

# An Exploratory Analysis of FDA Adverse Events Data

Onur R. Yoruk  
May 11<sup>th</sup>, 2020

*This slide deck & code notebook is available on:*  
[github.com/oryoruk/fda\\_adverse\\_events/](https://github.com/oryoruk/fda_adverse_events/)  
(or [bit.ly/azn\\_case](https://bit.ly/azn_case))

# Intro



- CS, Comp. Bio./Bioinformatics
- From Turkey
- Live in Philadelphia
- Will brew my first batch of beer this week

# Outline

- Background
- Exploratory Analysis of FAERS Data
- Questions from AstraZeneca Case Study
- Conclusion / Discussion / Next Steps

# FAERS: FDA Adverse Events Reporting System

General Information Report ID, receive date, etc.	
Patient or other information Age, weight, sex, etc.	
<b>Products</b>  Product A Product B Product C Product D Product E	<b>Patient reactions</b>  Reaction 1 Reaction 2 Reaction 3

- openFDA API

<https://api.fda.gov/drug/event.json?search=reactionmeddrapt:'headache'&limit=5>

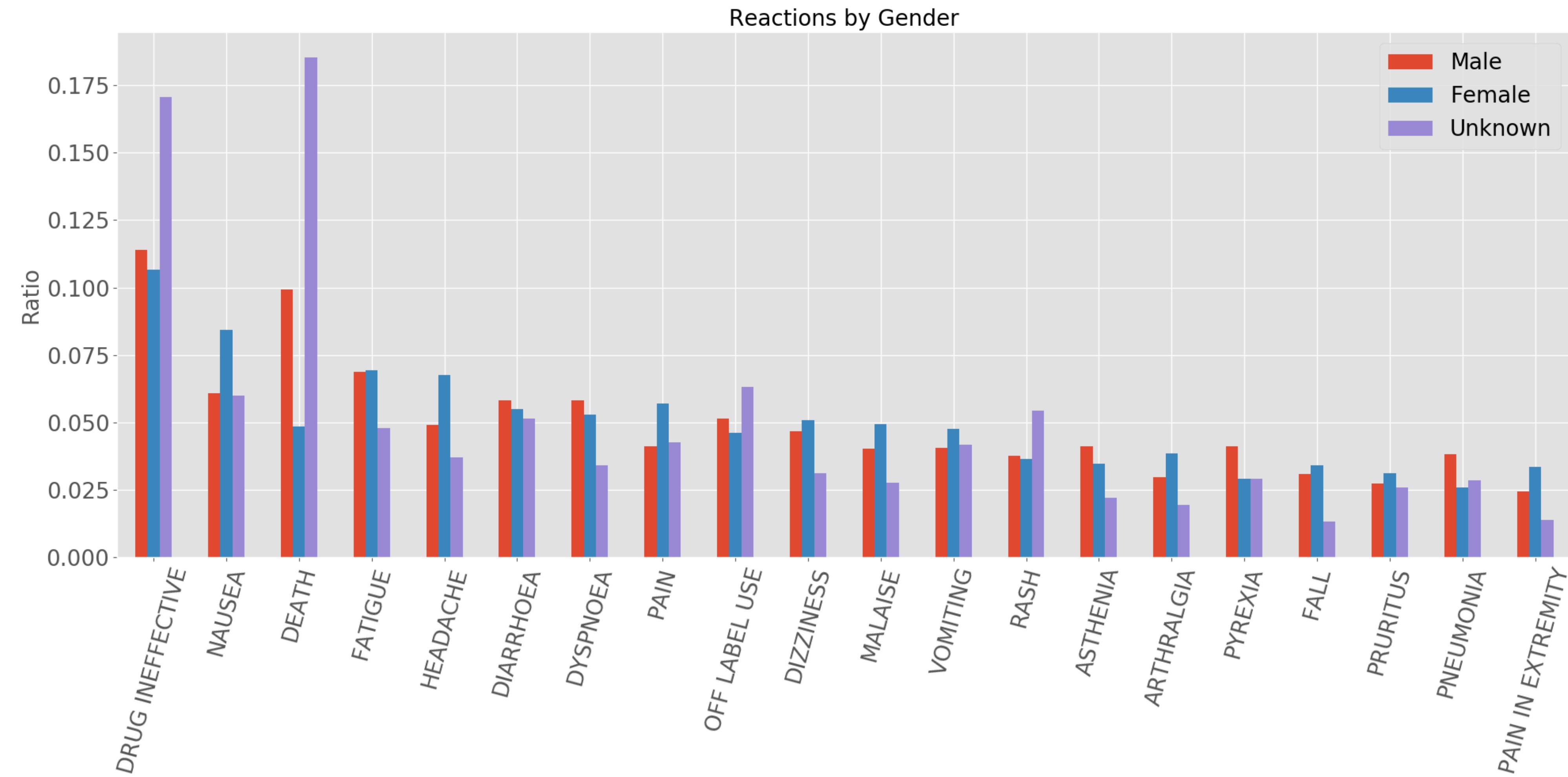
base endpoint

? search=

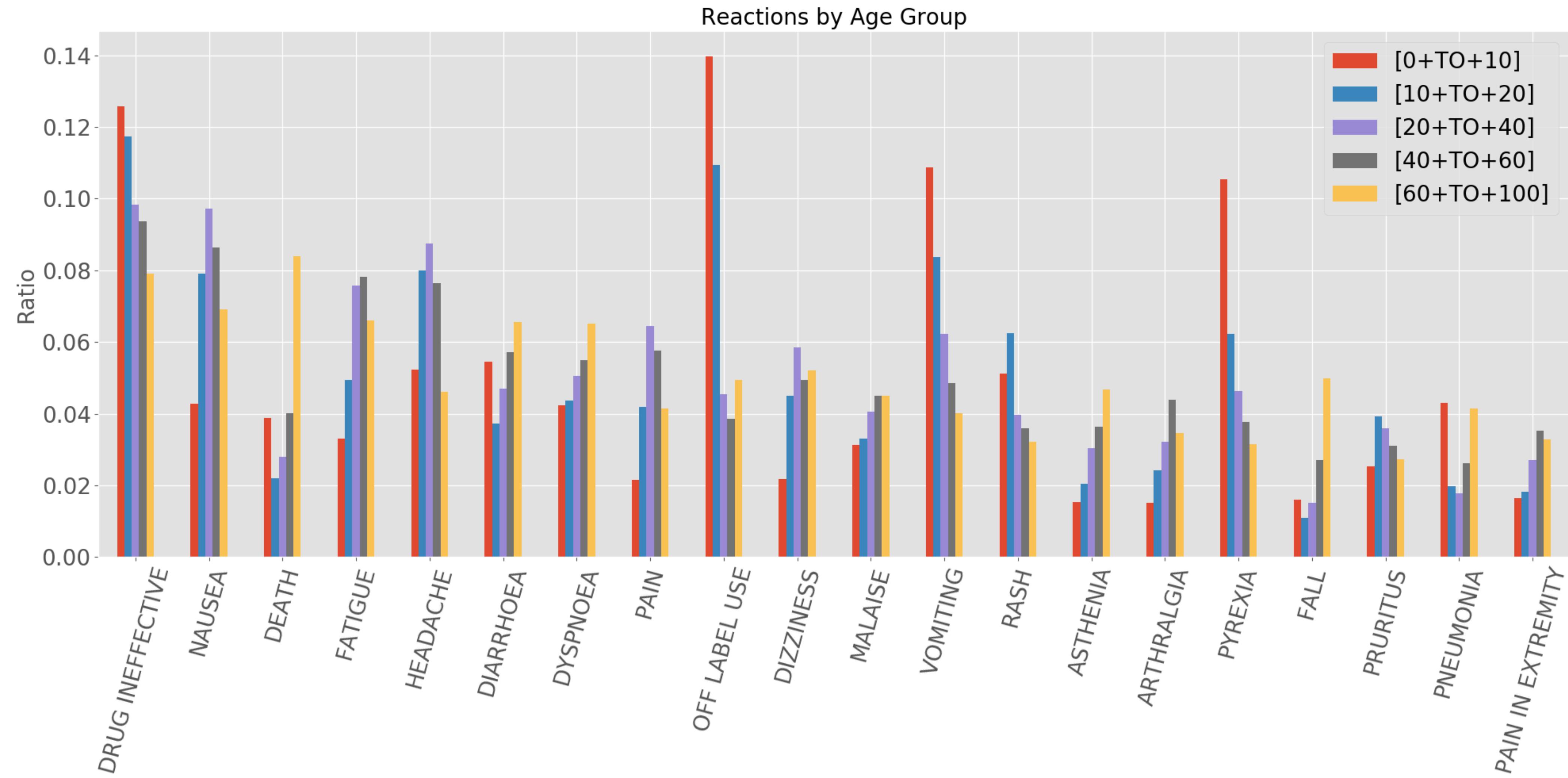
field:term

& limit

# Data Exploration Part I: Effect of Demographics on Reported Adverse Events



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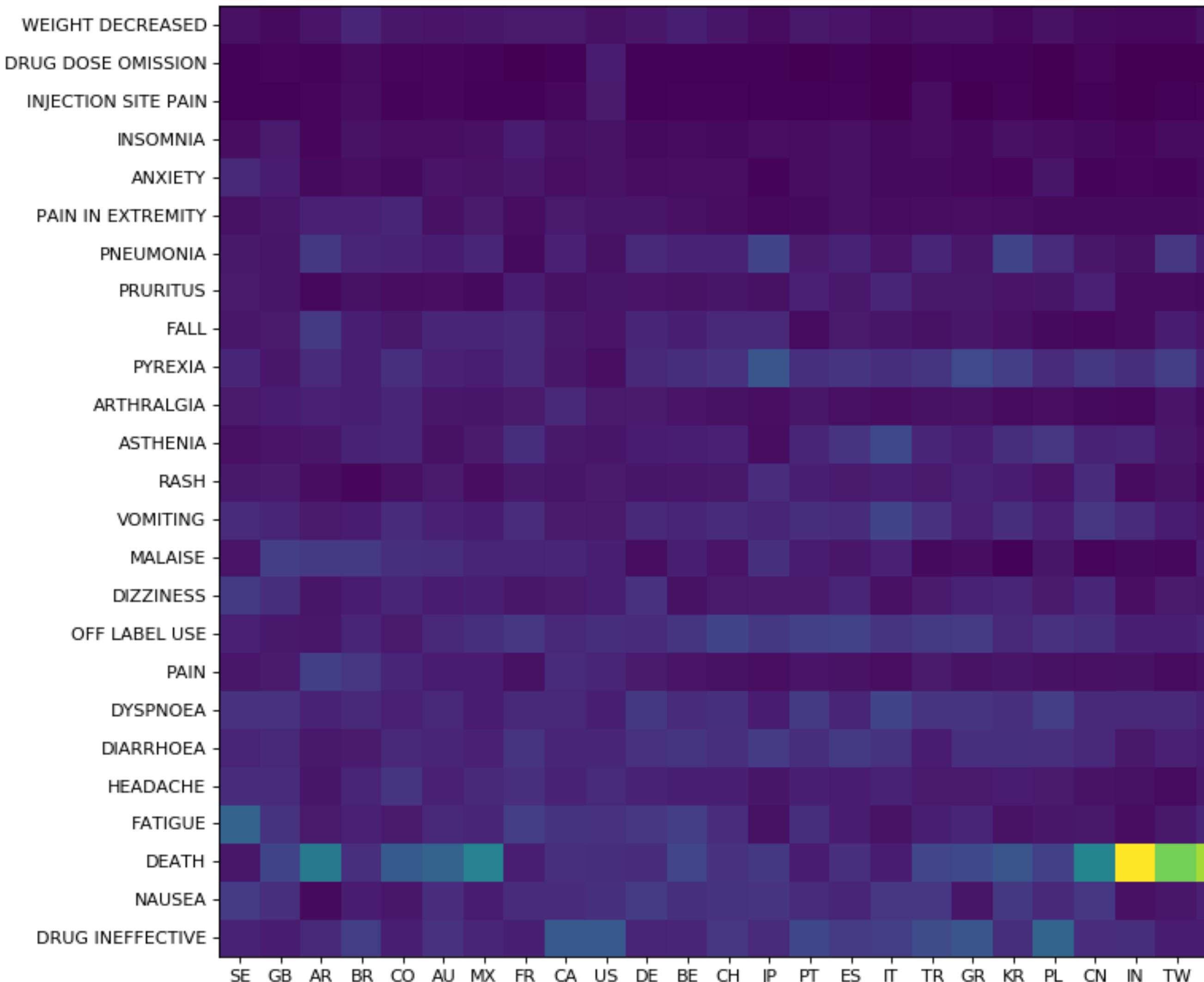
**Question 1: Are different adverse events reported  
in different countries?**

# Top Countries & Reactions

	term	count
0	US	6136862
1	GB	298758
2	CA	260177
3	JP	259359
4	FR	250505
5	DE	190403
6	IT	138001
7	BR	92823
8	ES	71442
9	AU	65305

