Opioids for Chronic Pain: Genie out of the bottle ?



DR NIRANJAN CHOGLE FFPMRCA

CONSULTANT IN ANAESTH & PAIN MEDICINE

JOINT INTERVENTIONAL PALLIATIVE PAIN SERVICE

SET

niranjan.chogle@setrust.hscni.net painclinicni@icloud.com

Dunstable GP surgery criticised over woman's opioid death

10 January 2024



Kirby Road Surgery, Dunstable, Bedfordshire, was Joy Ebanks's doctor's surgery

Alex Pope
BBC News, Bedfordshire

Mrs Ebanks suffered from fibromyalgia, arthritis, **agoraphobia** and was diagnosed with depression, Dr Cummings said.

She was prescribed venlafaxine and quetiapine - both used to treat mental health conditions - and took cannabis.

A coroner has criticised a doctors' surgery over the death of a woman who had been prescribed opioid drugs for about 14 years.

Joy Ebanks, 59, died from oxycodone toxicity in May last year.

Sean Cummings, the assistant coroner for Bedfordshire and Luton, said there was "no evidence" to suggest a plan was formed by Kirby Road Surgery in Dunstable to reduce the dosages.

The surgery said it would put together an action plan.

In his **prevention of future deaths report**, Dr Cummings said Mrs Ebanks was taking oxycodone and pregabalin as pain treatment and her primary cause of death was "oxycodone toxicity enhanced by pregabalin intake".

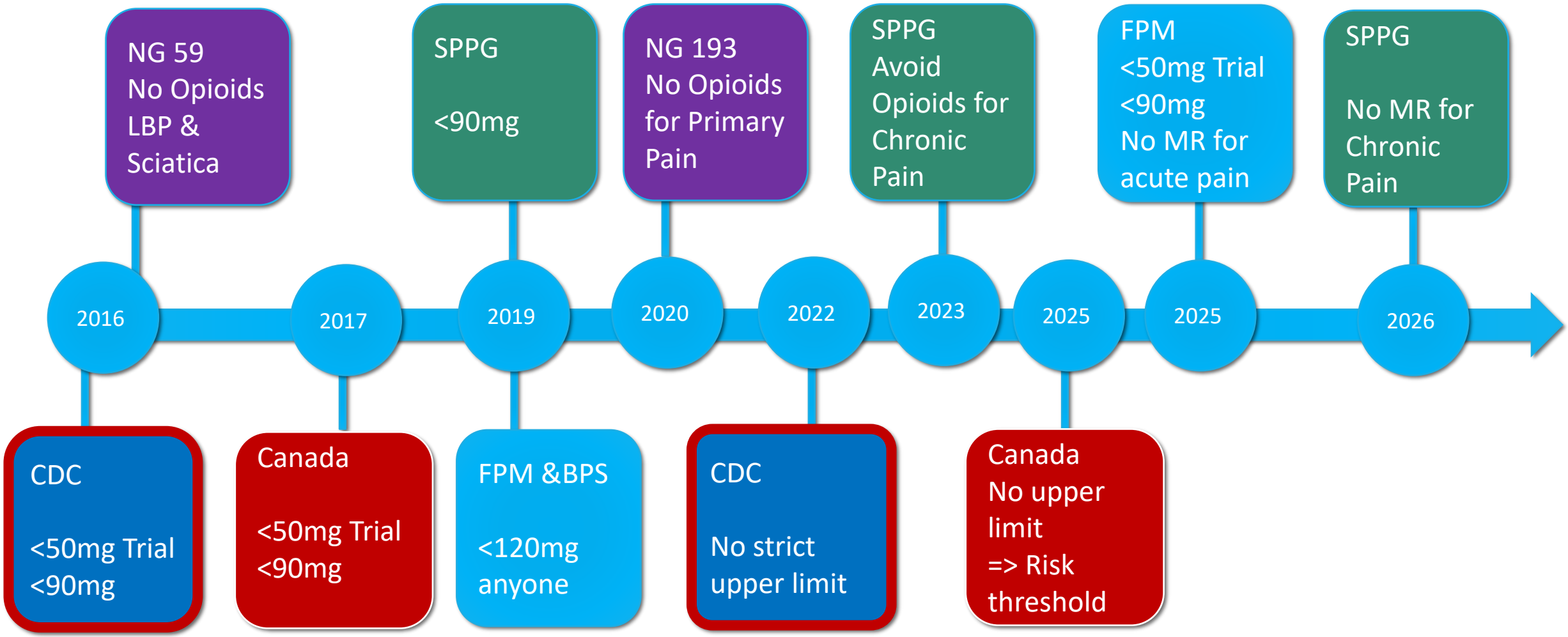
Disclosures

- Nil
- Opiophobia



Guidance

Guidance


NG 59
No Opioids
LBP &
Sciatica
SPPG
<90mg
NG 193
No Opioids
for Primary
Pain
SPPG
Avoid
Opioids for
Chronic
Pain
FPM
<50mg Trial
<90mg
No MR for
acute pain
SPPG
No MR for
Chronic
Pain
2016
2017
2019
2020
2022
2023
2025
2025
2026
CDC
<50mg Trial
<90mg
Canada
<50mg Trial
<90mg
FPM &BPS
<120mg
anyone
CDC
No strict
upper limit
Canada
No upper
limit
=> Risk
threshold

2025

Opioids Aware

A resource for healthcare professionals and patients to support prescribing of opioid medicines for pain



The Opioids Aware webpages are undergoing updates.

Sections

- Best Professional Practice ⊕
- Understanding Pain & Medicines for Pain ⊕
- Clinical Use of Opioids ⊕
- A structured approach to opioid prescribing ⊕
- Opioids & addiction ⊕
- Information for patients ⊕

Good Medical Practice

Stick to the latest recommendations ***(SSPG - NI Medication Management)***

Trial a medications only if **you** agree with someone else's recommendations

Organise **follow up, monitoring and wean**



Opioids for Acute Pain

Opioids remain important in the treatment of **moderate to severe acute pain**.

Chronic pain patients can have opioids for Acute pain

Avoid modified release opioids for the treatment of acute pain. Modified release opioids confer no benefit in the management of post operative pain and have a higher risk of opioid induced adverse events including **OIVI (opioid induce ventilatory impairment)**.

Modified release opioids is a risk factor for the development of persistent post operative opioid use (opioid use more than three months after surgery or trauma).

Opioids for Chronic Pain

No supportive evidence beyond 6 months

Trials lasting 12 months – No meaningful difference between placebo and opioids

Patients who do not achieve useful pain relief or improved function from opioids within 4 weeks are unlikely to gain benefit in the long term.

Short-term efficacy does **not guarantee long-term efficacy**

Opioids for Acute on Chronic Pain

Not to increase dose after stable dose

For a new acute pain problem, **a temporary increase may be trialled.**

Dose reduction when the acute issue has resolved.

Chronic pain management in the patient receiving opioid substitution therapy

- Close collaboration with drug services and the patient's GP is mandatory
- Regimens should avoid prescription of multiple opioids

For patients on Methadone

✓**Split dose** and give 12 hourly

For patients on Buprenorphine

✓**Split dose** and give 8-12 hourly

How come we spend 3 decades moving patients to MR preparation ?

Disclaimer: Must for all HCP



How did they do it ?

