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The Sentinel logo features the word "Sentinel" in a white serif font, with a white swoosh above the letters "i" and "n".

Sentinel Newsletter
Third Quarter 2023



[Six Years of the US Food and Drug Administration's Postmarket Active Risk Identification and Analysis System in the Sentinel Initiative: Implications for Real World Evidence Generation](#)

[The Use of Electronic Health Record Data for Drug Safety Signal Identification: A Scoping Review](#)

[New Sentinel Initiative's Video: The Strengths and Limits of Electronic Health Records and Claims-based Data](#)

Six Years of the US Food and Drug Administration's Postmarket Active Risk Identification and Analysis System in the Sentinel Initiative: Implications for Real World Evidence Generation

Since 2016, the FDA US Food and Drug Administration has used the congressionally mandated post-market Active Risk Identification and Analysis (ARIA) system through Sentinel to monitor the utilization and safety of drug and

The Use of Electronic Health Record Data for Drug Safety Signal Identification: A Scoping Review

The Sentinel Innovation Center (IC) was created in response to FDA's Medical Data Enterprise Initiative to build a new system containing electronic health records (EHR) from 10 million lives and the Sentinel Five-Year Strategy plan. While strides have been made in advancing signal detection methods and

biologic products. In this review, FDA and Sentinel Operations Center report on the safety concerns assessed and unable to be assessed in ARIA over the system's first 6 years (2016-2021). The findings presented in this review illustrate the accomplishments of the system and continued challenges in using administrative claims data, especially when used to define novel clinical concepts - while highlighting opportunities to improve the use of real-world data for post-market safety studies.

The most common situation for which ARIA was unable to assess a safety concern was for studies assessing adverse pregnancy and fetal outcomes following in-utero exposure. To address these shortcomings, Sentinel has responded through a number of initiatives. For example, Sentinel launched a Mother-Infant Linkage capability in 2018, creating a foundation for birth outcome studies. Sentinel further developed analytic tools for targeted signal evaluation in pregnancy using propensity score adjustment in 2019 and expanded signal identification tools to cover pregnant patients and their offspring in 2022. Also, in 2022, Sentinel added Medicaid data via the Transformed Medicaid Statistical Information System (T-MSIS) into ARIA; T-MSIS covers nearly half of all pregnancies in the United States. Lastly, FDA continues to expand approaches to pregnancy studies by agreeing to a series of demonstration projects focusing on pregnancy and post-market evidence generation by way of the latest installment of the Prescription Drug and User Fee Act (PDUFA) commitments. Read more about the results [here](#).

capabilities for administrative claims data, EHR data provides new opportunities to address the limitations of traditional approaches and promotes discovery-oriented pharmacovigilance. To evaluate the current state of EHR-based medication safety signal detection, the IC conducted a scoping literature review of studies aimed at identifying safety signals from routinely collected patient-level EHR data.

From 81 eligible studies, the authors extracted information on study design; EHR data utilized; analytic methods employed; drugs and outcomes evaluated; and key statistical and data analysis choices. Overall, the review found that variability in study design makes direct comparisons difficult, and studies varied widely in terms of methods, data, and statistical considerations. Additionally, despite broad interest in utilizing EHRs for safety signal identification, current efforts fail to leverage the full breadth and depth of available data or to rigorously control for confounding. The development of best practices and the application of common data models would promote the expansion of EHR-based pharmacovigilance. Read more about the results [here](#).

Engage with the Sentinel Community

[The 2023 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 Innovation Center and the Sentinel Operations Center. The Seminar Series describes emerging approaches in real world data utilization such as feature extraction, Natural Language Processing (NLP), machine learning, and techniques to advance causal inference improving Sentinel's capabilities.

2023 Sentinel Public Webinars:

- **Optimizing the Use of Post Approval Pregnancy Safety Studies Workshop:** On September 18, 2023, Duke-Margolis Center for Health Policy, under a cooperative agreement with the U.S. FDA, is convening a two-day hybrid Public Workshop that will discuss designs of post approval pregnancy safety studies for drug and biological products regulated by the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER). [Click here to view the full description of this event.](#)