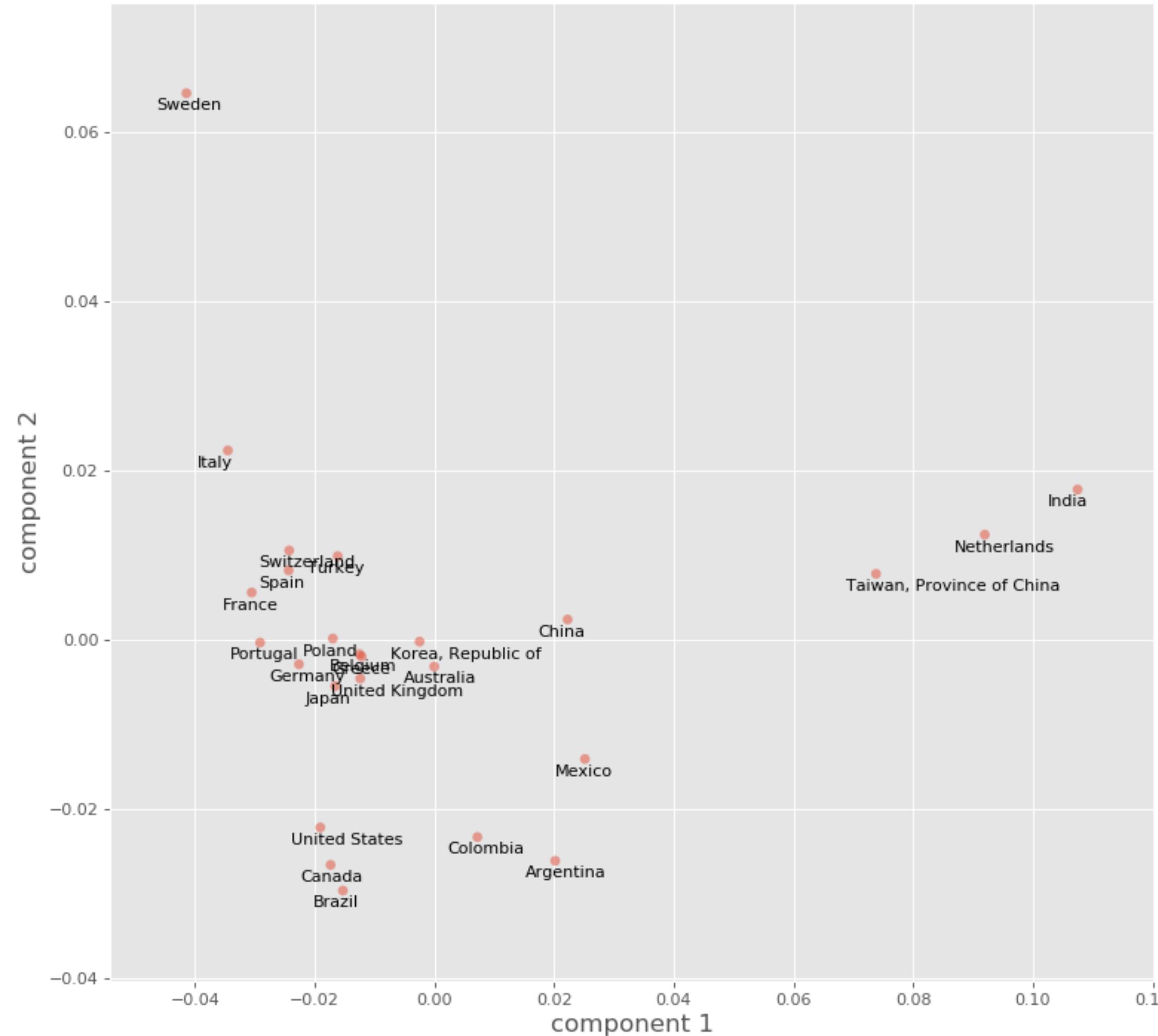
	term	count
0	DRUG INEFFECTIVE	733191
1	NAUSEA	485098
2	DEATH	474541
3	FATIGUE	439328
4	HEADACHE	388310
5	DIARRHOEA	359872
6	DYSPNOEA	344540
7	PAIN	326354
8	OFF LABEL USE	324957
9	DIZZINESS	313617

# “Death” Stands out as an Important Variable Separating Countries



# PC Analysis Groups

## Americas & Europe Separately



# Other Reactions Standing Out



# Answer 1

- Looks like YES, \*\*different adverse events\*\* are reported in \*\*different countries\*\*.
- Furthermore:
  - - We see that certain countries have similar patterns in terms of drug reactions reported:
  - - \*\*Netherlands, Taiwan and India\*\* cluster together because reports of Death seem to be very high from these countries.
  - - \*\*Sweden\*\* looks like an outlier because of very high relative number of reports around suicide/self harm
  - - The rest of the crowd is split into 2 clusters:
    - - Cluster 1: Europe and Asia
    - - Cluster 2: Americas
  - - When we do the PCA analysis, we see that the top 2 principal components that explain  $59\% = 47 + 12\%$  ( $79\% = 71 + 8\%$ ) of the variance in reported adverse event count distributions and correspond mainly to the following drug reactions:
    - - Death
    - - Combination of INTENTIONAL OVERDOSE, INTENTIONAL SELF-INJURY, TOXICITY TO VARIOUS AGENTS, DRUG INTERACTION, MALAISE, PAIN, DRUG INEFFECTIVE

**Question 1: Are different adverse events reported  
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# Answer 2

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# Data Exploration Part II: AstraZeneca in FAERS

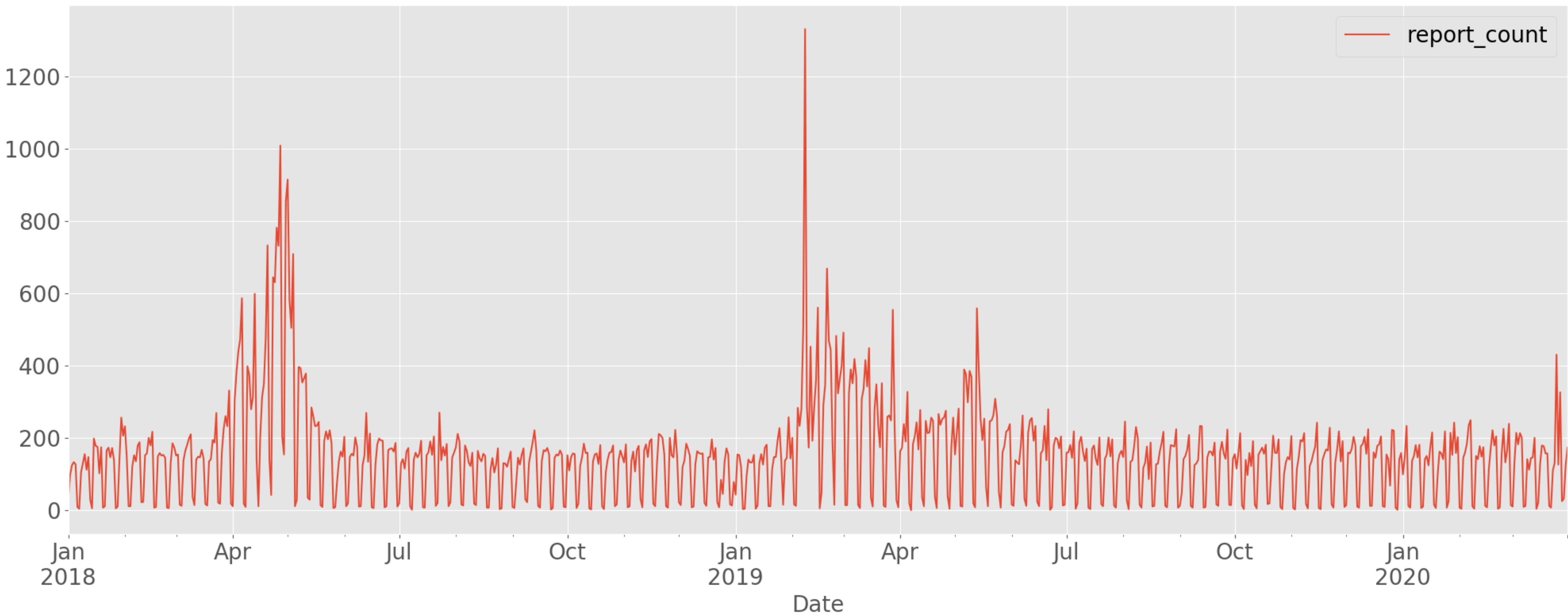
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	term	count
0	Mylan Pharmaceuticals Inc.	2143943
1	Aurobindo Pharma Limited	1933948
2	Teva Pharmaceuticals USA, Inc.	1749269
3	Actavis Pharma, Inc.	1736623
4	Cadila Healthcare Limited	1723934
5	Amneal Pharmaceuticals LLC	1671581
6	Zydus Pharmaceuticals (USA) Inc.	1649009
7	Sun Pharmaceutical Industries, Inc.	1545861
8	Sandoz Inc	1231388
9	West-Ward Pharmaceuticals Corp.	1201469