“Modified release opioids are **designed** for **Chronic Pain”**

“Modified release opioids do not cause **addiction”**

“Modified release opioids are **not associated** with **respiratory depression”**

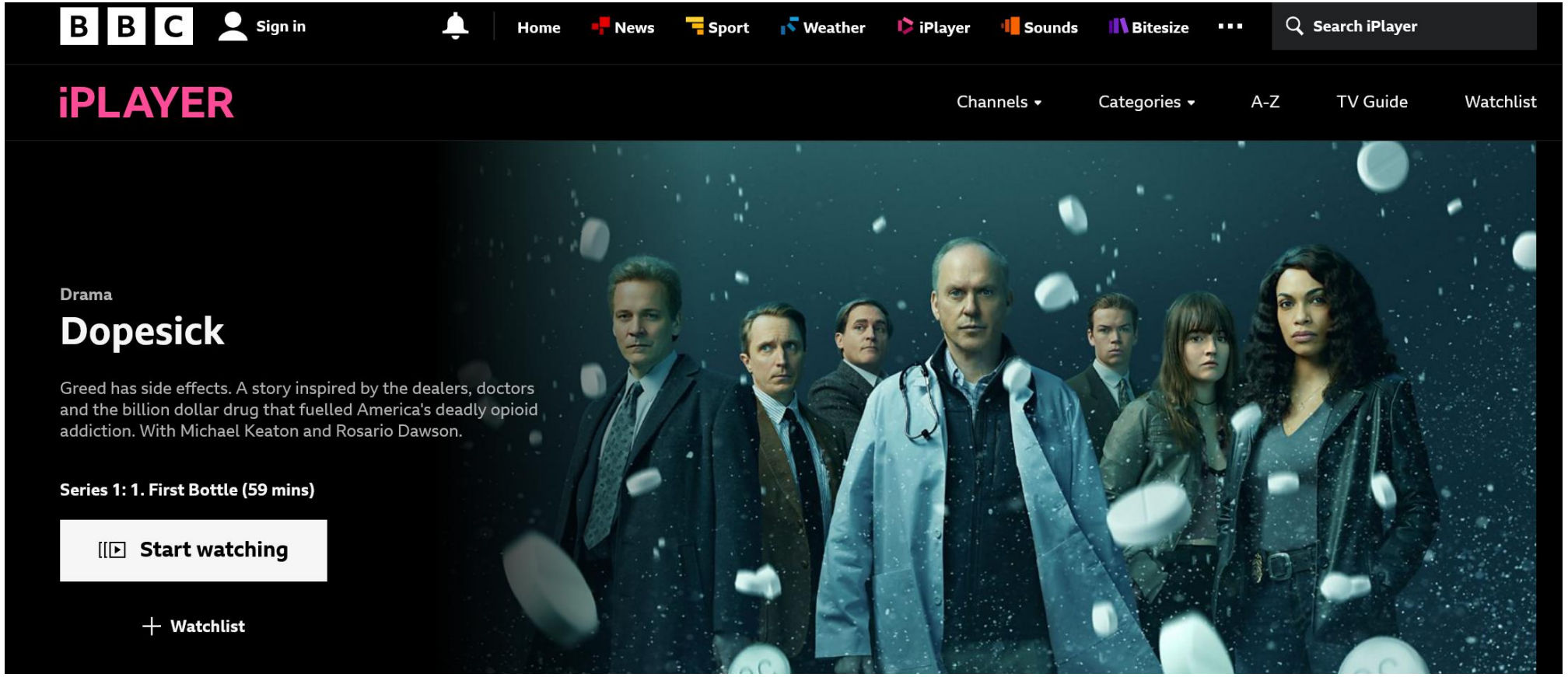
Pain as 5th vital sign

Funded patient support groups

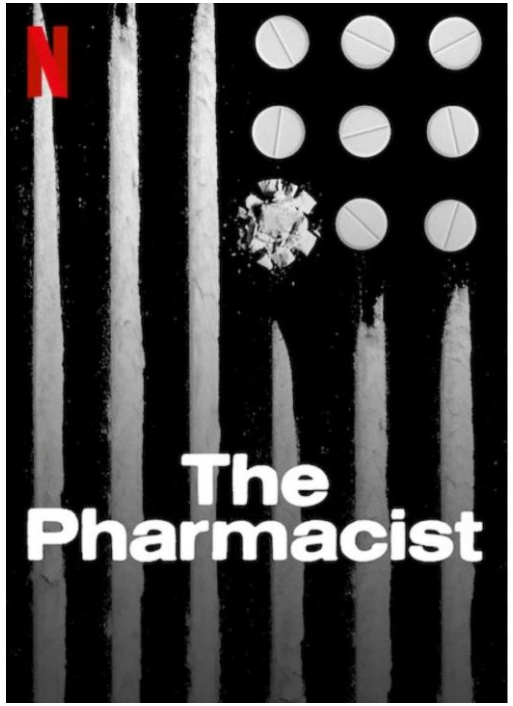
Funded Conferences

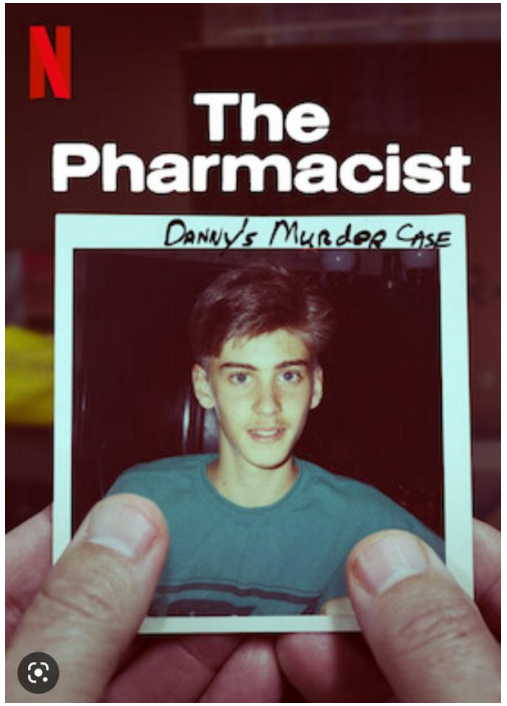
Funded Medical Societies

Disclaimer: Uncomfortable Viewing



Disclaimer: Uncomfortable Viewing



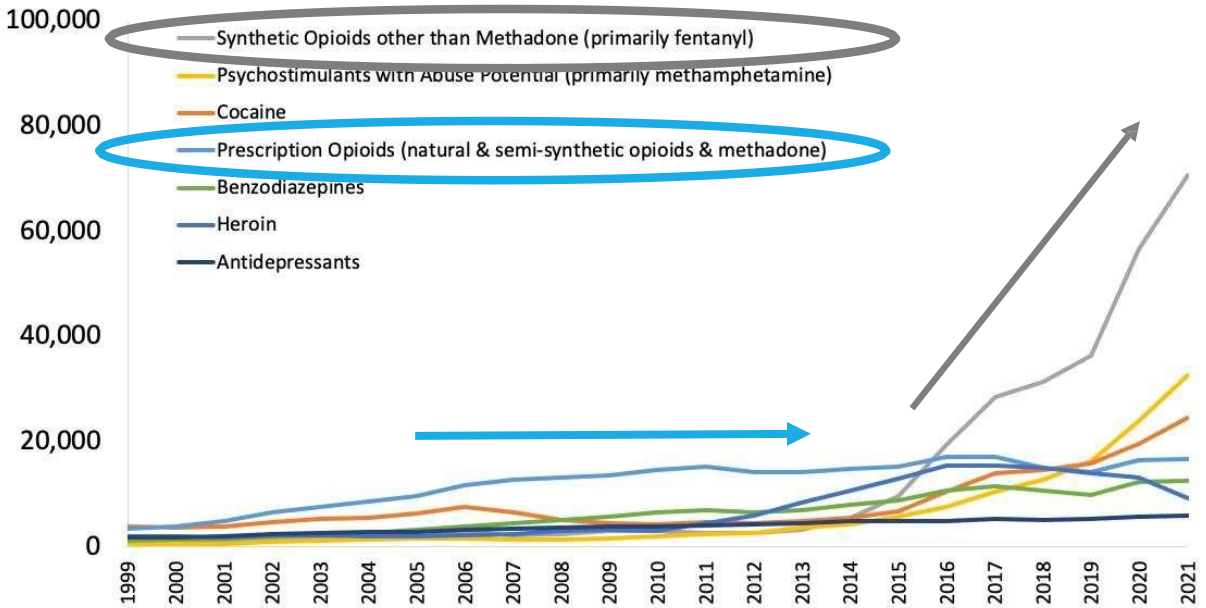




Netflix Jacqueline Cleggett

Dr. Jacqueline Cleggett was a pediatrician turned pain management doctor who was under investigation on allegations of running a pill mill in Louisiana.

