Active Surveillance: a Regulatory Perspective

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Active Surveillance Think Tank
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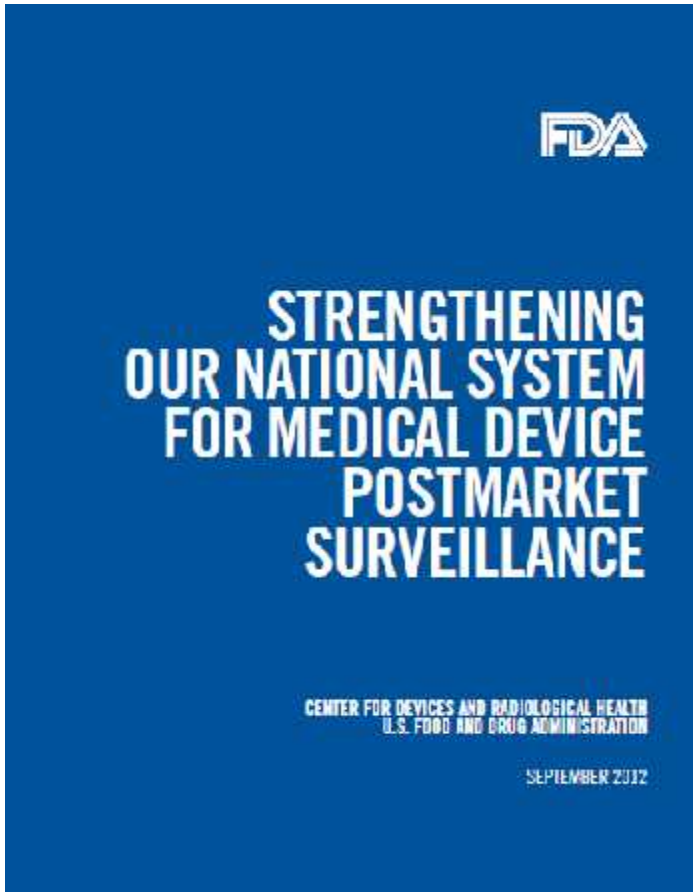
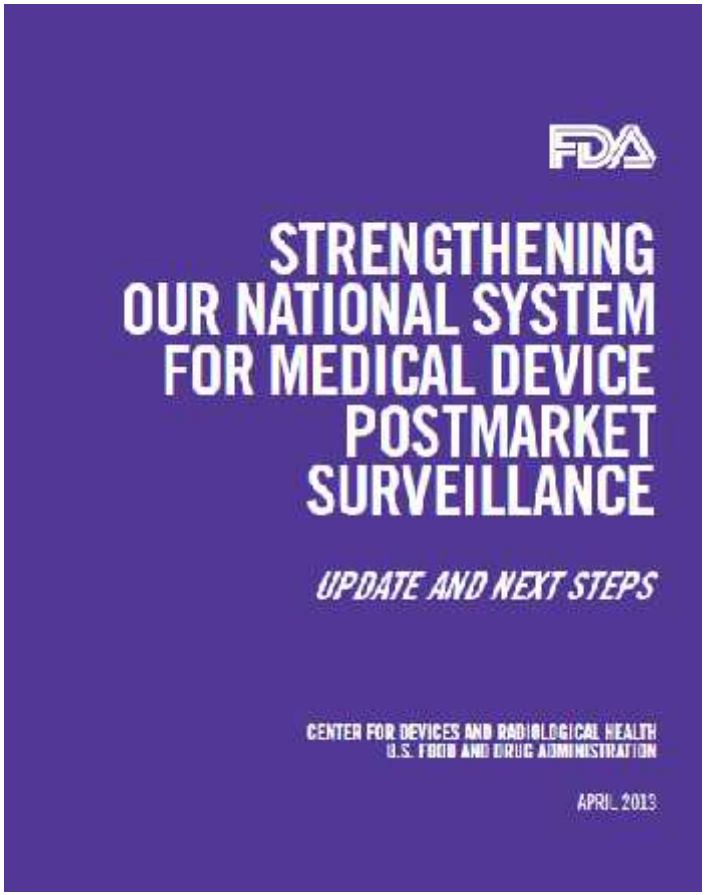
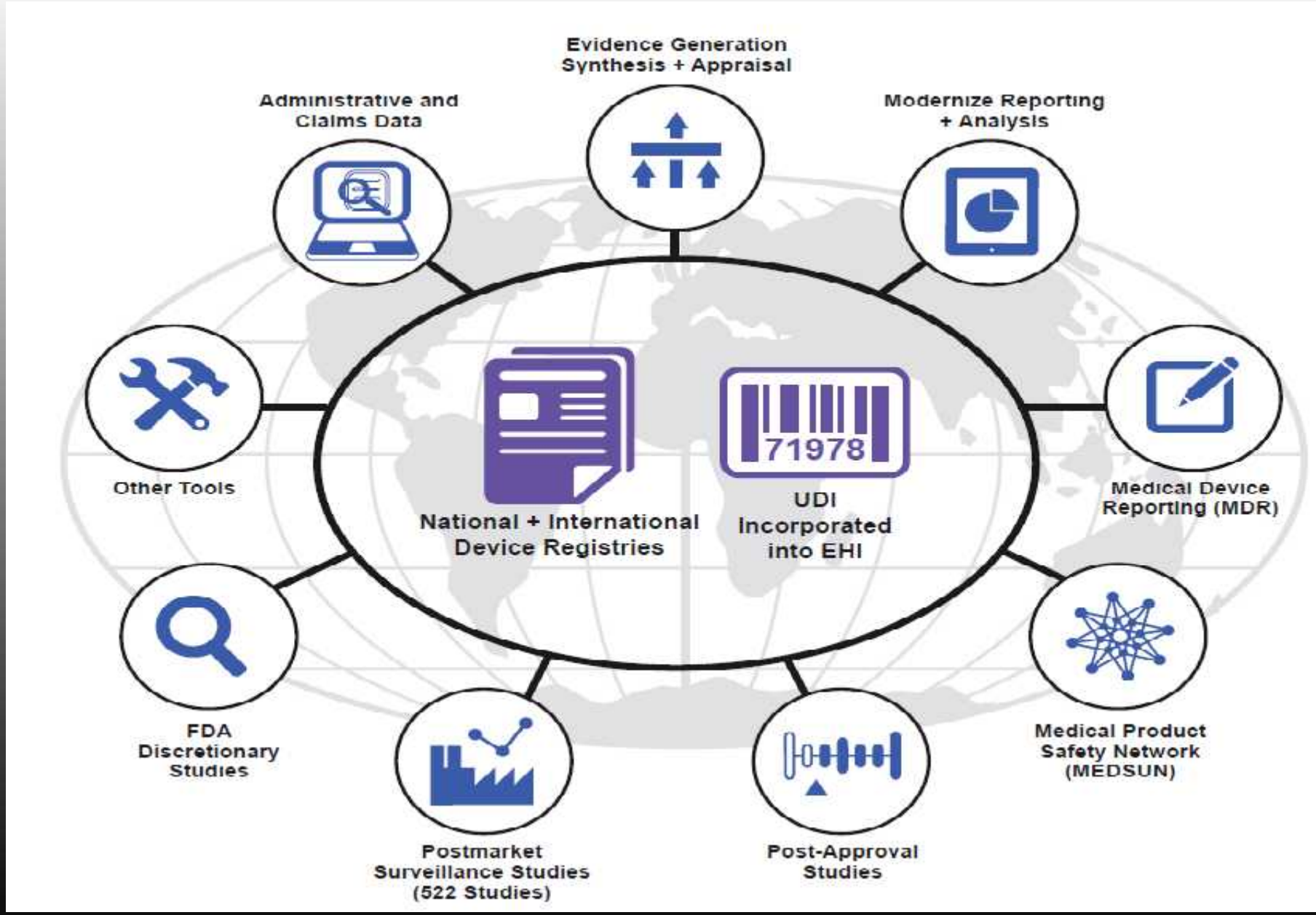
Strengthening Our National System

