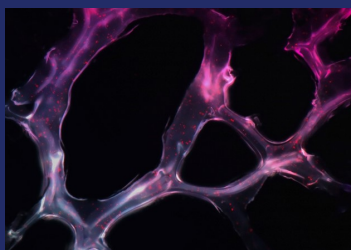# Sentinel Newsletter
Third Quarter 2022

Explore the **Sentinel YouTube Channel** and **Sentinel Website** for more information.

In This Issue:

Sentinel Presents Novel Research at ICPE 2022 Conference

Sentinel Innovation Center Uses Machine Learning in Computable Phenotyping Framing Project

Engage With Sentinel: New Sentinel Views Virtual Training

Sentinel Presents Novel Research at ICPE 2022 Conference

The **38th International Conference on Pharmacoepidemiology & Therapeutic Risk Management (ICPE)** was held in Copenhagen, Denmark on August 24-28, 2022. A variety of Sentinel-related work was featured, including symposia, oral presentations, spotlight posters, and a webinar. These materials can all be found on the <u>Sentinel Website here</u>.

See below for some additional presentation information:

Symposia

<u>Methods and Considerations for Hypothesis-Free Signal Detection Studies Accommodating Various Types of Medications, Populations, and Regions</u>

- This symposium provided a forum to explore considerations around conducting signal detection studies across different scenarios, and to obtain consensus on how to accommodate various medications, populations, regions, and settings.

<u>What Do Real World Data Validation Best Practices Look Like? Operationalizing Guidance for Real-world Studies Intended for Decision-making</u>

Sentinel Innovation Center Uses Machine Learning in Computable Phenotyping Framework Project

The Sentinel Innovation Center (IC) has been working on a computable phenotyping framework project that is set to be completed on September 30, 2022. The project, also known as "Health Outcome of Interest (HOI) 2.0," uses natural language processing (NLP) and machine learning (ML) to improve computable phenotype algorithms for identifying anaphylaxis and acute pancreatitis. The IC is also using this project to work towards developing a general framework for computable phenotyping in its Sentinel System analyses.

This activity is one of the pilots in a series being launched to support the Food and Drug Administration's (FDA) use of the

- This symposium explored approaches to assess and improve the validity of variable definitions, including those for exposures, outcomes, entry criteria, and confounders.

Data Harmonization, Standardization, and Quality Assessment in Distributed Health Data Networks: Lessons from Around the World

- This symposium discussed lessons learned, challenges, and opportunities related to federated health data networks, data standardization, harmonization, curation, and quality assessment for regulatory decision-making.

Oral Presentations

Arterial and Venous Thrombotic Events in Patients with COVID-19 Compared to Influenza

- This presentation explored the risk of inpatient arterial and venous thrombotic events in patients with COVID-19 and compared those risks to patients with influenza.

Systemic Corticosteroids for COVID-19 in U.S. Outpatient Settings

- This presentation examined new systemic corticosteroid use among non-hospitalized patients with COVID-19 from April 2020 - September 2021in four large U.S. databases.

Characterizing Medication Use Patterns of Pregnancies with COVID-19 in the Sentinel System

- This presentation discussed implementation of the CONSIGN study (COVID-19 infectiOn aNd medicineS In preGNancy). As part of an international collaboration across several countries, the study assessed the prevalence of medication use and characterized severity and clinical outcomes in pregnancies with COVID-19 compared to those without COVID-19 and reproductive aged patients with COVID-19.

Comparative Evaluation of Automated Approaches for Confounder Selection in Ultra High-dimensional Data with Rare Outcomes

- This presentation explored the performance of several lasso-based methods for large-scale confounder selection in ultra high-dimensional data with rare outcomes using simulated datasets.

Spotlight Posters

Racial Differences in U.S. COVID-19 Positivity, Hospitalization, and Mortality

- This poster examined racial differences in COVID-19 testing, positivity, hospitalization, and mortality during the first year of the pandemic.

Use of Valganciclovir/Ganciclovir [(v)GCV] for Treatment of Congenital Cytomegalovirus (cCMV) Infection in the United States: Evidence from the Sentinel Distributed Database, 2008-2020.

- This poster described (v)GCV use for the treatment of

post-market Active Risk Identification and Analysis (ARIA) system to assess the safety of its regulated medical products. The overall purpose of this pilot series is to develop a framework to leverage ML and NLP techniques in improving HOI identification algorithms that may later be used in the larger Sentinel Distributed Database to assess drug safety questions.

The project has three core aims:

- **Aim 1:** Expand on the Phase 1-2 anaphylaxis analysis plan and conduct additional secondary analyses.

- **Aim 2:** Develop and conduct a more scalable automated NLP feature engineering process (i.e., compare a PheNorm-like automated model to the current model, based on manual feature curation).

- **Aim 3:** Further develop the high-level general framework for HOI 2.0 identification into a more formalized and comprehensive guidance document for Sentinel (i.e., a publishable manuscript).