Figure 2. National Drug-Involved Overdose Deaths*, Number Among All Ages, 1999-2021



105,007 deaths

*Includes deaths with underlying causes of unintentional drug poisoning (X40–X44), suicide drug poisoning (X60–X64), homicide drug poisoning (X85), or drug poisoning of undetermined intent (Y10–Y14), as coded in the International Classification of Diseases, 10th Revision. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2021 on CDC WONDER Online Database, released 1/2023.

2023

Office for National Statistics

England

Deaths related to drug poisoning in England and Wales: 2024 registrations

Deaths related to drug poisoning in England and Wales from 1993 to 2024, by cause of death, sex, age and substances involved in the death.

Total opioid related deaths in 2024: **2,621** *(2,551 in 2023)*

Of all drug-poisoning deaths in 2024, other significant drugs that were mentioned on the death certificate were:

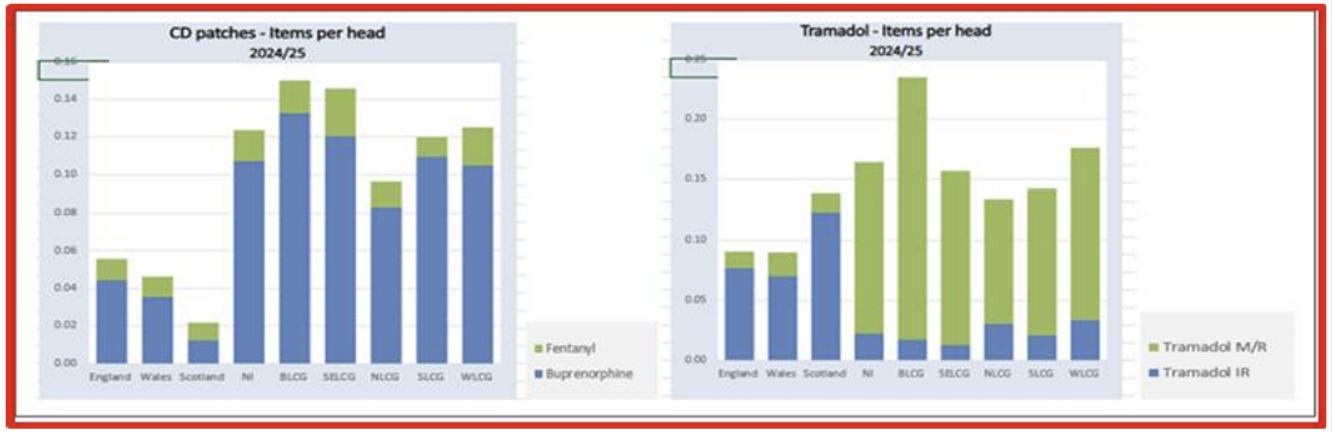
- Pregabalin, with 617 deaths
- Diazepam, with 302 deaths
- Amphetamine, with 111 deaths
- Fentanyl, with 60 deaths
- Ketamine, with 60 deaths

2026

NORTHERN IRELAND MEDICINES MANAGEMENT
Newsletter
Volume 17 Issue 1 January 2026

Avoid Modified-Release Opioids

Modified release (MR) opioids are associated with increased total opioid load, and related adverse effects including dependence. **MR opioids should be avoided** for chronic non-cancer pain unless clinical considerations or individual circumstances dictate otherwise. In Northern Ireland, prescribing of the following strong MR opioids in particular, is **significantly higher** than other parts of the UK - tramadol MR, fentanyl and buprenorphine patches.



Prescribers are reminded, for chronic non-cancer pain:

- Strong opioids are **not recommended** by NICE (exceptions only) and **not** included in the NI formulary.
- All patients prescribed opioids should be reviewed at least 6 monthly, educated on opioid risks and side-effects and alternatives to help manage pain, e.g. Community pain support programmes, "Live Well with Pain".

Offering Opioid for Non Cancer Chronic Pain



The Opioid Trial



Clearly defined pain associated with **identifiable organic disease** may respond to opioids

Poorly defined pain of uncertain aetiology (Chronic Primary Pain) or with pain disproportionate to imaging findings, would be less likely to respond to opioid therapy

