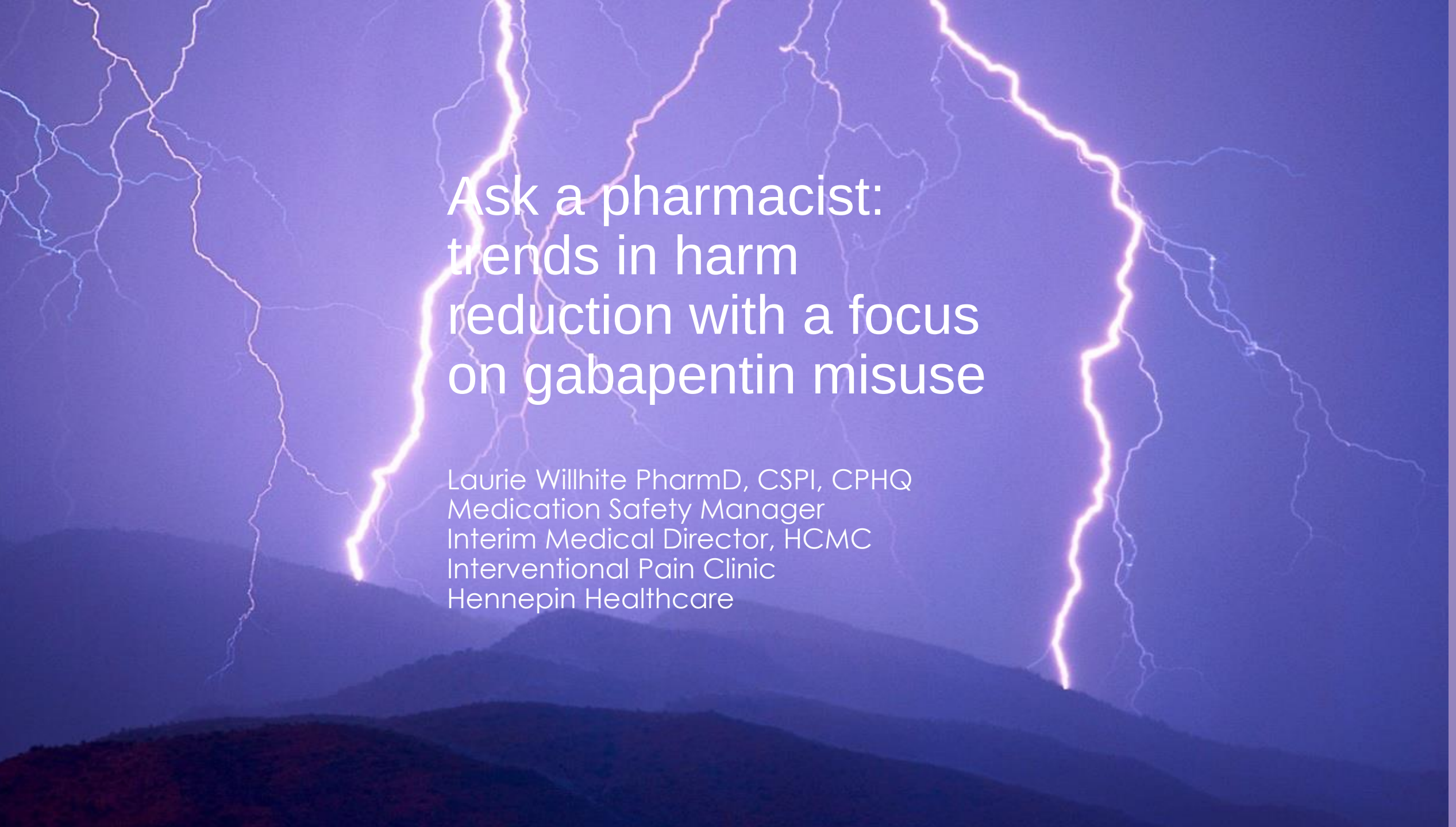


Ask a pharmacist: trends in harm reduction with a focus on gabapentin misuse

Laurie Willhite PharmD, CSPI, CPHQ
Medication Safety Manager
Interim Medical Director, HCMC
Interventional Pain Clinic
Hennepin Healthcare