Specifically, the IC created gold standard data for model training and evaluation. They utilized NLP and ML to improve models for identifying anaphylaxis and acute pancreatitis, among other phenotypes. Note that the NLP- and ML-enhanced models were proven to be transportable to an external study site, where the models perform well. The IC is currently exploring automated approaches to feature engineering that may improve the scalability of the algorithm development.

This project will ultimately improve the accuracy with which the IC identifies HOIs in Sentinel using electronic data. Note that the current activity is a continuation of Phase 1 and 2 activities involving the anaphylaxis example dataset.

For additional information about this project, please visit this page on the Sentinel Website.

Engage with the Sentinel Community

The 2022 Sentinel Innovation and Methods Seminar Series

The Sentinel Innovation and Methods Seminar Series features presentations by leading experts and innovators on topics related to the work of the IC and the Sentinel Operations Center (SOC). The Seminar Series describes the use of emerging technologies such as feature engineering, natural language processing, advanced analytics, and data interoperability to improve Sentinel's capabilities.

Visit the Sentinel Meetings, Workshops, & Trainings page to view past seminars, webinars, and workshops and to register for upcoming events in 2022.

Recent Seminars:

- Representing and Utilizing Clinical Textual Data for Real World Studies: An OHDSI Approach
- Deep Learning on Electronic Health Records for Research in Pharmacoepidemiology: Examples From the Field of Oncology
- Machine Learning for High-dimensional Proxy Covariate Adjustment in Healthcare Database Studies: An Overview of the Current Literature.
- Addressing Missing Data in Comparative Effectiveness Research Using EHR Data

### 2022 Sentinel Community Building and Outreach Center (CBOC) Informational Videos

The Community Building and Outreach Center has created informational videos to provide on-demand resources for individuals to become more familiar with Sentinel. **Click on the image below to be directed to the Sentinel Views Virtual Training video located on the Sentinel YouTube Channel.**
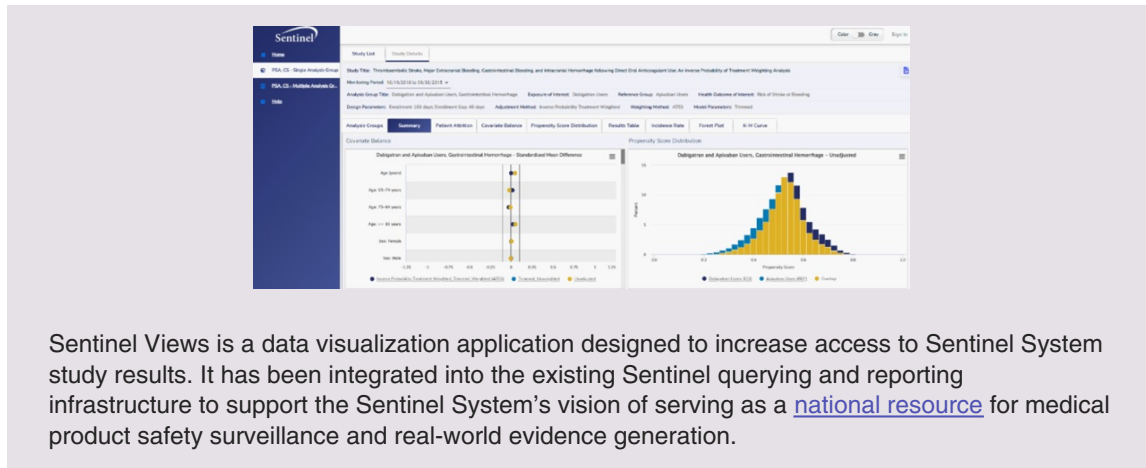
Sentinel Views is a data visualization application designed to increase access to Sentinel System study results. It has been integrated into the existing Sentinel querying and reporting infrastructure to support the Sentinel System's vision of serving as a national resource for medical product safety surveillance and real-world evidence generation.

Community Building and Outreach Center Webinar Series

The Community Building and Outreach Center has developed a webinar series to increase stakeholder awareness and engagement with the Sentinel System. **Click on the image below to view a recording of the recently released webinar titled "An Overview of Sentinel's Publicly Available Analytics Tools."**
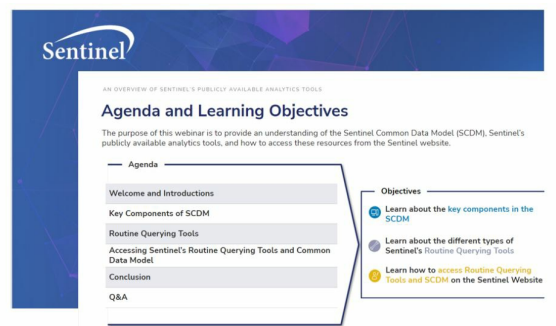
The Webinar provides an understanding of Sentinel's publicly available analytics tools, the Sentinel Common Data Model, and how to access those resources from the Sentinel website.

