Part 3: Prevention Strategies for Gabapentin Misuse in Communities

Kirk Evoy, PharmD, BCACP, BC-ADM, CTTS, FCCP, FTSHP

The University of Texas at Austin College of Pharmacy

University Health System

Conflict of Interest Disclosures

I have no conflicts of interest to disclose

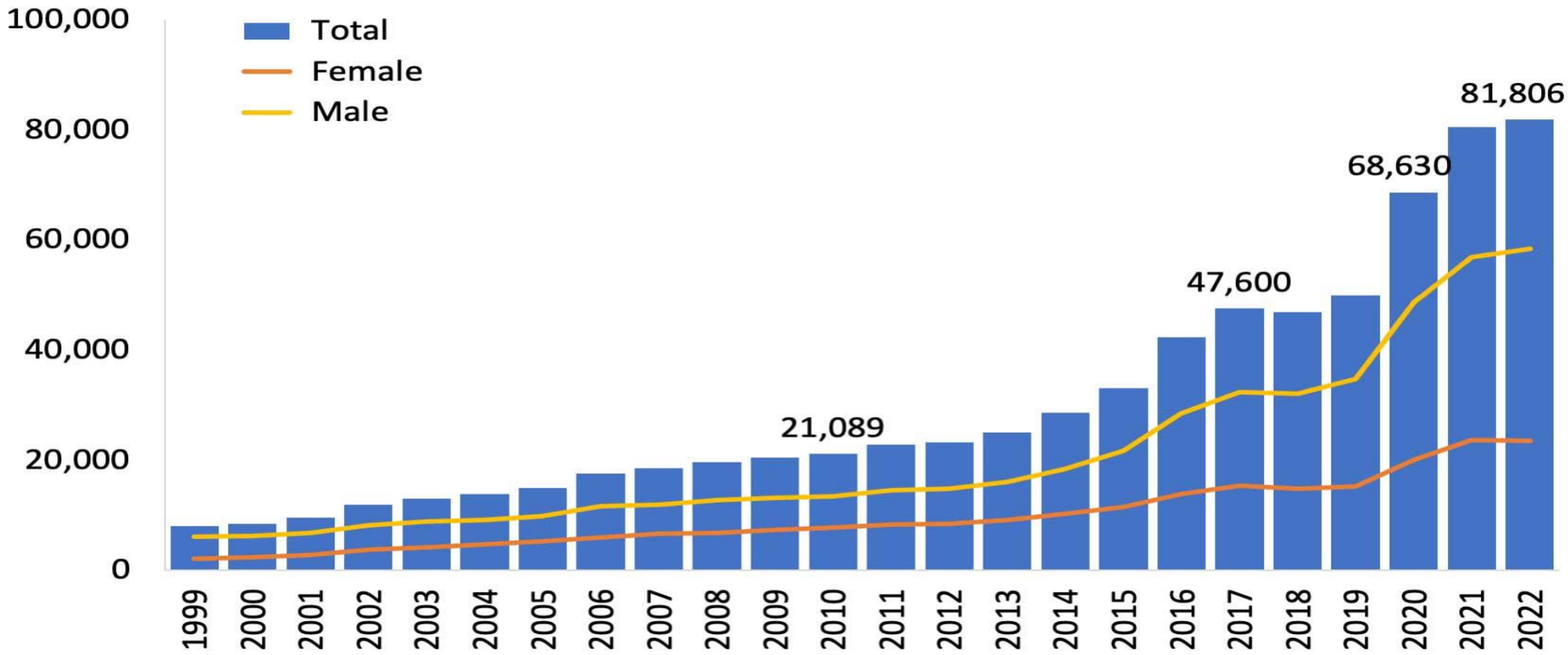
Learning Objectives

1. Gain insights on community-based prevention of gabapentin misuse
2. Articulate recommended prevention strategies for gabapentin misuse
3. Create plans to provide gabapentin misuse prevention services in communities

Evoy KE, et al. Drugs 2017;77(4):403-426.

Evoy KE, et al. Drugs 2021;81(1):125-156.