Mechanism of Pain: Old Classification



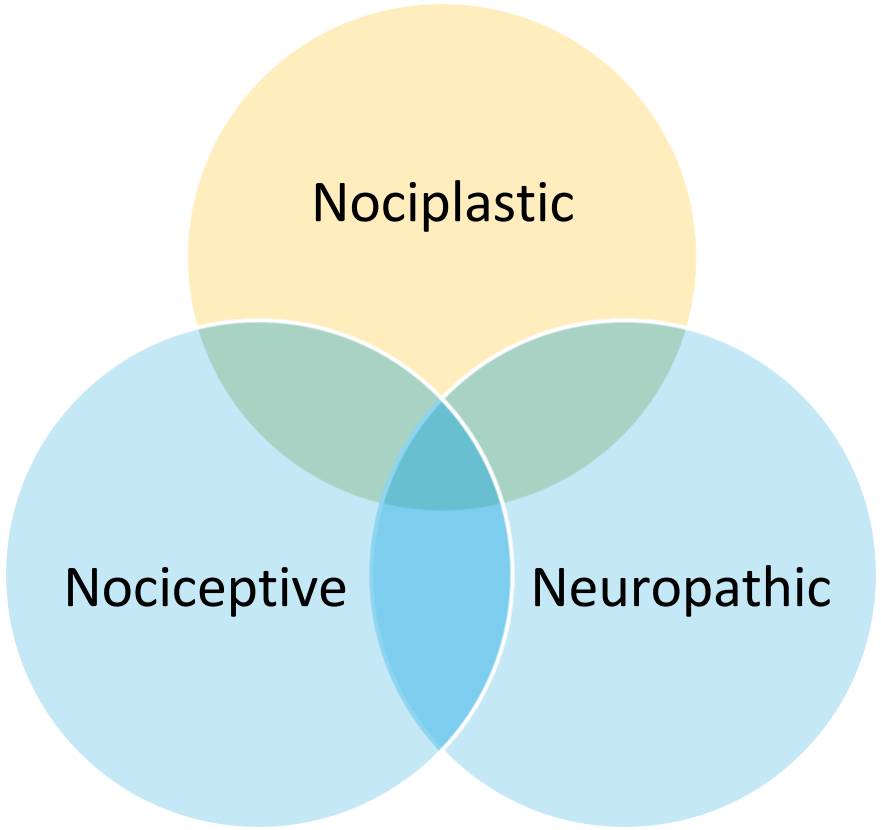
Nociceptive

Neuropathic



New

2017-2021 IASP Nociplastic Pain



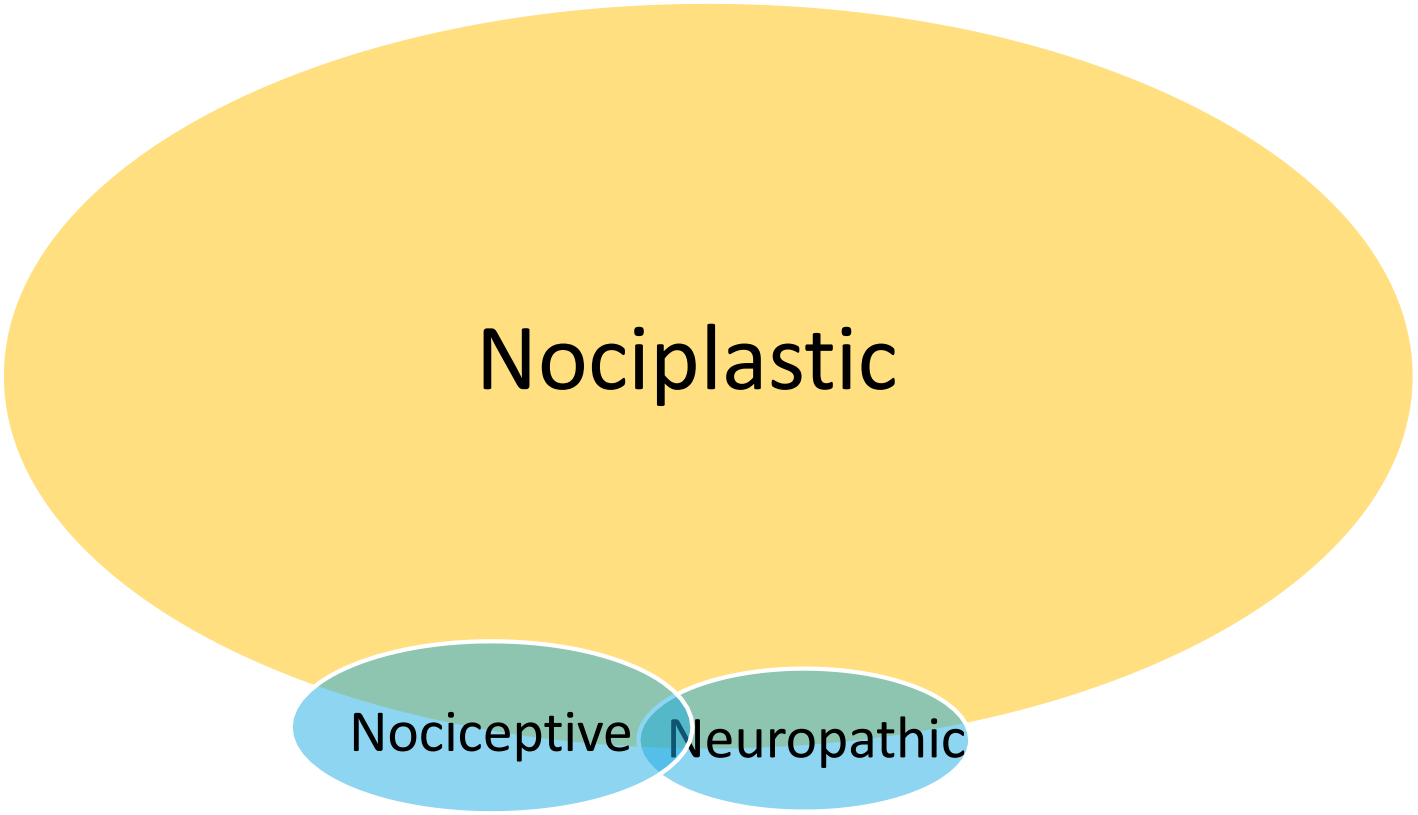
Nijs et al J Clin Med 2021 Aug.

New Classification

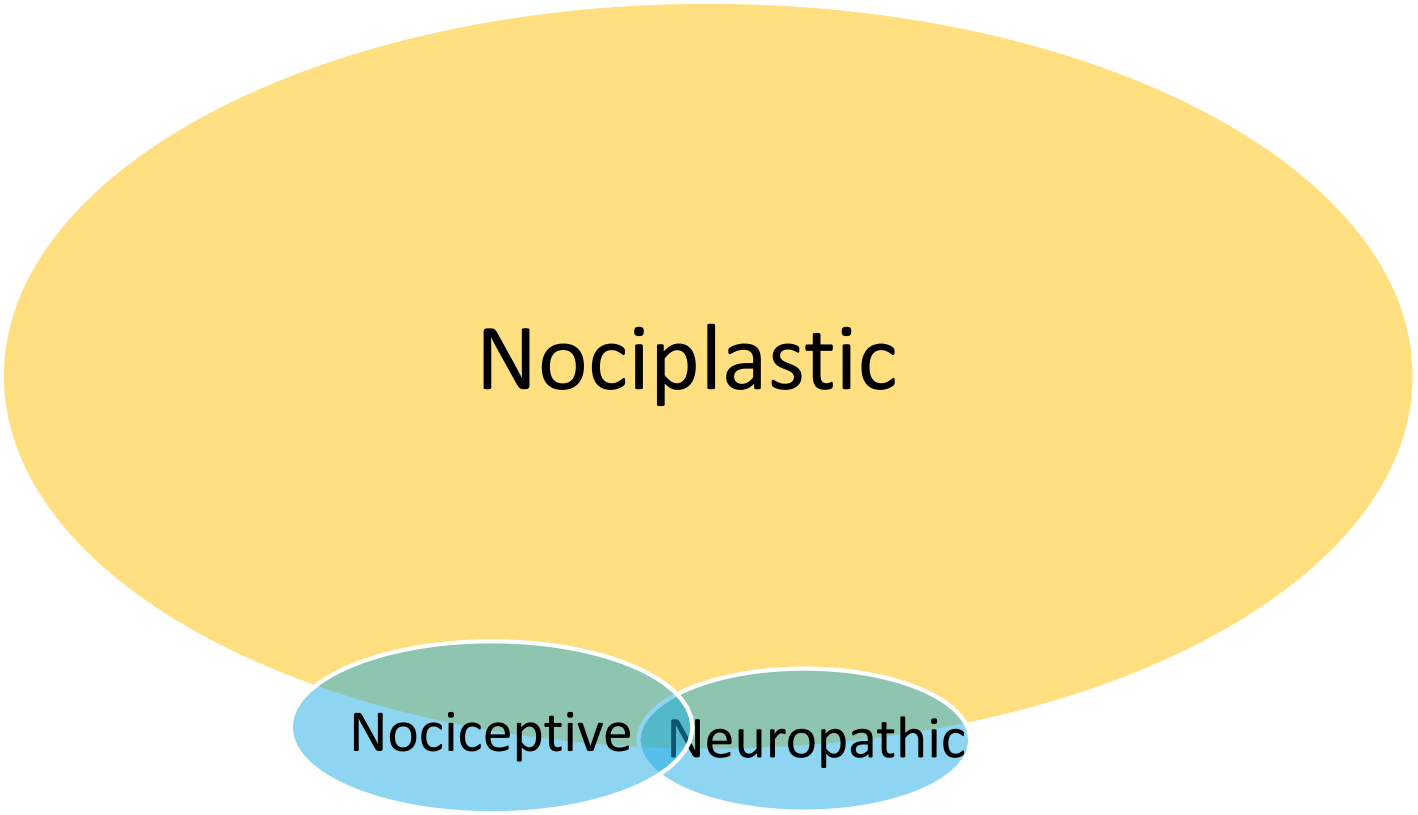
FM, IBS, Pelvic Pain (most),
BMS, Migraines, Low back pain (most)
TMD, Refractory TN, Whiplash inj,
Persistent Idiopathic Facial Pain

