Painkillers, opioids, pain management and addiction

Faculty of Addictions RCPsych Edinburgh 2016

Cathy Stannard – Bristol
cathystannard@doctors.org.uk
Session overview

• Prescribing for pain: current conversations and concerns
• About chronic pain and its treatment
• Using what we know to change what we do
The opioid conversation

• The prescription opioid epidemic in the US
• UK prescribing data
• Effectiveness of opioids for long-term pain
• Harms of opioid therapy
• Addiction to and misuse of opioid medicines
• Addiction to OTC medicines
• Managing pain in at risk populations
Prescription Cost Analysis
England 2015

Prescription items dispensed in the community in England and listed alphabetically within chemical entity by therapeutic class

Published 7 April 2016
Opioids: how we got to where we are

- Mid 1980s cancer patients dying in pain
- Late 1990s pain relief as a universal human right
- Small trials showing efficacy of opioids in non-cancer pain
- Early 2000s escalation of opioid prescribing paralleled by misuse, diversion and deaths
- Recognition of limitations of trial data
- Systematic reviews of efficacy
- Recognition of dose related harms
- 2012: 19 000 prescription opioid related deaths in US
- Opioid prescribing in UK x1.3
- 23 million prescriptions at cost of £314 million
Number of patients prescribed opioids

Zin C Chen L Knaggs R *Eur J Pain* 2014;18(9):1343-51
Variation Between Strategic Health Authorities in Prescribing of Opioid Analgesics (Quarter to March 2013)

- Tramadol
- Codeine
- Morphine
- Dihydrocodeine
- Buprenorphine
- Fentanyl
- Oxycodone
- Others 4.7.2

SHA median 92.8
Variation between Strategic Health Authorities in prescribing of Benzodiazepines (Quarter to March 2010) NHS prescribing services.
Figure 3. Variation between regional offices in prescribing of gabapentin and pregabalin (BNF 4.8.1)
Deaths related to drug poisoning in England and Wales 2014
Office for National Statistics 2015

Prescription opioid related deaths: Any mention

Drug-related deaths


- Other opiate
- Tramadol
- Dihydrocodeine not from compound formulation
- Codeine not from compound formulation
- Paracetamol & codeine compound formulation
Addiction to medicines. NDTMS *personal communication*
Drug Misuse: Findings from the 2014/15 Crime Survey for England and Wales

Statistical Bulletin 03/15
Edited by: Deborah Lader
July 2015

• 5.4% adults 16 to 59 misused a prescription-only painkiller not prescribed to them

• 7.2% 16 to 24 misused a prescription-only painkiller in the last year: 4.9% of 25 to 59 had done so

• Decline in misuse with age is less for prescription painkillers than other drugs

• Painkiller misuse less likely to be associated with misuse of other drugs (cf NPS)

• No association of painkiller misuse with alcohol misuse

• People with long-standing illness/disability more likely to have misused prescription-only painkillers and to have used illicit drug in the last year.

• Misuse of prescription painkillers distributed more evenly across the general population than use of illicit drugs

• Misuse of painkillers similar in both rural and urban areas
Risks of running into problems with high dose opioids

- **Patient factors**
  - Depression/common mental health diagnoses
  - Alcohol misuse/non-opioid drug misuse
  - Opioid misuse

- **Drug factors**
  - High doses
  - Multiple opioids
  - More potent drugs
  - Concurrent benzodiazepines/sedative drugs
Who gets long term opioid therapy?

*Increased risk includes:*

- **Patient factors**
  - Depression/common mental health diagnoses (x3-4)
  - Alcohol misuse/non-opioid drug misuse (x4-5)
  - Opioid misuse (x5-10)

  *and*

- **At risk patients are more likely to receive**
  - High doses
  - Multiple opioids
  - More potent drugs
  - Concurrent benzodiazepines/sedative drugs
Influences on opioid prescribing

- Patients' non-verbal communication
- Patient behaviour
- Gender of prescriber
- Experience of prescriber
- Cognitive load of prescriber
- Concerns about effectiveness and harms
- Availability of alternatives