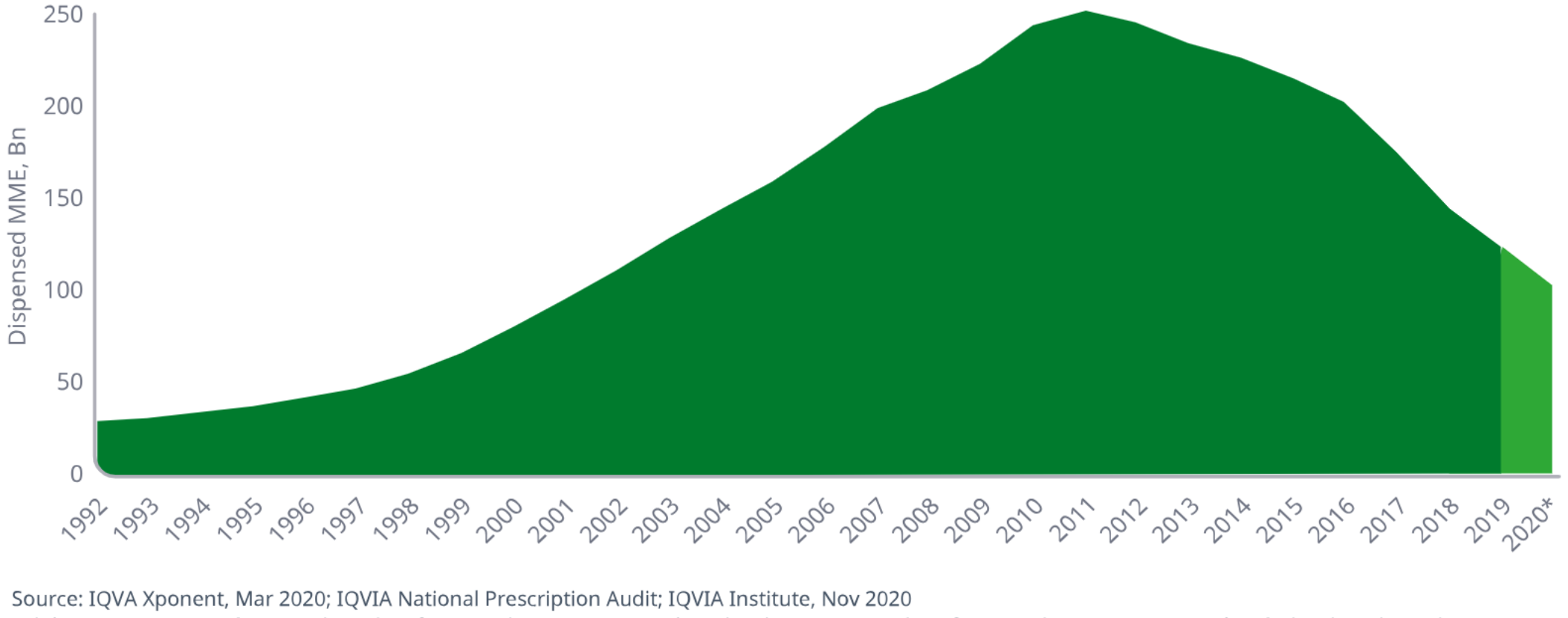
Figure 3. National Overdose Deaths Involving Any Opioid*, Number Among All Ages, by Sex, 1999-2022



*Among deaths with drug overdose as the underlying cause, the "any opioid" subcategory was determined by the following ICD-10 multiple cause-of-death codes: natural and semi-synthetic opioids (T40.2), methadone (T40.3), other synthetic opioids (other than methadone) (T40.4), or heroin (T40.1). Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2022 on CDC WONDER Online Database, released 4/2024.

