians as never before must demonstrate responsible stewardship of scarce National Health Service and other healthcare resources, but this is not all about costs. The clinical implications of increased opioid prescribing are straightforward to grasp with knowledge of the evidence, and these need to shine through in any analysis of prescribing statistics. Persistent pain is distressing and disabling, and if painkillers generally, or opioids in particular, were helpful in reducing pain, then increases in prescribing would be unarguably a good thing. The reality is that, however,

there are no data to demonstrate efficacy of long-term opioids, and probably fewer than one in ten patients prescribed the drugs in real life (as opposed to clinical trials) will be helped much at all, with benefit where it occurs being modest at best (but potentially life changing for the better when it occurs).^{13,14} We know that around 5% of patients in the UK are prescribed opioids at any time, and the figure from this paper suggests that, in 2012, 18% of the population in Scotland was prescribed an opioid.¹⁵ We know that most prescribing is for long-term pain, so we can assume there is a pretty large population taking opioids with little benefit. Around 80% of patients will experience at least one side-effect from opioids, and longer-term therapy is associated with increase in fractures, falls, and all-cause mortality, and of course, addiction and misuse.¹³ So, giving a prescription for something that is likely not to work is a clinical 'big deal' in relation to iatrogenic harm. Harms relate to dose and duration of treatment: Torrance and colleagues¹ can draw some conclusions about quantity prescribed by the use of the slightly unwieldy World Health Organization (WHO) metric of defined daily dose, but as they concede, this may reflect a small number of people using big doses or a larger population in whom dose would be less of a concern. It is difficult to draw conclusions about the proportion of patients receiving harmful high doses over long periods of time. The methodology of the analysis did not allow detailed comment on duration of opioid prescription, of critical interest given the harms data, but these data have been derived elsewhere, and indeed, we are not only prescribing medicines more than we did, but we are doing it for longer.^{15,16}

Opioid prescribing and pain severity

The issue of using reported pain severity as a measure of whether opioids, particularly strong opioids (which readers should note do include tramadol, as described in the British National Formulary), are being prescribed appropriately, which has recently come under question,¹⁷ is perhaps the most contentious conclusion of this paper. When pain is short term (acute), severity relates to the degree of tissue injury: a big operation hurts more than a small one. It is reasonable to prescribe strong medicines for severe acute pain, and treatment is usually successful. Persistent pain, however, is something quite other, and reported intensity of pain has almost nothing to do with tissue injury and a lot to do with anxiety, distress, previous experiences related and unrelated to the pain, and concerns about the implications of the pain.^{18,19} Many experienced pain practitioners believe that a report of 9 or 10 out of 10 is simply a measure of the degree to which the sufferer wants help. Reports of severe persistent pain should of course be taken seriously, but using strong opioids to treat distress is not the solution. The WHO analgesic ladder, designed to aid the treatment of cancer pain at the end of life, is well validated in the palliative care context where, as with acute pain, perceived pain severity relates to disease burden, and the premise of giving stronger medicines for stronger pain holds well. Understanding what the report of severity tells us about persistent pain confirms that the ladder has no role in the treatment of long-term pain, and indeed, the wholesale adoption of the ladder principle of 'titrate to effect' has led to the widespread overuse of opioids and the failed experiment of considering alleviation of persistent pain as a universal human right.²⁰ There is a

further consideration here: if a patient is taking opioids and has severe pain, the medicines are not working. The cohort identified in this study as being appropriately described opioids described severe pain: we do not know whether that was despite taking opioids (a real treatment failure) or was the reason they were being given opioids, a treatment failure of another sort, the failure to realise that we should not be guided by pain severity when prescribing opioids for long-term pain. Large cohort studies suggest that, even when controlling for pain intensity, opioid users are in worse pain than those not on opioids.²¹

It is also perhaps worrisome to frame, in any way, the staggering prevalence of persistent pain (in some reports up to 51% of the population: disease or normal human experience?—a debate for another day) as an opioid-deficiency problem.²² This paper identified a large population of patients describing severe pain (see preceding caveats) who were not taking any pain medicines. Given the poor evidence for effectiveness of any medicines for long-term pain, the statistic could be interpreted as a reflection of high-quality and judicious clinical decision making, embedding the principle of 'first do no harm' rather than neglect of the real needs of patients with pain.

Co-prescription of opioids and benzodiazepines

If hypnotics or other central-nervous-system depressants (including alcohol) are taken concurrently, the risks of overdose, disturbance of nocturnal respiratory control, accidents, and death increase.²³ Torrance and colleagues¹ have properly identified this as a potentially hazardous clinical practice and added to the literature that suggests that co-prescribing of these drug classes is more common than one might expect in well-run clinical circles. What Torrance and colleagues¹ do not explain is that there is rather more to this finding than meets the eye. The phenomenon of 'adverse selection', whereby the most risky drug regimens are prescribed to the patients most likely to be harmed by them, is most potently illustrated by the co-prescription of benzodiazepines and opioids.^{24,25} So, despite us knowing that the highest risks of prescribing are for patients with mental-health diagnoses, including substance-use disorder, and that the most risky regimens include high-dose opioids, multiple opioids, and co-prescription of benzodiazepines, the patients to whom we most frequently prescribe opioids are those with mental-health diagnoses/substance-use disorders, and these patients are prescribed the most risky drug schedules, including high-dose potent opioids and benzodiazepines in combination.^{23,26,27} We are never going to change the prescribing statistics without a better analysis of the complex antecedents of the decisions to prescribe for pain. This intricate dance between patient and prescriber needs an understanding of the importance of social context, patient expectations, and patient distress; clinician expectations and distress at not having enough time; frustration on both sides at the lack of effective alternatives; and the intractable inability of clinicians to sit on their hands and do nothing. In the messy reality of real-life clinical practice, all of these circumstances conspire to erode the objectivity of our decision making and result in us doing things that, despite our knowledge, are not in the patients' best interests.

So, what is in a number? Numbers give us a picture of how much of something we are prescribing, but not whether that is a marker of a compassionate society or a public health disaster. Numbers can confuse and confound us when assessing pain intensity, and we must spend long enough and look hard enough behind the number to see what our patients are trying to communicate. Numbers can tell us when we are probably getting things wrong, but we need much more than numbers to enter more constructive and less harmful relationships with patients in pain. That being said, these comments are of their time. We would be foolish, given what we have seen in North America, to let down our guard in relation to opioid prescribing, and we need to keep a finger on the pulse of trends in prescribing practices in the UK, so we do need Torrance and colleagues¹ and others to nuance the picture.

Declaration of interest

None declared.

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