McCracken L, Velleman S, Eccleston C
*Primary Health Care Research & Development* 2008; 9: 146–156


Influences on opioid prescribing

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- Cognitive load of prescriber
- Concerns about effectiveness and harms
- Availability of alternatives (NB doing nothing is a strategy)

McCracken L, Velleman S, Eccleston C
*Primary Health Care Research & Development* 2008; 9: 146–156


Understanding long-term opioid prescribing for non-cancer pain in primary care: a qualitative study

Carolyn McCrorie¹, S. José Closs², Allan House¹, Duncan Petty³, Lucy Ziegler¹, Liz Glidewell¹, Robert West¹ and Robbie Foy¹

Abstract

Background: The place of opioids in the management of chronic, non-cancer pain is limited. Even so their use is escalating, leading to concerns that patients are prescribed strong opioids inappropriately and alternatives to medication are under-used. We aimed to understand the processes which bring about and perpetuate long-term prescribing of opioids for chronic, non-cancer pain.

Methods: We held semi-structured interviews with patients and focus groups with general practitioners (GPs). Participants included 23 patients currently prescribed long-term opioids and 15 GPs from Leeds and Bradford.
Summary of McCrorie et al

Problems arise when

• Patients have consultations that don’t meet their needs
• GPs feel unable to negotiate non-medication approaches
• Therapeutic short-termism resulting from inconsistent clinical encounters
• Inadequate emotionally-charged consultations
Summary of McCrorie et al

Problems arise when

- Opioids prescribed to establish false therapeutic relationships
- Absence of mutually agreed formulations and management planning (prescribing as default reaction)

Importance of practice level planning
Gabapentin and Pregabalin: how we got to where we are

• Launched end of 20th century
• Novel compounds with action at α2δ subunit calcium channel
• Enthusiastically embraced by pain specialists
• Licensed for refractory epilepsy, neuropathic pain and (in UK) GAD
• Prescribing in the UK in last 5 years
  – Gabapentin ↑ x2.3
  – Pregabalin ↑ x3
• 10.5 million prescriptions annually
• Total cost £345 million annually
Gabapentin and Pregabalin: how we got to where we are

• Reports of misuse appeared around 2010
  – Population based studies
  – Secure settings
  – Patients presenting to addiction services

• Used in many multiples of therapeutic dose

• (Adverse selection may operate)
c350 Cochrane reviews of chronic pain interventions

- Pharmacologic interventions to reduce chronic post-surgical pain
- TENS
- Capsaicin
- CBT (small benefit, no active controls/unclear)!
- Multidisciplinary rehab
- Self Management Programmes (short term benefit in self efficacy and self related health, no improvement in psychological health)
- Spinal Cord Stimulation (2004 not been updated)
- Sympathectomy
- Radiofrequency lesioning
- Acupuncture
- Injections
- Medication for neuropathic pain
- Exercise for fibromyalgia
Expect analgesic failure; pursue analgesic success

Most analgesic drugs work well but in only a small percentage of people. Andrew Moore and colleagues argue that we need to move away from a focus on average response and seek out what works for each patient.

Andrew Moore professor\textsuperscript{1}, Sheena Derry senior research officer\textsuperscript{1}, Christopher Eccleston professor\textsuperscript{2}, Eija Kalso professor\textsuperscript{3}

\textsuperscript{1}Pain Research and Nuffield Division of Anaesthetics, University of Oxford, Churchill Hospital, Oxford OX3 7LJ, UK; \textsuperscript{2}Centre for Pain Research, University of Bath, Bath, UK; \textsuperscript{3}Pain Clinic, Department of Anaesthesiology, Helsinki University Central Hospital, Finland
Pain intensity

- Patients who report the highest pain intensity (10/10) respond less well to medications
- Pain intensity relates to anxiety and distress
- Reductions in pain intensity for any treatment (including CBT) are very modest
WHO analgesic ladder: a good concept gone astray

Our mistake is to treat chronic pain as if it were acute or end of life pain

Jane C Ballantyne professor of anesthesiology and pain medicine, Eija Kalso professor of pain medicine, Cathy Stannard consultant in pain medicine