Taking the Next Steps






Evidence Generation
Synthesis + Appraisal
Administrative and
Claims Data
Modernize Reporting
+ Analysis
Other Tools
National + International
Device Registries
71978
UDI
Incorporated
into EHI
Medical Device
Reporting (MDR)
FDA
Discretionary
Studies
Medical Product
Safety Network
(MEDSUN)
Postmarket
Surveillance Studies
(522 Studies)
Post-Approval
Studies

Surveillance: Epidemiology Perspective

- Surveillance
  - Continuous and systematic collection, analysis, interpretation and dissemination of information for monitoring health problems.

- Surveillance System
  - Network of people and activities that maintain this process and may function at a range of levels from local to national or international

- Public Health Surveillance
  - Most surveillance systems are operated by public health agencies that use surveillance to guide disease prevention and control activities.

Rothman & Greenland, Modern Epidemiology, Second Edition

Beyond Passive Surveillance

- Efforts from Passive to Active
  - Passive: reporter initiated (Medical Device Reporting System)
  - Enhanced/Stimulated Passive: target devices/events of interest amid passive reporting (Medical Product Safety Network, MedSun)
- Active Surveillance
  - Prospective, near real-time, pre-specified, rate-based
  - Active case finding
  - Not datamining, not research
  - Can embed studies in surveillance apparatus/system

Purposes for Surveillance

CDRH SIGNAL MANAGEMENT

- What is a Signal?
  - Information that may come from one or more sources; and
  - Suggests a new potentially causal association, or a new aspect of a known association, between a medical device and an event or set of related events; and
  - Might justify or require further evaluation and/or action by the Center

- What is Signal Management?
  - A set of activities to determine whether a safety signal represents a risk which may warrant further Center: 1) assessment; 2) communication; and /or 3) other risk mitigation actions and the actions undertaken accordingly.
  - An avenue for sharing knowledge and information about the performance of the products we regulate
  - Feedback to improve premarket review
  - Identification of science research needs

Important Differences Between Devices and Drugs: Implications for Postmarket Surveillance

Devices	Drugs
• Heterogeneous	• Homogeneous
• Complex components	• Pure molecules
• Iterative changes	• No changes
• Malfunctions	• Drug quality problems
• Design error	• No equivalent
• Packaging/Labelling error	• Similar
• Human Factors	• No equivalent
• Learning curve	• Straightforward use
• Unique Device Identifier	• NDC codes

Towards Active Surveillance

- Define exposures, outcomes, key covariates
- Choose analysis approach (design?, comparators?, confounders?)
- Active case finding (stimulated?, automated?, multi-modal?)
- Estimate the risk (models; crude, refined)
- Aggregate results over time (continuous, periodic)
- Apply alerting rules
- Report to FDA

Adapted from Info@mini-sentinel.org

Automated Enhanced Surveillance

ASTER-D (Adverse Event Spontaneous Triggered Electronic Reporting for Devices)

Reed et. al.: *J Clin Eng* 2016;41(2):83-89

- Device safety report triggered from within EHR or Incident Reporting System
- Data from HL7 Continuity of Care document to pre-populate safety report form
- Pre-specify event(s) of interest (more active approach)

