



Were Gabapentinoid-Opioid Co-Prescription Trends Affected by the United Stated Food and Drug Administration’s Safety Communications?

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INTRODUCTION

- **Gabapentinoids**, FDA-approved for the treatment of partial seizures, peripheral neuropathies, neuropathic pain syndromes, fibromyalgia and restless leg syndrome
- **‘Off-label’ effective agents** of perioperative multimodal analgesia

In December 2019, the **FDA issued a Drug Safety Communication: Serious risk of respiratory depression when co-prescribed gabapentinoids with other central nervous system depressants, particularly opioids.**

In this study, the impact of such a warning on gabapentinoid-opioid co-prescription rates was investigated.

METHODS

The **Merative MarketScan Commercial Claims database** was examined for pharmaceutical claims of all patients aged ≥ 18 years from February 2018 to December 2022.
Objective: Assessing gabapentinoid-opioid co-prescription rates (defined as any overlapping supply of opioids and gabapentin/pregabalin) before (23 months) and after (36 months) the FDA Communication.

We analyzed **co-prescription rates** on a patient level and performed an interrupted time series analysis to test the “real-world” effect of the FDA Communication.

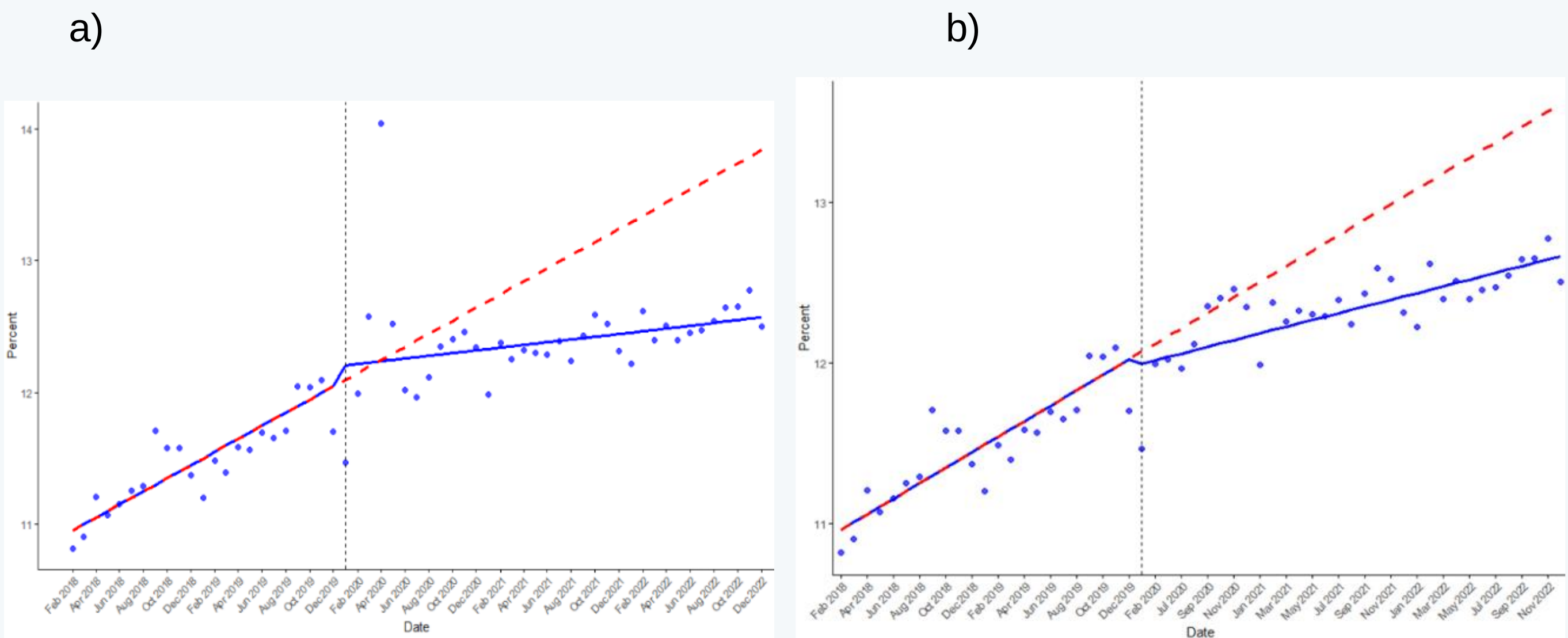


Figure 1 a) Trends in gabapentin-opioid co-prescriptions before and after the FDA warning in December 2019 and **b)** without the peak of COVID-19 first lockdown (March-May 2020). Blue dots represent monthly % of patients with co-prescriptions. Blue lines represent the co-prescription trend. Red-dotted line represents the hypothetical trajectory of the trend existing before December 2019, if the FDA warning was never issued. Black-dotted line marks the interruption point used for the interrupted series analysis.