Featured Sentinel Publication

Association of COVID-19 vs Influenza with Risk of Arterial and Venous Thrombotic Events Among Hospitalized Patients

A study conducted within Sentinel examined the risk of arterial and venous thrombotic events in patients hospitalized with COVID-19 before and during COVID-19 vaccine availability compared to patients hospitalized with seasonal influenza. The study found that hospitalization with COVID-19 was associated with a higher risk of venous thromboembolism within 90 days, but there was no significant difference in the risk of arterial thromboembolism within 90 days. The risk of death within 30 days of either event type was higher for patients with COVID-19 compared to influenza. This study was published in the Journal of the American Medical Association on August 16, 2022.

The US Food and Drug Administration Sentinel System: A National Resource for a Learning Health System

An article highlighting the Sentinel System as a national resource was published on September 12, 2022 in the Journal of the American Medical Informatics Association. The Sentinel System has completed hundreds of analyses, including many that have directly informed regulatory decisions. The Sentinel System also was designed to support a national infrastructure for a learning health system. The Sentinel System infrastructure now supports multiple non-FDA projects for stakeholders ranging from regulated industry to other federal agencies, international regulators, and academics.

New Analytic Packages, Methods, Tools and Reports

Methods Projects:

- Data Sandbox and Engagement Environment Discovery Project
- Approaches to Handling Partially Observed Confounder Data from Electronic Health Records (EHR) In Non-randomized Studies of Medication Outcomes

Tools:

- Sentinel Routine Querying System
- Sentinel Routine Querying System Reporting Tool
- Sentinel Common Data Model (SCDM) v8.1.0

Reports:

- Comparative Effectiveness of Azithromycin Relative to Roflumilast in Individuals With Uncontrolled Chronic Obstructive Pulmonary Disease Despite Triple Inhaled Therapy
- Use of Monoclonal Antibodies (mAbs) Under an Emergency Use Authorization (EUA) in Patients with COVID-19 Diagnosis: An Updated Descriptive Analysis
- Differences in COVID-19 Testing, Positivity, Hospitalization, and Mortality by Race and Ethnicity in the Sentinel Distributed Database: A Descriptive Analysis
- Women With Heart Failure & Pregnancy
- Utilization of Obesity Drugs: A Descriptive Analysis
- Counts and Characteristics of Individuals with Sodium-Glucose Co-transporter-2 (SGLT-2) Inhibitor Use: A Descriptive Analysis
- Hospitalization and Anaphylaxis Following Monoclonal Antibodies (mAb) Use in Patients with COVID-19: A Descriptive Analysis | Sentinel Initiative
- Utilization of Sodium Glucose Co-

- Seizure Algorithm Defined in "Seizures Following Gadolinium-Based Contrast Agents Exposure: A Self-Controlled Risk Interval Analysis"
- Seizures Following Gadolinium-Based Contrast Agents Exposure: A Self-Controlled Risk Interval Analysis
- Tacrolimus Use in Patients Following Liver or Kidney Transplants: A Descriptive Analysis
- Use of Monoclonal Antibodies (mAbs) Under an Emergency Use Authorization (EUA) in Patients with COVID-19 Diagnosis: A Descriptive Analysis
- Count and Duration of Follow up of New-Onset Cancer: An Updated Descriptive Analysis
- Characterizing Pregnant Women With and Without Evidence of Heart Failure and Non-Pregnant Women With Heart Failure: A Propensity Score Matched Analysis
- Bamlanivimab, Bamlanivimab and Etesevimab, and Casirivimab-Imdevimab Use in Patients with COVID-19: A Descriptive Analysis
- Outpatient Corticosteroid Use in Patients With COVID-19: An Updated Descriptive

Transporter-2 (SGLT-2) Inhibitor Drugs: A Descriptive Analysis

Analysis

- Characterization of Infants in the Mother-Infant Linkage Table in the Sentinel Distributed Database: An Updated Descriptive Analysis

Recent Publications and Presentations

- Data-Driven Approaches to Improve Phenotype Sensitivity Using EHR Data

- Identification of Obesity and Tobacco Use in Claims Compared to Electronic Health Record (EHR) Data

- Characterizing Infants in the Sentinel Distributed Database Mother-Infant Linkage Table

- Characterizing Pediatric Members in the Sentinel Distributed Database

- Switching Patterns of Mixed Amphetamine Salt Products in the FDA's Sentinel Distributed Database

- Inverse Probability Treatment Weighting Versus Propensity Score Matching in the Sentinel System: A Test Case

- Impact of Nitrosamine Contamination Recalls on Angiotensin-Receptor-Blocker (ARB) Utilization in the U.S., U.K., Canada, and Denmark

- Design Considerations for Using the Tree-based Scan Statistic in Surveillance of Maternal Outcomes Following Medication Use during Gestation

- Using TreeScan as a Signal Identification Approach to Screen for Adverse Maternal Outcomes of Medication Use in Pregnancy

- A Cohort Study to Assess Risk of Cutaneous Small Vessel Vasculitis Among Users of Different Oral Anticoagulants

- Novel Methods for Pregnancy Drug Safety Surveillance in the FDA Sentinel System

- New-Onset Cancer Cases in FDA's Sentinel System: A Large Distributed System of US Electronic Healthcare Data

Explore the *Sentinel YouTube Channel* and *Sentinel Website* for more information.