Assessing Aspirin and Cancers in FAERS: Mission Impossible

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Background

The US Food and Drug Administration (FDA) Adverse Event (AE) Reporting System (FAERS) is a global passive surveillance repository requiring mandatory updates by pharmaceutical manufacturers. Oral antiplatelet agents (OAA) including aspirin (ASA) are broadly used to prevent thrombosis, at expense of extra bleeding risks and potential cancer signal. However, the filing quality, and comparative patterns of ASA reports in FAERS are unknown. We assessed completeness of original annual FAERS reports for OAA with the special attention on ASA and cancer risks.

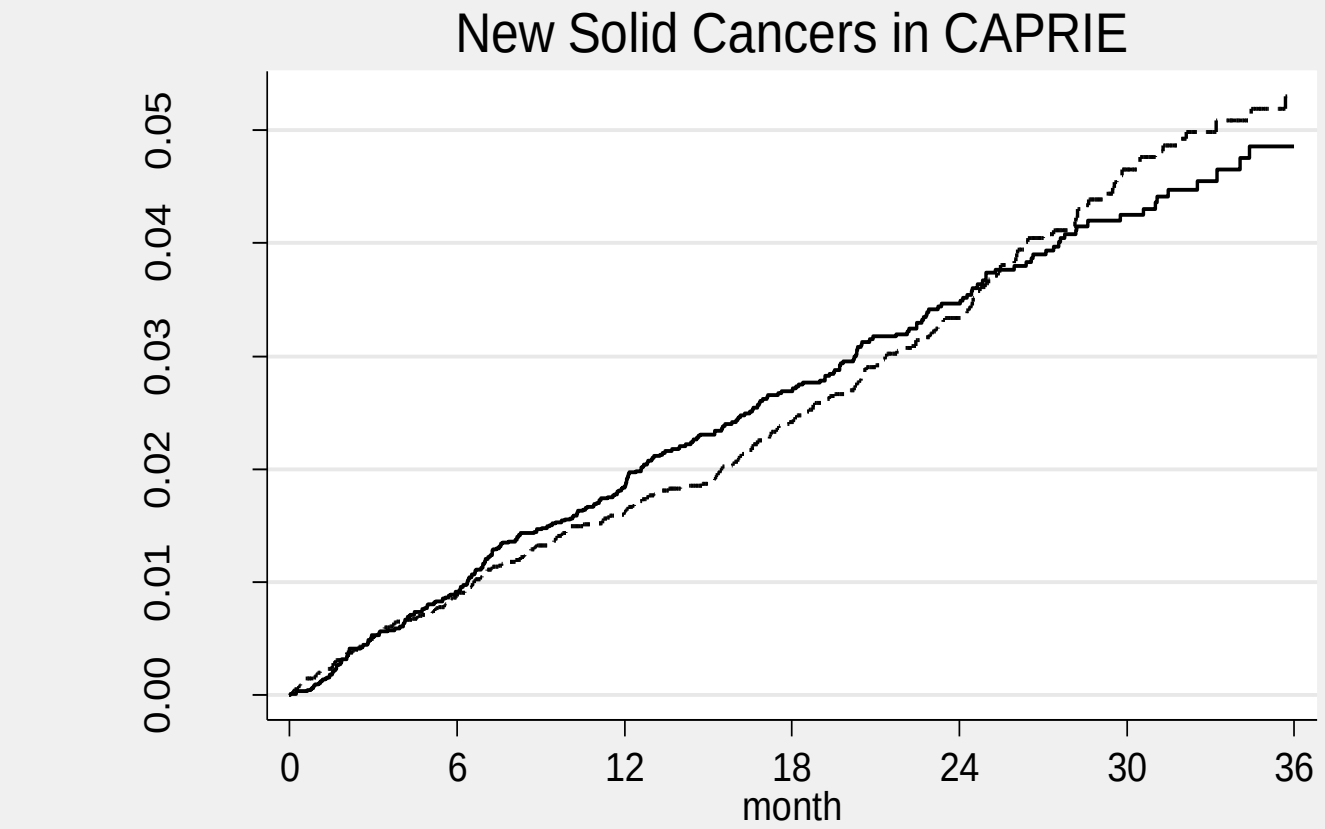
Results