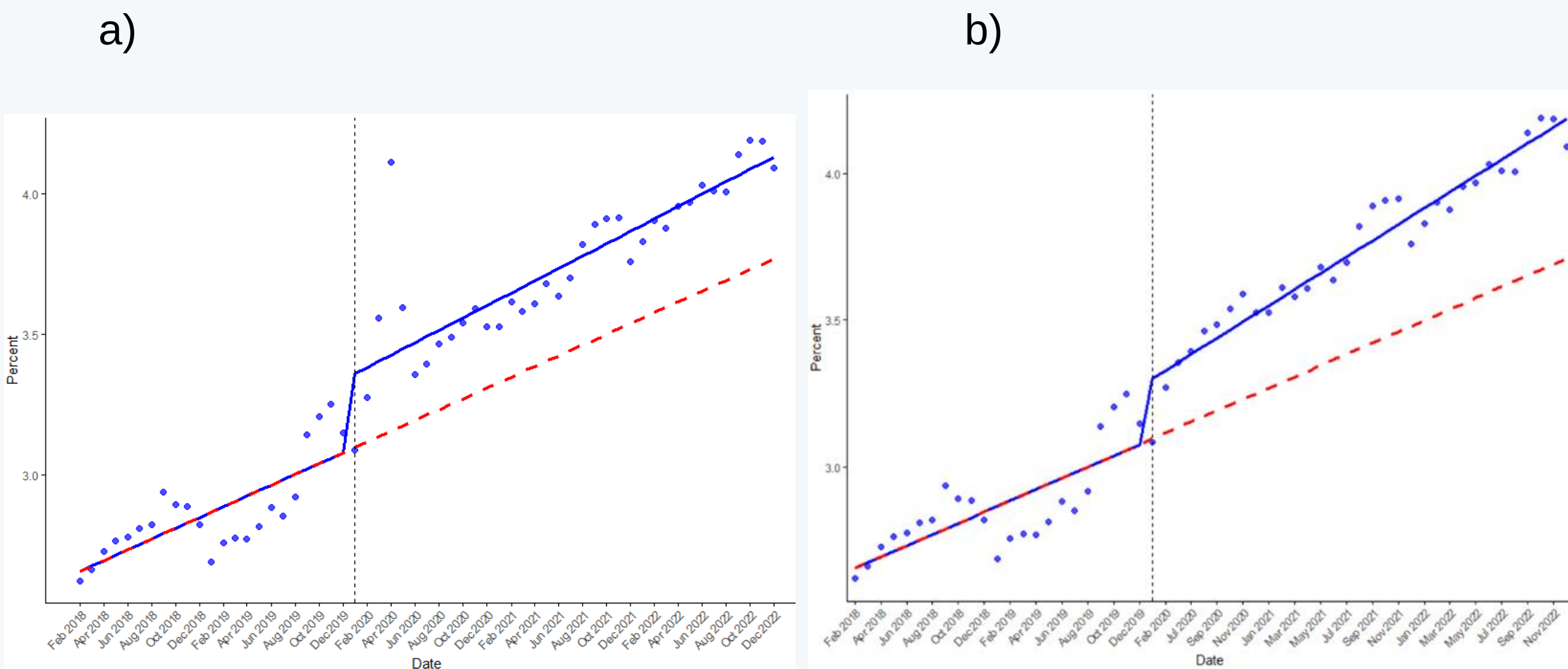


Figure 2 a) Trends in pregabalin-opioid co-prescriptions before and after the FDA warning in December 2019 and **b)** without the peak of COVID-19 first lockdown (March-May 2020). Blue dots represent monthly % of patients with co-prescriptions. Blue lines represent the co-prescription trend. Red-dotted line represents the hypothetical trajectory of the trend existing before December 2019, if the FDA warning was never issued. Black-dotted line marks the interruption point used for the interrupted series analysis.

RESULTS

n=2,119,239 patients with **gabapentin-opioid** and **n=583,344** patients with **pregabalin-opioid** co-prescriptions

Before the FDA Communication: Significant increasing monthly trends in both gabapentin-opioid and pregabalin-opioid co-prescriptions

After the Communication: Monthly trend was significantly reduced only for gabapentin-opioid co-prescriptions
Post-Communication an increasing trend remained

Excluding the peak of the first COVID-19 lockdown: Increase in the rate of month-to-month change in trends of pregabalin-opioid co-prescriptions and a negation of the immediate increase after the warning for gabapentinoid-opioid co-prescriptions

DISCUSSION

The literature on the impact of FDA warnings for pharmaceuticals is relatively sparse. For drugs such as codeine, varenicline and febuxostat prescription rates declined before the FDA’s first announcement, suggesting that physicians may already act on concerns from available literature before formal warnings. Gabapentinoid-opioid co-prescription rates still demonstrated a positive trend after the FDA’s December 2019 Communication, even though the change in monthly co-prescription trends was slower for gabapentin. The incongruity of our findings with the available literature could be attributed to gabapentinoids’ efficacy in neuromuscular pathologies and favorable risk-benefit ratio as multimodal analgesia components.



Abstract and References