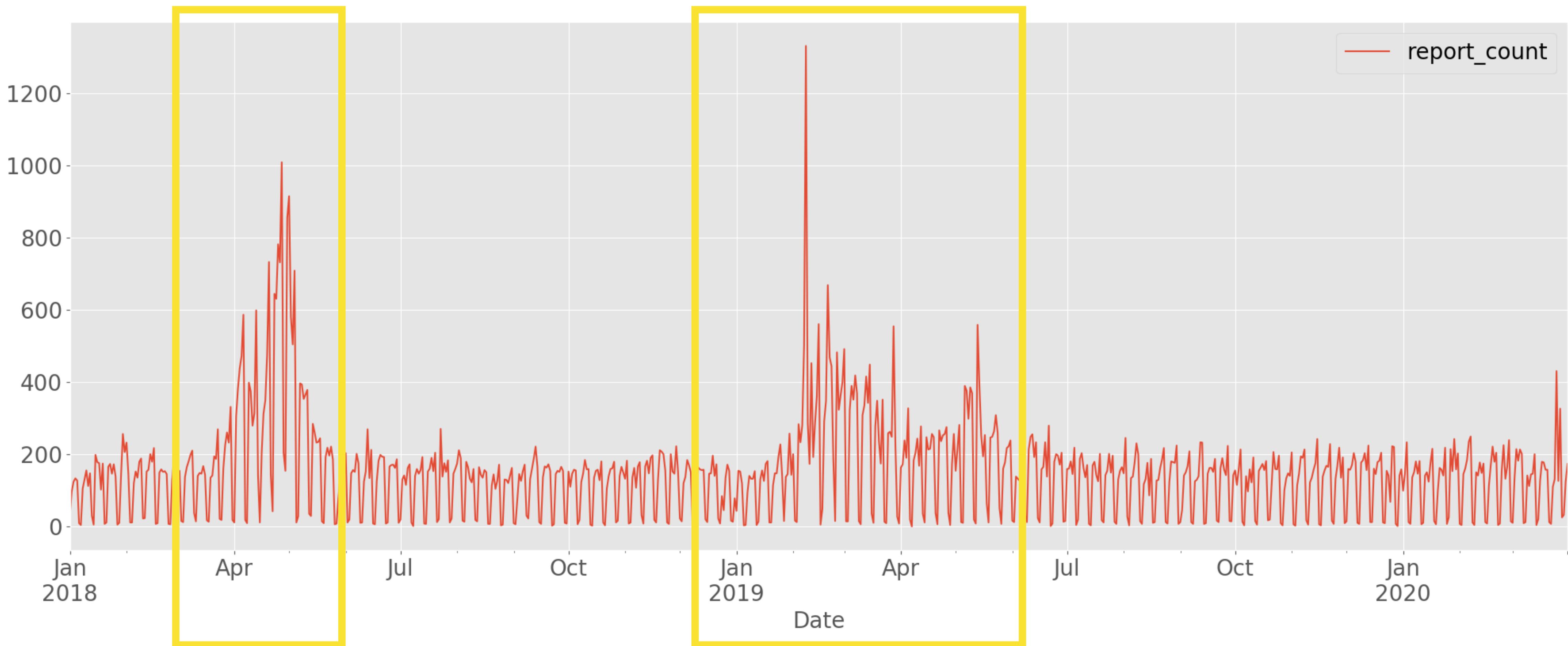
	term	count
146	AstraZeneca Pharmaceuticals LP	501107

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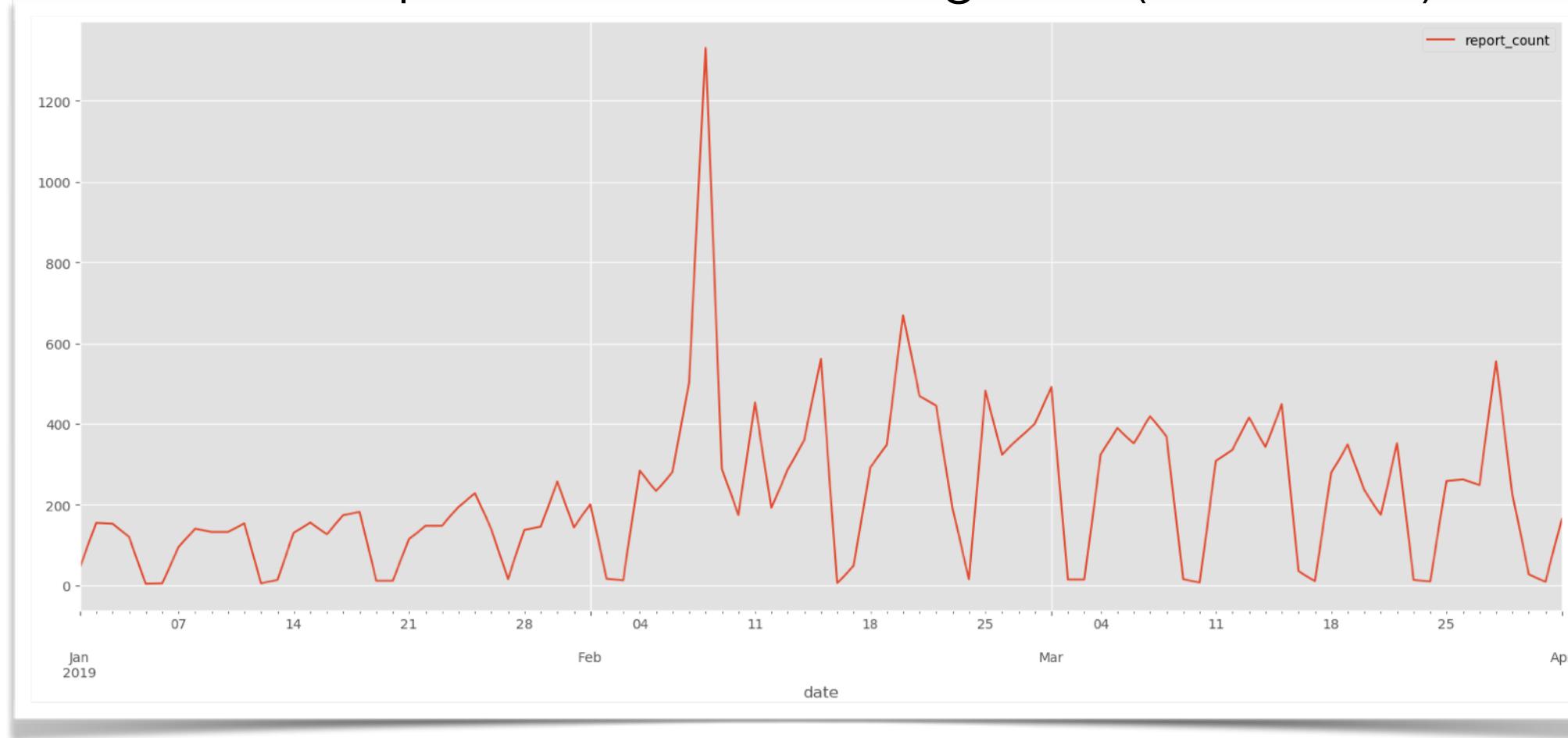