The total of 1,187,729 reports qualified. The majority (n=1,121,989) of them were silent, while 65,730 records contain reference of at least one OAA, including 47,900 ASA cases. Therapy with ASA was heavily (>50%) underreported when used with prasugrel or ticagrelor, but still dominant (72.8%) among OAA, followed by clopidogrel (18.7%), prasugrel (4.1%), ticagrelor (3.6%), and anecdotal vorapaxar (0.05%).

Results-II

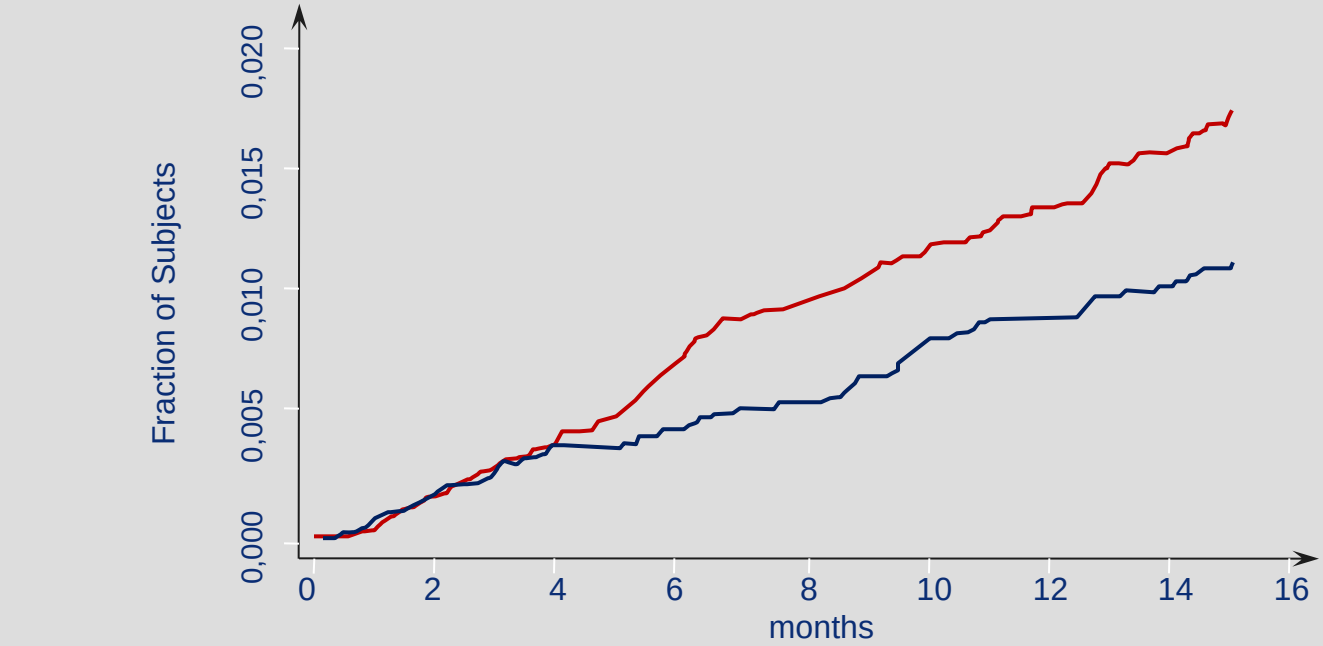
Despite current recommendations, some (0.73%) reports contain multi-OAA. The primary role of ASA in AE reporting was seldom (<1%), followed by clopidogrel (2.9%), prasugrel (3.7%), and highest for ticagrelor (9.3%). Missing gender after OAA was not common (< 10%), but age was missing in about 25% of reports. Bleeding was the most frequent AE associated with ASA.

