

# Existence of Notoriety Bias in FDA Adverse Event Reporting System (FAERS) Database and Its Impact on Signal Strength

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## Introduction

- Notoriety bias is defined as "a selection bias in which a case has a greater chance of being reported if the subject is exposed to the studied factor known to cause, thought to cause, or likely to cause the event of interest"
- This study aimed to determine the existence of notoriety bias in FAERS database and estimate the impact of potential notoriety bias induced by safety alerts on signal estimates using disproportionality analysis.

## Methodology

### DATABASE

- The FAERS is a database that comprises of AE reports, medication error reports and product quality complaints resulting in AEs that are submitted to FDA.
- The database is primarily designed to assist the FDA's post-marketing safety surveillance program for drug and therapeutic biologic products

### STUDY PROCEDURE

- Publicly available FAERS data was downloaded from FAERS website (<https://open.fda.gov/data/faers/>).
- Text file was extracted into excel worksheet for further analysis. 'New safety information' which is given by USFDA was considered as the source of safety signal.
- Thirty one drugs which had label change/safety alert issued by FDA from 2009 to 2013 were considered in this study.
- These drugs were reviewed four quarters before and after the safety alert notification for the existence of notoriety bias.
- Normalization of reports was done for ease of graphical representation.
- The highest count of the report of any of the 8 quarters of the drug was considered as 100 and remaining count of reports of that particular drug was normalized accordingly.
- The safety alert for biologicals and for drugs which had unspecific safety alert (Ex: Psychiatric events, skin reactions) were eliminated from the study.

### DISPROPORTIONALITY ANALYSIS

- The impact of notoriety bias induced by safety alerts were analyzed using Reporting Odds Ratio (ROR) and Proportional Reporting Ratio (PRR).
- ROR and PRR for the drugs were calculated two years before and after the safety alert were issued.
- Wilcoxon signed rank test was used to determine if there were statistical differences in signal strength before and after the safety alert.