Available at: https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates

U.S. Opioid Prescribing



Source: IQVA Xponent, Mar 2020; IQVIA National Prescription Audit; IQVIA Institute, Nov 2020

Available at: https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/prescription-opioid-trends-in-the-united-states/iqi-prescription-opioid-trends-in-the-us-1220-exhibit-1.svg?mw=1180&hash=99A85B2976FCB9998E372587EDF24BC4

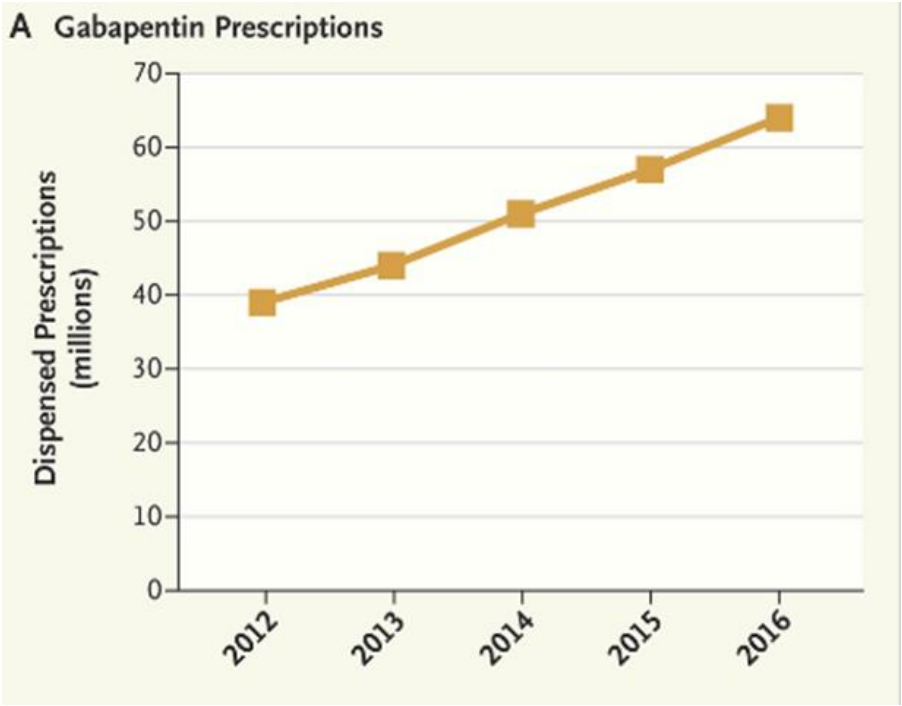
US Gabapentin Prescribing

1993: FDA approval

2001: Drug with the highest proportion of off-label use

2010–2015: Among top 20 most prescribed drugs

Today: 5th most commonly prescribed drug in US



Goodman CW, et al. N Engl J Med 2017 Aug 3;377(5):411-414.
Definitive Healthcare. Available at: https://www.definitivehc.com/resources/healthcare-insights/top-outpatient-prescription-medications

Gabapentin Fast Facts

- Brand Name: Neurontin®
- FDA-approved in 1993
- Mechanism of action (or misuse potential) not entirely understood
- Indicated for herpetic neuralgia and epilepsy
- Up to 95% of prescribing is off-label
- NOT a controlled substance according to DEA

Neurontin [package insert]. New York, NY: Pfizer Inc; Oct 2017.
Hamer AM, et al. J Managed Care Pharm. 2002;8(4):266-71.
Schifano F. CNS Drugs 2014;28:491-96.
Schifano F, et al. Psychother Psychosom. 2011;80(2):118-22.

Why Gabapentin?

- Potentiate desirable effects of other drugs
- Avoid detection on urine toxicology
- Attenuate withdrawal of other medications
- Self-medicate (e.g., pain, anxiety, withdrawal)
  - *Evoy, et al. (2021):* Lifetime "recreational" and "therapeutic" misuse rates reported among US general population sample were equivalent

Evoy KE, et al. Drugs 2017;77(4):403-426.

Evoy, et al. Int J Clin Pharm 2021;43(4):1055-1064.

Misuse Prevalence

Evoy, et al. (2021)

- Surveyed nationally distributed sample that mirrored US general population to estimate misuse prevalence and patterns associated
- Takeaway points:
  - 6.6% of US general population reported lifetime gabapentinoid *misuse or abuse*
  - 2.1% and 1.5% reported gabapentin or pregabalin *non-therapeutic* misuse, respectively
  - 50-70% co-administered opioids

Evoy, et al. Int J Clin Pharm 2021;43(4):1055-1064.

Much More Common in OUD Population

15-22% prevalence of gabapentin misuse among patients with an substance use disorder

Evoy KE, et al. Drugs 2017;77(4):403-426.