New Solid Cancers in CAPRIE



The FDA Secondary Prasugrel Review, 2009

All New Solid Cancers After 7 Days in TRITON



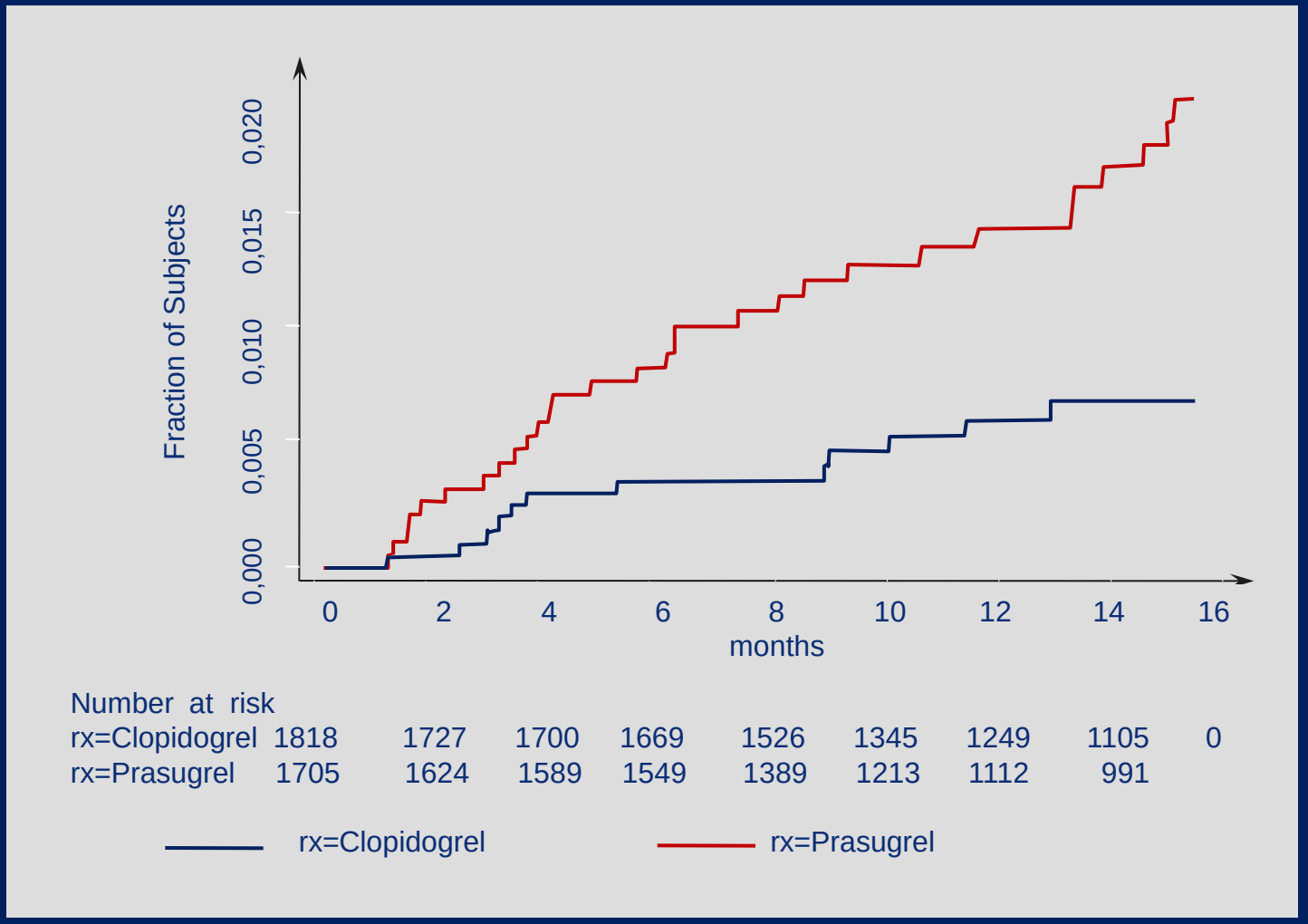
Number at risk

rx=Clopidogrel	6795	6508	6439	6327	5773	5120	4773	4286	0
rx=Prasugrel	6813	6558	6463	6318	5725	5097	4729	4227	0