1Department of Anesthesiology and Pain Medicine, University of Washington School of Medicine, Seattle, WA 98104, USA; 2Intensive Care and Pain Medicine, University of Helsinki and Helsinki University Hospital, Finland; 3Pain Clinic, Southmead Hospital, Bristol, UK

In 1986, the World Health Organization (WHO) developed a simple model for the slow introduction and upward titration of analgesics, which became known as the WHO analgesic stepladder. Before this, people were dying in unnecessary pain because drug regulations introduced earlier to the century had increased the stigma and fear associated with both prescribing and taking opioids.

The underlying principle was that analgesics should be used incrementally, starting with non-opioids, progressing through mild and finally strong opioids, dosed in accordance with the patient’s reported pain intensity. It was expected that opioids would be needed in increasing doses to overcome pain as cancer progressed. The goal was to allow patients to be as comfortable and interactive as possible during the short march towards death. Risks of addiction and hastened death were accepted in the principle of double effect: comfort is paramount.

The stepladder approach had tremendous value when it was introduced because it institutionalized the use of opioids, overcoming prejudicial and regulatory stigmas that had hampered compassionate care, especially for patients dying from cancer. The success of opioid treatment in terminal ill cancer patients set the stage for extending the same moral imperative and treatment principles to the treatment of chronic pain, where previously opioids were considered too risky or not effective.

Suddenly, because chronic pain is ubiquitous and open ended, the floodgates opened. Over the past 30 years, in much of the developed world, we have seen more patients treated with opioids at higher doses than ever before. The extent to which the more liberal use of opioids would cause harm was not predicted.

The increase in opioid prescribing and its adverse consequences are nowhere more obvious than in the United States, where sales increased fourfold between 1999 and 2010 with parallel increases in prescription opioid deaths and admissions for misuse. These alarming statistics are an indication that unfermented use of opioids in the community can have disastrous social consequences. But patients treated with opioids can experience many other adverse consequences (including higher rates of addiction than previously envisaged, cognitive impairment, general lack of wellbeing, dysfunctional relationships and poor quality of life, hormonal effects, and higher accident rates), with no clear evidence that the treatment is actually relieving pain in the long term.

Rates of harm have been directly correlated with dose, which in turn is correlated with continuous use, the precise dosing principles promoted by the WHO stepladder. This is compounded by the phenomenon of “adverse selection” whereby the highest and most harmful doses tend to be prescribed for the people in the greatest distress, who in turn, are those most at risk.

The somatosensory component of pain of whatever aetiology is always managed by cognitive and affective influences, but these may assume greater prominence in chronic pain than in acute or cancer related pain. Functional neuroimaging has shown that pain that is initially associated with brain regions linked with the corresponding anatomical area becomes increasingly associated with emotional and reward brain circuits. Thus, prolonged pain becomes linked less with nociception and more with emotional and psycological factors. So what does the report of pain intensity actually mean when pain is chronic, and to what extent is the report of pain an attempt to communicate distress, which cannot be well addressed by opioids?

Our mistake, we believe, was to treat chronic pain as if it were acute or end of life pain. These short lived pain states tend to exhibit a predictable and linear trajectory, they tend to respond well to opioids, and titrating opioids against pain intensity usually works well. Chronic pain, on the other hand, does not have a predictable or linear trajectory and often does not respond well to opioids other than early in the course of treatment. Not only the report of pain, but also the experience of pain, is altered by mood, circumstance, stress, duration, meaning, acceptance, expectation, and fear. With so many factors altering chronic pain as it is experienced and reported, it is not surprising that pain scores do not respond in any predictable fashion to opioids.

In fact, attempts to lower pain scores using opioids has led to overuse and adverse outcomes without any appreciable lowering of the chronic pain burden at the population level.

