Overview of Anticipated Procedures for Active Surveillance of New Medical Products

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Mini-Sentinel Protocol Core

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Goal

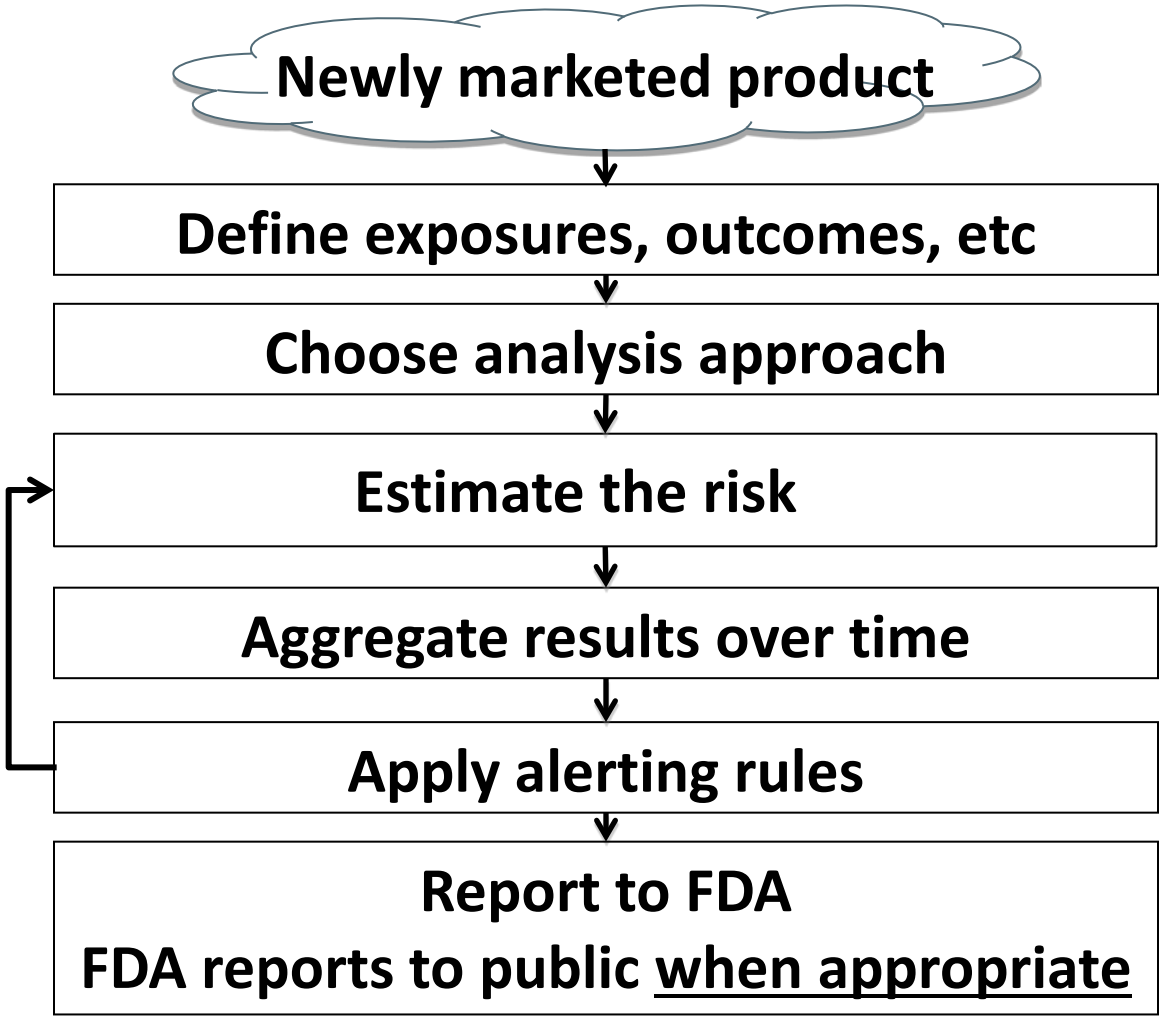
- Relatively standardized
- Prospective
- Dozens of products simultaneously
- Signal *potential* excess risk for subsequent follow-up

