Assessing Exposure to Recently Approved Medications to Inform Feasibility for Signal Identification Analyses in the FDA's Sentinel System

Thuy Thai[1]; José J. Hernández-Muñoz[2]; Leah Herity[2]; Jamal T. Jones[2], James M. Kidd[2], Jummai Apata[2]; Natasha Pratt[2]; Yong Ma[3]; Bahareh Rasouli[1]; Mayura Shinde[1]; Sruthi Adimadhyam[1]; Jennifer G. Lyons[1]; Celeste Ewig[1]; Iara Costa[1]; June O'Neill[1]; Gifty Brisbane[1]; Amelia Thyen[1]; Derek Campbell[1]; Monica A. Muñoz[2]

[1] Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, MA, USA
[2] Office of Surveillance and Epidemiology, Center for Drug Evaluation and Research, United States Food and Drug Administration, Silver Spring, MD
[3] Office of Biostatistics, Office of Translational Sciences, Center for Drug Evaluation and Research, United States Food and Drug Administration, Silver Spring, MD

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BACKGROUND

- At the time of approval, information regarding safety of new medications i.e., new molecular entity (NME) drugs and therapeutic biologics, are often limited to results from clinical trials.
- The U.S. Food and Drug Administration (FDA) primarily depends on spontaneous reporting systems and other passive information sources for identifying new safety signals after approval.
- Recently, the FDA began implementing an active surveillance approach by applying tree-based scan statistics to the Sentinel Distributed Database (SDD) to enhance post-marketing safety surveillance activities. However, the effectiveness of tree-based scan statistics relies heavily on the size of the exposed population.

OBJECTIVES

To identify medications with adequate population exposure, approved by the FDA from 2017-2021, for effective post-marketing surveillance using tree-scanned based statistics.

METHODS

Data source: Sentinel Distributed Database (the number of Data Partners and their available data depended on the time at the query distribution for each run in each NME approval year)

Exposures of interest: 260 medications for 256 NMEs approved 2017-2021 (48 in 2017, 60 in 2018, 48 in 2019, 53 in 2020, and 51 in 2021).

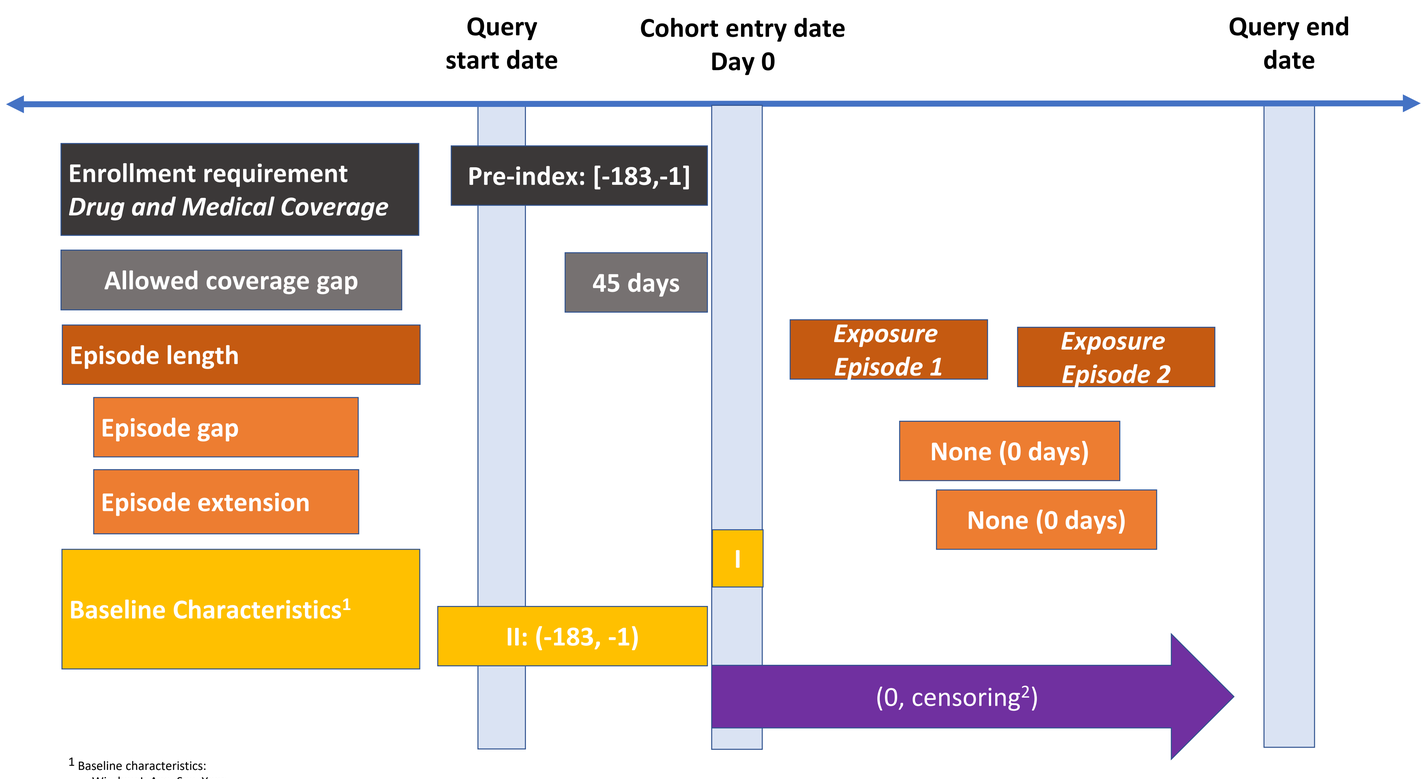
- As the number of medications in each NME approval year is large, we split each NME approval year into two or three runs to maintain the query size and efficiency (e.g., in 2019, the 1st run included 26 medications with approval dates from Jan 1st to Aug 31st and the 2nd run included the 22 remaining medications)
- Some NMEs have medications with both single ingredient and more than one ingredient. We included medications with more than one ingredient as separate analyses

