Part 1: Overview of Gabapentin Misuse and Importance of Prevention in the United States

Morning Coffee Break Series on Gabapentin Misuse| August 1, 2024

UNC GILLINGS SCHOOL OF GLOBAL PUBLIC HEALTH

UNC INJURY PREVENTION RESEARCH CENTER

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Learning Objectives

1. Introduce gabapentin usage and trends in the United States.
2. Define gabapentin misuse potential and associated harms.
3. Summarize state-level actions to address gabapentin misuse.
4. Identify reasons for the prevention of gabapentin misuse in the United States.

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1

GABAPENTIN USAGE & TRENDS

Introduction to Gabapentin

- Anticonvulsant and nerve-pain medication, orally administered[1,2]
- Only available via prescription
- Common brand names: Gralise, Horizant, Neurontin (also available as a generic)

Gabapentin in Animals[3]

- Dogs: Chronic pain relief, anxiety, and seizures
- Cats: anxiety and fear

Function in the Body

- Gamma aminobutyric acid (GABA) analogue[1,2]
- Binds to proteins in the cortical membranes[1,2]
- "Reduces the excitability of nerve cells in the brain"[4], preventing pain response and seizure activities[1,2]
- Exact mechanism of action is still being understood
- Recommended dosage varies by desired treatment[5]

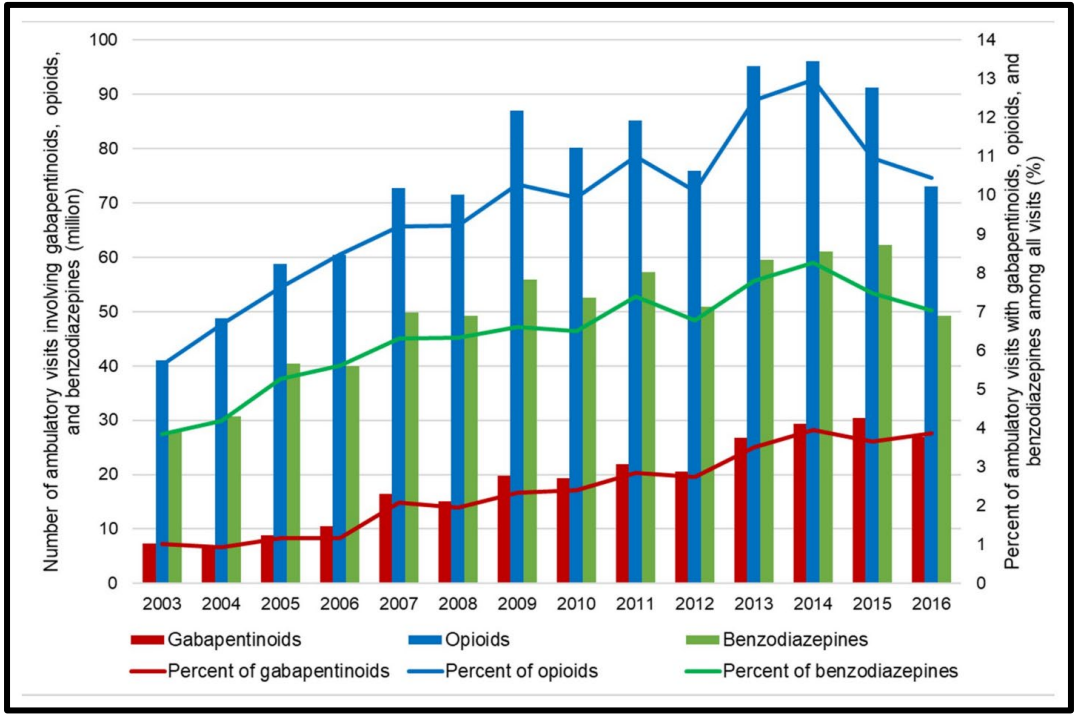
Common Side Effects[1,6]

- Dizziness
- Drowsiness
- Peripheral oedema
- Weight gain
- Ashtenia
- Headache
- Dry Mouth

Uses with FDA-Approval[7,8]

- Partial onset seizures in adults and children
- Postherpetic neuralgia in adults and children
- Moderate-to-severe restless legs syndrome in adults (extended-release only)

Trends in use of gabapentinoids, opioids, and benzodiazepines in the US ambulatory care settings: 2003–2016 National Ambulatory Medical Care Survey (NAMCS)[9]



Off-label prescribing of gabapentin is estimated between 83-95%.[10,11]