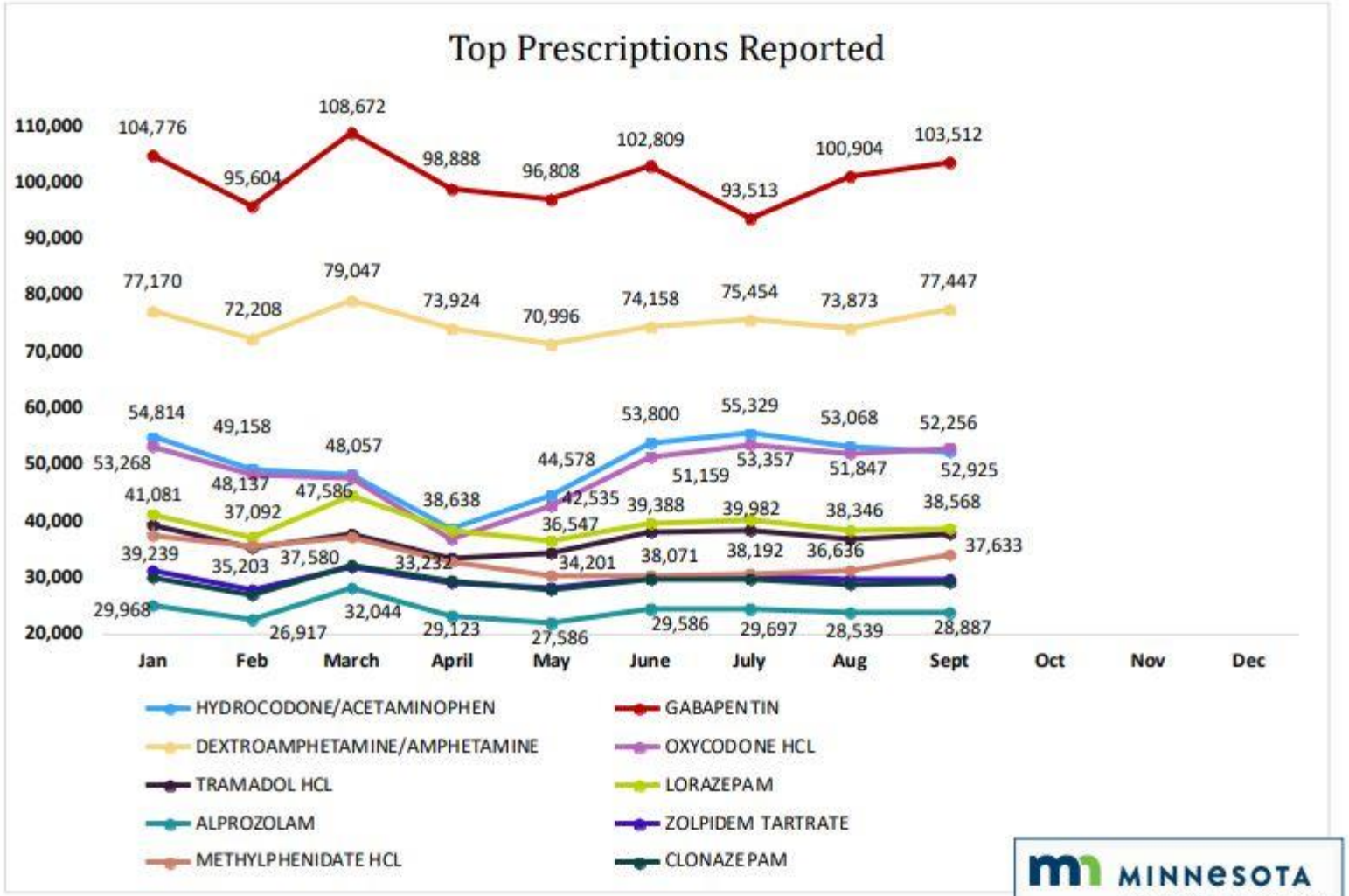
Objectives

- At the end of this presentation, the participate will be able to

  - Discuss prescribing trends of opioid pain medication and other controlled substances
  - Weight the risks and benefits of gabapentin and opioid prescribing together
  - Discuss the adverse effects and misuse of gabapentin

