

# Gabapentinoids-Use, Misuse and Diversion

Carolyn Warner-Greer MD

**BOWEN**  
CENTER

# Gabapentoids

- Gabapentin (Neurontin, Horizant, Gralise)
- Pregabalin (Lyrica)
- Structurally similar to GABA
  - Do not act on GABA receptors
  - Act on voltage gated  $\text{Ca}^{2+}$  channels → increase GABA in brain
  - Produce relaxation and euphoria
  - NNT GABA ~NNT NSAID (better safety profile in most)
  - Most pronounced with first uses as well as supratherapeutic doses

# Pregabalin vs. Gabapentin

- Pregabalin-Schedule V medication
  - Higher affinity to VACC
  - Bioavailability of 90%
  - Rapid oral absorption
  - Post marketing data (2007) coincided with emergence of opioid crisis
- Gabapentin
  - Bioavailability decreases with increased doses (60% with 900 mg vs 27% with 4,500 mg)
  - Released in 1993



# FDA Approved Indications

- Pregabalin
  - Diabetic neuropathy
  - Post-herpetic neuropathy
  - Fibromyalgia
  - Neuropathic pain with spinal cord injury
  - Partial seizures

# FDA Approved Indications

- Gabapentin
  - Partial seizures
  - Post-herpetic neuralgia
  - RLS (gabapentin enacarbil only)
- HOWEVER
  - 83-94% (90% of RX) are written for off-label uses, 5<sup>th</sup> highest RX for Indiana Medicaid
  - Off label uses have limited/no evidence
  - Pfizer fined \$420 million for illegal marketing of gabapentin
  - To date, off labeled marketing → \$755 million in fines

# Prevalence of RX

- Between 2012-2016
  - # Pt. who filled GABA RX: 8.3 M→13.1 M
  - # Pt. who filled PREGAB: 1.9 M→2.1 M
- 14-20% of RX for GABA in 2016 also included OPI
- Goal to “prescribe something besides BZP and OPI”

# Vital Tool for Pain Management

- Alone, minimal addictive potential
- Individuals with central sensitization/neuropathic pain
  - Neuropathic vs. sensitization
- NNT~3-8 (similar to NSAID's)
- Safety profile due to dose limiting absorption
- This can be mistakenly extrapolated to “ANYONE” with pain



# Utility in Treating AUD

- Reduced SX associate with withdrawal
- Improved rates of abstinence
- Improved rates of reduction in heavy drinking days
- Improved measures of:
  - Mood
  - Sleep
  - Cravings



# “Opportunistic Drug Of Abuse”

- Low cost
- Poor oral bioavailability → supratherapeutic doses RX
- Current classification as a non-controlled substance
- Increased rates of off label prescribing
- HCP desire to prescribe “non-addicting” medication for pain, anxiety

## Accidental opioid overdose increases when opioids are co-prescribed with gabapentin



**60%** Increase in odds of accidental opioid-related death when opioids are co-prescribed with moderate and high dose gabapentin compared to opioid use alone.

**2x** The risk of accidental opioid overdose nearly doubled with a co-prescription of very high dose gabapentin and opioids.

**46%** Of all gabapentin users were co-prescribed an opioid in 2013, making the risk of overdose particularly concerning as these drugs are often used together.

**ODPRN**

Gomes et al. Gabapentin, opioids and the risk of opioid-related death: A population-based nested case-control study. PLoS Medicine, 2017.



**St. Michael's**  
Inspired Care.  
Inspiring Science.



As of May 2017:  
**GABAPENTIN**  
became **5<sup>th</sup>** AS THE MOST  
PRESCRIBED  
MEDICATION

In the United States under  
hydrocodone, levothyroxine,  
prednisone, and amoxicillin.

