

Pregabalin Plus Opioids Correlated with Greater Risk of Opioid Use Disorder Than Opioids Alone

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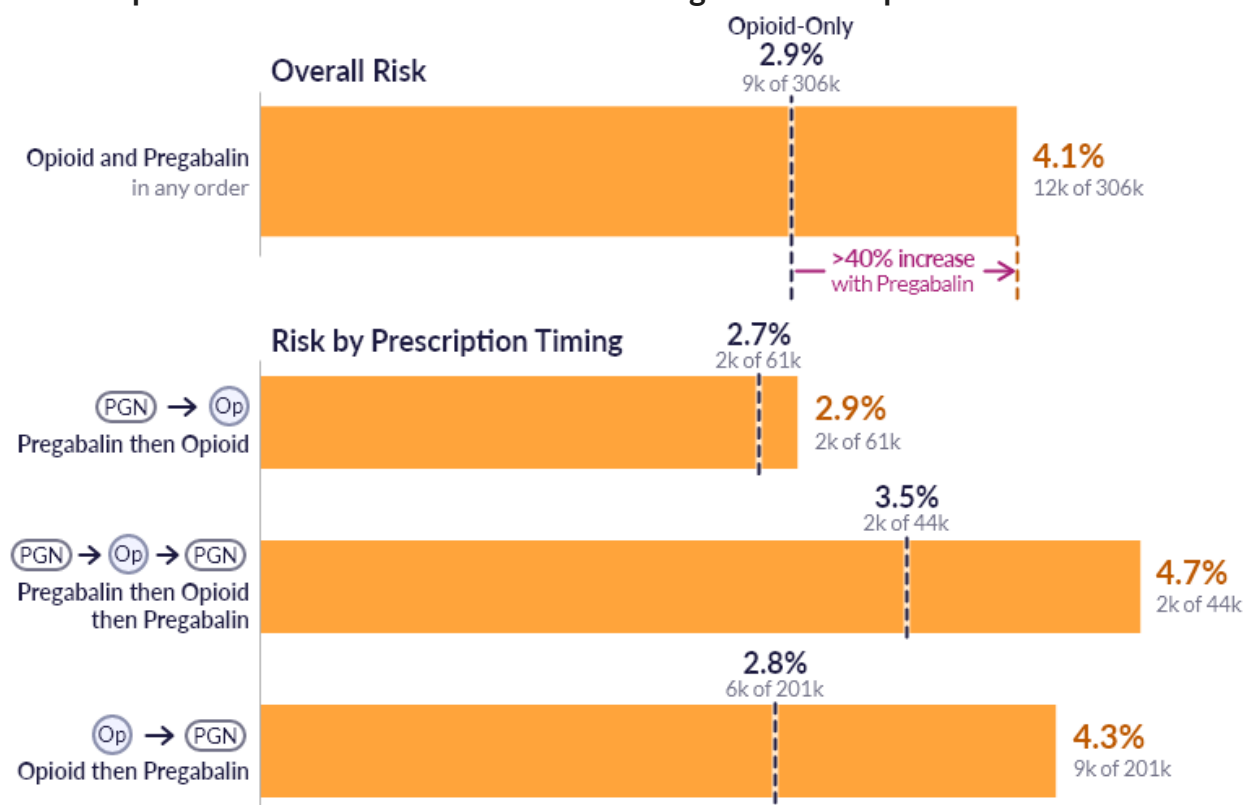
Key Findings:

- Patients prescribed pregabalin and opioids have a 42% greater risk of developing OUD or experiencing an opioid overdose than patients only prescribed opioids.
- Patients prescribed pregabalin both before and after and only after their opioid prescription have an increased risk of OUD or opioid overdose compared to patients prescribed pregabalin only before their opioid prescription.

Gabapentin and pregabalin, anti-convulsant medications sometimes prescribed for pain, are both part of a class of medications called gabapentinoids.¹ We previously published [that gabapentin, when prescribed with opioids, is correlated with an increased risk of opioid use disorder \(OUD\)](#)² for patients when compared to opioid use alone, and we wanted to understand whether there might be similar risks for patients prescribed pregabalin and opioids.