Partial List of Off-Label Uses of Gabapentin[12]

Off-Label Use	**Level of Efficacy**
Bipolar disorder	No significant difference compared to placebo
Neuropathic pain	May be effective for certain presentations
Diabetic neuropathy	Effective
Complex regional pain syndrome	Ineffective
Attention deficit disorder	Insufficient evidence
Trigeminal neuralgia	Evidence favors efficacy
Periodic limb movement disorder of sleep	Ineffective
Migraine	Evidence favors efficacy
Drug and alcohol withdrawal	Ineffective

Franklin v. Parke-Davis[13]

US District Court for the District of Massachusetts

Gabapentin is not a controlled substance at the federal level. However, pregabalin, a closely related medication, has been for over 20 years.

2 GABAPENTIN MISUSE & ASSOCIATED HARMS

Estimated lifetime prevalence of gabapentin abuse in the general population is low (ranging from 1.1-2.1%).[14,15]

Potential for abuse and misuse is higher among people with current or prior opioid or substance use disorder.[15-21]

Abuse and Misuse Among Individuals with SUD

- **Prior treatment for substance use disorder** was predictive of gabapentinoid misuse, abuse, and obtainment[15]
- **15%** of current, nonmedical users of prescription opioids surveyed in Appalachian Kentucky reported **using gabapentin to get "high"** in the past 6 months[18]

Abuse and Misuse Among Individuals with SUD

- **22% of opioid dependent patients** in a Massachusetts detoxification facility used higher amounts of gabapentin than prescribed or used gabapentin without a valid prescription.[19]
- Among patients at a substance misuse clinic, **19% reported gabapentin misuse** (Scotland)[17]

Abuse and Misuse Among Formerly-Incarcerated Individuals

- In a sample of 250 formerly-incarcerated individuals, **16% reported lifetime non-medical use of gabapentin**.[21]
- In the same sample, among those with opioid use disorder, **26% reported illegally obtaining, overusing, or falsifying illness** to obtain gabapentin.[21]

Motivations for Misuse or Abuse[16,22]

- To become intoxicated or “high”
- To increase the effects opioids or methadone
- As a substitute for opioids or other drugs
- Management of pain or withdrawal

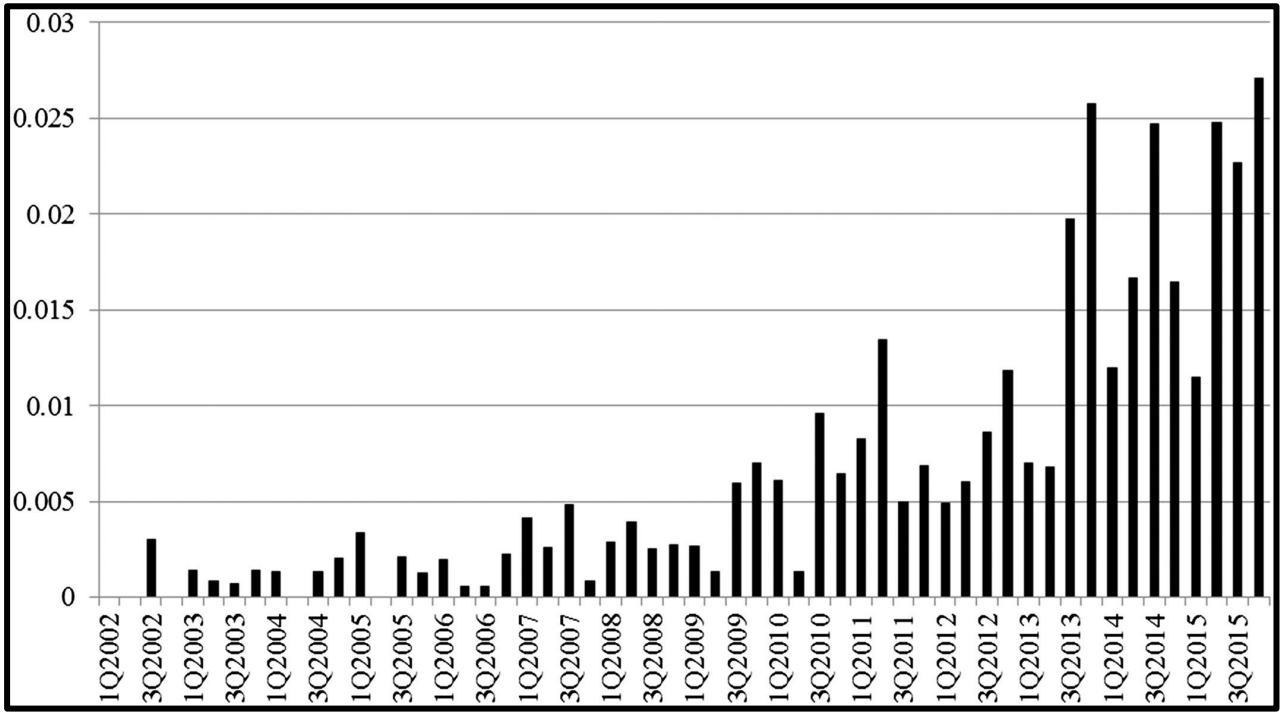
Obtainment of Gabapentinoids[14]

