ENGELBERG CENTER for Health Care Reform at BROOKINGS

Sentinel Initiative Public Workshop

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Prospective Routine Observational Monitoring Program Tools (PROMPT): Current Status of Development

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PROMPT Goal

To develop capacity to conduct active safety surveillance on medical products:

- Relatively standardized
- Prospective, near real-time
- Semi-automated
- High capacity for multiple products/outcomes simultaneously

PROMPT Goal

- Apply multivariate confounder adjustment and sequential monitoring
- Signal *potential* excess risk for subsequent follow-up

PROMPT Building Blocks

- Created electronic algorithms to:
  - identify health outcomes of interest (HOI)
  - identify standard cohorts
  - define core confounders
- Although all algorithms are not validated.

Library of Health Outcomes

- Agranulocytosis
- **Anaphylaxis**
- Angioedema
- Aplastic anemia
- Asthma exacerbation
- Bell's palsy
- Bleeding, GI
- CVA, all acute
- CVA, hemorrhagic
- CVA, ischemic
- Diabetes, type I
- Erythema multiforme major
- Fracture, hip
- Guillain-Barré syndrom
- Hearing loss, sudden
- Hypertension, pulmonary
- Hypertensive emergency
- Inflammatory bowel disease
- Intussusception
- Kawasaki disease
- **Kidney injury, acute**
- **Liver injury, acute severe**
- **Myocardial infarction, acute**
- Neuropathy, peripheral
- Neutropenia
- Pancreatitis, acute
- Premature delivery
- Pulmonary fibrosis
- Purpura, Henoch-Schönlein
- Purpura, idiopathic thrombocytopenic
- Purpura, thrombotic thrombocytopenic
- Respiratory failure, acute
- Rhabdomyolysis
- Rheumatoid arthritis, juvenile
- Seizure, febrile
- Sepsis
- Stillbirth / spontaneous abortion
- Sudden cardiac death / ventricular arrhythmia
- Suicide
- Systemic lupus erythematosus
- Tendon rupture, achilles
- Thrombocytopenia
- Tuberculosis
- Valvulopathy
- Venous thromboembolism

Library of Standard Cohorts

Persons with:

- Asthma
- Chronic kidney disease
- Coronary artery disease
- Dementia
- Depression
- Diabetes, type I or II
- Tobacco use, diagnosed
- Obesity
- High risk for influenza complications
- Hypertension
- Immunocompromised including exposure to certain immunologics, certain cancers, or HIV
- Nursing home residence

Library of Core Confounders

Demographics

- Age
- Sex
- Calendar time
- Data partner

Lifestyle factors

- Tobacco use, diagnosed
- BMI
- Combined Charlson-Elixhauser comorbidity index

Healthcare utilization in baseline period

- No. visits to ED
- No. ambulatory visits
- No. hospitalizations
- No. distinct drugs ordered / dispensed
- No. prescriptions ordered / dispensed

Tools for PROMPT Design Decisions

- Developed an Operations Manual
  - Steps for implementation
- Incorporated Taxonomy guidance aimed at “pre-thinking” major design and analysis considerations
- 4 design and analytic modules