  Time for questions at the end: fentanyl, benzodiazepines

Minnesota PMP data

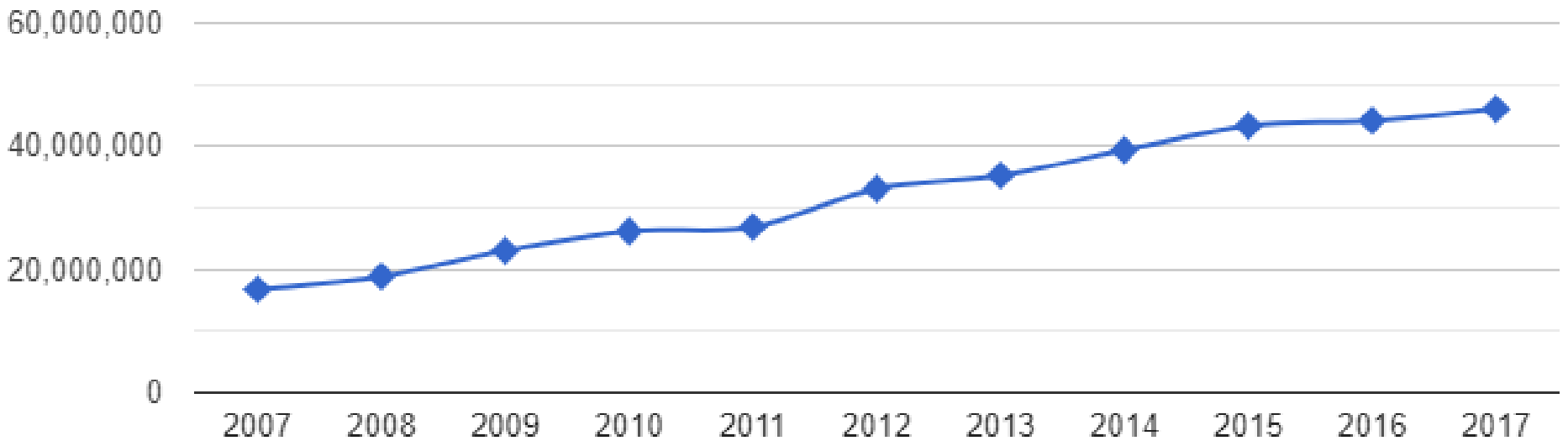


MINNESOTA BOARD OF PHARMACY
PRESCRIPTION MONITORING PROGRAM

Contact: Minnesota Prescription Monitoring Program minnesota.pmp@state.mn.us 651.201.2836