Query start date: January of the year of approval
Query end date: the most recent available data at the query distribution time.

Sex: male and female; **Age**: no restriction

Outcome of interest: Number of initiators with at least one exposed episode of the evaluated NME during the query period

The study design diagram is shown in Figure 1



[1] Baseline characteristics:
Window I: Age, Sex, Year
Window II: The Centers for Medicare and Medicaid Services (CMS) Chronic Conditions Data Warehouse (CCW): Acute Myocardial Infarction, Alzheimer's Disease and related conditions, Atrial Fibrillation, Diabetes, Heart Failure, Hyperlipidemia, Hypertension, Depression, Ischemic Heart Disease, Rheumatoid Arthritis/Osteoarthritis, Stroke/Transient Ischemic Attack (TIA), Breast Cancer, Colorectal Cancer, Prostate Cancer, Lung Cancer, Endometrial Cancer, Acquired Hypothyroidism, Anemia, Asthma, Benign Prostatic Hyperplasia, Chronic Kidney Disease, COPD and Bronchiectasis, Glaucoma, Osteoporosis; and Other: Obesity Diagnosis/Procedure, Obesity NDCs, Overweight, Smoking Diagnosis/Procedure, Smoking NDCs, Alcohol Abuse or Dependence, Drug Abuse or Dependence, History of Cardiac Arrest, History of Coronary Angioplasty or Bypass

[2] Censoring: earliest of death, disenrollment, data partner data end date, query end date