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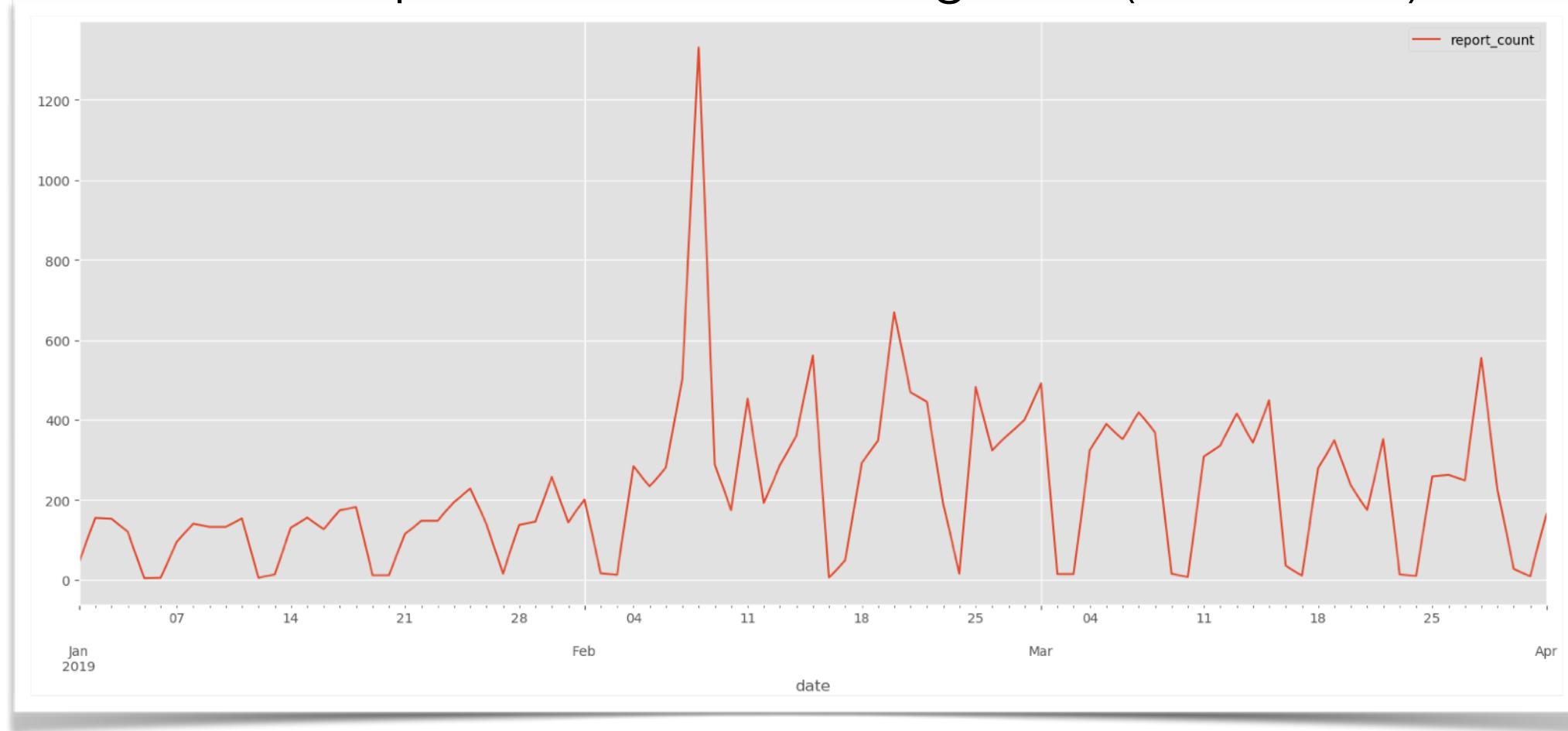
# Multiple Spikes in Reports over the Years Point to Problematic Drugs: New Spikes Can Warn Proactively

Report Counts Including AZN (Over Time)



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## Drugs

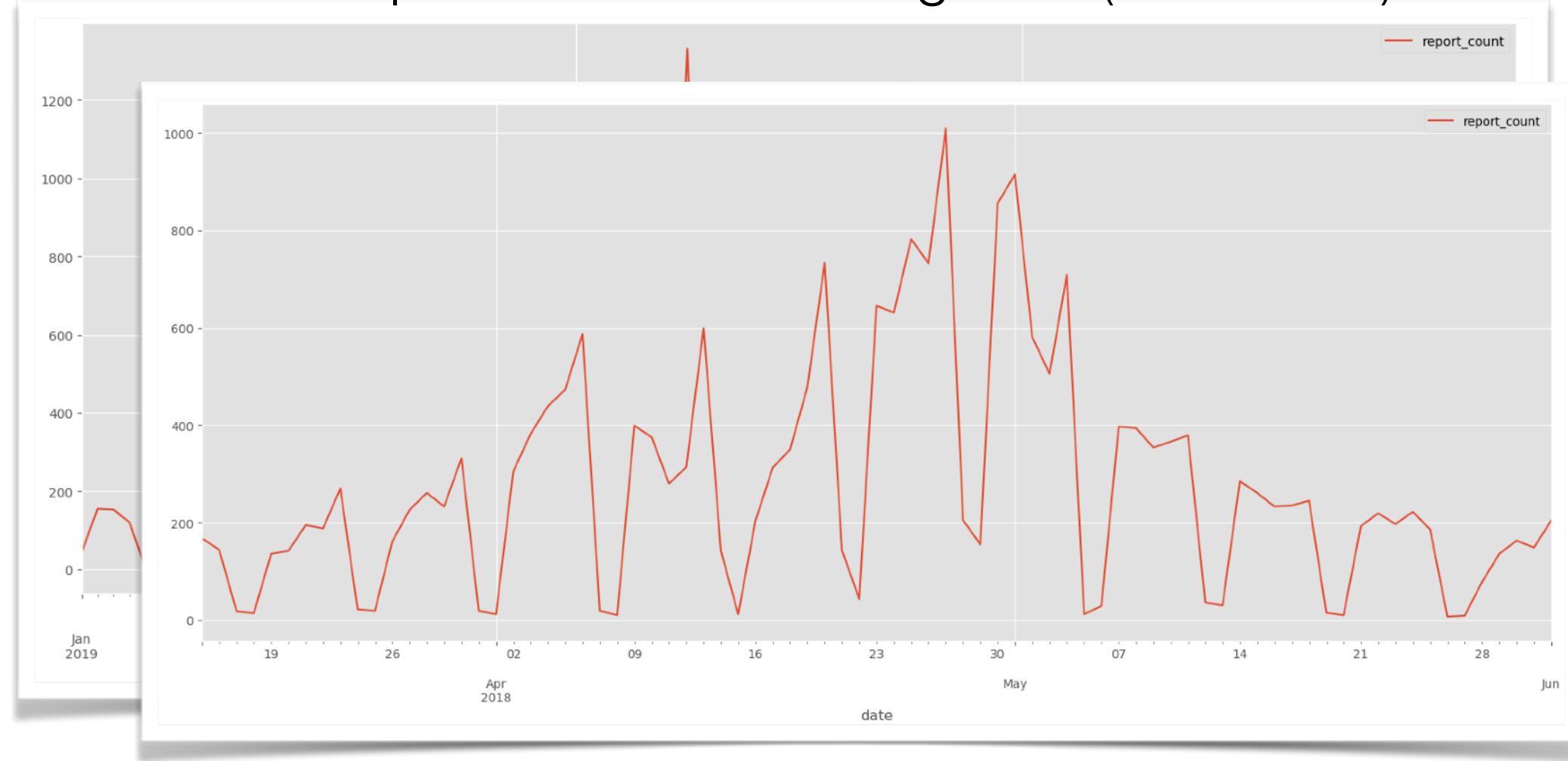
	term	count
0	NEXIUM	2441
1	NEXIUM I.V.	2430
2	PRILOSEC	1818
3	PREVACID 24 HR	1449
4	PREVACID	1386

## Reactions

	term	count
0	CHRONIC KIDNEY DISEASE	2322
1	RENAL INJURY	1525
2	RENAL FAILURE	1437
3	ACUTE KIDNEY INJURY	1185
4	END STAGE RENAL DISEASE	697