Gabapentin Rxs in the US

https://clincalc.com/DrugStats/Drugs/Gabapentin



Gabapentin: What it is used for

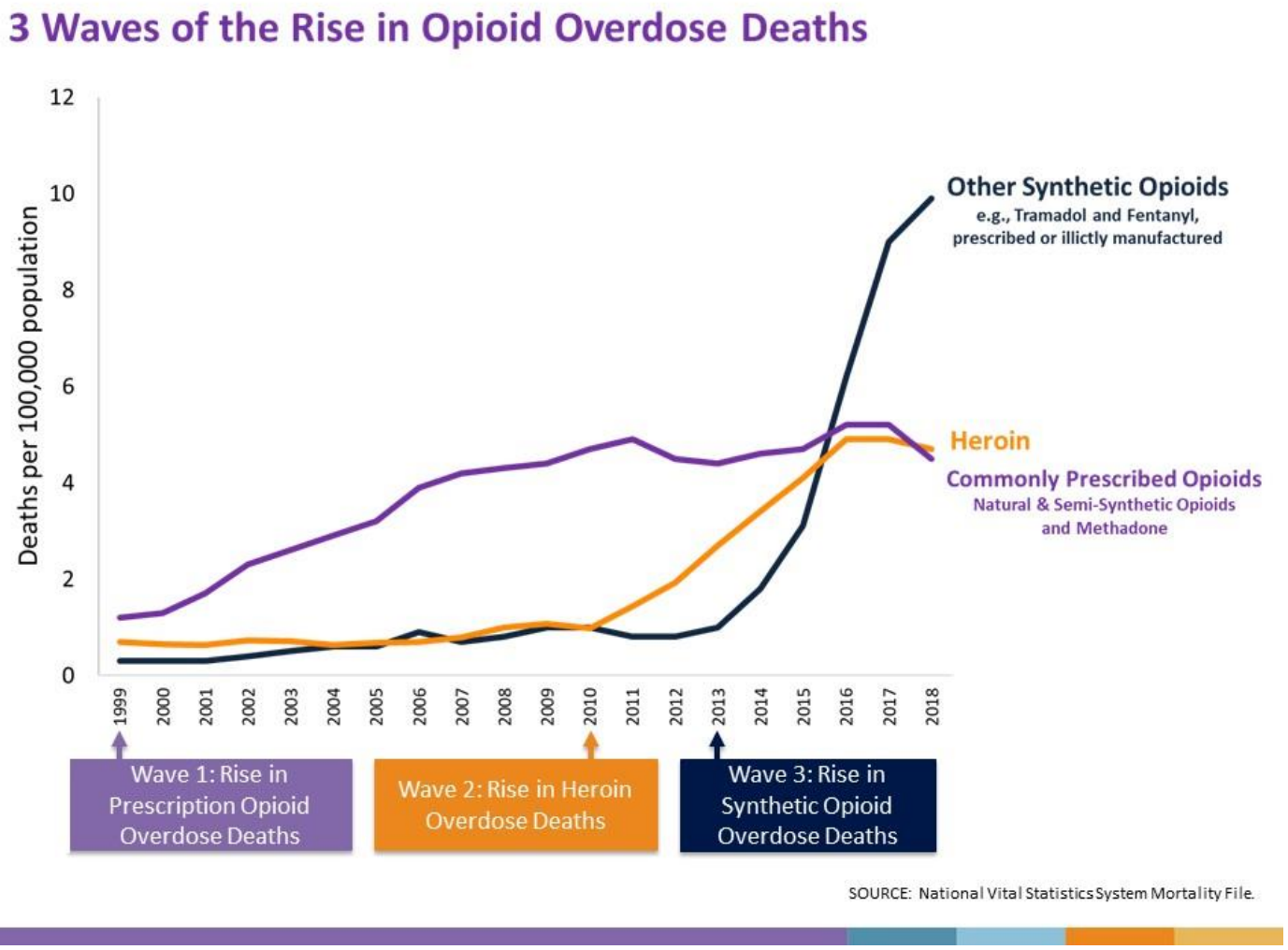
FDA Approved

- Seizures
- Nerve pain from shingles

Other uses

- Nerve pain from spinal cord injury, post herpetic neuralgia, diabetic peripheral neuropathy, chemotherapy and HIV
- Non neuropathic pain disorders
- Fibromyalgia
- Restless legs syndrome
- Anxiety

Why gabapentin?



Why gabapentin

- A legacy of off-label marketing for pain, manufacturers fined $
  - gabapentin (remember, only approved for shingles pain
  - pregabalin (approved for fibromyalgia, diabetic neuropathy and PHN)
- Ibuprofen and acetaminophen don’t work, aren’t tolerated or are the patient cannot use them
- Patient satisfaction
- Non pharmacologic therapies such as pain psychology, alternative therapies, referral to a comprehensive pain program may not be well accepted or readily available