Healthcare (63%)

Family or acquaintances (58%)

Internet (47%)

Rates of gabapentin diversion per 100,000 population by quarter, 2002 to 2015[23]



Harms Associated with Gabapentin Abuse and Misuse

- Increased healthcare utilization[24,25]
- Poisonings[26-28]
- Death[27,29-36]
- Adverse Events[37]

Harm: Increased Healthcare Utilization

Individuals with sustained overuse of gabapentin had **increased odds of an all-cause inpatient stay** and **increased odds of a drug-related inpatient stay** compared to individuals utilizing gabapentin without overuse.[24]

Adverse effects from gabapentin appear to be greatest when combined with opioids.

Harm: Increased Healthcare Utilization

Concurrent gabapentin and opioid use **doubled the odds of all-cause inpatient stays**, even if neither medication were overused.[24]

Harm: Increased Healthcare Utilization

Sustained overuse of both gabapentin and opioids **quadrupled the odds of all-cause inpatient stays**.[24]

Harm: Adverse Events

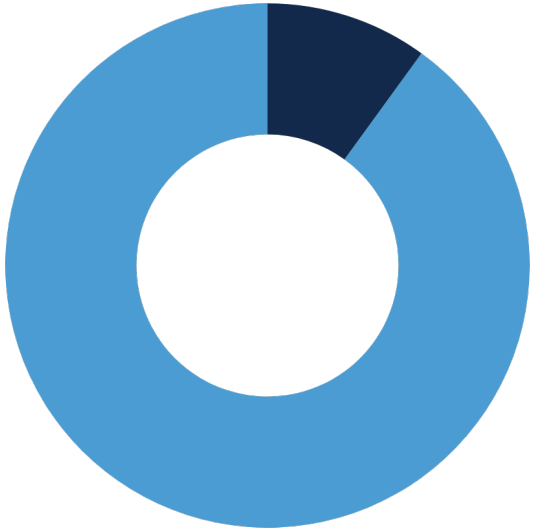
23% of all gabapentin reports in the FDA Adverse Event Reporting System were likely **related to abuse of the medication**.[37]

Harm: Poisonings

From 2006 to 2014, poison center calls for gabapentinoids increased four-fold.[26]

Harm: Death

Individuals exposed to gabapentin and opioids in the prior 120 days had increased odds of opioid-related death compared to those exposed only to opioids.[29]



10% of all fatal overdoses involved gabapentin between 2019-2020 across 23 states and DC.[33]

Harm: Intentional Overdose & Suicide

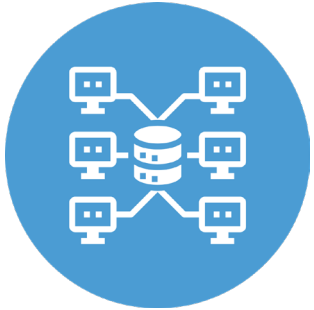
Intentional overdose of gabapentin in combination with other medications has proven to be fatal.[36]

3 STATE-LEVEL ACTIONS TO ADDRESS MISUSE

Interventions have historically fallen into 5 main categories

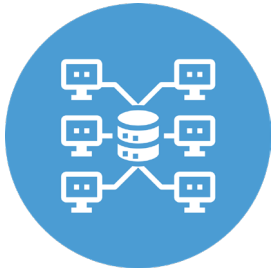
For gabapentin specifically, interventions have primarily focused on prescribing regulations.

