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### Welcome Message from Dr. Gerald Dal Pan



My name is Dr. Gerald Dal Pan and I am the Director of the Office of Surveillance and Epidemiology (OSE) within the FDA Center for Drug Evaluation and Research (CDER). I am also the Executive Sponsor of the Sentinel System. I hope that this newsletter will help you learn more about the exciting activities happening within Sentinel and how you can get involved.

Created in 2008 by the FDA, Sentinel develops new ways to assess the safety of marketed medical products. It uses advanced statistical methods to study relationships and patterns in medical billing information and electronic health records. Since its inception, Sentinel has constantly looked for new ways to use Real-World Data to advance regulatory science and innovation. For example, Sentinel is conducting a study of the natural history of coagulopathy in COVID-19 patients and leading efforts by a group of collaborators as part of the Reagan-Udall Foundation for the FDA and Friends of Cancer Research COVID-19 Evidence Accelerator. More information on this project, as well as a list of other COVID-19-related activities, can be found [here](#).

The goal of this newsletter is to keep those who are interested in Sentinel informed and aware of new innovations and to show ways in which you can get involved. Stay tuned—we have lots of exciting news to come!

### Upcoming Events

Sentinel is excited to share the following events taking place soon:

- **The Development and Validation of a Real-World Mortality Variable:** Tuesday, March 30th, 2021; 2:00 PM - 3:00 PM Eastern Time
- **Advanced Approaches for Evaluating Drug Safety in Pregnancy:** Monday, April 26th, 2021; 12:00 PM - 1:00 PM Eastern Time
- **Measure What You Treasure: The Challenges and Opportunities of Collecting Real World Endpoints:** Tuesday, June 22nd, 2021; 1:00 PM - 2:00 PM Eastern Time

## Redesigned Sentinel Website

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The redesigned Sentinel website has become a focal point for engaging stakeholders and sharing knowledge to support FDA's vision of a more robust Sentinel System. Since January 2020, Sentinel has fully redesigned its website.

The first two releases focused on a brand new homepage design and developing a more intuitive site navigation. The upcoming third release will focus on improving search, developing a dedicated "Engage with Sentinel" page, and creating a "Training Center" with easy-to-navigate trainings, webinars, and workshops in a single location.

[Explore the redesigned Sentinel website](#)

## Sentinel Launches Projects to Advance Innovation

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Sentinel is currently working on several projects to advance innovation. Two recently launched projects are highlighted below:

### **Horizon Scan of Electronic Health Record Databases**

The purpose of this project is to develop and implement a horizon scan and series of interviews to:

(1) Identify electronic health record (EHR) sources and registries, and (2) conduct initial feasibility assessment of these potential partners for enhancing the Sentinel System.

This specific project will involve three phases:



The horizon scan will search U.S. EHR resources with a particular focus on identifying and evaluating potential sources of data on pediatric, cancer, and pregnancy/birth outcomes, as well as cause of death. Furthermore, the horizon scan will consider EHR data sources that will be useful to address questions related to a variety of drug safety and public health issues.

### **Enhancing Causal Inference in the Sentinel System: An Evaluation of Targeted Learning and Propensity Scores for Confounding Control in Drug Safety**

Improving causal inference from Real-World Data (RWD) for purposes of evaluating safety and effectiveness of medical products is an important goal of Sentinel. Current causal inference approaches implemented in the Sentinel System include methods based on propensity scores for control of confounding. Targeted Learning, which incorporates machine learning (ML) methods for causal inference, has been proposed as an alternative and potentially better approach.

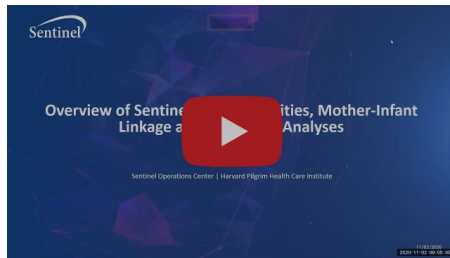
The goal of this project is to evaluate the potential use of Targeted Learning methods within the Sentinel System compared to existing approaches. As Sentinel expands its data resources to include EHR, the project will focus on comparing the performance of Targeted Learning methods with causal inference approaches currently available to Sentinel in data environments that include linked insurance claims and EHR data. The project will further assess practical aspects of the feasibility of how such approaches might be implemented in a distributed environment.