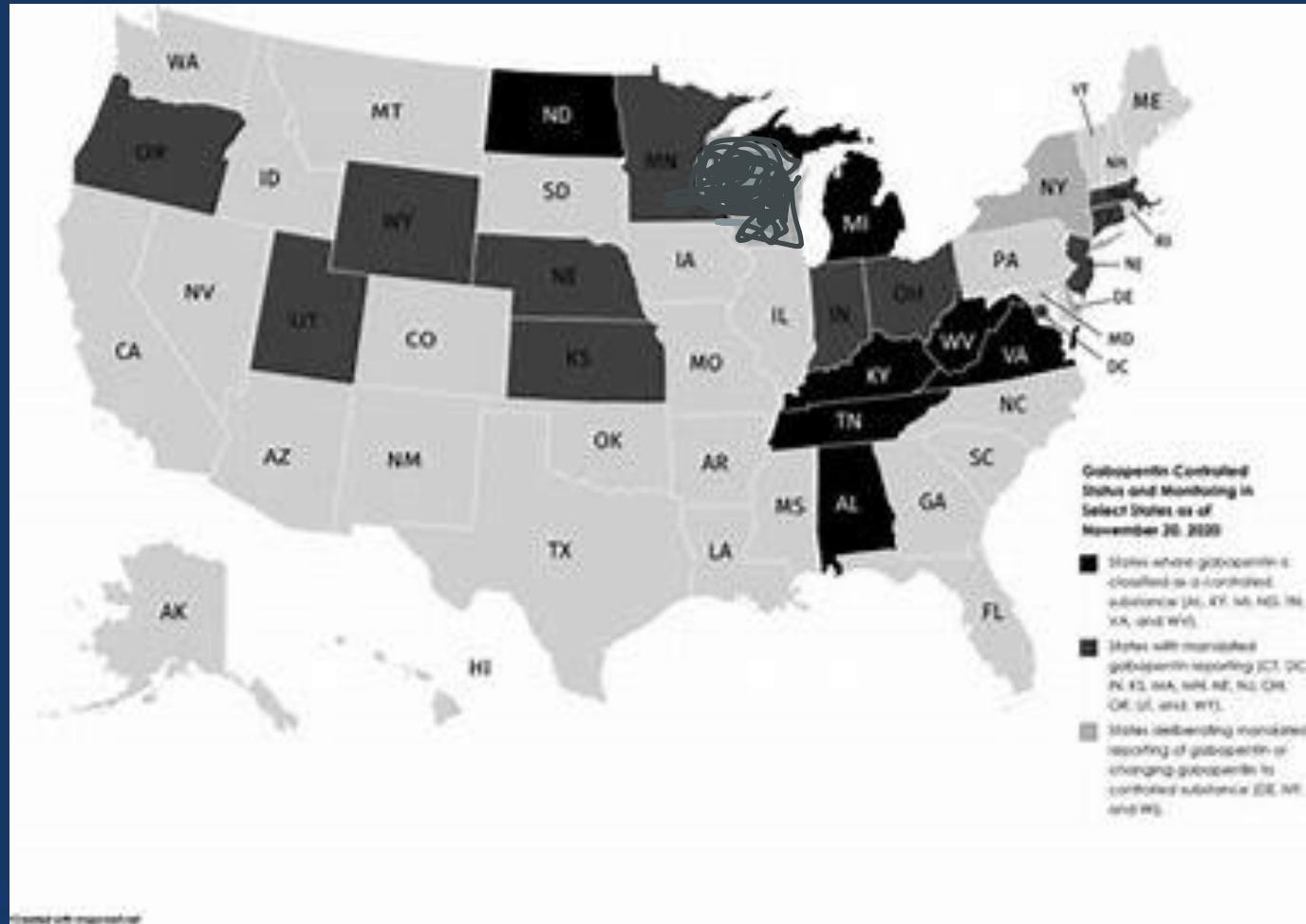
RehabCenter.net





# Scheduling and Controlled Substances

- As of 11/2020
  - GABA Schedule V: AL, KY, TN, MI, ND, WV, VA
  - GABA mandated reporting to PDMP: CT, DC, IN, OH, KS, MA, MN, NE, NJ, OR, UT, WY (and WI in 2021)
  - Active legislation to change GABA to Schedule V: NY, DE
- Another way to view this is→





# Cited reasons for misuse

- Euphoria
- Potentiate effect from MOUD
- Control mood/anxiety
- Self harm
- Pain
- Treat withdrawal symptoms