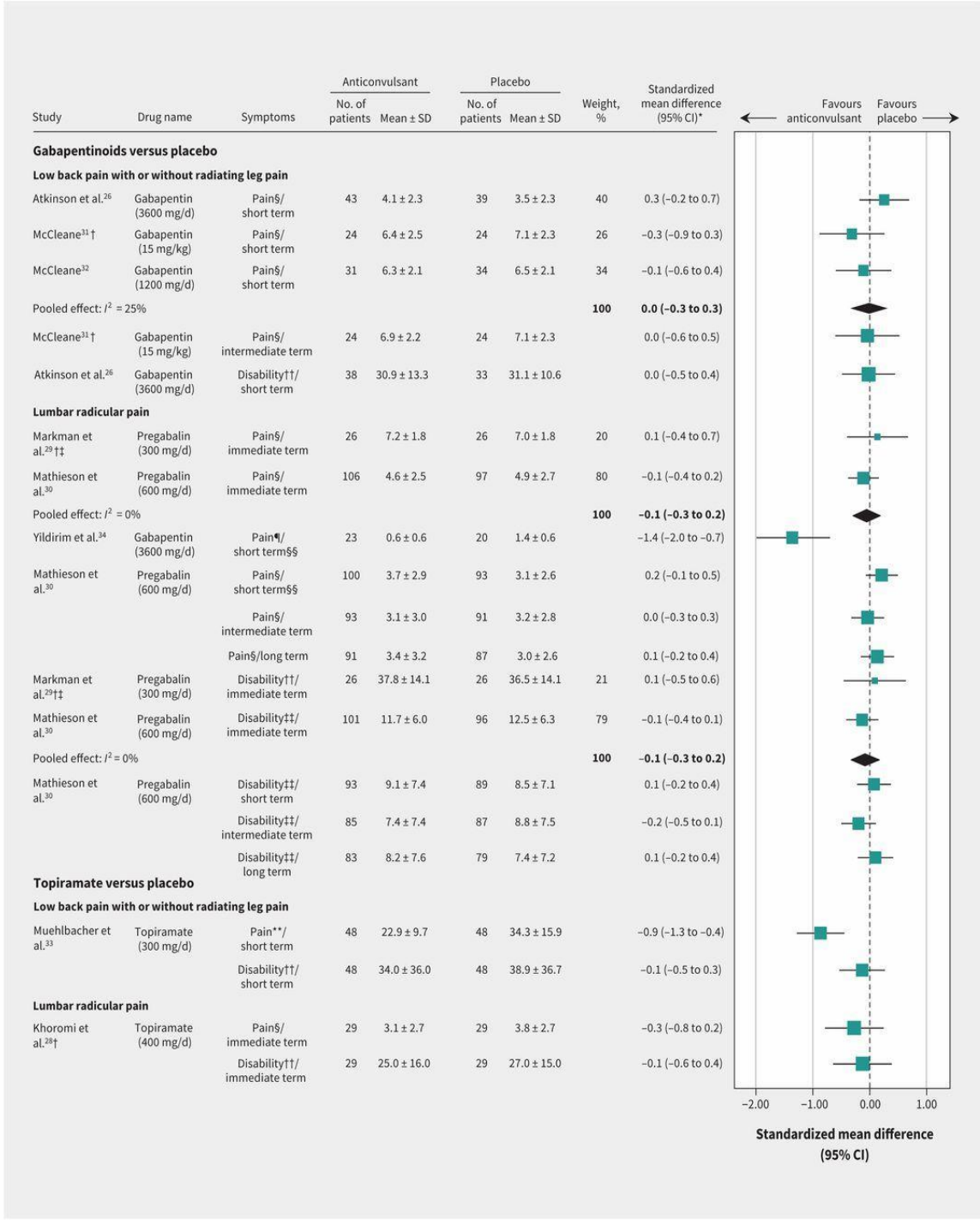
What is the problem

- Reinforces the tendency to view the treatment of pain as something you need pills for
- Side effects
- Misuse

Back pain

Low evidence if any to support gabapentin for back pain

https://www.cmaj.ca/content/190/26/E786



Duloxetine

Indication	Starting Dose	Target Dose	Maximum Dose
MDD (2.1, 2.2)	40mg/day to 60mg/day	Acute Treatment: 40 mg/day (20 mg twice daily) to 60 mg/day (once daily or as 30 mg twice daily); Maintenance Treatment: 60 mg/day	120 mg/day
GAD (2.1)	60 mg/day	60 mg/day (once daily)	120 mg/day
DPNP (2.1)	60 mg/day	60 mg/day (once daily)	60 mg/day
FM (2.1)	30 mg/day	60 mg/day (once daily)	60 mg/day
Chronic Musculoskeletal Pain (2.1)	30 mg/day	60 mg/day (once daily)	60 mg/day

- Some patients may benefit from starting at 30 mg once daily.
- There is no evidence that doses greater than 60 mg/day confers additional benefit, while some adverse reactions were observed to be dose-dependent.
- Discontinuing Cymbalta: A gradual dose reduction is recommended to avoid discontinuation symptoms (5.6).

