Adverse event profiles after brand and generic clopidogrel in the Food and Drug Administration Adverse Event Reporting System (FAERS)

Victor Serebruany, MD, PhD
Heart*Drug*™ Research LLC;
Johns Hopkins University;
Busan, December, 2018

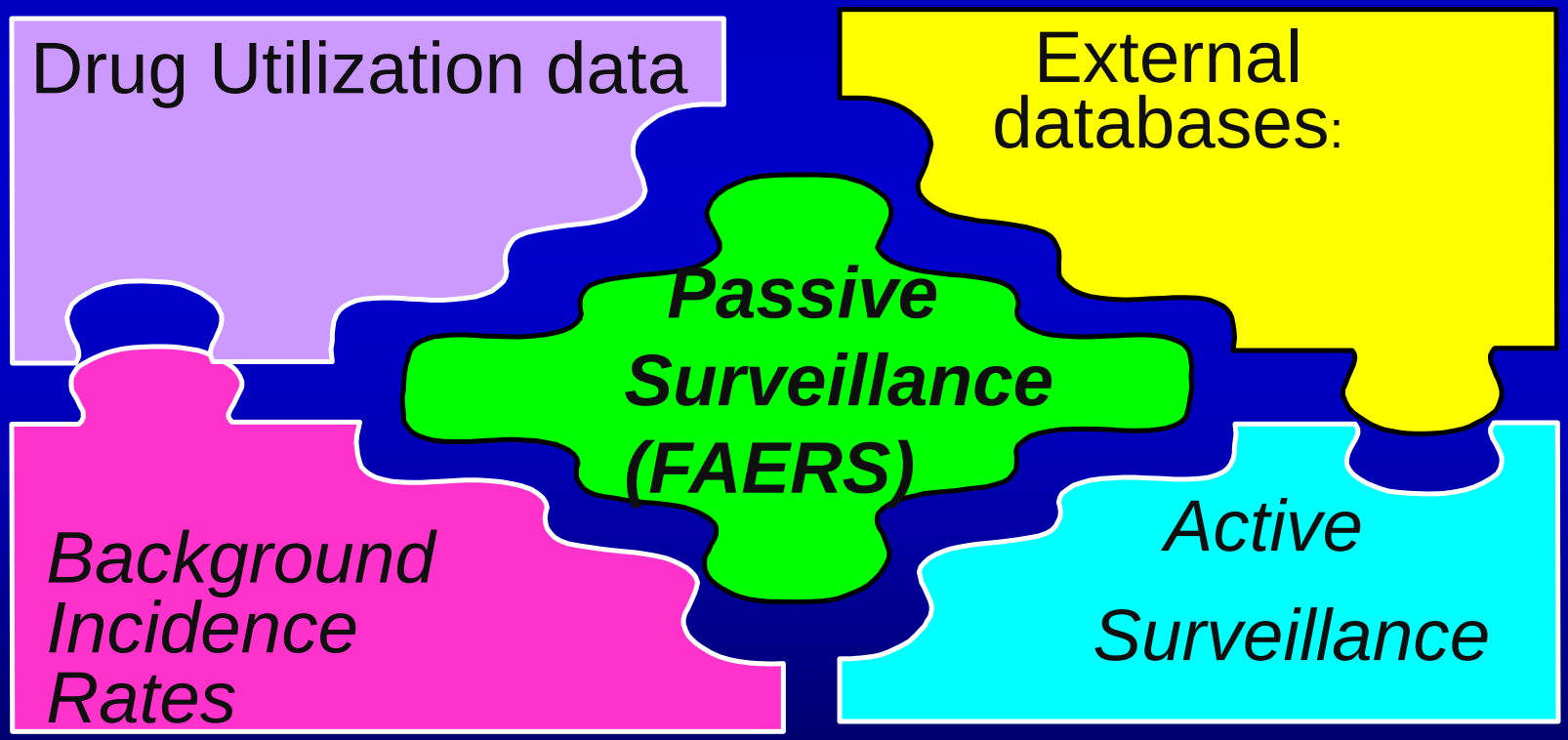
Background

Brand clopidogrel (BC) is used as bisulfate salt, while the preparation used in generic formulations (GC) varies. The clinical usefulness of BC has been proved in a wide variety of large scale clinical trials, while GCs have been approved for clinical use based solely on small bioequivalence studies. Importantly, trials are focused predominantly on efficacy thrombotic vascular outcomes and bleeding risks, while adverse events are usually not under the scope, underpowered, and commonly underreported, or missing. Since post-trial surveillance data are so scarce, the evidence from large, uniform, government-mandated datasets are useful.