# Combination Use

- DUI cases with GABA involved
  - 7%-GABA alone
  - 44%-BZP and GABA
  - 43%-OPI and GABA
  - 6%-ETOH
- Postmortem
  - 75% with GABA also have OPI (primarily methadone)

# Source of gabapentinoids

- HCP-52-63% of misused GABA comes from RX
- Viable street market for GABA
  - DEA has cited concern for trading or selling
  - Value- \$1-10/pill (usually \$1/100 mg)
- Unsuspecting family members
- Market is “flooded with gabapentin”



# Risk Factors for Misuse

- Opioid use disorder treated with MOUD (15-22% vs 1% in general population)
- Other RF
  - Mood disorders
  - History of SUD
  - History of misuse of RX medication

# **“Preliminary evidence of pregabalin misuse among prescription and/or illicit opioid (mis)users”**

- Butram, Kurtz J Psychoactive Drugs April 2021
- Mixed method interviews: OPI and Lyrica use
- N-5
- Describe
  - Treatment of pain
  - Desired psychoactive effects
  - Treat withdrawal

# **“A qualitative analysis of gabapentin misuse and diversion among people who use drugs in Appalachian Kentucky”**

- N-33 patients who reported gabapentin misuse
- Prominent drug of misuse among patients with OUD
- Cited low cost and easily escalated doses
- First exposure always RX-off label indication
- Many noted painful withdrawal from gabapentin in jail



# “Gabapentin misuse inside treatment settings”

- Butram, et al. September 2020 J Stud Alcohol Drugs
- Studied within large study on gabapentin misuse (n-91)
- Structured Interview
  - “Attempting to get high”
  - “Cheeking” pills to take in higher quantities
  - Feign symptoms to get prescribed (sciatica)
  - “Fruitless activity” (25%)
  - Take edge of withdrawal
  - “Freelapse”/pass drug test

## Gabapentin's link to fatal drug overdoses draws concern



- CDC report 5/13/21 90% of gabapentin OD included fentanyl
- CDC report 6/28/21 Gabapentin detected in 1/10 US overdose deaths
- Public Citizen-petitioned FDA and DEA to schedule gabapentin
  - Prevalence of misuse
  - “Extraordinary” level of off label prescribing



# “Gabapentin controlled substance status”

- Campbell, et al. J Am Pharm Assoc Jan 2021
- Risk factors for misuse:
  - OUD
  - Mental illness
  - History of drug misuse
- Recommend:
  - UDT monitoring to detect use without RX
  - Therapeutic serum monitoring for safety
  - Reclassify gabapentin as Schedule V/add to state PDMP



HEALTH NEWS

DEC. 20, 2019 / 1:20 AM

## FDA: Gabapentin, opioid combination may cause breathing problems

By HealthDay News



Dec. 20 -- New warnings about the risk of dangerous breathing difficulties when gabapentinoids are used with opioids or by certain patients must now appear on product labels, the U.S. Food and Drug Administration announced Thursday.



Centers for Disease Control and Prevention  
CDC 24/7: Saving Lives, Protecting People™