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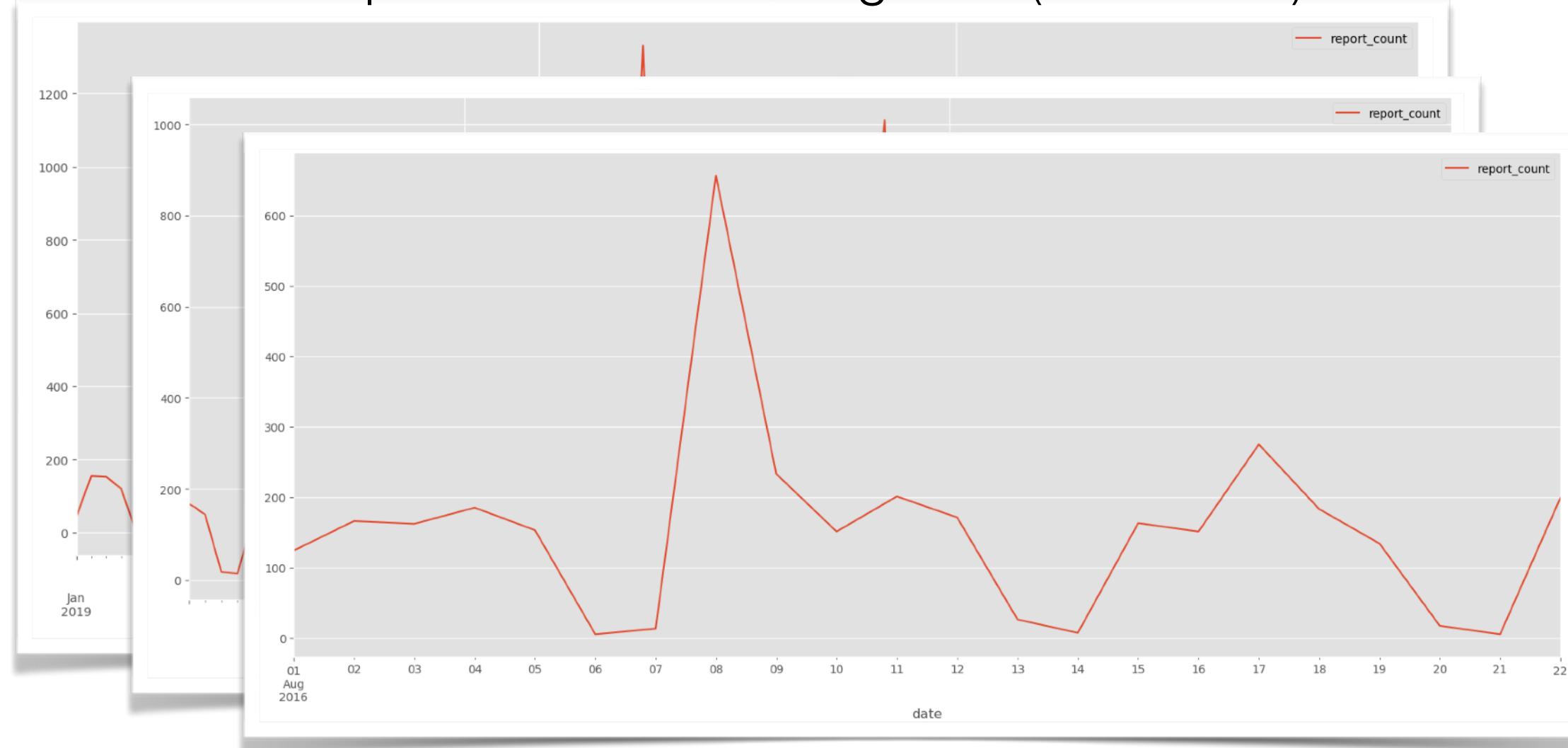
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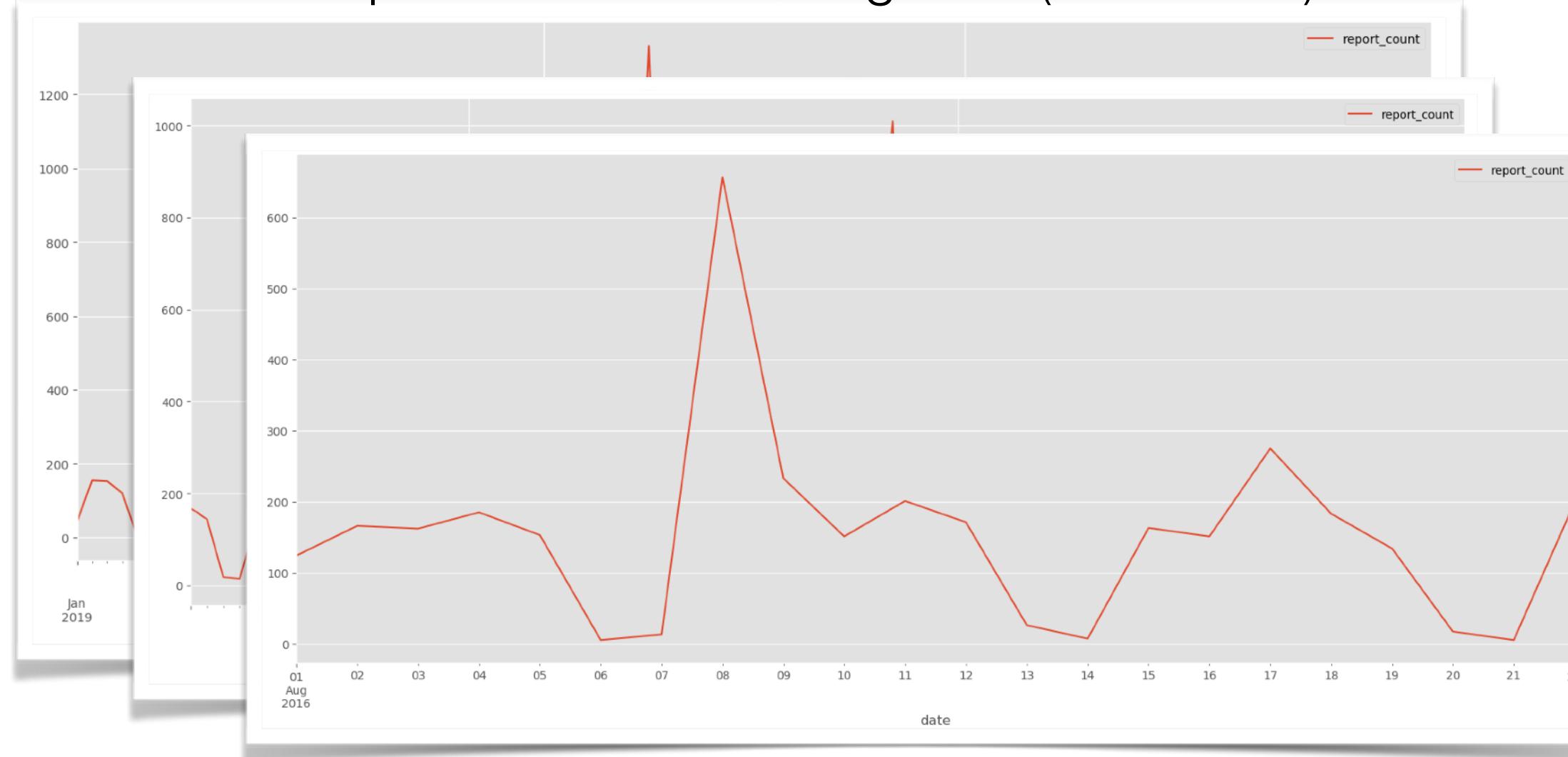
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## Kidney Problems May be Caused by Nexium and Prilosec

### Severe Kidney Problems Linked to Prilosec and Nexium

Nexium and Prilosec are used to treat conditions such as chronic heartburn. Both Nexium and Prilosec have topped the nationwide sales of over the last 20 years. Consumers can obtain Nexium and Prilosec by prescription or by simply buying it over-the-counter. The FDA approves Proton Pump Inhibitors (PPIs), like Nexium and Prilosec, for use up to four weeks at a time. However, many people have taken Prilosec or every day for decades. Extended use of Prilosec and Nexium can cause severe kidney problems, such as [Acute Interstitial Nephritis \(AIN\)](#).