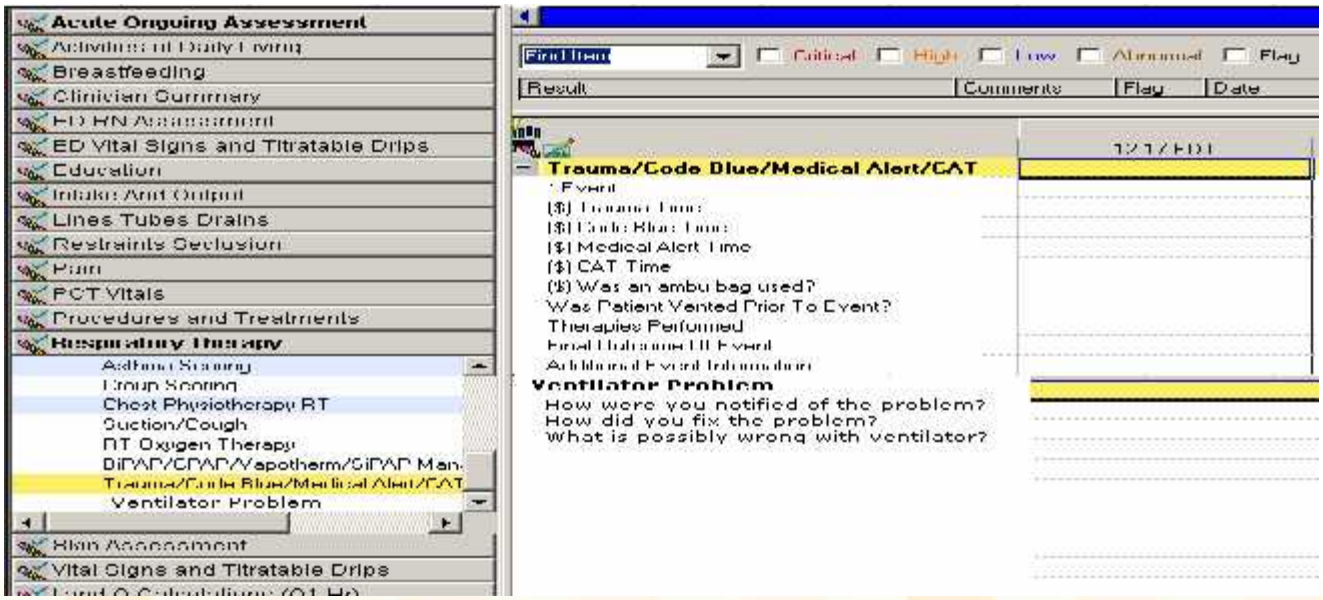
Detection of Ventilator-Associated Adverse Events

Stockwell et. al. (unpublished)

- Ventilator change out during patient care as a flag for potential device issues

Ventilator Surveillance

- iView section of EHR: automatic flag for change in ventilator ID
- Respiratory Therapist documents reason for the change in ventilator ID and sent to biomedical engineering
- Transmission to CDRH of evaluated event