Workshop Registration

- **Scalable Incident Detection via Natural Language Processing and Probabilistic Language Models:** On September 20, 2023, Dr. Colin G. Walsh will describe a scalable approach to identifying clinical events at the health system scale using natural language processing (NLP) and probabilistic language models. Our methods will be discussed and demonstrated in two challenging and clinically important use-cases: suicide prevention and sleep-related behaviors. This approach has implications for post-market safety surveillance, for clinical prevention, population health, and more. [Click here to view the full description of this event and register for this webinar.](#)
- **Leveraging Missing Data and Measurement Error Approaches in Propensity Score-Based Analyses of Real-World Data Webinar:** On August 21, 2023, Dr. Rebecca Hubbard presented an evaluation of measurement error and missing data approaches to this problem motivated by a real-world study of the comparative effectiveness of treatments for advanced urothelial cancer and conclude with reflections on how to embrace modern advances in data sources and methodology while preserving time-tested principles that support research rigor and reproducibility. [Click here to view the full description of this webinar.](#)
- **Multi-wave Validation Sampling to Improve Estimates Derived from Electronic Health Record Data:** On July 11, 2023, Dr. Bryan E. Shepherd described his experience performing a multi-wave validation study to target informative records for validation and then combining the validated data (~1000 records) with error prone EHR data (~10,000 records) to estimate the association between maternal weight change during pregnancy and the risk of her child developing obesity. [Click here to view the full description of this event for this webinar.](#)

2023 Sentinel Events:

- **15th Annual Sentinel Initiative Public Workshop:** This workshop will serve as an opportunity for attendees to hear about recent achievements and developments to date. This event will be virtual and in-person at the National Press Club, Washington, D.C. The keynote speaker for this event will be Dr. Janet Woodcock, FDA's Principal Deputy Commissioner. [Click here to view the full description and register for this event.](#)

Workshop Registration

2023 Sentinel ICPE Conference Awards:

- **Ronald D. Mann Best Paper Award:** *Pharmacoepidemiology & Drug Safety* awarded Sentinel paper, "[Novel Methods for Pregnancy Drug Safety Surveillance in the FDA Sentinel System](#)" with the Ronald D. Mann Best Paper Award at this year's ICPE conference. This award is given annually to the best paper published in *Pharmacoepidemiology & Drug Safety*. Congratulations to the following authors: Elizabeth A Suarez, Michael Nguyen, Di Zhang, Yueqin Zhao, Danijela Stojanovic, Monica Munoz, Jane Liedtka, Abby Anderson, Wei Liu, Inna Dashevsky, David Cole, Sandra DeLuccia, Talia Menzin, Jennifer Noble, Judith C Maro. This is the second time Sentinel is honored with this award.

2023 ICPE Conference Participants & Presentations:

- [Introducing CoLab: The Evolution of US-Canada International Collaboration on Drug Safety and Effectiveness](#) (*Symposium*)
- [Hospitalized Arterial or Venous Thrombotic Events in Patients Diagnosed in the Ambulatory Setting with COVID-19 Compared to Influenza](#) (*Oral Presentation*)
- [Investigating Potential Differences in the Safety Profiles of Biosimilars Relative to Originator Products using a Tree-Based Scan Statistic](#) (*Oral Presentation*)
- [Principled Approaches to Handle Partially Observed Confounder Data from Electronic Health Records: A Plasmode Simulation Study](#) (*Oral Presentation*)
- [Triple Challenges – Small Sample Sizes in Both Exposure and Control Groups When Scanning Rare Maternal Outcomes in Signal Identification: A Simulation Study](#) (*Oral Presentation*)
- [Variation in Mother-Infant Linkage Rates by Jurisdiction in U.S. Medicaid Data](#) (*Oral Presentation*)
- [Characterizing Medication Use Patterns Among Pregnant and Non-Pregnant Patients with COVID-19 in the Sentinel System](#) (*Lightning Presentation*)
- [Utilization of Beta-blockers Among the Pediatric Population in the United States: A Study in the FDA's Sentinel System from 2008 to 2022](#) (*Spotlight Poster*)
- [Association Between Race and COVID-19 Outcomes in the United States \(2020-2021\)](#) (*Poster*)
- [Diversifying the FDA's Sentinel System with Rigorous Quality Inclusion Rules for the U.S. Medicaid Population](#) (*Poster*)