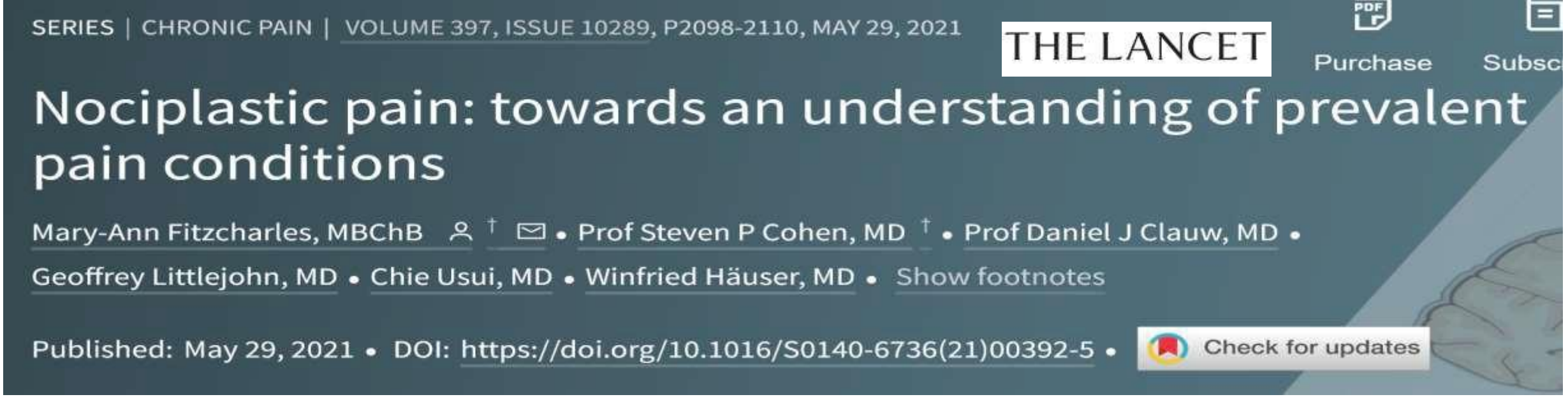
Nociplastic

Pain Clinic attendees: Predominantly Nociplastic pain picture



GP's heart-sink attendees: Predominantly Nociplastic pain picture





It is important to recognise this type of pain, since it will respond to different therapies than nociceptive pain or neuropathic pain, with a **decreased responsiveness to peripherally directed therapies such as**:

I. **Anti-inflammatory drugs**
II. **Opioids**
III. **Surgery**
IV. **Injections.**

Nociplastic Pain

2025

NORTHERN IRELAND MEDICINES MANAGEMENT

Newsletter Supplement:
Chronic Pain Management – Important Messages

April 2025

Nociplastic Pain

What is chronic pain?

Chronic (or persistent) pain, is pain that lasts for more than 3 months. Most people return to normal after an acute pain episode, e.g. after surgery or injury, however, sometimes the pain continues, or occurs without any such history. **Chronic pain is less about injury/damage and more about changes to sensitivity of the nervous system.**

Types of chronic pain

There are 2 types of chronic pain:

Chronic primary pain	No clear underlying condition, or pain impact is disproportionate to observable injury/disease, e.g. fibromyalgia, chronic primary headache/ musculoskeletal pain.
Chronic secondary pain	A symptom of an underlying condition, e.g. osteoarthritis, sciatica, neuropathic pain If medication is considered necessary, use alongside alternative strategies, and according to the relevant NICE guidance and Northern Ireland (NI) Formulary.

Note: both primary and secondary chronic pain can co-exist.

How should chronic pain be managed?

Factors such as personal beliefs, emotions and past experiences can turn the pain 'volume' up or down. **The most important aspect of chronic pain management is retraining the brain using a biopsychosocial approach.** This involves keeping active, mind-based activities and social connections. It is important to listen to the patient's pain story and use this to agree an individualised management plan.

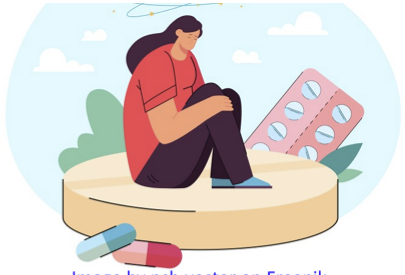


Image by pch.vector on Freepik

In this issue

- What is chronic pain?
- How should chronic pain be managed?
- Types of chronic pain
- Patient education
- Alternative strategies to manage chronic pain
- Reducing risks — Key points (opioids and gabapentinoids)
- Modified-release opioids – Increased dependence risk
- Risky opioid combinations
- Lidocaine plasters
- Further resources

Cochrane for Clinicians

Putting Evidence into Practice

Controlled-Release Oxycodone for Neuropathic Pain and Fibromyalgia in Adults

Conclusion:

Oxycodone CR has limited effectiveness for the treatment of diabetic neuropathy or post herpetic neuralgia.

Evidence is lacking regarding treatment benefit for other neuropathic pain syndromes (sciatica) or fibromyalgia.

Cochrane for Clinicians March 1, 2015 ◆ Volume 91, Number 5

2023

HSC

Department of Health
An Roinn Sláinte
Männystrie O Poustie
www.health-ni.gov.uk

NORTHERN IRELAND MEDICINES MANAGEMENT

January 2023 Volume 14, Issue 1 NEWSLETTER Strategic Planning and Performance Group

In This Issue



- Avoid opioids for chronic non-malignant pain
- NI Formulary Correction
- Appropriate prescribing of Calcium and Vitamin D supplements
- Strep A Update: Refer to these links for current guidance
- NICE Guidance — Recently Published

Avoid Opioids for Chronic Non-Malignant Pain



Opioids should **not** routinely be prescribed for chronic non-malignant pain.

There has generally been a move away from the use of medication for treatment of chronic pain due to its limited benefit (estimated 30% only). **Pharmacological treatment when considered necessary,** should be in line with NICE Guidance for Chronic Pain, where opioids have a limited role; see table for examples. Opioids are also associated with significant risks.