Regulations to Alter Prescribing



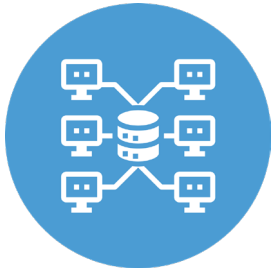
Prescription Drug Monitoring Programs (PDMPs)

Controlled Substance Designations



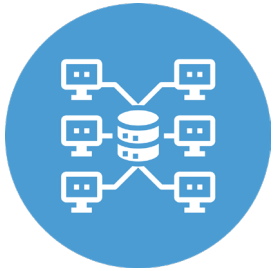
Prescription Drug Monitoring Programs[38]

Electronic databases that track controlled substance prescriptions (or other prescriptions mandated by the state)



Prescription Drug Monitoring Programs[38]

- Identify patients with signs of problematic use at risk of developing SUD or experiencing an overdose
- Help eliminate concerns of “doctor shopping”
- Identify providers with questionable prescription histories
- Provide stability throughout a patient’s continuum of care



Prescription Drug Monitoring Programs[38]

- Help providers discuss harms related to a patient's medical regime, including increased risks of respiratory depression and overdose if concurrently using multiple gabapentinoids or gabapentin and an opioid

Prescription Drug Monitoring Programs[38]

Practitioners should not dismiss patients from their care based on information found in the PDMP.

Controlled Substance Designations/Scheduling [39]

Classify drugs and substances based on the drug's "acceptable medical use" and its "abuse or dependency potential"[39]

Controlled Substance Designations/Scheduling [39]

5 levels of drug scheduling (Schedules I-V) where Schedule I is the highest level of scheduling and Schedule V is the lowest

Schedule I [39]

No currently accepted medical use and high potential for abuse, with use potentially leading to severe psychological or physical dependence

Examples: heroin, LSD, cannabis, ecstasy

Schedule II [39]

High potential for abuse

Examples: Vicodin, cocaine, methamphetamine, oxycodone, fentanyl, and Adderall

Schedule III [39]

Moderate to low potential for physical and psychological dependence

Examples: Tylenol with codeine, ketamine, anabolic steroids, testosterone

Schedule IV [39]

Low potential for abuse and low risk of dependence

Examples: Xanax, Valium, Ativan, Ambien, Tramadol

Schedule V [39]

Lower potential for abuse than Schedule IV

Examples: Robitussin AC, Lyrica (**pregabalin)**, Lomotil

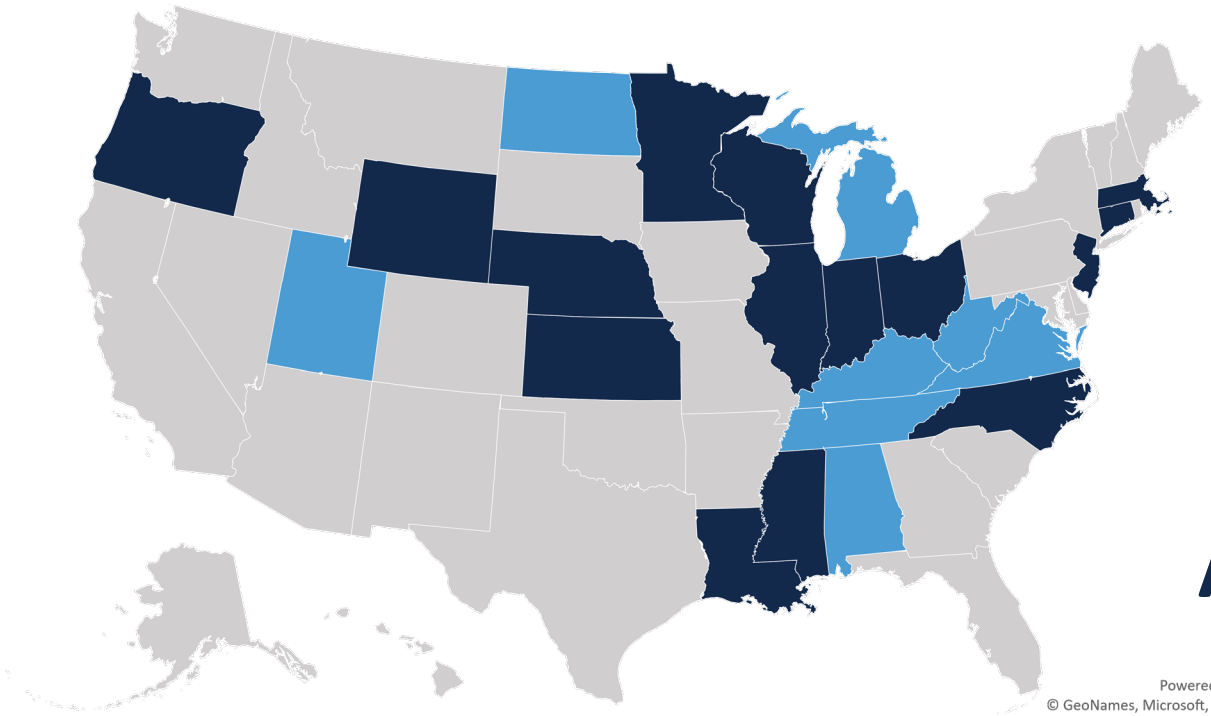
Gabapentin is not a controlled substance at the federal level. However, pregabalin, a closely related medication, has been for over 20 years.