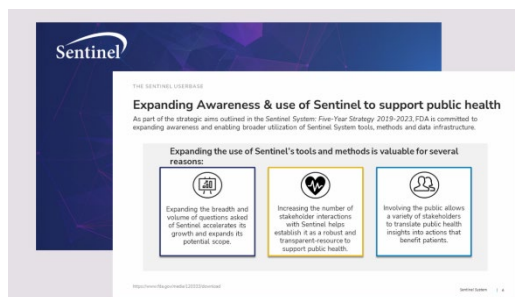
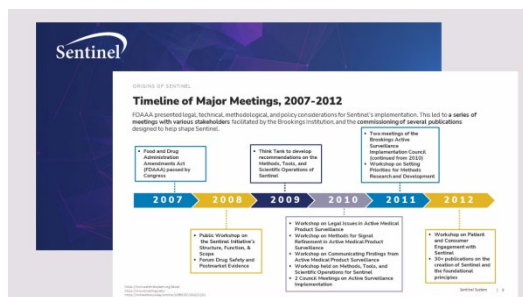
- [Expanding Capabilities for Unapproved Cannabis-Derived Product Surveillance in the United States, TriNetX, July 1, 2018 – June 30, 2022 \(Poster\)](#)
- [Exploring the Use of Electronic Health Records \(EHR\) Data for Active Safety Surveillance of Epidiolex in PCORnet, July 1, 2018- July 1, 2022 \(Poster\)](#)
- [High Dose Dexamethasone for COVID-19 Not Common in a Large US Hospital Network \(Poster\)](#)
- [NLP Detection of Mortality Information from Publicly Available Data using Deep Learning Modelling \(Poster\)](#)
- [Percutaneous Transluminal Septal Myocardial Ablation and Common Procedural Complications Before and After the Approval of Ablysinol \(Poster\)](#)
- [Racial and Ethnic Differences in Hospitalized and Critical COVID-19 Treatment, January 2021-April 2022 \(Poster\)](#)
- [Using Real-World Data to Evaluate Comparative Effectiveness Cohorts of Azithromycin Relative to Roflumilast in Individuals with Uncontrolled Chronic Obstructive Pulmonary Disease \(Poster\)](#)
- [Utilization of Gonadotropin-Releasing Hormone Agonist Products in Adolescents \(Poster\)](#)

Visit the [Sentinel Meetings, Workshops, & Trainings page](#) to view past seminars, webinars, and workshops and to register for upcoming events in 2023.

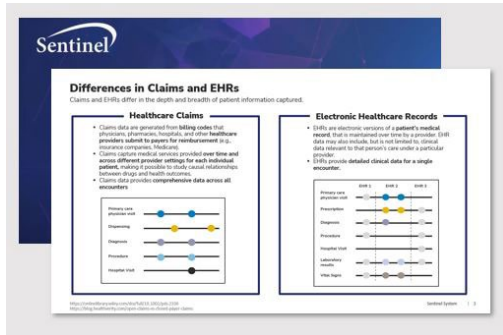
Sentinel Community Building and Outreach Center (CBCO) Training Series

CBCO INFORMATIONAL VIDEOS

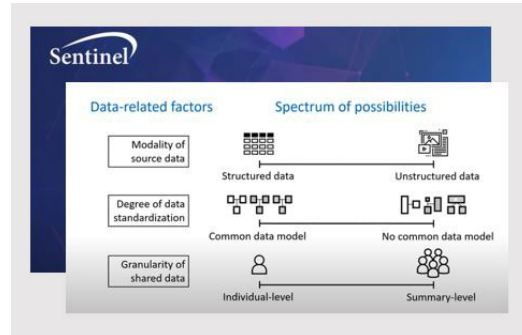
The Community Building and Outreach Center has created informational videos to provide on-demand resources to become more familiar with Sentinel. Click below to learn more about two recently released videos.



MAJOR MOMENTS details the evolution of Sentinel as a national resource, starting from the Mini-Sentinel pilot in 2009 to Sentinel today. [Click here to view the video.](#)



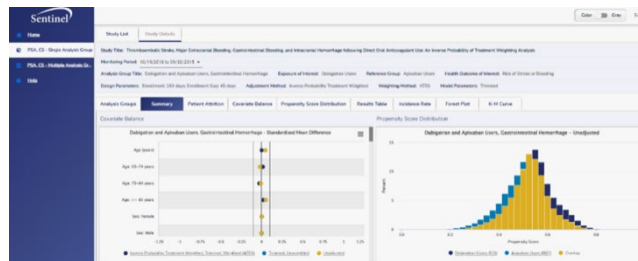
THE SENTINEL USERBASE highlights various groups of stakeholders that can use Sentinel as a resource to inform their work. [Click here to view the video.](#)