We studied 612,246 patients, half with opioid prescriptions and half with both pregabalin and opioid prescriptions, to determine their risk of OUD. We matched the two populations based on age, sex, morphine equivalent daily dose, comorbidities, and length of time for follow-up. We found that patients prescribed both pregabalin and opioids were more than 40% more likely to be diagnosed with OUD or experience an opioid overdose.

Risk of Opioid Use Disorder or Overdose for Pregabalin and Opioids



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Figure 1. Risk of OUD or opioid overdose by whether the patient is prescribed pregabalin and the timing of the pregabalin prescription.

Similar to what we observed with gabapentin, patients prescribed pregabalin both before and after and only after opioids have the greatest risk of developing OUD or experiencing an opioid overdose. These results suggest that, like other gabapentinoids, concomitant use of opioids and pregabalin is correlated with an increased risk of OUD or opioid overdose.

These data come from Cosmos, a HIPAA-defined Limited Data Set of more than 193 million patients from 208 Epic organizations including 1,197 hospitals and more than 25,400 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

- Chincholkar M. Gabapentinoids: pharmacokinetics, pharmacodynamics and considerations for clinical practice. *Br J Pain*. 2020;14(2):104-114. doi:10.1177/2049463720912496
- Little D, Stamp T, et al. Opioids plus gabapentin associated with increased risk of opioid use disorder over opioids alone. *Epic Research*. [Opioids Plus Gabapentin Associated with Increased Risk of Opioid Use Disorder Over Opioids Alone \(epicresearch.org\)](https://epicresearch.org). Published April 7, 2023. Accessed July 3, 2023.

Data Definitions

Term	Definition
Study period	1/1/17 to 5/1/23
Study population	Age of 18-100 History of outpatient opioid use

	More than two pre-opioid encounters More than three post-opioid encounters No documented history of OUD before the study period or first documented outpatient opioid use
Exposures	A prescription for pregabalin
Outcomes	Receive one of the following ICD-10 diagnoses post outpatient opioid use: F11*, T40.2X1A, T40.2X1D, T40.2X2A, T40.2X2D, T40.2X2S, T40.2X4A, T40.2X4D, T40.2X4S
Comorbidities	Anxiety Depression Epilepsy Chronic Pain Bipolar Diabetes Insomnia Shingles
Model Specifications	Patients were matched on age, length of time in the observation period, prescribed opioid amount (aka MEDD), shared comorbidities, and sex. For age and length of time in the observation period, patients were partitioned into 4 equal groups and matched to patients in the same group. MEDD used roughly the same matching technique, but patients with opioid orders were split into 10 equal buckets instead of 4. For shared comorbidities, patients were matched exactly on their list of studied comorbidities. Sex was also matched exactly. After completing the 1:1 patient matching described above, we calculated the risk ratios and 95% confidence intervals seen in Table 1. Since some subset of the patients in the “Pregabalin Use” row are also included in the samples tested in proceeding rows, we used Bonferroni Correction to adjust our confidence intervals for testing multiple hypotheses.

Table 1: Risk of Opioid Use Disorder or Overdose for Pregabalin and Opioids

Exposure Description	Case OUD	Case No OUD	Control OUD	Control No OUD	Case Risk	Control Risk	Case Confidence Interval (+/-)	Control Confidence Interval (+/-)
Pregabalin Use	12,431	293,692	8,725	297,398	4.0608	2.8502	0.07995	0.06740
Pregabalin Before Opioids	1,773	59,630	1,643	59,760	2.8875	2.6758	0.15144	0.14594
Pregabalin Before & After Opioids	2,082	41,997	1,530	42,549	4.7233	3.4710	0.22644	0.19538
Pregabalin After Opioids	8,576	192,065	5,552	195,089	4.2743	2.7671	0.10120	0.08206