Using the Sentinel System to Assess Generic Drug Safety in the Post-Approval Setting

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What I’ll Cover

• What is Sentinel?
• How does Sentinel fit into generic drug review and monitoring?
• Who can use Sentinel?
• What’s next for Sentinel?
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Sentinel’s Origins

• Developed in response to Section 905 of Food and Drug Administration Amendments Act (FDAAA; 2007)
  • Mandated creation of an active electronic postmarket surveillance system for regulated products
Sentinel’s Timeline

- **2007**: Congress passes Food and Drug Administration Amendments Act (FDAAA)
- **2008**: FDA launches Sentinel Initiative
- **2009**: FDA launches Mini-Sentinel Pilot
- **2011**: Mini-Sentinel distributed dataset reaches 100 million lives marked mandated by FDAAA
- **2012**: Mini-Sentinel has suite of reusable programming tools for routine queries
- **2016**: FDA launches Sentinel System
Sentinel Characteristics

- Primarily claims data
- Common data model
- Distributed data network
Claims Data

Bob’s Story

- Lives in Boston, MA
- Has appendectomy
- Diagnosed with hypertension
- Routine Office Visit

2011
- Encounter: Office Visit Diagnosis: Influenza with pneumonia
- Dispensings: Prescription: Antibiotic
  - 1/1/2011

2012
- Encounter: Emergency Department Procedure: Appendectomy
  - 3/15/2012
- Hospital: Inpatient stay
  - 3/15/2012 - 3/18/2012

2013
- Encounter: Office Visit Diagnosis: Hypertension
- Dispensings: Prescription: Anti-hypertensive
  - 12/11/2012

2014
- Encounter: Office Visit Diagnosis: Hypertension
  - 10/31/2013

https://www.sentinelsystem.org/sentinel/data
Claims Data

Advantages

• Capture all reimbursed healthcare usage
• Data are longitudinal and can produce incidence rates
• Use for payment contributes to data quality
• Common billing standards allow aggregation into large sample sizes

Disadvantages

• Data are not collected specifically for research
• Economic incentives affect data
• Missing OTC, low-cost generics paid out of pocket, drug samples, etc.
• Challenging to get key lifestyle factors (e.g., smoking, diet, exercise)
Sentinel System: Data Snapshot

- 223 million members* 2000-2016
  - 178 million members* with both medical and pharmacy benefits
- 425 million person-years of observation time
- 43 million people currently accruing new data
- 5.9 billion pharmacy dispensings
- 7.2 billion unique medical encounters
- 42 million people with at least one laboratory test result

*Counts distinct patient ID values in the database

https://www.sentinelinitiative.org/sentinel/snapshot-database-statistics
Sentinel Common Data Model

- Enrollment
- Demographics
- Medical utilization
- Pharmacy prescriptions
- Diagnoses
- Procedures
- Lab tests
- Vital signs

Data Partners transform data locally into the Common Data Model, which enables them to run standardized computer programs that run identically at each Data Partner site.
Common Data Model

Data Partners (DPs) hold data in Common Data Model format:
- Enrollment
- Demographics
- Medical Utilization
- Pharmacy Prescriptions
- Diagnoses
- Procedures
- Laboratory Tests
- Vital Signs

Queries Distributed to Data Partners (DPs)

Sentinel Operations Center (SOC)

Query Results Reviewed and Returned to SOC (all direct identifiers removed)

Data transferred securely

https://www.sentinel system.org/sentinel/data/distributed-database-common-data-model
Distributed Database: A Hub-and-Spoke Model

SOC – Sentinel Operations Center
DP – Data Partner
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Generic Drug Surveillance

What evidence can utilization and switching patterns provide on generic substitution in the real-world?
Generic Drug Surveillance

• What is prompting the switchback?
  • Adverse events
  • Effectiveness
  • Other factors
Design and Analysis Considerations: Studying Generic Drugs

- **Confounding**
  - Patients switch to newly-released generic, leading to difficulty identifying an appropriate comparison group

- **Selection bias**
  - Patients who stay on brand when generic is available may be different in some way

- **Outcome ascertainment**
  - Outcome of interest may be no difference between groups

- **Secular factors**
  - Pharmacy inventory; provider preference
Strategies: Studying Generic Drugs

• Confounding
  – Self-controlled design; propensity score (PS) matching; historical controls

• Selection bias
  – Censoring; appropriate comparator group selection; restriction/stratification

• Outcome ascertainment
  – Power

• Secular factors
  – PS matching; restriction/stratification; instrumental variables
Sentinel Methods Development: Generic Drug Surveillance Tool

• Aims:
  – Design, develop, test and evaluate a flexible and reusable prototype analytic tool that could be used to conduct rapid population-based assessments on new generic products in the future; and
  – Use the Sentinel System to characterize utilization and switching patterns associated with the two use-cases for modified-release products

• Can handle multiple switch patterns and product groupings

• No outcomes yet, but planned for future development

• In progress – stay tuned!
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IMEDS

• Innovation in Medical Evidence Development and Surveillance from the Reagan-Udall Foundation
• Supports FDA’s vision of providing the Sentinel System as a broader resource for public health and medical evidence generation
• Launched and running analyses
Who Can See What Sentinel Does?

- All analyses are ultimately posted on the Sentinel public website and are available for viewing
- Other avenues of communication:
  - Presentations at scientific conferences
  - Publications in journals
  - Public workshops and meetings
New Sentinel Webpage
www.sentinelinitiative.org
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Sentinel: What’s Next

• Medicare data expansion: Fall 2017
  – >50 million beneficiaries

• Yearly infrastructure and tool enhancements
  – Mother-baby linkage (launched)
  – Generic switching tool (launched)

• Continued scientific collaboration and outreach

• Develop a comprehensive training program for review staff

• Ongoing standardization of processes and communications

• Evaluate new ways to enhance access to Sentinel for stakeholders
Links

• Sentinel website: https://www.sentinelinitiative.org/
• Switching methods protocol: https://www.sentinelinitiative.org/sites/default/files/Meth ods/Sentinel_Methods_Manufacturer-Level-Drug-Utilization-Switching-Patterns.pdf
• PDUFA VI: https://www.fda.gov/forindustry/userfees/prescriptiondruguserfee/ucm446608.htm
• IMEDS: http://reaganudall.org/innovation-medical-evidence-development-and-surveillance
• Sentinel interim and final assessments: https://www.fda.gov/ForIndustry/UserFees/PrescriptionDr ugUserFee/ucm464042.htm
Thank you!

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