EHR v. CLAIMS: CBOC explores how claims and electronic health records (EHR) data may be used to address different dimensions of a scientific question or problem. This video details the limits and strengths of each identified resource and how they both affect the outcomes of scientific studies. [Click here to view the video.](#)

Machine Learning in Distributed Data Networks: This video discusses how access to larger amounts and more complex types of electronic health data in distributed data networks like the FDA Sentinel System has created a growing interest in the use of data-adaptive machine learning techniques. [Click here to view the video.](#)

CBOC & IC VIRTUAL TRAINING SESSIONS



SENTINEL VIEWS is a data visualization application designed to increase comprehension of the Sentinel System study results. It has been integrated into the existing Sentinel querying and reporting infrastructure, to support the work of the Sentinel System. The Sentinel Views web graphics are interactive and help to visualize results. The tool also includes a public facing dashboard accessible to the general public. [Click here to view the virtual training.](#)

Feedback Poll

Which section of this Newsletter applied to you most?

Spotlight: Six Years of the US Food and Drug Administration's Post Market ARIA System

Highlight: The Use of Electronic Health Record Data for Drug Safety Signal Identification

Engage with Sentinel Training Section

New Analytic Packages, Methods, Data, and Tools Projects

Recent Reports, Publications, and Presentations

New Analytic Packages, Methods, Data, and Tools Projects

- [Characterization of COVID-19 Genomic Data in Sentinel Distributed Database](#)
- [Effectiveness of Fixed Triple Combination Inhaled Corticosteroid \(ICS\), Long-Acting Beta-Agonist \(LABA\), and Long-Acting Muscarinic Antagonist \(LAMA\) Products vs. Multiple Inhaler ICS, LABA, LAMA Therapy in Patients With COPD](#)
- [Data Expansion Implementation: Linking the National Death Index \(NDI\) data to the Sentinel Distributed Database \(SDD\)](#)
- [Subset Calibration Methods](#)
- [Creating a Sentinel Linked Electronic Health Record \(EHR\)-claims Development Network](#)
- [Medical Literature and Data on Cannabis Use](#)
- [Development and Evaluation of Electronic Health Record \(EHR\) Information Extraction Pipeline and Tree-Based Scan Statistic \(TBSS\) Methods for EHR-Based Signal Detection \(DA2\)](#)
- [Monitoring of Safety and Effectiveness of COVID-19 Therapeutics: Aim 1 Protocol Development](#)

- [Inclusion of Semi-Structured and Unstructured Electronic Health Record \(EHR\) Data in Confounding Adjustment and Outcome Ascertainment](#)
- [Onboarding of Commercial Electronic Health Record \(EHR\) Data Partners](#)
- [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](#)

Recent Reports, Publications, and Presentations

- [Using Real-World Data to Evaluate Comparative Effectiveness Cohorts of Azithromycin Relative to Roflumilast in Individuals with Uncontrolled Chronic Obstructive Pulmonary Disease](#)
- [Percutaneous Transluminal Septal Myocardial Ablation and Common Procedural Complications Before and After the Approval of Ablysinol](#)
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- [Triple Challenges – Small Sample Sizes in Both Exposure and Control Groups When Scanning Rare Maternal Outcomes in Signal Identification: A Simulation Study](#)
- [Principled Approaches to Handle Partially Observed Confounder Data from Electronic Health Records: A Plasmode Simulation Study](#)
- [Pragmatic Guidance for Embedding Pragmatic Clinical Trials in Health Plans: Large Simple Trials Aren't So Simple](#)
- [Risk of Admission to Hospital with Arterial or Venous Thromboembolism Among Patients Diagnosed in the Ambulatory Setting with COVID-19 Compared with Influenza: Retrospective Cohort Study](#)
- [An Assessment of the Sentinel System: Focus on the Active Risk Identification and Analysis \(ARIA\) System](#)
- [Valsartan, Losartan and Irbesartan Use in the USA, UK, Canada and Denmark After the Nitrosamine Recalls: A Descriptive Cohort Study](#)
- [Active Surveillance of Medical Product Use in the FDA's Sentinel System: A Focus on Pediatric Populations](#)

Explore the [Sentinel YouTube Channel](#) and [Sentinel Website](#) for more information.

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