Hospital-Based Active Surveillance

Emergency Department (ED) Device-Associated Events

Hefflin et. al.: *Am J Prev Med* 2004;27(3):246-253

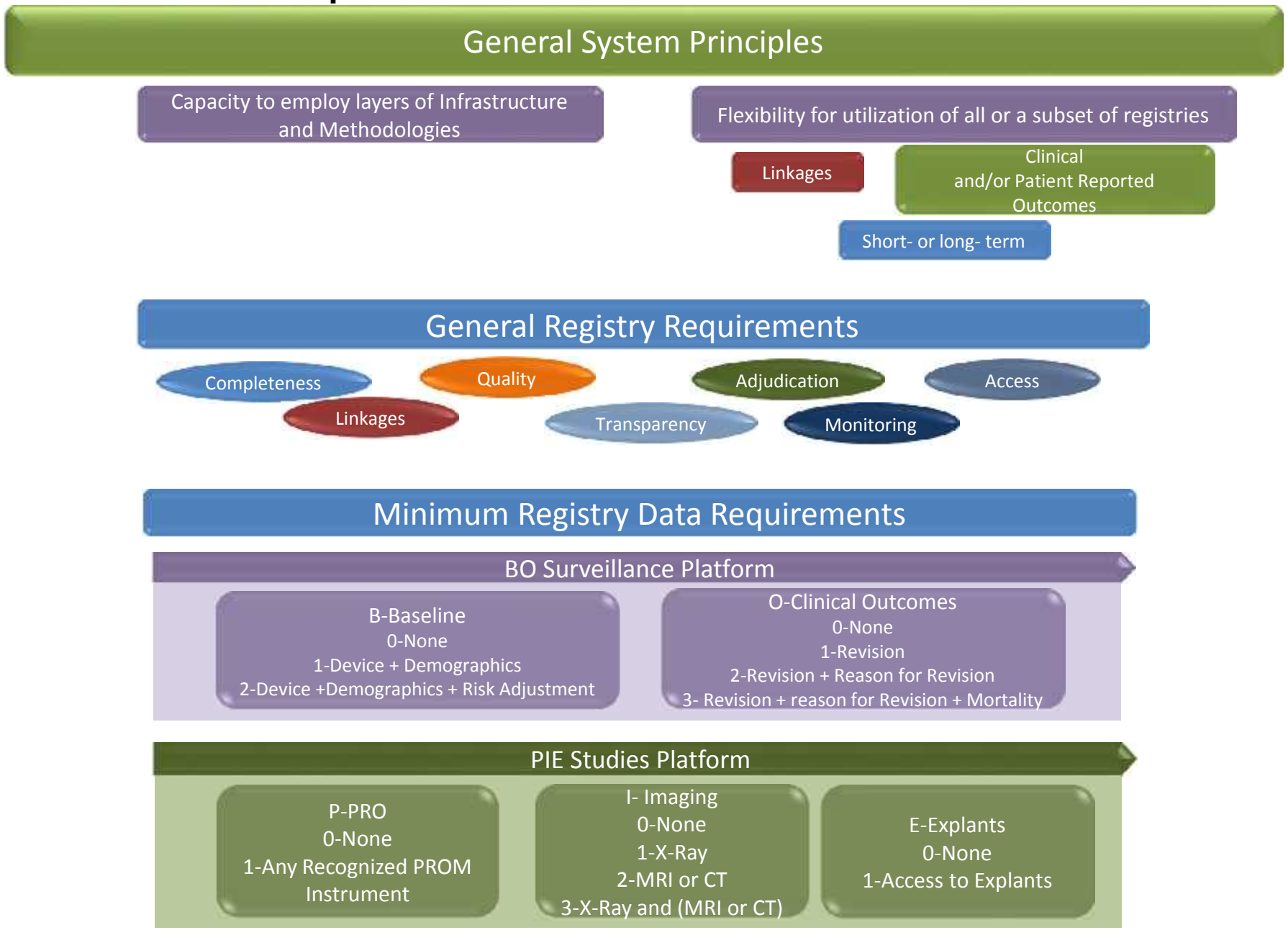
- Explored ED records using CPSC's National Electronic Injury Surveillance System (national stratified probability sample)
- FDA trained NEISS staff in coding and case ascertainment
- National estimates vary by age, gender, device type: overall--454K (1999) and 489K (2004)

Multi-Modal Event Surveillance in Tertiary Care Facility

Samore et. al.: *JAMA* 2004;291:325-334

- Reliability of e-surveillance in detecting device events
- Rates (per 1000 admissions) varied by method
  - From Incidence reports (1.6) to Computer Flags (27.7) to ICD-9 Discharge Codes (64.6) with Overall Estimate (83.7)