Adverse Effects and Risks

- Somnolence
- Dizziness
- Weight gain/edema
- Misuse
- Increased opioid overdose risk
- Dependence and Withdrawal

Evoy KE, et al. Drugs 2017;77(4):403-426.
Evoy KE, et al. Drugs 2021;81(1):125-156.

Increased Opioid Overdose Risk

- ***Peckham, et al. (2018)***
  - Gabapentin MISUSE in setting of high-dose prescription opioid use increased all-cause (OR 4.08 (95% CI 2.58-6.46) and drug-related hospitalization (OR 4.72, 95% CI 2.67-8.37)
- ***Macleod, et al. (2019)***
  - Gabapentinoid use among patients receiving opioid maintenance therapy increased all-cause mortality (HR 1.71, 95% CI 1.33-2.20)
- ***Gomes, et al. (2017)***
  - Concomitant gabapentin and opioid prescriptions increased risk of opioid-related deaths (adjusted OR 1.49, 95% CI 1.18-1.88)
- ***Khan, et al. (2021)***
  - Concomitant gabapentin and opioid prescriptions increased risk of opioid overdose (OR 1.16, 95% CI 1.04-1.28)

Peckham, et al. Drug Saf. 2018;41(2):213-28.
Gomes T et al. *PLoS Med*. 2017;14(10).
Khan NF et al. *Clin Pharmacol Ther*. 2021;110(4):1011-1017.
Macleod J et al. PLoS Med. 2019;16(11).

Dependence and Withdrawal

- Reports of cravings, self-titration, and seeking suggest dependence possible
- Benzodiazepine or alcohol-like withdrawals reported
  - Alleviated rapidly with resumption of gabapentinoid
  - Not relieved with benzodiazepines
  - Taper protocols not well-defined; consider weekly 25% dose reductions
- Increased neonatal withdrawal risk; may require administration of both opioids and gabapentinoids

Evoy KE, et al. Drugs 2017;77(4):403-426.
Evoy KE, et al. Drugs 2021;81(1):125-156.
Huybrechts KF, et al. BMJ 2017;358:j3326.
St. Louis EK, et al. Epilepsy Behav 2007;11:222-234

Access to Gabapentin

- *Evoy, et al. (2021)*
  - Health care providers: 71.8%
  - Family or acquaintances: 43.6%
  - Purchase from dealer or internet: 10.3%
- *Smith, et al. (2015)*
  - Physicians: 52%
  - Illicit dealers: 36%
- *Wilens, et al. (2014)*
  - U.S. opioid dependent patients in OUD treatment:
    - 40% GBP and 50% PRG misuse among patients prescribed those meds
    - 13% GBP and 6% PRG misuse among those NOT prescribed a gabapentinoid

Evoy, et al. Int J Clin Pharm 2021;43(4):1055-1064. Smith RV, et al. Am J Psychiatry. 2015;172(5):487-8. Wilens T, et al. Am J Addict. 2015 Mar;24(2):173-7.

How Can We Reduce Gabapentin Misuse?

Provider Education and Awareness

- Promote provider awareness through:
  - Live or virtual continuing education
  - Conference presentations
  - Academic literature
  - Professional school curriculum
  - Academic detailing

Evoy et al. TSHP Journal 2018;17(1):12-15.
Evoy KE, et al. J Am Pharm Assoc 2019;60(1):81-86.

Identifying Risk Factors and Signs of Misuse

- Primary risk factor: opioid use disorder
- Lesser risk factors: young males; other SUDs; psychiatric comorbidities; H/O incarceration
- Need to develop validated risk-assessment tool
- Signs of prescription drug misuse:
  - Requesting specific drugs or higher doses during appointment
  - Doctor shopping or filling at multiple pharmacies in short succession
  - Requesting not to bill insurance
  - Requesting early refills
  - Claiming medications were lost or stolen

Evoy KE, et al. Drugs 2017;77(4):403-426.
Evoy KE, et al. Int J Clin Pharm 2021;43(4):1055-1064.
Gahr M, et al. J Addict Med. 2013 Mar-Apr;7(2):147-9.
Carrus D, et al. J Clin Psychopharmacol. 2012 ;32(6):839-40.