Controlled Substance Designations/Scheduling

Determines **how** the drug can be prescribed and **who** can prescribe the medication[40]

Controlled Substance Designations/Scheduling

States have autonomy to add additional drugs to their state-level controlled substance listing



Policies to Address Harms

Classified gabapentin as a schedule V controlled substance and mandate reporting in the state's PDMP

Mandate reporting in the state's PDMP without a controlled substance designation

Calls for State and National Scheduling of Gabapentin

- North Carolina mandated reporting in the PDMP in March 2024
- Utah classified gabapentin as schedule V in May 2024
- Nationally: FDA denied a petition to initiate proceedings to schedule gabapentin in January 2023[41]

Do these state-level approaches work?

Scheduling Gabapentin and Impact on Medicare Prescriptions

Mean total days' supply of gabapentin per Medicare enrollee per year

- Decreased by 8.37 (CI: -10.34, -6.39) total days after schedule V regulations[42]
- Decreased by 1.01 (CI: -1.74, -0.29) total days after PDMP regulations[42]

Other Evidence for Regulatory Interventions

Opioid restriction laws: shown to significantly decrease opioid prescribing[43-46]

Carisoprodol (Schedule IV): Federal scheduling showed an immediate decline and decreasing trend in prescription fills[47]

Unintended Effects

Potential to limit prescribing to patients who need the medication to function

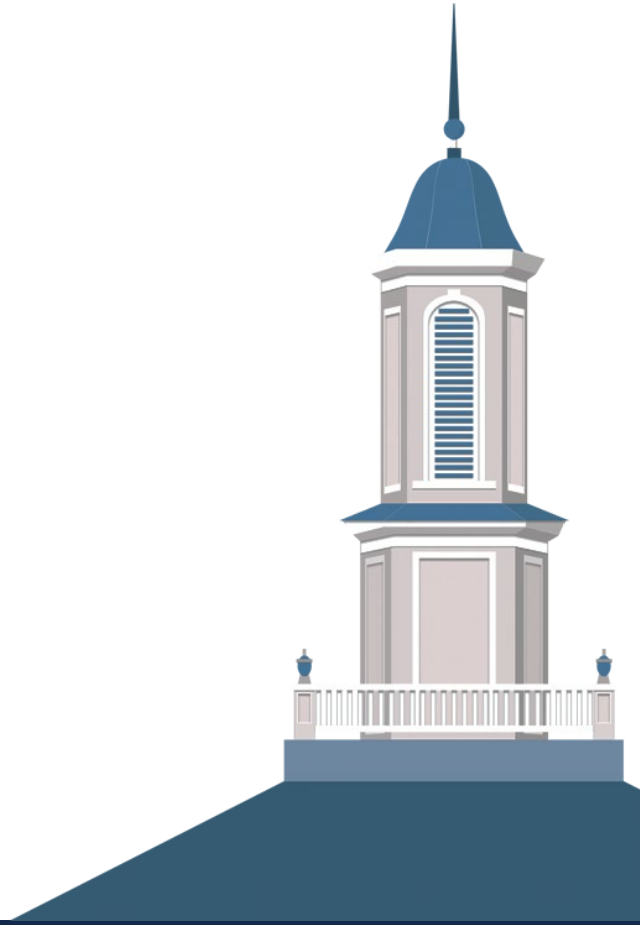
4 REASONS TO PREVENT GABAPENTIN MISUSE

Key Reasons to Prevent Gabapentin Misuse

- Reduce documented harms, particularly for populations with SUD/OUD
- Reduce burden on the healthcare system
- Reduce societal costs, monetarily and metaphorically
- Confront the drug overdose crisis

We have a duty to promote rationale use of medications.[48]

Thank you!



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Q&A

Additional questions? Feel free to contact me at kgoracombs@unc.edu.