Neuropathic Pain

Causes

- Diabetic neuropathy
- Cervical or lumbar radiculopathy
- Post herpetic neuralgia
- Spinal cord injury
- Trigeminal neuralgia
- Chemotherapy-related neuropathic pain
- HIV-related neuropathic pain
- Post stroke pain

How does this pain feel?

- Pain
  - Paresthesia –tingling, foot falling asleep)
  - Allodynia
  - Burning, shooting pain
  - Pain with walking (ie walking over hot or cold, walking over glass)
  - Sensations of heat or cold
  - Usually more severe at night (causes sleep disturbance)
- Associated symptoms
  - Sleep disturbances
  - Balance problems, falls

Assessment Tools

Neuropathic Pain Questionnaire – Short form

Tingling Pain

0 ←= =→ 100

No Tingling Pain	Worst Tingling Pain Imaginable	Please rate your <u>usual</u> pain: ________

Numbness

0 ←= =→ 100

No Numbness Sensation	Worst Numbness Imaginable	Please rate your <u>usual</u> pain: ________

Increased pain due to touch

0 ←= =→ 100

No Increase At All	Greatest Increase Imaginable	Please rate your <u>usual</u> pain: ________

Backonja, Clinical J Pain 2003

Assessment of neuropathic pain – DN4 Questionnaire

Interview of the patient			
Question 1	Does the pain have one or more of the following characteristics?		
	1. Burning	☐ Yes	☐ No
	2. Painful cold	☐ Yes	☐ No
	3. Electric shocks	☐ Yes	☐ No
Question 2	Is the pain associated with one or more of the following symptoms in the same area?		
	4. Tingling	☐ Yes	☐ No
	5. Pins and needles	☐ Yes	☐ No
	6. Numbness	☐ Yes	☐ No
	7. Itching	☐ Yes	☐ No

Examination of the patient			
Question 3	Is the pain located in an area where the physical examination may reveal one or more of the following characteristics?		
	8. Hypoesthesia to touch	☐ Yes	☐ No
	9. Hypoesthesia to prick	☐ Yes	☐ No
Question 4	In the painful area, can the pain be caused or increased by:		
	10. Brushing	☐ Yes	☐ No

Diabet Med 2011.

Treating Neuropathic Pain: Expert Guidelines

American Diabetes Association Position Statement: Diabetic Neuropathy 2017

- Pregabalin or duloxetine as the first- line agents [A]
- Gabapentin may also be used as a second-agent, taking into account patients' socioeconomic status, comorbidities, and potential drug interactions. [B]
- Tricyclic antidepressants are also effective, but should be used with caution given the higher risk of serious side effects. [B]
- Use of opioids, including tapentadol or tramadol, is not recommended as first- or second-line agents. [E]

ADA= American Diabetes Association
Diabetes Care 2017 Jan; 40(1): 136-154

Pharmacotherapy for Neuropathic Pain : Recommendations from ISAP

First line	Second line	Third line
• SNRIs: Venlafaxine and duloxetine (High;Strong)* • Gabapentin and pregabalin (High; Strong) • Tricyclic antidepressants (Moderate; Strong)	• Capsaicin 8% patches (High; Weak) • Tramadol (Moderate; Weak) • Lidocaine patches (Low; Weak)	• Strong opioids (Moderate; Weak) • Botulinum Toxin A (Moderate; Weak)

ISAP= International Association for the Study of Pain

Lancet Neurol 2015; 162–73

* Eg high quality of evidence/strong recommendation for use

Pharmacotherapy for Neuropathic Pain in Adults- expert guidelines

Strong recommendations AGAINST use	Weak recommendations AGAINST use	Inconclusive recommendations
•Levetiracetam •Mexiletine	•Cannabinoids •Valproate	•Combination therapy •Capsaicin cream •Carbamazepine •Clonidine topical •Lacosamide •Lamotrigine •NMDA antagonists •Oxcarbazepine •SSRI •Tapentadol •Topiramate •Zonisaminde

HennepinHealthcare

ISAP= International Association for the Study of Pain
NeuPSIG- Neuropathic Pain Special Interest Group
Lancet Neurol 2015; 162–73

Gabapentin + Opioids

- Opioids slow down the gut, increasing gabapentin absorption by 44%

- Patients on gabapentin doses >900 mg per day with opioids were 60% more likely do die from an opioid related death even when opioid dose is controlled for.
    - http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1002396http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1002396

Using gabapentin safely

Consider tapering down from doses >1800 mg.