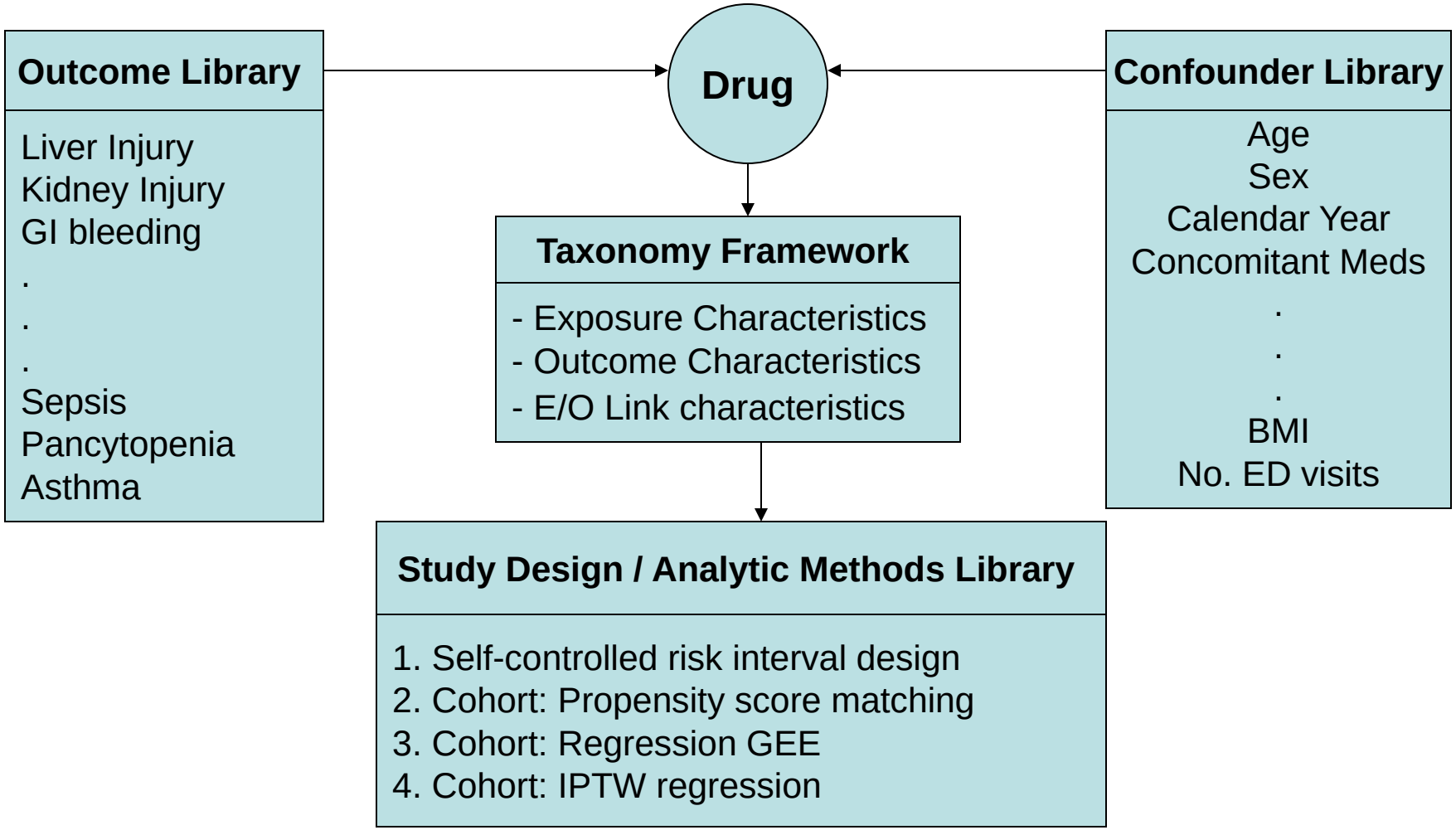
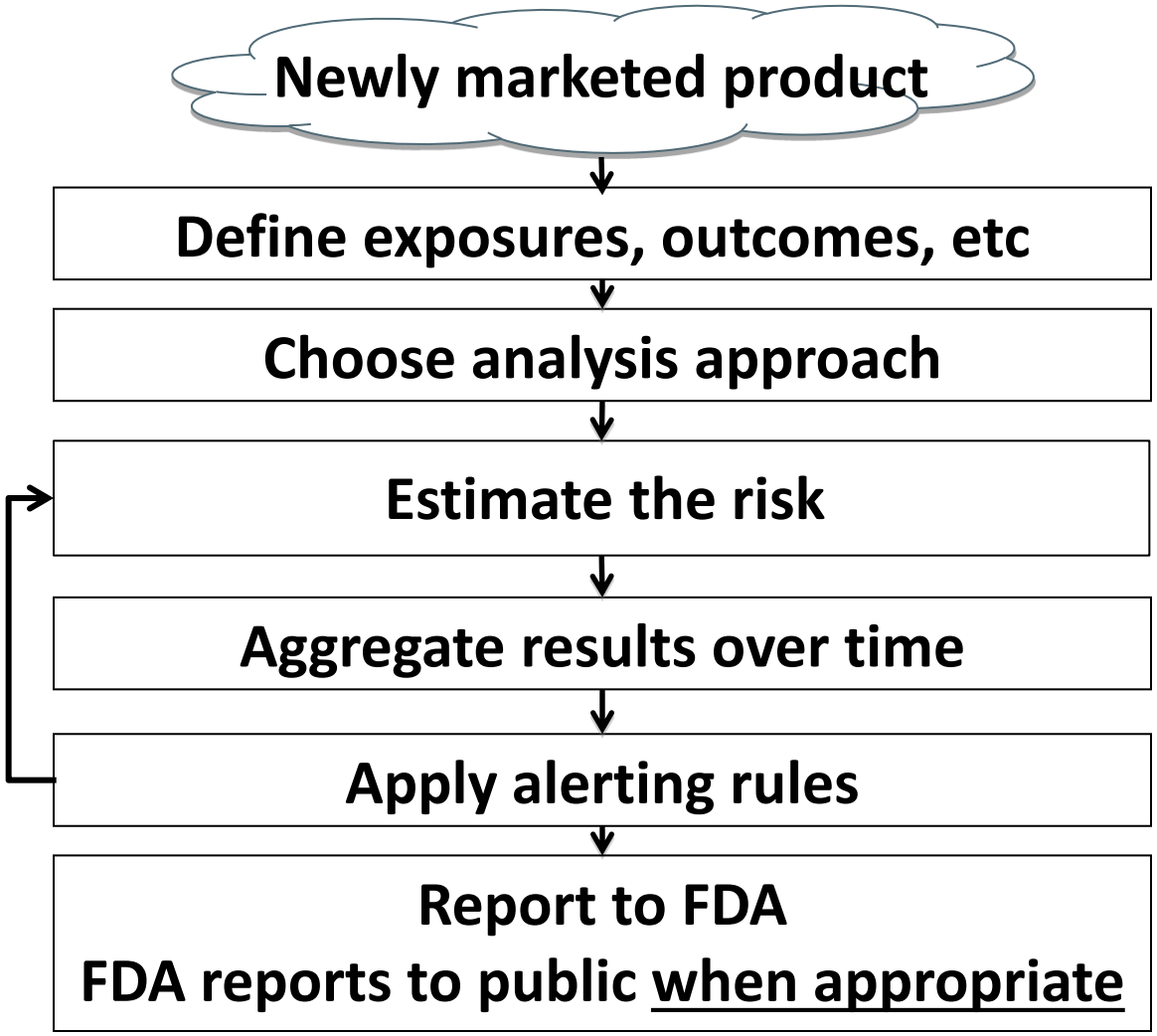
Sequential Monitoring Design

- Input a range of specified sequential design parameters
  - Timing and frequency of tests
  - Stopping threshold used at each test point to signal a potential safety problem
  - Overall false positive error rate

4 PROMPT Modules

Module 1	Module 2	Module 3	Module 4
Self-controlled risk interval design	Cohort design Propensity score (exposure) matching	Cohort design Regression adjustment Generalized Estimating Equations	Cohort design Inverse probability of treatment weighted regression adjustment

PROMPT at a Glance



PROMPT at a Glance