MINI-SENTINEL STATEMENT OF WORK

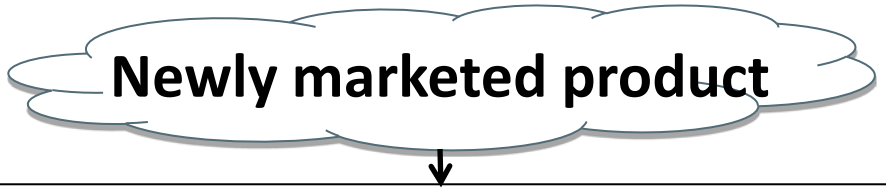
ROUTINE PROSPECTIVE SAFETY SURVEILLANCE FOR NEW DRUGS, VACCINES, AND OTHER BIOLOGIC PRODUCTS

- http://www.mini-sentinel.org/work_products/Assessments/Mini-Sentinel_Prospective-Surveillance-Statement-of-Work.pdf

Prospective surveillance at a glance

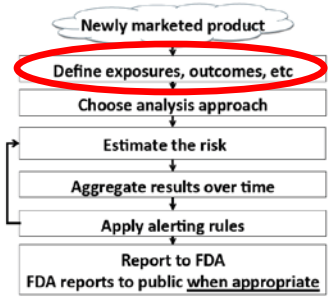


Prospective surveillance: who, what, when



Define exposures, outcomes, etc

- **FDA: Product in need of surveillance**
- **6 mo prior to desired start**
- **Planning team:**
  - **Which outcomes?**
  - **Post-exposure time window?**
  - **Which design?**
  - **Which data?**
  - **Plan for promptly evaluating signals?**



