Fatal Outcomes from Drug Interactions
Insights from the FDA Adverse Event Reporting System

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Background

Drug-drug interaction harms are difficult to assess and evidence in this field is limited

Objective

This study aims to describe the characteristics of the recipients and drugs involved in fatal drug interactions reports in the FDA Adverse Event Reporting System (FAERS)

Methods

- Observational study

- FAERS 2022 reports with Death as outcome and mentioning the following MedDRA Preferred Terms (PTs) as the adverse reaction:
  - Drug interaction
  - Inhibitory drug interaction
  - Potentiating drug interaction
  - Labelled drug-drug interaction issue
  - Labelled drug-drug interaction medication error

- De-duplication and manual review of cases for categorization of the implicated drugs based on their pharmacological action

FAERS uses the Medical Dictionary for Regulatory Activities (MedDRA) Preferred Terms (PTs) -single medical concept- for classification of the adverse events

Results

- 10,202 reports involving drug interaction were identified
  - 798 (7.8%) reported death as the outcome
  - 151 duplicative reports were removed
- Report characteristics are shown in Table 1
- Therapeutic classes for reports are shown in Figure 1
- The most prevalent report involved antidepressants
- Interquartile range (IQR) of number of medications per report IQR 1-3 was 2 to 7

Figure 1. Percentage of Reports with Fatal Outcome by Drug Class involved

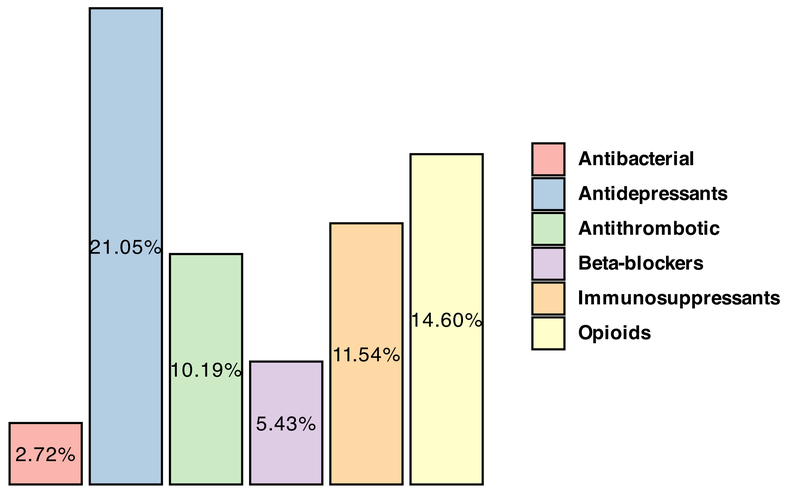

Table 1. Reports Characteristics

Reports	N=647 (100%)
Sex Female (N, %)	210 (32.5)
Missing	77 (12)
Age (years, SD)	57.3 (22.1)
Missing	142 (22%)
Severity Outcomes*	
Death only	170 (73.7)
Life Threatening	109 (16.8)
Hospitalized	266 (41.1)
Congenital Anomaly	4 (<0.01)
Disable	37 (5.7)
Other Outcomes	416 (64.3)
Total drugs by report Mean (SD)	6.1 (10.2)
MedDRA PT for the interaction†	
Drug Interaction	462 (71.4)
Inhibitory drug interaction	2 (0.3)
Potentiating drug interaction	12 (1.8)
Labelled drug-drug interaction issue	14 (2.2)
Labelled drug-drug interaction medication error	50 (7.7)
Reporter	
Consumer	94 (17.2)
Healthcare Professional	549 (84.8)
Missing	4 (<0.01)
Country Event Occurring	
US	80 (12.3)
Rest of the world	502 (77.6)
Missing	65 (10.1)

SD standard deviation; MedDRA PT: Medical Dictionary for Regulatory Activities-Preferred Term;
*Apart from "Dead" there could be more than one severity outcome in the same report
†Could be more than one PT in the same report

Conclusions

- FAERS database provides crucial insights into fatal outcomes associated with drug-drug interactions
- Despite the high frequency of reports involving specific therapeutic classes, not all fatal adverse reactions due to drug interactions are reported to FAERS and some reports may be misclassified

References

1. FDA Adverse Event Reporting System (FAERS) Public Dashboard. https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-public-dashboard
2. Medical Dictionary for Regulatory Activities. MedDRA. https://www.meddra.org/