

# Opioids Plus Gabapentin Associated with Increased Risk of Opioid Use Disorder Over Opioids Alone

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## Key Findings:

- Patients prescribed gabapentin in combination with opioids are at a 47% greater risk of developing opioid use disorder (OUD) or experiencing opioid-related overdose than patients who are taking opioids without gabapentin.
- Patients with gabapentin prescriptions both before and after their opioid prescription have the greatest risk of OUD or opioid overdose.

Gabapentin is a non-opioid medication used to treat chronic pain conditions, including shingles and diabetic neuropathy.<sup>1</sup> It is also used for other medical conditions, including seizures, restless legs syndrome, and anxiety. Recently, gabapentin was recommended as part of surgical recovery protocols to reduce opioid use while maintaining satisfactory post-operative pain control.<sup>2</sup>

A previous study found that use of gabapentin and opioids together may increase the risk of opioid-related overdose,<sup>3</sup> while another study found an increased risk of mortality for patients prescribed both gabapentin and opioids compared to those only prescribed opioids.<sup>4</sup> However, there is little known about the prevalence of OUD in patients who are prescribed both gabapentin and opioids.

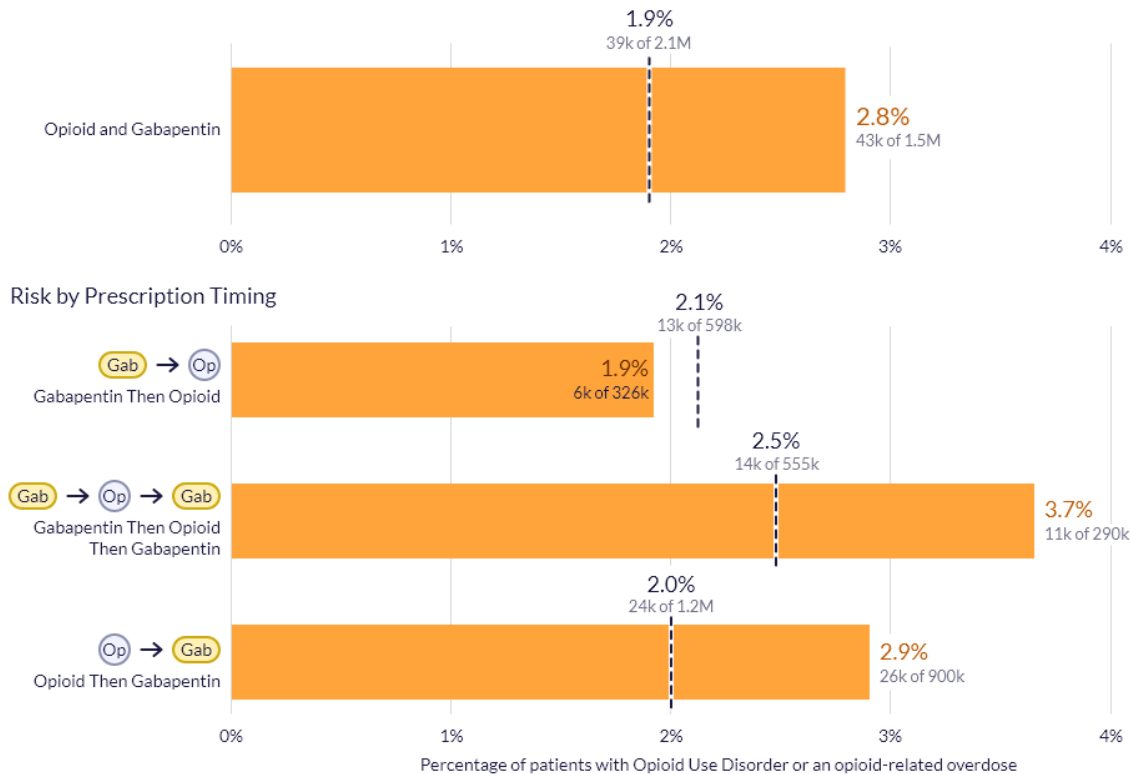
To better understand how use of gabapentin and opioids may influence a patient's risk of developing opioid-related conditions, we matched 1.5 million patients with both gabapentin and opioid prescriptions to 2.1 million patients with only opioid prescriptions and evaluated their likelihood of being diagnosed with OUD or having an opioid-related overdose. Patients were matched by prescribed opioid amount, age, at least one shared comorbidity, and length of time in the observation period.

We found that patients taking gabapentin in combination with opioids are 47% more likely to develop OUD or experience an opioid-related overdose than patients who are solely prescribed opioids, as shown in Figure 1. While we observed slight differences in risk based on which comorbidities a patient has, an increased risk is seen across all comorbid factors assessed.

To further evaluate whether gabapentin and opioid prescribing timing influenced risk, we compared patients who had gabapentin prescriptions only before, only after, or both before and after their opioid prescription. We found that the greatest risk of OUD or opioid overdose is seen in patients who had gabapentin prescribed both before and after their opioid prescription.