## Looking Back: Sentinel Annual Public Workshop & Public Training

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The **12th Annual Sentinel Initiative Public Workshop** was convened on October 14, 2020 by the Robert J. Margolis, MD,

Center for Health Policy under a cooperative agreement with the FDA. The online workshop provided an opportunity to discuss recent achievements and engage with the broader community of patients, consumers, and scientific stakeholders.



During the **2020 Sentinel Public Training**, epidemiologist investigators presented on Sentinel's database and analytic capabilities. Participants discussed pregnancy-related analyses including how Sentinel links and uses mother and infant data, cohort identification approaches for assessing medical product use during pregnancy, and a case study involving a new inferential analysis tool.

## Looking Back: The Sentinel Innovation Center (IC) Webinar Series

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The IC webinar series features presentations by leading experts and innovators on topics relevant to the Innovation Center's Master Plan.

Below are details for all past webinars, which are publicly available:

- Electronic Health Records + Natural Language Processing + Machine Learning = Improved Sentinel Outcome Detection Algorithms
- Unsupervised Approaches for Phenotyping Using Electronic Health Record Data
- Overview, Considerations, and Challenges in Integrating Structured and Unstructured Electronic Health Record Data into Common Data Models
- Harmonizing Electronic Health Records from Heterogeneous Systems via Automated Translation of Medical Concepts
- Portability and Scalability of Computable Phenotypes: Trade Offs and New Trajectories
- Data Curation in PCORnet® - Lessons Learned and Implications for Regulatory Decision-Making
- Targeted Learning: The Bridge from Machine Learning to Statistical and Causal Inference

**Sentinel would like to congratulate Patrick J. Heagerty, PhD, MS, a member of the Sentinel Innovation Center Executive Leadership Team, for his 2020 election to the National Academy of Medicine!**

## Sentinel Study Results

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- Thromboembolic Stroke, Intracranial Hemorrhage, Gastrointestinal Bleeding, and Major Extracranial Bleeding following Dabigatran, Rivaroxaban, and Apixaban Use in Patients with Atrial Fibrillation: A Propensity Score Matched Analysis
- Serious Infections following Ustekinumab Use: A Descriptive Analysis

## Methods, Data, and Tools

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- A New Propensity Score Matched Analysis Tool for Pregnancy: Replicating A Study of Oral Clefts following Topiramate Use during the First Trimester of Pregnancy
- Oral Clefts Algorithm Defined in "A New Propensity Score Matched Analysis Tool for Pregnancy: Replicating A Study of Oral Clefts following Topiramate Use during the First Trimester of Pregnancy"
- Routine Querying System: Version 10.3.0

## Recent Publications

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- Risk of Non-Melanoma Skin Cancer in Association with Use of Hydrochlorothiazide-Containing Products in the United States
- The FDA MyStudies App: A Reusable Platform for Distributed Clinical Trials and Real-World Evidence Studies
- Incidence of Uterine Bleeding following Oral Anticoagulant Use in Food and Drug Administration's Sentinel System
- Complementary Use of U.S. FDA's Adverse Event Reporting System and Sentinel System to Characterize Direct Oral Anticoagulants-Associated Cutaneous Small Vessel Vasculitis
- Leveraging the Capabilities of the FDA's Sentinel System To Improve Kidney Care

## Recent Presentations

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- SER 2020 Presentation: Validation of an Electronic Algorithm for Hodgkin and Non-Hodgkin Lymphoma in ICD-10-CM
- SER 2020 Presentation: Using Prenatal Tests to Estimate Pregnancy Start in Health Insurance Claims Data
- 2020 ICPE Presentation: Natural History of Coagulopathy in Patients with COVID-19 in a Real-World Electronic Health Data Network
- 2020 ICPE Presentation: Validation of Claims-based Algorithms to Identify Hospitalized COVID-19 Events within the FDA Sentinel System
- 2020 ICPE Symposia: When Decisions Can't Wait: Delivering Rapid Real World Studies