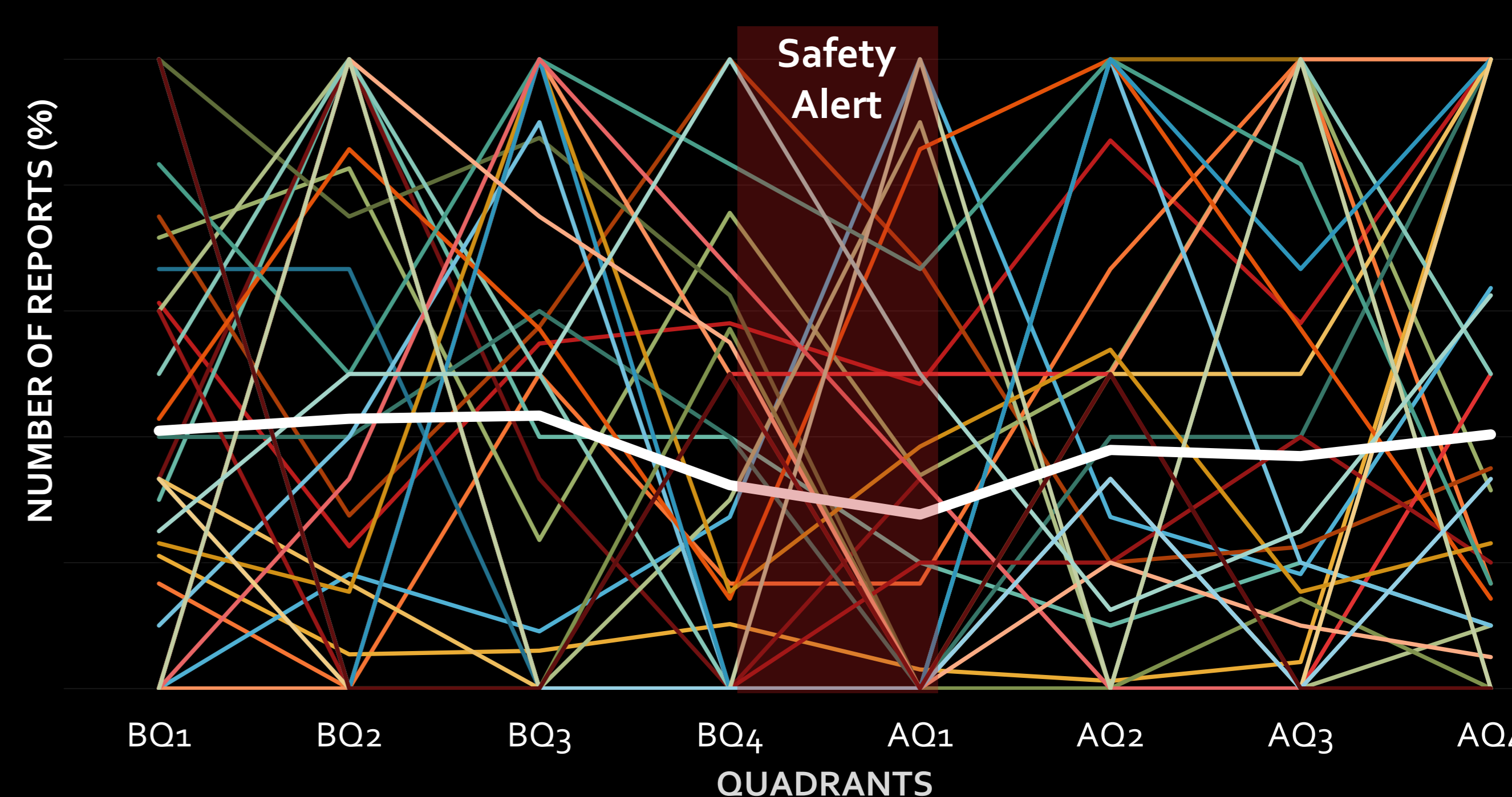
## Result

- The analysis was performed for thirty one drugs which had safety alert/label change notification by FDA between 2009 and 2013.
- There was increased reporting for 11 drugs after the safety alert/label change by FDA. Drugs included Zoledronic acid, Ceftriaxone, Varenicline, Trazodone, Solifenacin, Finasteride, Lanthanum carbonate, Bevacizumab, Solifenacin succinate, Tropicium chloride and Tolterodine tartrate. An average increase of  $17.18 \pm 31.63$  was observed for the above mentioned drugs.
- The reporting of 20 drugs decreased or remained unchanged after the safety alert/label change by FDA. Drugs included Montelukast, Didanosine, Propylthiouracil, Orlistat (104; 58), Minocycline, Tapentadol hydrochloride, Oxybutynin chloride, Doxycycline hyclate, Simvastatin, Dutasteride, Leuprolide acetate, Dronedarone HCl, Infliximab, Voriconazole, Adalimumab, Drospirenone, Pegloticase, Fesoterodine fumarate, Dalfampridine, Lacosamide.

## Descriptive Statistics

		N	Mean
Number of reports	Before	31	26.9355
	After		25.8387
Signal strength using ROR	Before	31	29.2003
	After		37.1373
Signal strength using PRR	Before	31	38.6842
	After		44.5129

## Reporting Trend of 31 Drugs, 4 Quarters Before and After the Safety Alert



## Wilcoxon Signed Rank Analysis

		N	Mean Rank	Sum of Ranks	Z value	p value
Number of reports	Negative Ranks	18 <sup>a</sup>	14.58	262.50	-0.974 <sup>d</sup>	0.330
	Positive Ranks	11 <sup>b</sup>	15.68	172.50		
	Ties	2 <sup>c</sup>				
Signal strength using ROR	Negative Ranks	17 <sup>a</sup>	14.76	251.00	-0.059 <sup>d</sup>	0.953
	Positive Ranks	14 <sup>b</sup>	17.50	245.00		
	Ties	0 <sup>c</sup>				
Signal strength using PRR	Negative Ranks	17 <sup>a</sup>	14.91	253.50	-0.108 <sup>d</sup>	0.914
	Positive Ranks	14 <sup>b</sup>	17.32	242.50		
	Ties	0 <sup>c</sup>				

a. after < before, b. after > before, c. after = before, d. Based on positive ranks

- It was observed that there is no statistically significant difference with respect to the number of reports and signal strength, before and after the safety alert.

## Conclusion

- Although, few FDA safety alert/ warnings had strong and immediate impact, many had no impact on reporting of AE and signal strength.
- This study found that over reporting due to notoriety bias does not exist in the FAERS database and the overall disproportionality in signal estimates is not altered by safety alert.
- Even though few drugs exhibited increase in reporting, it was not found to be significant.
- Future studies are required to assess the impact of confounding factors on notoriety bias.

## Reference

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