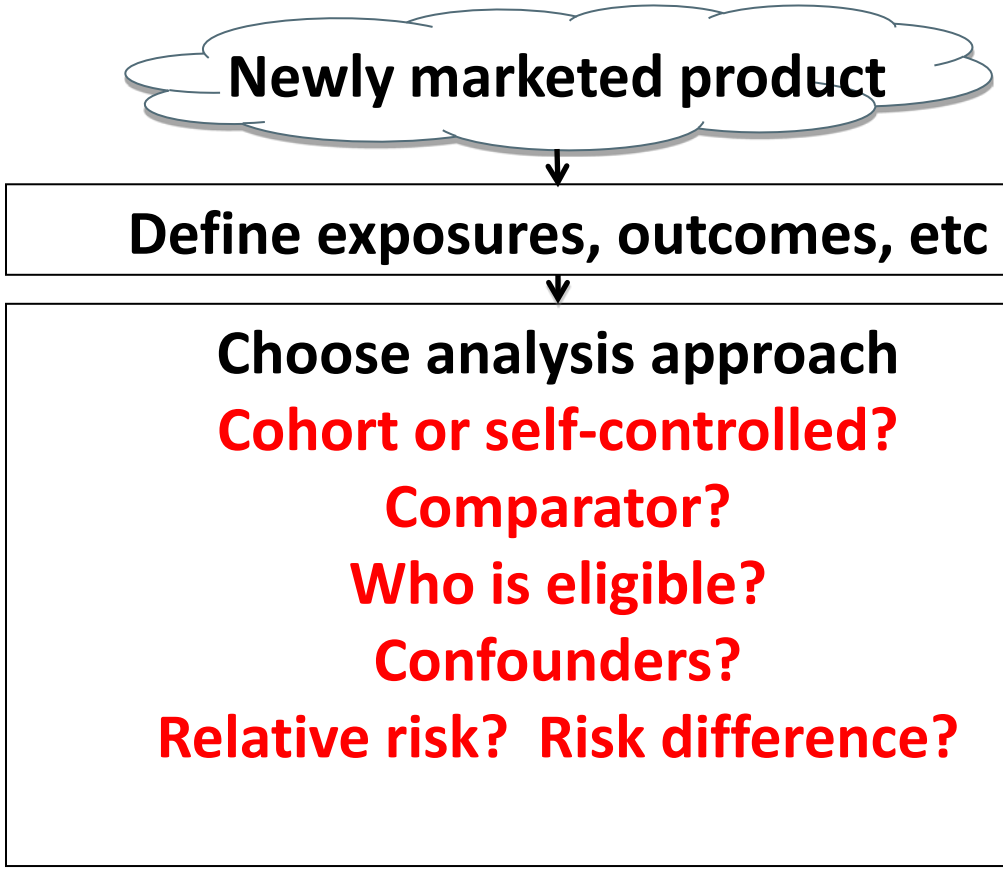
Standard outcome algorithms

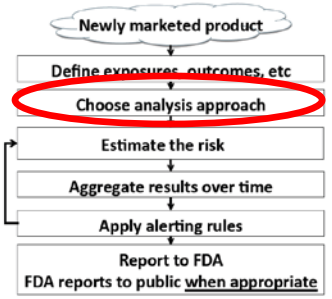
GI bleeding
Pancreatitis
Premature delivery
Pulmonary Fibrosis
Hypertensive crisis
Agranulocytosis
Aplastic Anemia
Bronchospasm
CVA
Venous Thromboembolism
Hemorrhagic CVA
Ischemic CVA
Neutropenia
Bell's Palsy
Spontaneous abortion/Stillbirth
Acute Respiratory Failure
Sepsis
Deafness
Thrombotic thrombocytopenic purpura
Systemic lupus erythematosis
Inflammatory Bowel Disease
Juvenile RA
Tuberculosis
Erythema multiforme major
Idiopathic thrombocytopenic purpura
Thrombocytopenia
Henoch Schonlein purpura
Peripheral neuropathy
Guillan-Barre syndrome
Tendon rupture
Seizure, febrile
Suicide
Valvulopathy
Hip fracture
Pulmonary hypertension
Rhabdomyolysis
Sudden cardiac death
Diabetes

Standard Outcome Definitions:

Outcome	Algorithm	Rationale	Reference
Acute Ischemic Stroke	**Recommended Primary**: 434, 436 in first position of a hospital claim	Some algorithms also included 433.x1 and excluded 434.x0 (see Recommended Secondary), however 433.x1 may also have low PPV and the PPV for 434 (without exclusion) in first position is good (>85%). PPV diminishes slightly when any position, or when community vs tertiary care.	22262598 12105309
	Recommended Secondary: 433.x1, 434 (excluding 434.x0), 436 in first position of a hospital claim	Algorithm that included 433.x1, 434 (excluding 434.x0), and 436 performed well. 433 (other than 433.x0) had very low PPV. One study found 433.x1 PPV=71%	22262598 12364739
	Also Observed (but not recommended): 433, 434, 436 in first position	433 had very low PPV . 433.x0 PPV was 2%, 433.x1 PPV was only 20%	9707200

Prospective surveillance: how





What affects the choice? Exposure-outcome characteristics

Table 1. Scenario characteristics inherent to the specific exposure-outcome pair (i.e., scenario) that might affect design and analytic choice

Exposure characteristics			Characteristics of the (potential) exposure-HOI link				HOI characteristics	
					Strength of confounding			
Background frequency of use in population	Utilization trend in population	Use pattern	Onset of exposure risk window	Duration of exposure risk window	Between person	Within person	Background frequency	Expected degree of onset misclassification
More frequent	Uniform	Short-term (including intermittent)	Immediate	Short	Negligible	Negligible	Infrequent	Negligible (e.g., HOI is mortality captured by vital statistics)
Less frequent	Changing (increasing, decreasing, cyclical)	Long-term	Short	Long	Needs to be addressed	Needs to be addressed	Rare	Pertinent (e.g., cancer)

Stakeholder preferences affect the choice

Table 2. Scenario characteristics determined by stakeholder/investigator that might affect design and analytic choice		
Effect measure of interest	**Number of comparison groups**	**Comparison exposure**
Difference measure	One	Active comparator
Relative measure	Multiple	Truly unexposed

Standard cohort algorithms

- Persons with coronary artery disease
- Persons with mood disorders
- Persons with end-stage renal disease
- Hypertensives
- Smokers
- Asthmatics
- Persons with dementia
- Persons who received fluoroquinolones for post-exposure prophylaxis
- First responders
- Nursing home residents
- Pregnant women
- Live births
- Premature babies
- Persons at high risk for influenza complications
- Immunocompromised persons
- Type 1 diabetics
- Type 2 diabetics
- Obese persons