Figure 1. Design diagram

RESULTS

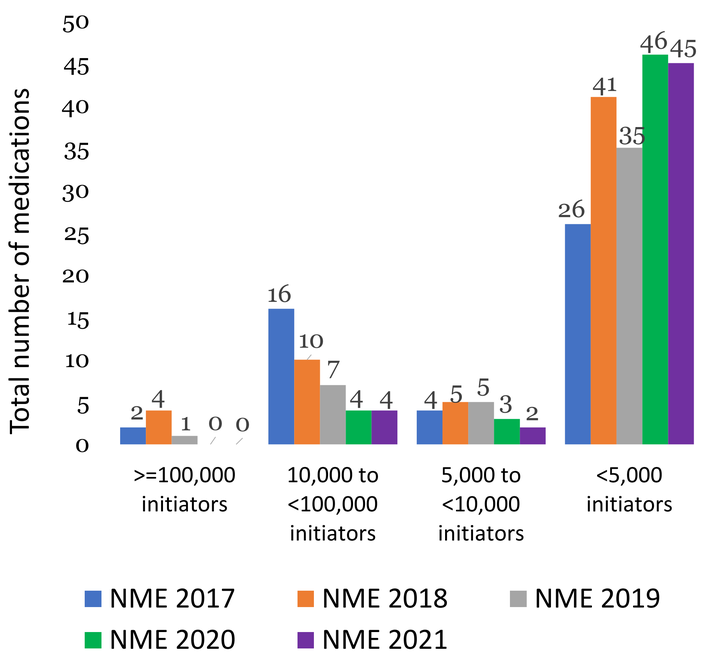
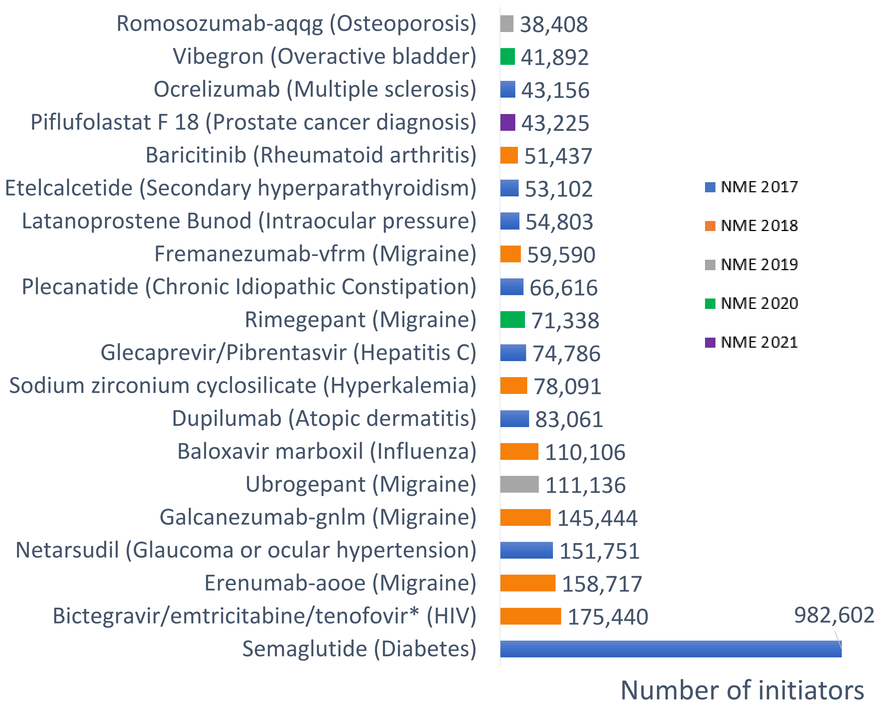


Figure 2. Number of NME approved medications with different cut-off categories of utilization



Note: The listed indication is the indication when NME was first approved. There could be other indications post approval
** Bictegravir sodium, emtricitabine, tenofovir alafenamide*

Figure 3. Top 20 NME medications with highest utilization

Table 1. Number of Data Partners and Years of Available Data by NME Approval Years

NME approval year	Run	Number of Data Partners included	Number of years and months with available data**
2017	1	14	5 years and 11 months
	2	14	6 years
2018	1	13	5 years and 5 months
	2	13	5 years and 5 months
2019	1	13	4 years and 5 months
	2	13	4 years and 5 months
2020	1	14	2 years and 8 months
	2	13	3 years
	3	12	3 years
2021	1	12	2 years and 5 months
	2	13	2 years and 6 months

*** Number of years and months with available data was counted from January of the approval year to the most recent available data at the query time.*

CONCLUSION

- Few of the analyzed medications accrued enough new initiators since approval to be robust candidates for signal identification analysis using tree-based scan statistics and most of NMEs with highest number of initiators were approved in or before 2019.
- Most of the evaluated NME medications (74%) had fewer than 5000 new initiators, which makes them weak candidates for signal identification analyses.
- However, in the initial years post-approval, several new medications have recently undergone successful tree-based scan analyses in the Sentinel Distributed Databases.
- To facilitate the application of active surveillance strategies for products with lower initial uptake, periodic exposure assessments will be needed.

LIMITATIONS

- The analyses for each NME approval year (as shown in Table 1) were conducted at different times. Thus, number of Data Partners and the available data were not the same across NMEs 2017-2021.

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- TNT, BR, MS, SA, JGL, IC, JO, GB, AT, and DC are employees at HPHCI, an organization that conducts work for government and private organizations, including pharmaceutical companies. Others have no conflicts of interest to disclose.