### Study Linking Prilosec and Nexium to Severe Kidney Problems

Dr. Ziyad Al-Aly is a kidney specialist and researcher on a [current study regarding PPI use](#) and kidney problems. Dr. Al-Aly found that PPI users were more likely than people on other heartburn medication to develop kidney problems, such as chronic kidney disease or kidney failure. Dr. Al-Aly recommends using Prilosec or Nexium when absolutely necessary and for the shortest time possible.

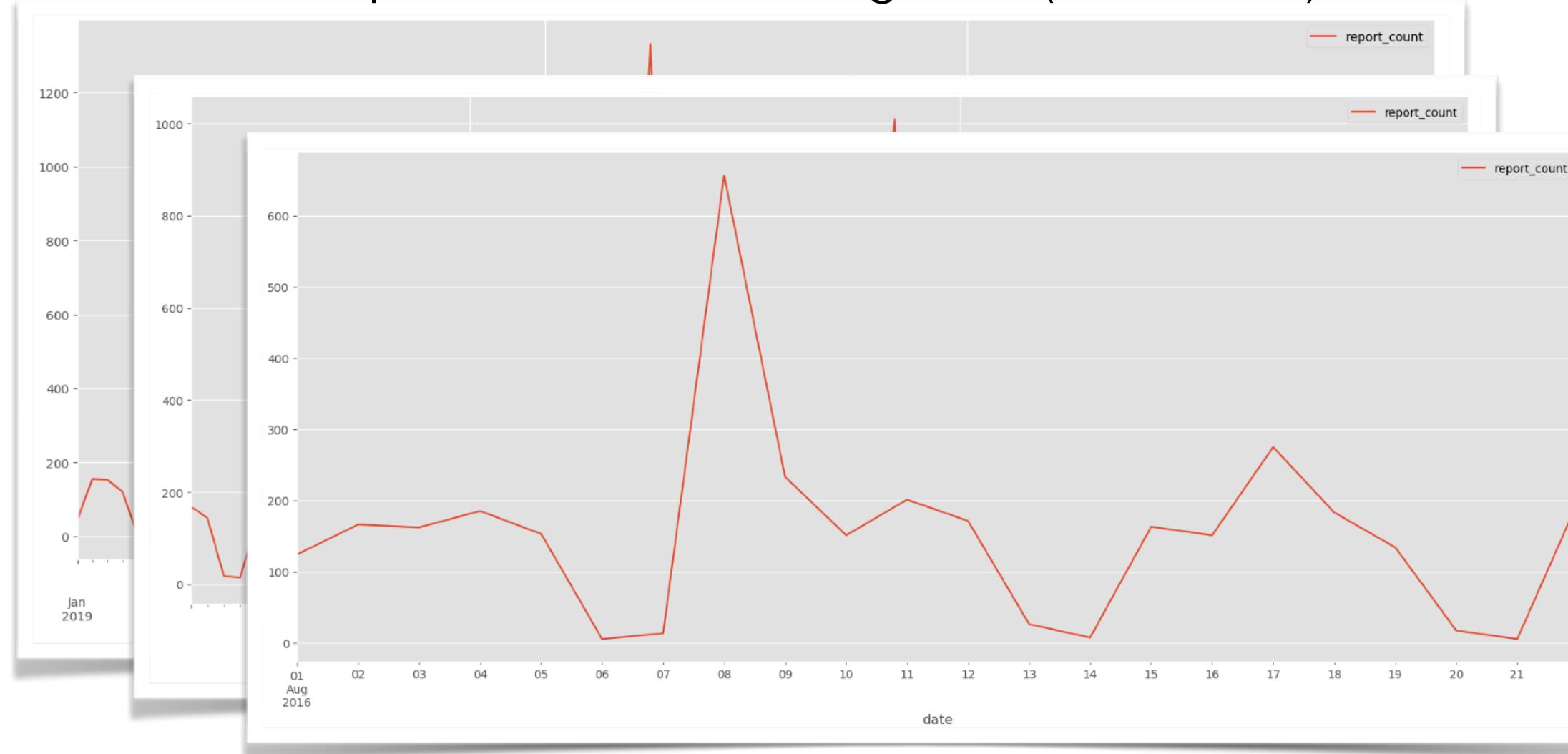
The study revealed chronic kidney disease in 15% of PPI users, opposed to 11% in those who took heartburn medication. Even more alarming, the study noted end-stage kidney failure rates were twice as high among PPI users. More studies are underway to evaluate the risk of kidney problems caused by Nexium and Prilosec. Previous studies linked Prilosec and Nexium use with Acute Interstitial Nephritis and Acute Kidney Injury. Prolonged use of PPIs may also worsen heartburn (gastroesophageal reflux disease), making it harder for users to stop using the drug.

### Profits Prevent Warning on Kidney Problems

AstraZeneca, the manufacturer of Nexium and Prilosec, has made \$80-\$100 billion dollars in revenue in the past twelve years. The company modified their formula to maintain a longer patent and make versions of the drug that wouldn't be available as a generic. The company created

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## Kidney Problems May be Caused by Nexium and Prilosec

**Severity**  
Nexium & Prilosec over the counter drugs have been linked to kidney problems.  
Problems include chronic kidney disease, acute kidney injury, renal failure, and heart damage.

**Levin Papantonio**  
Thomas | Mitchell | Rafferty | Proctor | P.A.

**800.277.1193**  
[Click Free Case Review](#)

### Nexium & Prilosec Lawsuits

Nexium & Prilosec are drugs called proton pump inhibitors (PPIs). They are used to treat gastroesophageal reflux disease (GERD), by reducing the amount of acid in a person's stomach.

The Nexium and Prilosec lawsuits claim the long-term use of these drugs can increase the likelihood of strokes, bone fractures, acute kidney injury, renal failure, and heart damage.

Our law firm is accepting clients who took Nexium or Prilosec and suffered chronic kidney disease or acute interstitial nephritis.