## Morbidity and Mortality Weekly Report (*MMWR*)

CDC

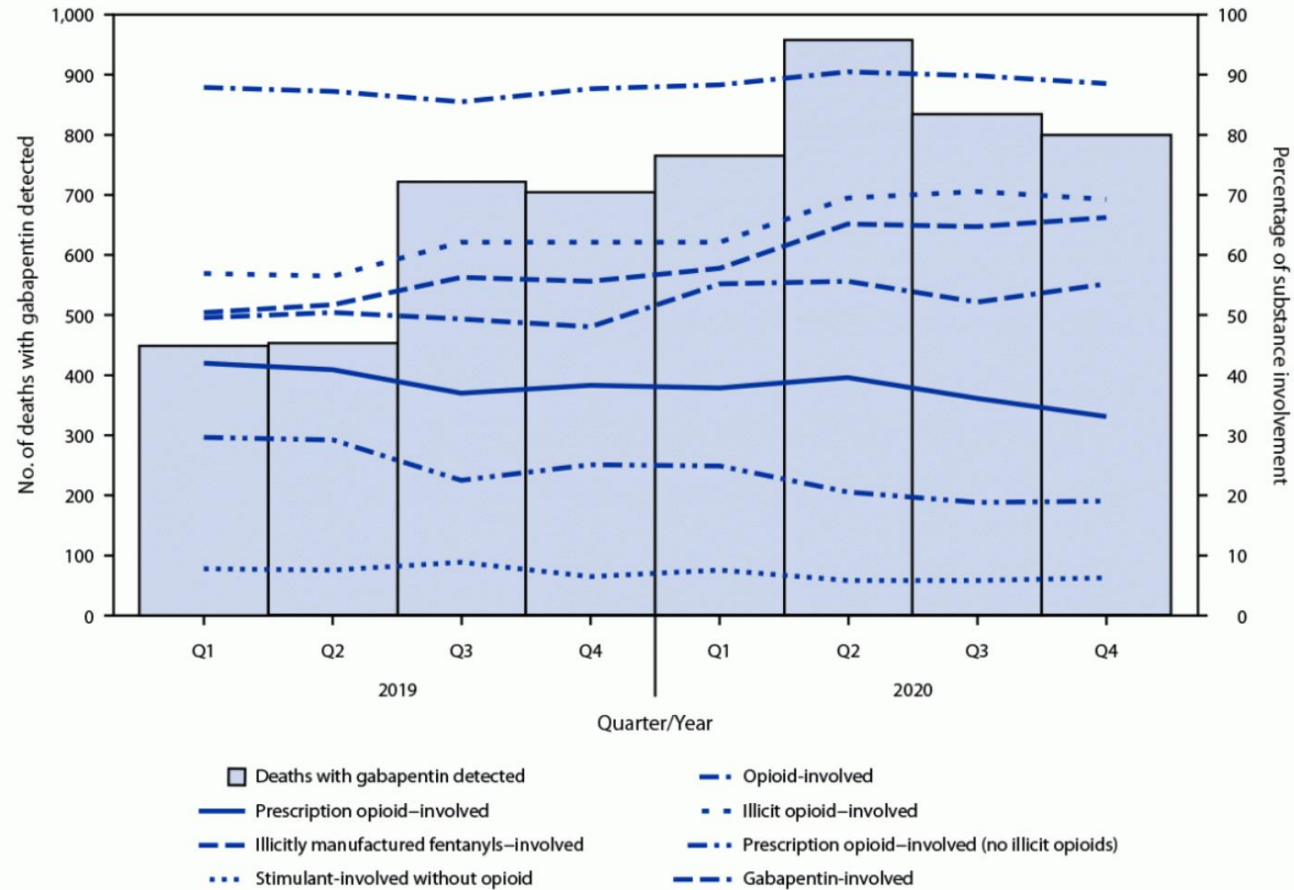
# *Notes from the Field:* Trends in Gabapentin Detection and Involvement in Drug Overdose Deaths — 23 States and the District of Columbia, 2019–2020

*Weekly* / May 13, 2022 / 71(19);664–666

Christine L. Mattson, PhD<sup>1</sup>; Farnaz Chowdhury<sup>2</sup>; Thomas P. Gilson, MD<sup>3</sup> ([VIEW AUTHOR AFFILIATIONS](#))

[View suggested citation](#)

FIGURE. Quarterly trends in gabapentin detection and involvement of gabapentin and other substances in drug overdose deaths among decedents in whom gabapentin was detected, by substance involvement\* — 23 states and the District of Columbia,† 2019–2020



Abbreviation: Q = quarter.

\* Substances determined to have caused death. When nonspecific terminology was used in an overdose cause of death statement (e.g., multidrug overdose), all drugs detected in postmortem toxicology were included as involved in the death. For example, if the cause of death was “multidrug overdose,” and toxicology results were positive for five drugs, all five were classified as involved.



# Recommendations

- Be aware of the misuse potential of gabapentin/pregabalin
- Avoid prescribing to higher risk populations
- Check PDMP (all states)
- Frequent small RX/mid RX pill counts
- Monitor for signs of misuse/diversion:
  - Requesting gabapentin RX
  - Receiving RX from multiple providers
  - Lost/stolen RX
  - Check UDT-non prescribed use/serum toxicology-appropriate use
- Education re: off label use and indications