Correspondence to: J C Ballantyne jdb12@uw.edu
Shape shifting pain: chronification of back pain shifts brain representation from nociceptive to emotional circuits

Javeria A. Hashmi,1 Marwan N. Baliki,1 Lejian Huang,1 Alex T. Baria,1 Souraya Torbey,1 Kristina M. Hermann,1 Thomas J. Schnitzer2 and A. Vania Apkarian1,3,*

1 Department of Physiology, Feinberg School of Medicine, Northwestern University, Chicago, Illinois, 60611, USA
2 Department of Rheumatology, Feinberg School of Medicine, Northwestern University, Chicago, Illinois, 60611, USA
3 Departments of Anaesthesia and Surgery, Feinberg School of Medicine, Northwestern University, Chicago, Illinois, 60611, USA

Correspondence to: A. Vania Apkarian, PhD,
Department of Physiology,
303 E. Chicago,
Torry Bldg. 5-703,
Chicago, IL 60611
E-mail: a-apkarian@northwestern.edu
CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016
WHY GUIDELINES FOR PRIMARY CARE PROVIDERS?

- Primary care providers account for approximately 50% of prescription opioids dispensed.
- Nearly 2 million Americans, aged 12 or older, either abused or were dependent on prescription opioids in 2014.
- An estimated 11% of adults experience daily pain.
- Millions of Americans are treated with prescription opioids for chronic pain.
- Primary care providers are concerned about patient addiction and report insufficient training in prescribing opioids.

MYTH VS. TRUTH

1. Opioids are effective long-term treatments for chronic pain.
   - Myth: While evidence supports short-term effectiveness of opioids, there is insufficient evidence that opioids control chronic pain effectively over the long term, and there is evidence that other treatments can be effective with less harm.

2. There is no unsafe dose of opioids as long as opioids are titrated slowly.
   - Myth: Daily opioid doses close to or greater than 90 MME/day are associated with significant risks, and lower doses are safer.

3. The risk of addiction is minimal.
   - Myth: Up to one quarter of patients receiving prescription opioids long term in a primary care setting struggle with addiction. Certain risk factors increase susceptibility to opioid-associated harms. History of overdose, history of substance use disorder, higher opioid dosages, or concurrent benzodiazepine use.

WHAT CAN PROVIDERS DO?

First, do no harm. Long-term opioid use has uncertain benefits but known serious risks. CDC’s Guideline for Prescribing Opioids for Chronic Pain will support informed clinical decision making, improved communication between patients and providers, and appropriate prescribing.

PRACTICES AND ACTIONS

USE NONOPIOID TREATMENT
Opioids are not first-line or initial therapy for chronic pain (Recommendation #1).
- In a systematic review, opioids did not differ from nonopioid medication in pain reduction, and nonopioid medications were better tolerated, with fewer improvements in physical function.

REVIEW PDPMP
Check prescription drug monitoring program data for high doses and prescriptions from other providers (Recommendation #9).
- A study showed patients with one or more risk factors (i.e. excess prescriptions, 4 or more pharmacies, or dosage >100 MME/day) accounted for 15% of all opioid deaths.

OFFER TREATMENT FOR OPIOID USE DISORDER
Offer or arrange evidence-based treatment (e.g., medication-assisted treatment and behavioral therapies) for patients with opioid use disorder (Recommendation #12).
- A study showed patients prescribed high doses of opioids long-term (>60 days) had 3.22 times the risk of opioid use disorder compared to patients not prescribed opioids.

START LOW AND GO SLOW
When opioids are started, prescribe them at the lowest effective dose (Recommendation #1).
- Studies show that high doses (>100 MME/day) are associated with 7 to 9 times the risk of overdose compared to <20 MME/day.

AVOID CONCURRENT PRESCRIBING
Avoid prescribing opioids and benzodiazepines concurrently whenever possible (Recommendation #1).
- One study found concurrent prescribing to be associated with a near quadrupling of risk for overdose death compared with opioid prescription alone.

LEARN MORE | www.cdc.gov/drugoverdose/prescribing/guideline.html
## Table 1. Responding to Prescription Opioid Abuse.