OBJECTIVE:

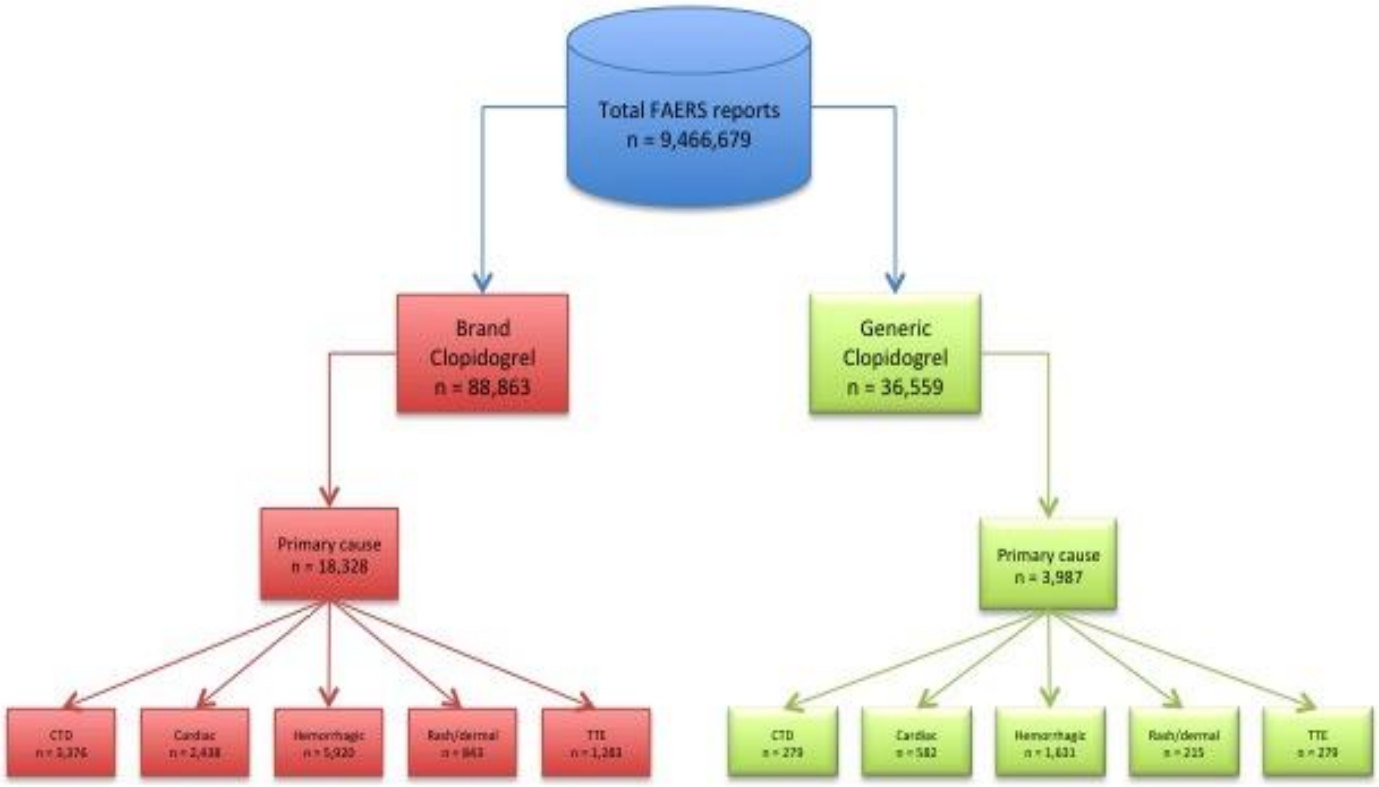
To assess completeness and quality of original FAERS cases comparing outcomes after brand and generic clopidogrels.