#### What Do We Know About the Nexium & Prilosec Lawsuits



**Nexium & Prilosec Case Evaluation**

First Name:

Last Name:

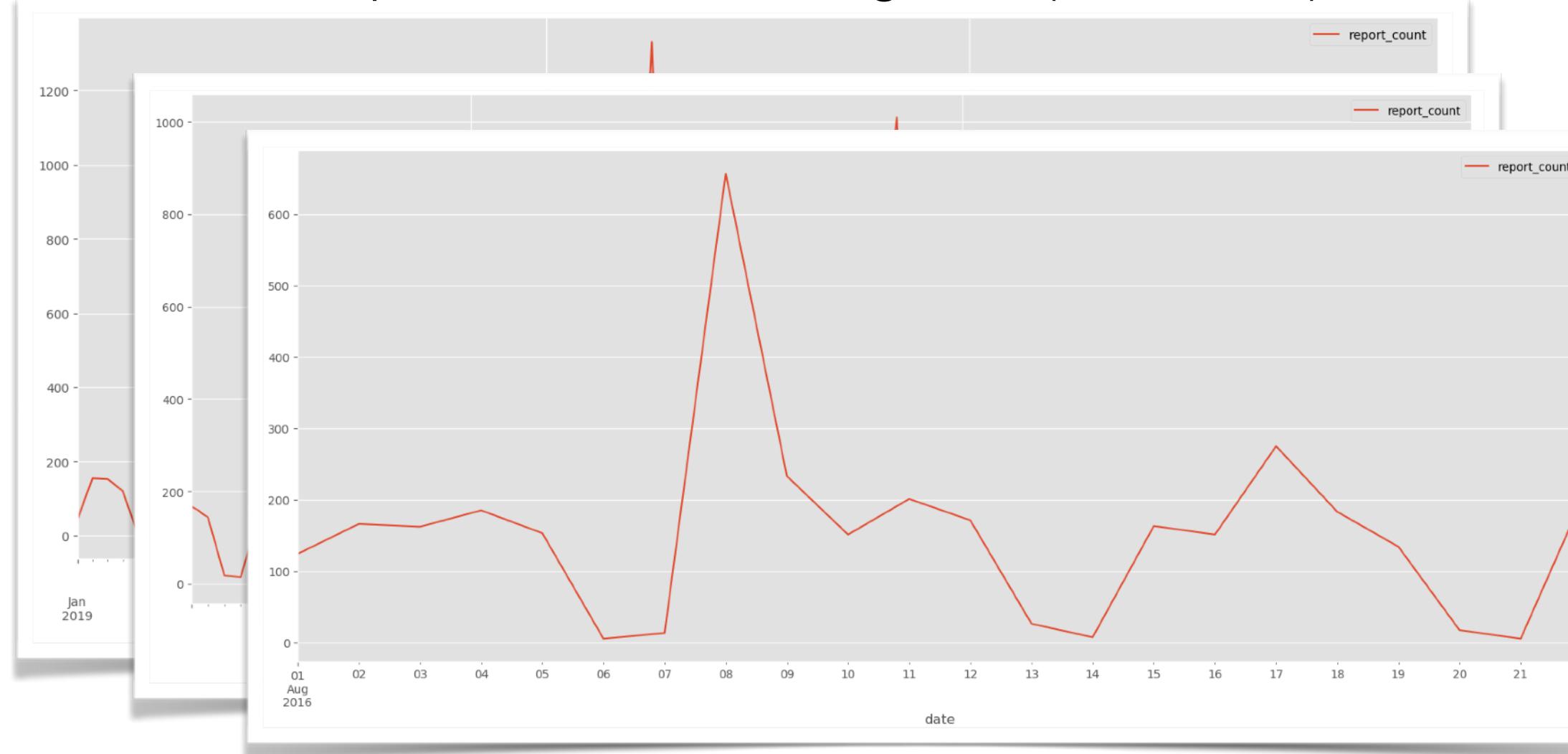
Email:

Phone Number:

Describe your Nexium or Prilosec injury:

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### Nexium & Prilosec Lawsuits

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Popular heartburn drugs linked to gradual yet 'silent' kidney damage

Most patients don't experience acute kidney problems beforehand

Date: February 22, 2017

Source: Washington University in St. Louis

Summary: The sudden onset of kidney problems often serves as a warning for doctors to discontinue patients' use of proton pump inhibitors (PPIs), sold under brand names Prevacid, Prilosec, Nexium and Protonix, among others. But a new study indicates that more than half of patients who develop chronic kidney damage while taking the drugs don't experience acute kidney problems beforehand, according to researchers.

Most Popular this week

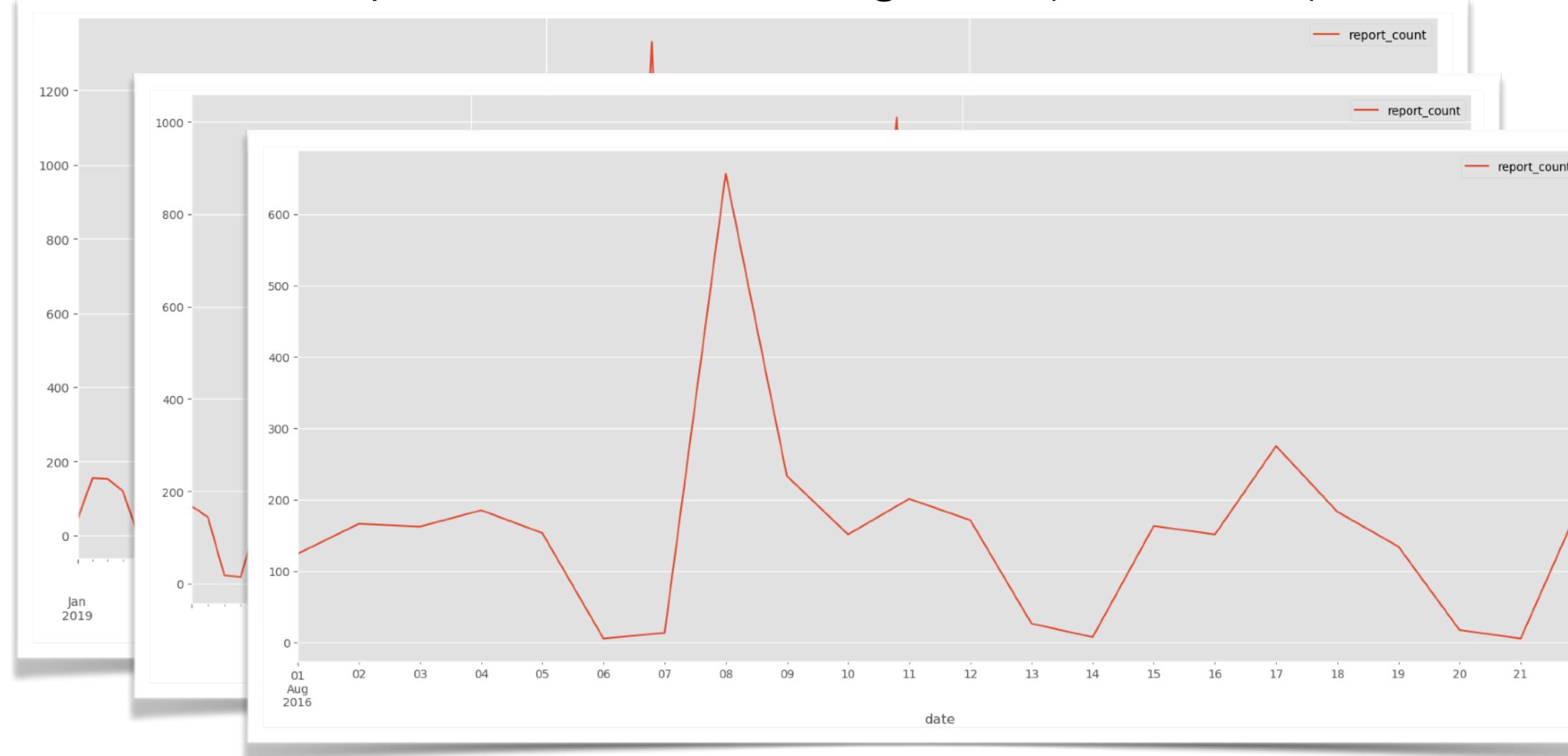
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Vitamin D Levels Appear to Play Role in COVID-19 Mortality Rates

Antibody Blocks Infection by the SARS-CoV-2 in Cells, Scientists Discover

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# Conclusions & Next Steps

- Different countries have different adverse event reporting patterns
- Different disease areas
- Co-reported drugs
- Warning / Monitoring Dashboard Tool could be useful