# Risk of Opioid Use Disorder or Overdose for Gabapentin and Opioids

Overall Risk



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Figure 1. Percentage of patients with an OUD or opioid overdose diagnosis between January 2017 and January 2023 stratified by medications prescribed and timing of gabapentin and opioid prescriptions. Opioid-only risk is assessed for patients matched to the opioid plus gabapentin populations based on prescribed opioid amount, age, observation time, and at least one shared comorbidity.

These findings add to the previous literature on the increased risk of opioid-related conditions with concomitant use of gabapentin and opioids.<sup>2,3</sup> While we did match patients on several characteristics, we did not study all potential factors that might contribute to the increased risk, such as level of pain control or social vulnerability index.

*These data come from Cosmos, a HIPAA-defined Limited Data Set of more than 183 million patients from 199 Epic organizations including 1,141 hospitals and more than 24,500 clinics, serving patients in all 50 states and Lebanon. This study was completed by two teams that worked independently, each composed of a clinician and research scientists. The two teams came to similar conclusions.*

## References

1. AFHS Drug Information Essentials. American Society of Health System Pharmacists, 2004-2022. Accessed March 15, 2023.
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3. Olopoenia A, Camelo-Castillo W, Qato DM, et al. Adverse outcomes associated with concurrent gabapentin, opioid, and benzodiazepine utilization: A nested case-control study. *Lancet Reg Health Am.* 2022;13:100302. Published 2022 Jun 23. doi:10.1016/j.lana.2022.100302
4. Waddy SP, Becerra AZ, Ward JB, et al. Concomitant Use of Gabapentinoids with Opioids Is Associated with Increased Mortality and Morbidity among Dialysis Patients. *Am J Nephrol.* 2020;51(6):424-432. doi:10.1159/000507725

## Data Definitions

Term	Definition
<b>Case patient</b>	Patient with an initial opioid prescription and an initial gabapentin prescription documented between 1/1/2017 and 1/28/2023, at least two face-to-face encounters prior to first opioid prescription, at least three encounters in the study period, and no documented history of OUD or opioid use
<b>Control patient</b>	Patient with an initial opioid prescription documented between 1/1/2017 and 1/28/2023, at least two encounters prior to first opioid prescription, at least three face-to-face encounters in the study period, and no documented history of OUD or opioid use
<b>Opioid prescription</b>	Medication orders with a pharmaceutical subclass of Opioid Agonists, Opioid Combinations, Opioid Partial Agonists or corresponding to one of the following RxNorm codes: 2670, 3423, 6378, 6754, 6813, 7052, 7238, 480, 1819, 1841, 7804, 7814, 8001, 56795, 10689, 73032, 4337, 5489, 787390, 477468, 1007785, 7676, 23088, 17933, 8143, 3290, 22713, 6761, 7894, 8119, 8354, 8785, 10597, 32926, 2001357, 2392230
<b>Gabapentin prescription</b>	Medications with a generic ingredient of gabapentin or gabapen*
<b>Opioid use disorder (OUD) or opioid-related overdose</b>	Any diagnosis of the following ICD-10 codes: F11*, T40.2X1A, T40.2X1D, T40.2X2A, T40.2X2D, T40.2X2S, T40.2X4A, T40.2X4D, T40.2X4S
<b>Comorbidity</b>	Patient has received at least one of the following diagnoses at any point in time: <ul style="list-style-type: none"> <li>• Chronic Pain (SNOMED 82423001)</li> <li>• Diabetes Mellitus, excluding gestational diabetes (SNOMED 73211009, and not 199223000)</li> <li>• Epilepsy (ICD-10 Codes: G40*)</li> <li>• Anxiety Disorder (SNOMED 197480006)</li> <li>• Insomnia (SNOMED 194437008)</li> <li>• Shingles (SNOMED 4740000)</li> <li>• Depression (SNOMED 35489007)</li> <li>• Bipolar Disorder (SNOMED 13746004)</li> </ul>

**Table 1: Risk of Opioid Use Disorder for Gabapentin and Opioids**

Opioid Use – Control Population			Opioid Use & Gabapentin Use – Case Population		
Total Count	OUD Count	% of Patients with OUD	Total Count	OUD Count	% of Patients with OUD
<b>2,098,636</b>	39493	1.9%	<b>1,516,087</b>	42934	2.8%

**Table 2: Risk of Opioid Use Disorder by Gabapentin Timing**

Group	Group total	OUD or Overdose	No OUD or Overdose	Risk of OUD or Overdose
Gabapentin then Opioid	325,831	6,260	319,571	1.92%
Matched Opioid Only Patients	597,650	12,676	584,974	2.12%
Gabapentin then Opioid then Gabapentin	290,087	10,578	279,509	3.65%
Matched Opioid Only Patients	555,490	13,755	541,735	2.48%
Opioid then Gabapentin	900,169	26,096	874,073	2.90%
Matched Opioid Only Patients	1,220,021	24,359	1,195,662	2.00%