The Opioid Trial – Look out for

Nociplastic Pain

h/o Substance misuse

Other addictions

Psychological distress

Trauma

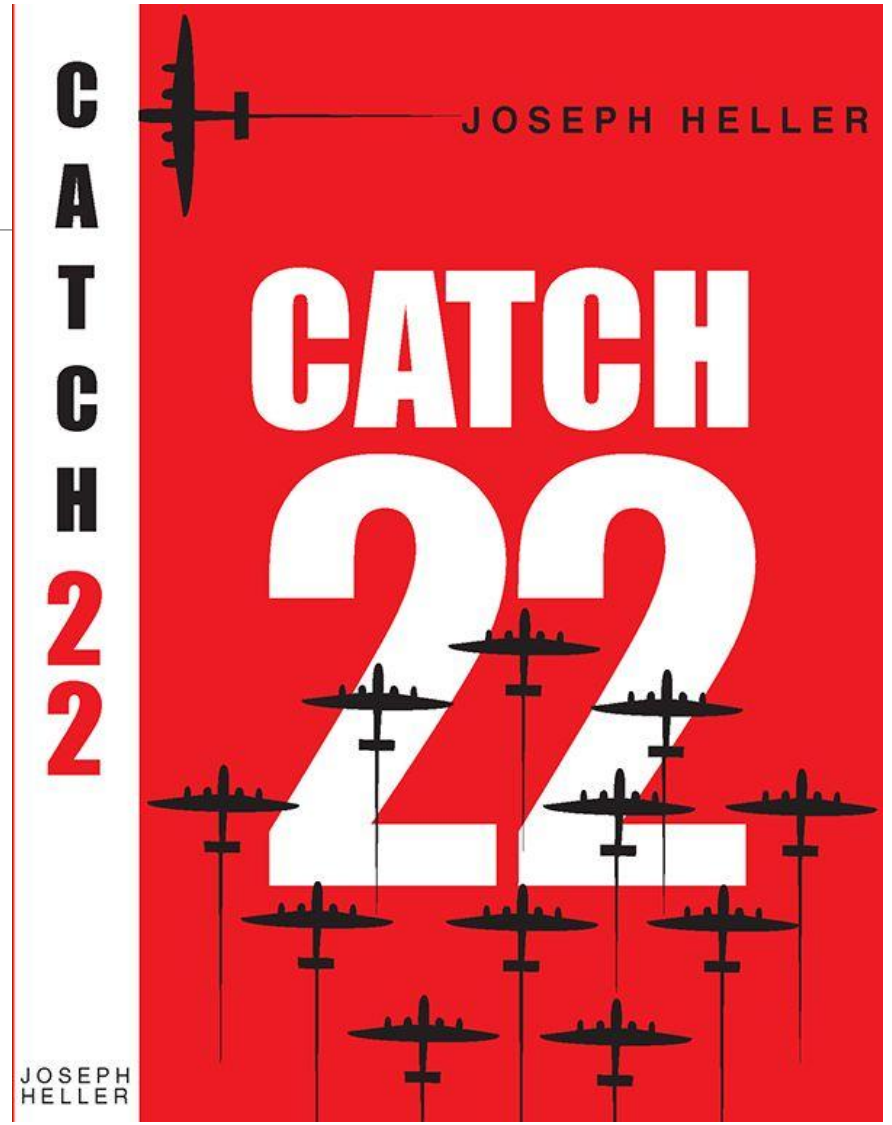
Major psychiatric co-morbidities

h/o self harm



The Opioid Trial

- Nociplastic Pain
- h/o Substance misuse
- Other addictions
- Psychological distress
- Trauma
- Major psychiatric co-morbidities
- h/o self harm



The Opioid Trial



Agree outcomes- importance on function

Duration of trial:

- **2 weeks max if pain is constant**
- **2-4 week if pain is episodic**

Choice of opioid

- a short (1-2 week supply) of immediate release morphine tablets.
- 5-10mg morphine. If 20mg Oral IR morphine tablet doesn't help – non Mu opioid responsive pain
- **Max 50mg OME**

Taper over 1 week if unsuccessful to achieve outcomes

Common opioids



	Potency	Equivalent dose to **50mg oral morphine** in 24hr	Equivalent dose to **90 mg oral morphine** in 24hr
Codeine phosphate	0.1	*240mg*	
Dihydrocodeine	0.1	*240mg*	
Hydromorphone	5	**10 mg**	**18mg**
Methadone	*	*	
Morphine	1	**50 mg**	**90mg**
Oxycodone	1.5	**33 mg**	**60mg**
Tapentadol	0.4	**125 mg**	**225mg**
Tramadol	0.1	*100mg*	
Buprenorphine	100	***20ug/hr (Butec)***	**35ug/hr (Transtec)**
Fentanyl	**100**	***25ug/hr***	**37ug/hr**

Buprenorphine

Only MR opioid preparation with some indications

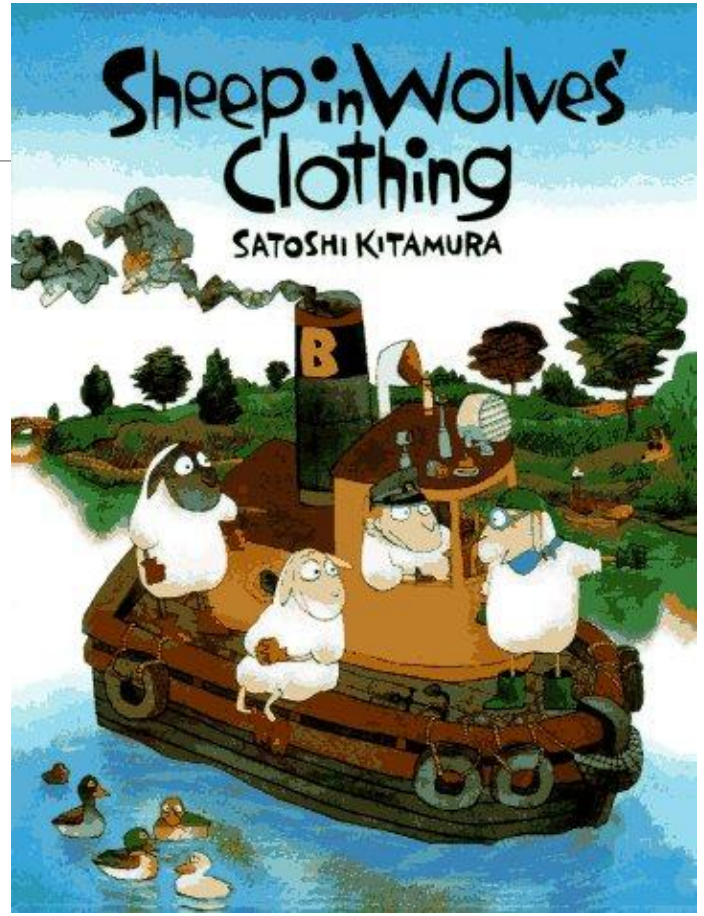
Partial mu agonist

Respiratory depression is rare (5ug-20ug/h)

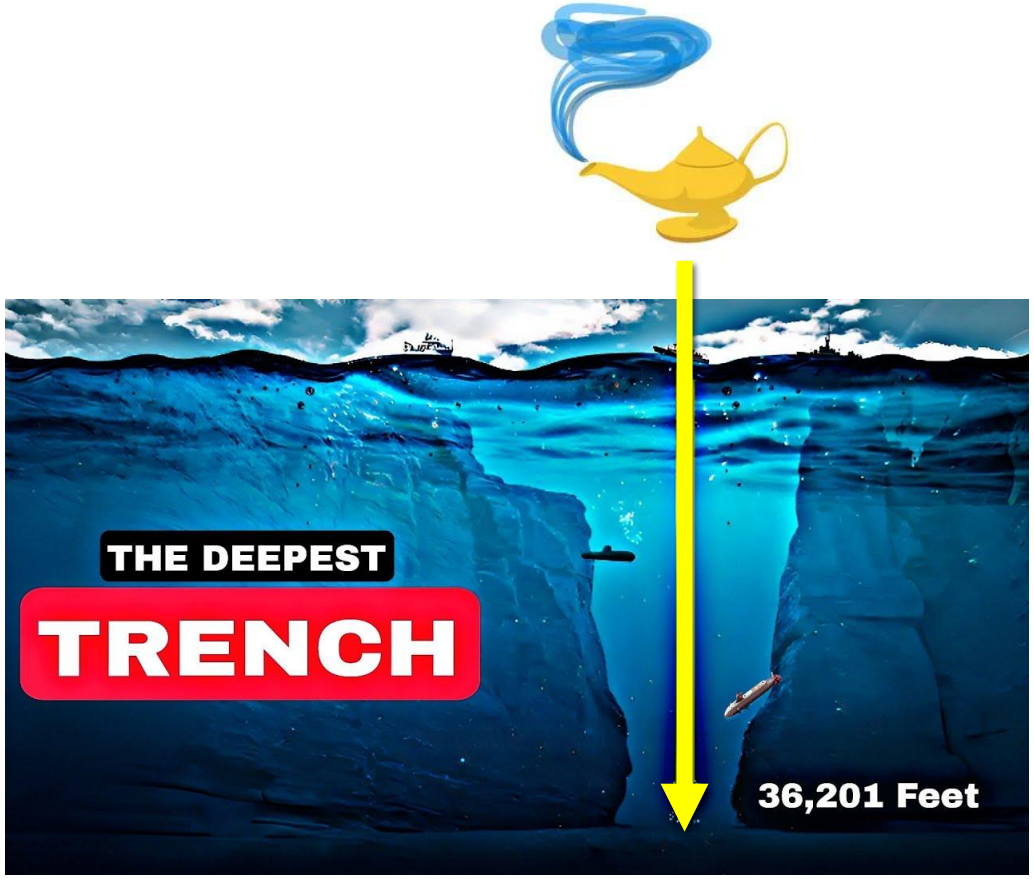
Addiction is rare

Least Sensitising opioid

Least Serotonergic opioid



Fentanyl



50mg OME / 90mg OME



Seem arbitrary

2024

Pain

RMD Open
Rheumatic & Musculoskeletal Diseases

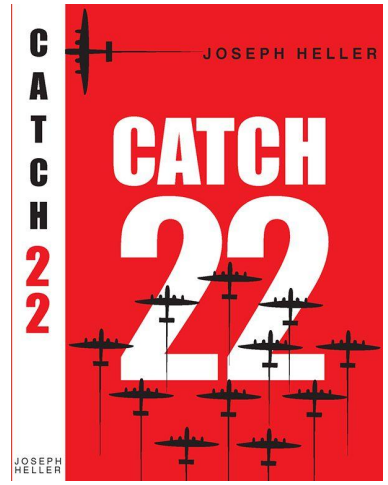
ORIGINAL RESEARCH

Machine learning identifies risk factors associated with long-term opioid use in fibromyalgia patients newly initiated on an opioid

