

# FDA's Mini-Sentinel Program to Evaluate the Safety of Marketed Medical Products

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# Mini-Sentinel

- 5-year pilot developed in response to the FDA Amendments Act of 2007
- Develop scientific operations for active medical product safety surveillance
- Create a coordinating center with continuous access to automated healthcare data systems, and the following capabilities:
  - Develop and evaluate scientific methods that might later be used in a fully-operational Sentinel System.
  - Offer FDA the opportunity to evaluate safety issues in existing automated healthcare data system(s) and learn more about barriers and challenges.

# Selected Mini-Sentinel Activities

- Descriptive analysis
  - Most can be done using aggregate data
- One-time assessment
  - Similar to typical epidemiological studies
- Evaluation of the impact of FDA regulatory actions
- Sequential analysis as new data accrues

# Stages of Postmarket Surveillance



Aim = Identify excess risk	All (suspected and unanticipated) adverse events (AEs), all products	Specific AE:product pairs of concern	A highly suspected AE:product pair
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# Mini-Sentinel Partner Organizations



KAI SER PERMANENTE®

Humana  
Pharmacy Solutions®



RUTGERS  
Institute for Health

# The Mini-Sentinel Distributed Database

- Populations with well-defined person-time for which medically-attended events are known
- 126 million individuals\*
  - 345 million person-years of observation time (2000-2011)
  - 44 million individuals currently enrolled, accumulating new data
  - 27 million individuals have over 3 years of data

\*As of 12 December 2011. The potential for double-counting exists if individuals moved between data partner health plans.

# Why a Distributed Database?

- Avoids many concerns about inappropriate use of confidential personal data
- Data Partners maintain physical control of their data
- Data Partners understand their data best
  - Valid use / interpretation requires their input
- Eliminates the need to create, secure, maintain, and manage access to a complex, central data warehouse

# Rapid Postmarket Assessment of Varenicline Safety

## □ New-user design

- First varenicline or bupropion use with a 180-day “wash-out” period
- Aged 20 years or older
- No diagnosis of outcomes of interest in the 180 days preceding treatment initiation

## □ Further restricted to

- New users with a tobacco use disorder code (ICD-9-CM 305.1)
- New users of products approved for smoking cessation

## □ Composite cardiovascular outcome

- Acute myocardial infarction (ICD-9-CM code 410.xx)
- Intermediate coronary syndrome or unstable angina (411.1), or
- Acute coronary occlusion without myocardial infarction (411.81)

Cohort	New users	Follow-up (in years)	Composite CV outcome	Incidence per 1,000 persons (95% CI)	Incidence rate per 1,000 person-years (95% CI)	Mantel-Haenszel incidence rate ratio (95% CI) *
<b>Initiators with a tobacco use code</b>						
Varenicline	89,519	11,197.01	56	0.63 (0.47, 0.81)	5.00 (3.78, 6.49)	<b>1.02 (0.71, 1.47)</b>
Bupropion	113,378	22,942.15	118	1.04 (0.86, 1.25)	5.14 (4.26, 6.16)	
<b>Initiators of smoking cessation products</b>						
Varenicline	260,660	32,070.43	109	0.42 (0.34, 0.50)	3.40 (2.79, 4.10)	<b>0.98 (0.43, 2.23)</b>
Bupropion	11,203	1,462.38	6	0.54 (0.20, 1.17)	4.10 (1.51, 8.93)	
<b>All initiators</b>						
Varenicline	260,660	32,070.43	109	0.42 (0.34, 0.50)	3.40 (2.79, 4.10)	<b>1.52 (1.21 1.91)</b>
Bupropion	745,004	209,477.70	452	0.61 (0.55, 0.66)	2.16 (1.96, 2.37)	

\* Adjusted for age, sex, and health plan

# Challenges

- Many different exposures
- Many different outcomes
- Many patient types
- Many and diverse data environments
  
- Need for timeliness in both detection and follow-up
- Need to avoid false alarms
- Need for multiple simultaneous activities
- Need for surge capacity

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## Welcome to Mini-Sentinel

Mini-Sentinel is a pilot project sponsored by the U.S. Food and Drug Administration (FDA) to inform and facilitate development of a fully operational active surveillance system, the Sentinel System, for monitoring the safety of FDA-regulated medical products.

Mini-Sentinel is one piece of the Sentinel Initiative, a multi-faceted effort by the FDA to develop a national electronic system that will complement existing methods of safety surveillance.

Mini-Sentinel Collaborators include Data and Academic Partners that provide access to health care data and ongoing scientific, technical, methodological, and organizational expertise.

**NEW POSTINGS**

- [Drugs that act on RAAS and angioedema](#)
- [Smoking cessation drugs & cardiovascular outcomes](#)
- [Angiotensin II receptor blockers & celiac disease](#)
- [Anti-diabetes drugs & acute myocardial infarction](#)
- [Mini-Sentinel Common Data Model v2.0](#)
- [MSDD At-a-Glance – December 12, 2011](#)

# The annotated Mini-Sentinel

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ORIGINAL REPORT

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The U.S. Food and Drug Administration's Mini-Sentinel program

- Supplement to *Pharmacoepidemiology and Drug Safety*
- 34 peer reviewed articles
- Goals, organization, privacy policy, data systems, systematic reviews, stats/epi methods, record retrieval and review, protocols for drug/vaccine studies...
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