If increasing dosing to >900 mg per day with opioids, carefully document and assess risk/benefit, and provide naloxone

Avoid using with opioids, benzodiazepines, other meds that cause drowsiness.

The FDA has required new warnings for gabapentin about the risk of life-threatening or fatal breathing problems in patients with lung disease, elderly

Avoid gabapentin and hydrocodone together in particular

Need to adjust dose if kidney problems

Gabapentin misuse: Why?

- Widespread availability
- Not a controlled substance in Minnesota
- Sedating and euphoric effects
- Not commonly detected on urine drug screens

Gabapentin misuse

- Increases effects of opioids
- Cocaine users use it alone or in combination with quetiapine (Seroquel)
- Both drugs have been restricted from correctional facility formularies
  - 2004 audit in a Florida correctional facility showed that only 20% of the gabapentin was in possession of the intended patient
  - Switched to a PA system with tablets only, not capsules

- Annals Pharmacotherapy 2016;50:229-233.
- Am J Addict 2004;13:321-323.

Gabapentin misuse

- Among 503 misusers of prescription opioids in KY not currently in addiction treatment
  - 15% were misusing using gabapentin
  - Oxycodone, Suboxone and benzodiazepine use common
  - Sources:
    - Prescribers 52%
    - Illicit sources 36%
      - Am J Psychiatry 2015;172:5.
- About 20% of a large sample of UDS in a toxicology laboratory were positive for non-prescribed gabapentin

AACC mtg abstract B 324 http://www.abstractsonline.com/Plan/ViewAbstract.aspx?sKey=67c97692-b33b-48a8- 9fb5-1bf308bcfba5&cKey=723b5fa2-bc2a-4c02-9a6e-6516bc026c5a&mKey=d4cbe046-6d73-41d9-840f- d1d61d62bcab#

Trends in Gabapentin Misuse Reported to Poison Centers, 2012-2015

- Review of gabapentin abuse reported to the National Poison Data System (NPDS) between January 2012 and December 2015, using search terms, "gabapentin" and "abuse".
- Results:
  - 6239 cases of gabapentin abuse reported to poison centers during the study period.
  - Gabapentin was the sole agent of abuse in 2195 (35.2%) cases.
  - Major effects were observed in 5.48% of patients, 28.7% had moderate effects, and 31.8% described minor effects.
  - Mean annual prevalence of gabapentin abuse reported to poison centers rose from 2.69 cases per million in 2012 to 9.18 cases/million in 2015.
  - West Virginia and Kentucky have the highest average prevalence during this period (35.5 and 33.6 cases/million, respectively).
  - Intubation occurred in 369 cases, and of these, only 34.9% were associated with gabapentin abuse alone.
  - Sedation was the most common reported effect in 45.9% of cases of gabapentin abuse alone.
  - Deaths comprised 22 cases, and were more likely to be associated with polysubstance ingestion (95%).
- Discussion: Reports of gabapentin abuse to PCs have tripled between 2012- 2015. Approximately 2/3rds of gabapentin abuse occurs with other substances

NACCT 2017 abstract #184

Gabapentin Withdrawal

- Onset 12h to 7 days after last use (usually 24-48 hours)
- Symptoms reported in case reports:
  - Agitation (>50%)
  - Confusions and disorientation (45%)
  - Sweating (36%)
  - GI symptoms (23%)
  - Less common:
    - Tremor, tachycardia, hypertension and insomnia

Summary: Appropriate gabapentin use

- Use only for conditions in which it is effective, titrate up to 900 mg - 1800 mg and talk to your doctor about stopping it if

- Check MN PMP

provide naloxone if patient using opioids

- Monitor for early refill requests, other concerning behavior

- Be mindful of patients at increased risk

- Use more non medication therapies; medication alternatives are duloxetine, acetaminophen, oral and topical NSAIDs

Other topics

Fentanyl

Fentanyl test strips

Medications for Opioid Use Disorder

Questions?