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| **Balancing individual need and societal risk.**  
Patients require access to safe and effective pain medication, but both individuals and society must be protected from the effects of opioid misuse. | The FDA will consult with partners including the National Academy of Medicine to craft a framework for opioid review, approval, and monitoring that balances individual needs for pain control with the risk of addiction, as well as the broader public health consequences of opioid abuse and misuse. |
| **Meeting the need for timely action.** The evolving threat of opioid abuse requires a flexible interim approach while the full policy framework is in development. | The FDA Science Board will convene in March to advise on the role of pharmaceuticals in pain management, development of alternative pain medications, and postmarketing surveillance activities. Multiple other actions will also occur over the next several months, including an evaluation of the existing Risk Evaluation and Mitigation Strategy (REMS) requirements for extended-release/long-acting (ER/LA) opioids. An advisory committee will consider this review and offer advice regarding possible expansion of the scope and content of prescriber education and whether to expand the REMS program to include immediate-release opioids, potentially increasing the number of prescribers |
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“We are also working closely with industry and the National Institutes of Health to develop additional alternative medications that alleviate pain but do not have the addictive properties of opioids. Nonpharmacologic approaches to pain treatment are also an urgent priority. The FDA has approved nonopioid medications for treatment of various chronic-pain syndromes, including gabapentin (Neurontin), pregabalin (Lyrica), milnacipran (Savella), duloxetine (Cymbalta), and others, and a number of promising development programs are in the pipeline.”
http://www.rcoa.ac.uk/faculty-of-pain-medicine/opioids-aware
A Public Health England funded project

Good practice in prescribing opioid medicines for pain should reflect fundamental principles in prescribing generally. The decision to prescribe is underpinned by applying best professional practice; understanding the condition, the patient and their context and understanding the clinical use of the drug. This resource, developed by UK healthcare professionals and policymakers, provides the information to support a safe and effective prescribing decision.

1. Opioids are very good analgesics for acute pain and for pain at the end of life but there is little evidence that they are helpful for long term pain.

2. A small proportion of people may obtain good pain relief with opioids in the long-term if the dose can be kept low and especially if their use is intermittent (however it is difficult to identify these people at the point of opioid initiation).

3. The risk of harm increases substantially at doses above an oral morphine equivalent of 120mg/day but there is no increased benefit.

4. If a patient is using opioids but is still in pain, the opioids are not effective and should be discontinued, even if no other treatment is available.

5. Chronic pain is very complex and if patients have refractory and disabling symptoms, particularly if they are on high opioid doses, a very detailed assessment of the many emotional influences on their pain experience is essential.
Opioids are very good painkillers for acute pain and pain at the end of life but there is little evidence that they are helpful for long term pain.

There may be a small number of people who do well with opioids in the long term if the dose can be kept low and particularly if use is intermittent (it is difficult to identify these people at the point of opioid initiation).

The risks of harm increases substantially at doses above an oral morphine equivalent 120mg/day, but there is no increased benefit.

If a patient has pain and they are on opioids it means they are not working and should be stopped, even if no other treatment is available.

Chronic pain is very complex and if patients have refractory and disabling symptoms, particularly if they are on high opioid doses, a very detailed assessment of the many emotional influences on their pain experience is essential.
Raising awareness of problems of gabapentin and pregabalin

• Advice to prescribers 2014

• ACMD recommend GBP and PG controlled under Misuse of Drugs Act and scheduled under Misuse of Drugs Regs
Explaining the etiology of Complex Regional Pain Syndrome (CRPS) from the psychogenic model is exceedingly unsophisticated, because neurocognitive deficits, neuroanatomical abnormalities, and distortions in cognitive mapping are features of CRPS pathology. More importantly, many people who have developed CRPS have no history of mental illness. The psychogenic model offers comfort to physicians and mental health practitioners (MHPs) who have difficulty understanding pain maintained by newly uncovered neuro inflammatory processes. With increased education about CRPS through a biopsychosocial perspective, both physicians and MHPs can better diagnose, treat, and manage CRPS symptomatology.
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Bringing together physical and mental health
A new frontier for integrated care

Authors
Chris Naylor
Preety Das
Shilpa Ross
Matthew Honeyman
James Thompson
Helen Gilburt

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