rx=Clopidogrel rx=Prasugrel

The FDA Secondary Prasugrel Review, 2009

All New Solid Cancers in Women After 7 Days in TRITON



The FDA Secondary Prasugrel Review, 2009

Cancers and antiplatelet agents in FAERS

	Number of Cases NOT Reporting Cancer	Number of Cases Reporting Some Form of Cancer	Total Number of Cases	% of Total Cases Reporting some form of Cancer	Risk Ratio	Risk Ratio (95% interval)	p-value	comment
clopidogrel (no aspirin)	59994	2797	62791	4.45%	1.0551	(1.0006 - 1.1125)	0.047432	cancer reported more frequently w/ clopidogrel alone (compared to clopidogrel + aspirin)
clopidogrel + aspirin	55648	2453	58101	4.22%				
prasugrel (no aspirin)	4245	119	4364	2.73%	0.6794	(0.5383 - 0.8574)	0.001048	cancer reported more frequently w/ prasugrel + aspirin (compared to prasugrel alone)
prasugrel + aspirin	3874	162	4036	4.01%				
ticagrelor (no aspirin)	8268	144	8412	1.71%	0.4654	(0.3763 - 0.5757)	< 0.0001	cancer reported more frequently w/ ticagrelor + aspirin (compared to ticagrelor alone)
ticagrelor + aspirin	5107	195	5302	3.68%				
aspirin (no clopidogrel, no prasugrel, no ticagrelor)	441387	20984	462371	4.54%	1.0749	(1.0318 - 1.1198)	0.000526	cancer reported more frequently w/ aspirin alone (compared to aspirin + clopidogrel)
clopidogrel + aspirin	55648	2453	58101	4.22%				
aspirin (no clopidogrel, no prasugrel, no ticagrelor)	441387	20984	462371	4.54%	1.1307	(0.9718 - 1.3155)	0.110995	cancer reported more frequently w/ aspirin alone (compared to aspirin + prasugrel)
prasugrel + aspirin	3874	162	4036	4.01%				
aspirin (no clopidogrel, no prasugrel, no ticagrelor)	441387	20984	462371	4.54%	1.234	(1.0745 - 1.4171)	0.00273	cancer reported more frequently w/ aspirin alone (compared to aspirin + ticagrelor)
ticagrelor + aspirin	5107	195	5302	3.68%				
clopidogrel (no aspirin)	59994	2797	62791	4.45%	1.6336	(1.3633 - 1.9574)	< 0.0001	cancer reported more frequently for clopidogrel (no aspirin) compared to prasugrel (no aspirin)
prasugrel (no aspirin)	4245	119	4364	2.73%				
clopidogrel (no aspirin)	59994	2797	62791	4.45%	2.6021	(2.2043 - 3.0718)	< 0.0001	cancer reported more frequently for clopidogrel (no aspirin) compared to ticagrelor (no aspirin)
ticagrelor (no aspirin)	8268	144	8412	1.71%				
prasugrel (no aspirin)	4245	119	4364	2.73%	1.5929	(1.253 - 2.0251)	0.000127	cancer reported more frequently for prasugrel (no aspirin) compared to ticagrelor (no aspirin)
ticagrelor (no aspirin)	8268	144	8412	1.71%				

Conclusions

1. The reporting quality for ASA and cancer signal in FAERS are not good.
2. Heavy ASA underreporting during dual antiplatelet therapy, and missed demographic variables challenge outcome research capacities for establishing drug interactions in FAERS.
3. The FAERS quality can be improved by stricter FDA rules, better surveillance, and enforcements.