Carlos Raúl Ramírez Medina ,[1] Mengyu Feng,[1] Yun-Ting Huang ,[1]
David A Jenkins,[2] Meghna Jani [1,3,4]

28,552 FM patients

26% ended up as long term users



2024

Pain

RMD Open
Rheumatic & Musculoskeletal Diseases

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Initial Trial dose <50mg OME	1
Initial Trial dose > 120 mg OME	31.9
Initial Trial dose 50-119 mg OME	7.5
Morbid Obesity	2.4
Substance use disorder	2
Obesity	1.6

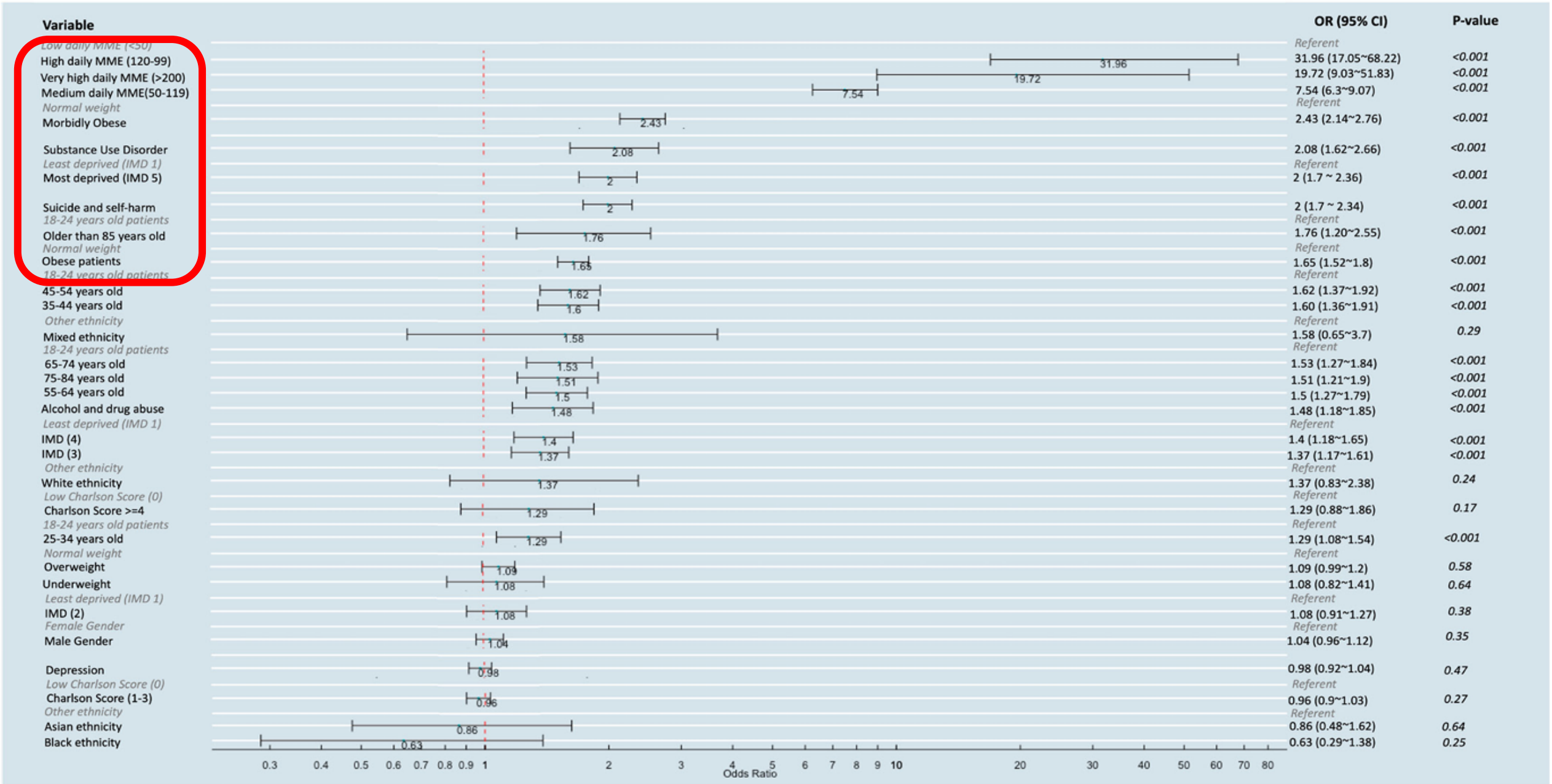


Figure 2 Factors associated with long-term opioid use in fibromyalgia patients ranked by adjusted Odds Ratio. IMD, Index of Multiple Deprivation; MME, morphine milligram equivalents.

Only one way to wean



Only one way to wean





Motivational Interviewing

A change can be successfully implemented if the reason for change comes from within

Long term harm opioids

Unintentional overdose- Patches & Long acting preparations

Sexual dysfunction and infertility ★

Falls and Fractures ★

Osteoporosis ★

Increased risk of MI

Reduced immunity ★

Adrenal insufficiency

Central Sensitisation (OIH) ★

Opioid Induced Androgen Deficiency (OIAD)

as short as **one week** exposure.

One systematic review and meta-analysis found that **hypogonadism is present among approximately 63% of male patients** on long-term opioids.

Opioids and Their Endocrine Effects: A Systematic Review and Meta-analysis. *The Journal of Clinical Endocrinology & Metabolism.* 2019;105(4):1020-1029.

Opioid Induced Androgen Deficiency (OIAD)

Sex hormone deficiency	Adrenal insufficiency
Anaemia **decreased libido** decreased muscle mass depression **erectile dysfunction** fatigue menstrual irregularities **osteoporosis** vasomotor instability **weight gain**	Fatigue malaise abdominal discomfort, anorexia orthostatic hypotension

Opioid-induced endocrinopathy. *Journal of Osteopathic Medicine*. 2009;109(1):20-25

Opioids and Their Endocrine Effects: A Systematic Review and Meta-analysis. *The Journal of Clinical Endocrinology & Metabolism*. 2019;105(4):1020-1029.

Fracture and Falls risk

OR **4.49** **risk of Fractures in opioid users** vs non opioid users

Falls risk is increased at initiation and escalation of opioids

400% increased risk of fall & fracture

Opioids and the Risk of Fracture: A Self-Controlled Case Series Study in the Clinical Practice Research Datalink. Am J Epidemiol. 2021 Jul

Opioid Induced Immunosuppression

Bind to **μ-opioid receptor on immune cells**

Act by activating the descending pathways of the HPA axis and the sympathetic nervous system, **glucocorticoids are released**, along with **noradrenaline**, both acting on leucocytes resulting in reduction of immune response.

Very relevant to those with an **immunosuppressed status, due to frailty, disease such as cancer or HIV, or those who have undergone invasive surgery** should be considered when treating with opioids.