Safe Prescribing

- Prescribe primarily for well-studied indications
- Routinely assess safety/efficacy and discontinue if ineffective
- Use alternative treatments (e.g., SNRIs, TCAs, lidocaine, capsaicin) and multi-modal care when appropriate
- Use caution with:
  - Concomitant opioid use
  - Multiple CNS depressants
  - Elderly and chronic kidney disease

Neurontin [package insert]. New York, NY: Pfizer Inc; Oct 2017.
Hamer AM, et al. J Managed Care Pharm. 2002;8(4):266-71.
Peckham AM, Subst Abuse 2018;12:1-8.
Samuel MJ, et al. J Am Geriatr Soc. 2023;71:2052-2081.

Naloxone Co-Prescribing

- Opioid overdose reversal agent
- Can be administered by layperson in event of overdose
- Available via prescription, pharmacy naloxone access laws, over-the-counter
- Patients prescribed opioids + gabapentin should receive counseling and naloxone prescription

Evoy KE, et al. JAMA 2018;320(18):1934-1937.
Lai RK, et al. J Am Pharm Assoc 2022;62(6):1725-1740.
Torres E, et al. J. Pain Palliat. Care Pharmacother 2022;36(3):178-186.
Evoy KE, et al. Integr Pharm Res Pract 2021;10:13-21.
Evoy KE, et al. Subst Abuse 2020;14:1-4.

De-prescribing and Withdrawal Prevention

- Avoid abrupt discontinuation to prevent withdrawal
- Return unused gabapentin to safe disposal sites
- Rehab centers offering gabapentin use disorder treatment now available
- Maternal use during pregnancy can cause fetal withdrawal syndrome

Evoy KE, et al. Drugs 2017;77(4):403-426.
Evoy KE, et al. Drugs 2021;81(1):125-156.
Huybrechts KF, et al. BMJ 2017;358:j3326.
St. Louis EK, et al. Epilepsy Behav 2007;11:222-234

Increased Access to Care

- Adequately control pain, anxiety, OUD to reduce need for self-medication
- Need greater access to specialty providers and OUD treatment
- Incorporate multi-disciplinary team based approach when able

Patient Education and Awareness

- Among US patients receiving opioids + gabapentinoids in outpatient setting:
  - SUD counseling provided in 3.1% of visits
  - Naloxone rarely co-prescribed
- Improve patient education to minimize misuse and overdose risk
- Develop community resources and public health campaigns

Evoy KE, et al. Subst Abuse 2020;14:1-4.

Regulatory Changes

State pharmacovigilance

- Gabapentin reclassified as Schedule-V in several US states
- Added to prescription drug monitoring program in other states

Federal pharmacovigilance

- US FDA: “We’ve tasked our surveillance and epidemiology group inside FDA, who are focused on spotting early patterns of misuse of controlled substances, with investigating the use patterns of the gabapentinoids.”

https://www.fda.gov/NewsEvents/Speeches/ucm596893.htm *Peckham. Risk Manag Healthc Policy*. 2018 31;11(1):523. Karavolis ZA. Am J Health Syst Pharm 2022;79(9):e143-e148.

Pros vs. Cons of Scheduling

PROS

- **Prescribing restrictions**
  - Restricted refills/drug quantity
- **Restricted access**
  - Barriers to doctor shopping and diversion
- **Increased monitoring**
  - Easier to identify signs of misuse
- **More judicious prescribing**

CONS

- **Restricted patient access**
  - ‘Punishes’ patients with legitimate medical need or in rural areas
  - More office visits
- **Provider burden**
  - More ‘red tape’/documentation for pharmacists
  - More refill requests to prescribers
- **Patients may be undertreated**

Peckham, et al. Expert Opin Drug Saf. 2017;17(5):519-23.

Covvey JR, et al. Res Social Admin Pharm 2023;19(4):599-609.

Continued Research

- Continued epidemiologic characterization is important, but need more research into solutions
- Report events for ongoing post-marketing surveillance
- Stay abreast of ongoing research and policy updates

Conclusion

- Gabapentinoids maintain important role in treating many chronic conditions
- Misuse of GBP and PRG growing
- Need greater emphasis on identifying risk factors for and signals of misuse
- Safe prescribing of gabapentinoids should be emphasized

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