Conducting protocol-based assessments in the Mini-Sentinel pilot

Process & Lessons learned

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On behalf of the Mini-Sentinel angioedema workgroup

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## Mini-Sentinel angioedema workgroup

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Overarching goals of the project

- To assess selected drug-event associations
  - Drugs targeting renin-angiotensin-aldosterone system & angioedema

- To build general strategies for safety assessments of medical products on the market for >2 years

- NOT designed to provide definitive evidence of a causal relation
Mini-Sentinel partner organizations
Process to conducting a MS protocol-based assessment

- FDA identifies topic
Mini-Sentinel distributed analysis

1. Workgroup creates and submits query (a computer program)

2. Data partners retrieve the query

3. Data partners review and run query against their local data

4. Data partners review results

5. Data partners return results via secure network

6. Results are aggregated and returned
Cohort creation

Total population in Mini-Sentinel as July 2011
~99,000,000

Applying eligibility criteria
(age, medical history, etc)

ACEIs
1,845,138

ARBs
467,313

Aliskiren
4,867
Cohort creation

Total population in Mini-Sentinel as July 2011
~99,000,000

Applying eligibility criteria
(age, medical history, etc)

ACEIs 1,845,138
ARBs 467,313
Aliskiren 4,867
ß-blockers 1,592,278
Statistical analysis

- Propensity score approach
  - Condensing information from a large number of variables into a non-identifiable measure

- Case-centered approach and meta-analysis
  - Needing only aggregated data to complete the analysis
Timeline

Kick-off meeting: Mar 11

Protocol finalized: Aug 11

1st workplan sent: Sep 11

Analysis complete: Jan 12

Draft final report: Feb 12

Total time from start to completion: ~11 months
Results

Adjusted relative risk

ACEIs

* Beta-blockers as the common reference group

Toh et al, Arch Intern Med 2012;172:1582-1589
Results

* Beta-blockers as the common reference group

Toh et al, Arch Intern Med 2012;172:1582-1589
Results

Toh et al, Arch Intern Med 2012;172:1582-1589

* Beta-blockers as the common reference group
More results can be found here

- **Report:**

- **Manuscript:**

- **Presentation:**
Summary of overarching goal #1

- Largest assessment on this topic to date

- Replicated known ACEIs–angioedema association
  - With much more precise risk estimates

- Provided new information on angioedema risk for
  - Aliskiren (caveat: based on 7 exposed cases)
  - ARBs
Summary of overarching goal #2

- Developed a time and cost efficient process to perform medical product safety assessments within a large distributed data system

- Developed analytic strategies to perform robust statistical analysis without sharing identifiable information
Thank you