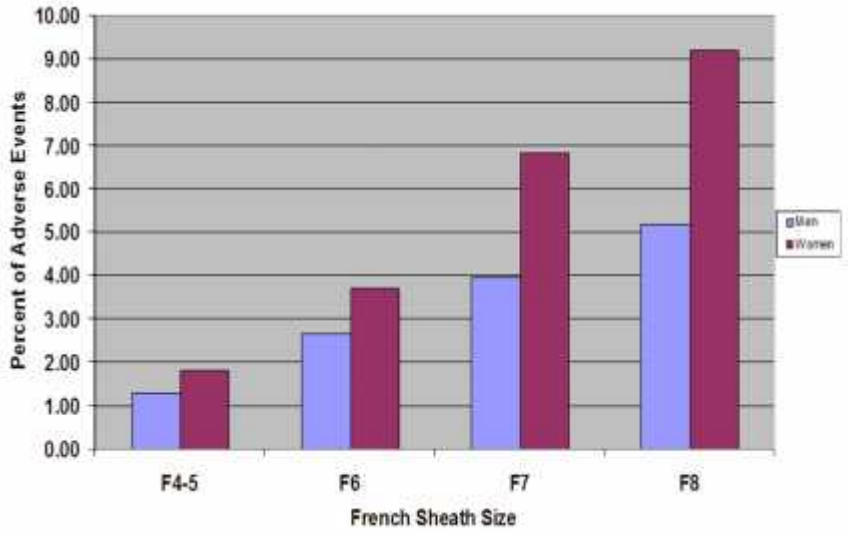
Registry-Based Surveillance: Crude to Refined
Proposed BO-PIE Model within ICOR-USA



Registry-Based Surveillance: Flexibility

- Primary study in cathPCI registry (>200 sites)
- Results suggested significant gender-related differences
- Second study done using additional data collection
  - Device brand
  - Sheath size
- Demonstrates flexibility in potential surveillance model

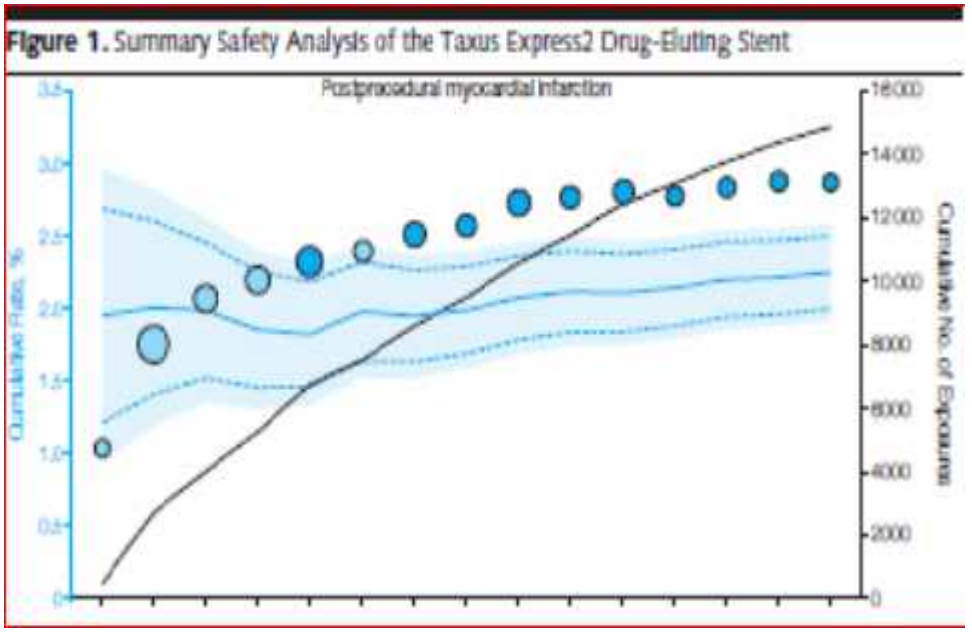
Relative Risk of Any Vascular Complications Following Cardiac Catheterization by Gender



Tavris et. al., *Pharmacoepidemiol Drug Safety* 2007;16:125-131

Automated Active Surveillance

Automated Surveillance to Detect Postprocedure Safety Signals of Approved Cardiovascular Devices



Issues to Consider

- Appropriate data source (relevant/reliable)
- Device complexity, heterogenity, identification
- Means of case ascertainment and validation
- Timeliness of surveillance and data lags
- Diffusion rate, person-years of follow-up, effect estimates
- Crude versus refined models
- Methods issues (analytic approach, multiple comparisons)

Thanks for Your Attention!