Opioids and the immune system. Palliative medicine. 2006;20(8_suppl):9-15.

Non-analgesic effects of opioids: mechanisms and potential clinical relevance of opioid-induced immunodepression. Current pharmaceutical design. 2012;18(37):6034-6042.

Opioid Induced Hyperalgesia

Abnormal pain sensitivity, where patients receiving opioid therapy become more sensitive to pain

Central Sensitisation caused or worsened by opioids

Management:

- Non Cancer Pain -> **slow wean**
- Cancer pain -> **wean and switch**

*Patients who started with **Nociplastic disorders are naturally at a risk** of OIH*

A comprehensive review of opioid-induced hyperalgesia. *Pain physician.* 2011;14(2):145

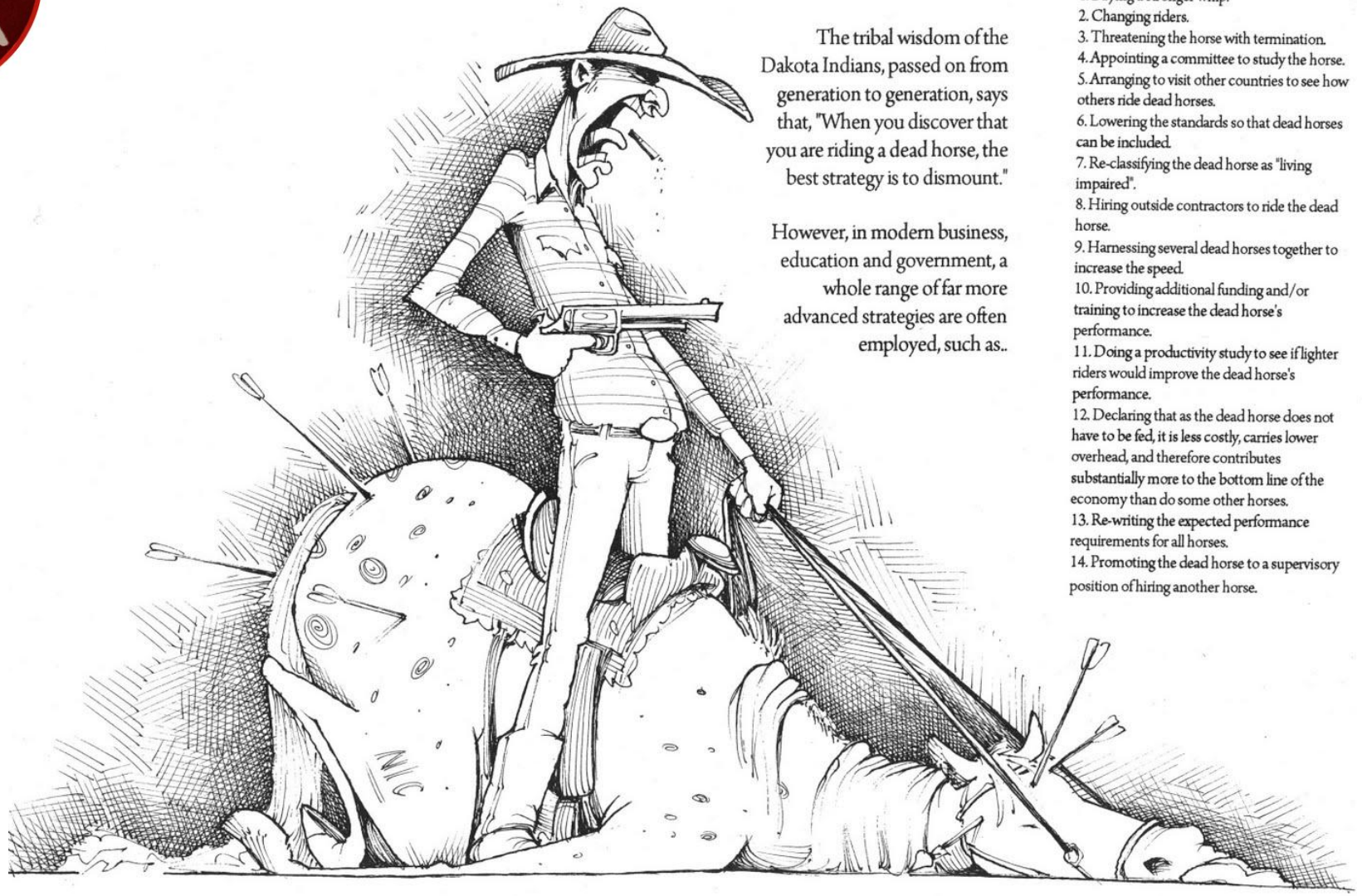
Only one way to wean

- **Patient should feel the need to wean**
- **No replacement strong opioids**
- **Flareups will happen- that is natural for all Ch. Pain** (even if they don't wean)
- **Pause during a wean is permissible**; shared decision
- **Reduce by** 5-10% between 2-6 weekly
- Usually stopping medicines makes no difference to the pain but can **make people feel better** (being more awake, more energy, engage with surrounding)
- Switching to another strong opioid is generally applicable to palliative setting

What happens in the real world ?



THE DEAD HORSE THEORY



The tribal wisdom of the Dakota Indians, passed on from generation to generation, says that, "When you discover that you are riding a dead horse, the best strategy is to dismount."

However, in modern business, education and government, a whole range of far more advanced strategies are often employed, such as..

1. Buying a stronger whip.
2. Changing riders.
3. Threatening the horse with termination.
4. Appointing a committee to study the horse.
5. Arranging to visit other countries to see how others ride dead horses.
6. Lowering the standards so that dead horses can be included.
7. Re-classifying the dead horse as "living impaired".
8. Hiring outside contractors to ride the dead horse.
9. Harnessing several dead horses together to increase the speed.
10. Providing additional funding and/or training to increase the dead horse's performance.
11. Doing a productivity study to see if lighter riders would improve the dead horse's performance.
12. Declaring that as the dead horse does not have to be fed, it is less costly, carries lower overhead, and therefore contributes substantially more to the bottom line of the economy than do some other horses.
13. Re-writing the expected performance requirements for all horses.
14. Promoting the dead horse to a supervisory position of hiring another horse.













D HORSE THEORY



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End result:

- Ineffective Polypharmacy
- Opioid / Gabapentinoid related deaths
- Serotonin Toxicity
- Anticholinergic crisis
- **Dependence**
- **Tolerance**
- **Drug seeking behaviour**

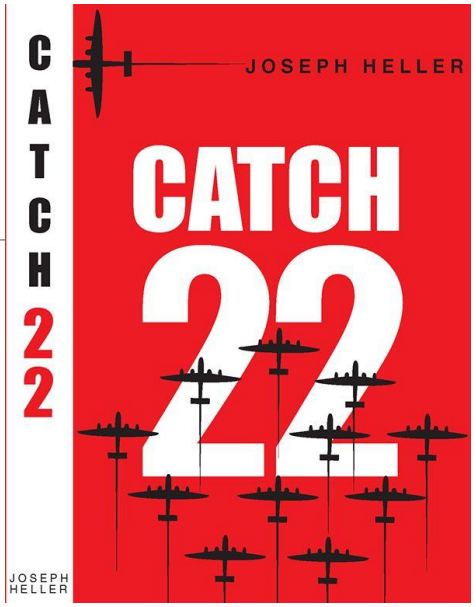
Long term

- ……..we wish, we hadn't let the genie out !



Summary

- **Opioids are great for acute pain in ALL patients**
- Think about **Catch 22** before you let the **genie out**
- MR preparations are problematic
- **50mg OME** is the STOP line for an opioid trial.
- **90mg OME** is the **'Risk Threshold'**
- Easier to implement change if the **need for that change comes from within**
- **Replace** rather than **Add**
- **The only option while riding a dead horse is to dismount**



Questions ?