FDA Postmarketing Surveillance



FDA should monitor FAERS

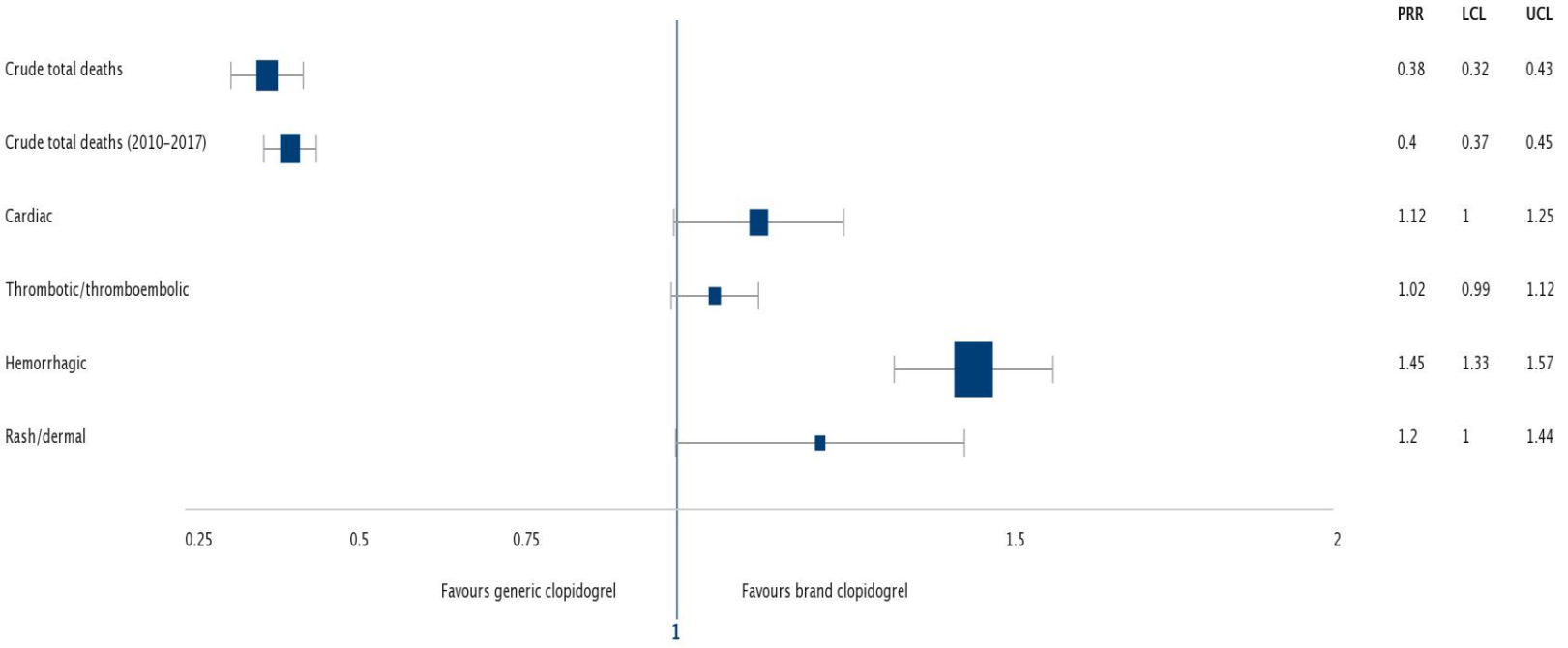
- Daily “in-box” review of reports
  - All serious unlabeled reports;
  - Serious direct reports;
  - Periodic and “enhanced pharmacovigilance” reports
- Periodic safety reports
- Main mission: identify and monitor “Safety Signals”
- Work with epidemiologists, and doctors



CTD = crude total deaths
TTE = thrombotic/thromboembolic

Variable	Brand Clopidogrel n, (%)	Generic Clopidogrel n, (%)
Age (<75 y.o.)	7,193 (39.2%)	1,787 (44.8%)
Age (> 75 y.o.)	4,178 (22.8%)	1,091 (27.4%)
Age missing	6,957 (38.0%)	1,109 (27.8%)
Gender (Female)	5,667 (30.9%)	1,513 (37.9%)
Gender (Male)	7,955 (43.4%)	1,782 (44.7%)
Gender missing	4,706 (25.7%)	692 (17.4%)
Diabetes	308 (1.68%)	42 (1.06%)
Hypertension	586 (3.2%)	123 (3.1%)
Renal failure	165 (0.9%)	24 (0.6%)
Total	18,328 (100%)	3,987 (100%)

Proportional reporting ratios for selected primary cause events



Conclusion

- The primary-caused adverse profiles differ with brand and generic clopidogrel in FAERS. While deaths reports were higher, the rates of cardiac, hemorrhagic, and skin complications were less common for Plavix.
- It seems that generic manufacturers heavily underreport deaths to the FDA, while the overall adverse event profile suggests potentially better safety of brand over generic formulations.