

# **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

Name	Affiliation	Role
Marsha Reichman	OSE/CDER/FDA	Co-Lead
Monika Houstoun	OSE/CDER/FDA	Co-Lead
Sean Hennessy	University of Pennsylvania	Co-Lead
Darren Toh	Harvard Pilgrim Health Care Institute	Co-Lead
Xiao Ding	OTS/CDER/FDA	Member
Adrian Hernandez	Duke University School of Medicine	Member
Mark Levenson	OTS/CDER/FDA	Member
Lingling Li	Harvard Pilgrim Health Care Institute	Member
Carolyn McCloskey	OSE/CDER/FDA	Member
Azadeh Shoaibi	OMP/CDER/FDA	Member
Mary Ross Southworth	OND/CDER/FDA	Member
Eileen Wu	OSE/CDER/FDA	Member
Gwen Zornberg	OSE/CDER/FDA	Member

# Overarching goals of the project

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- ❑ **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

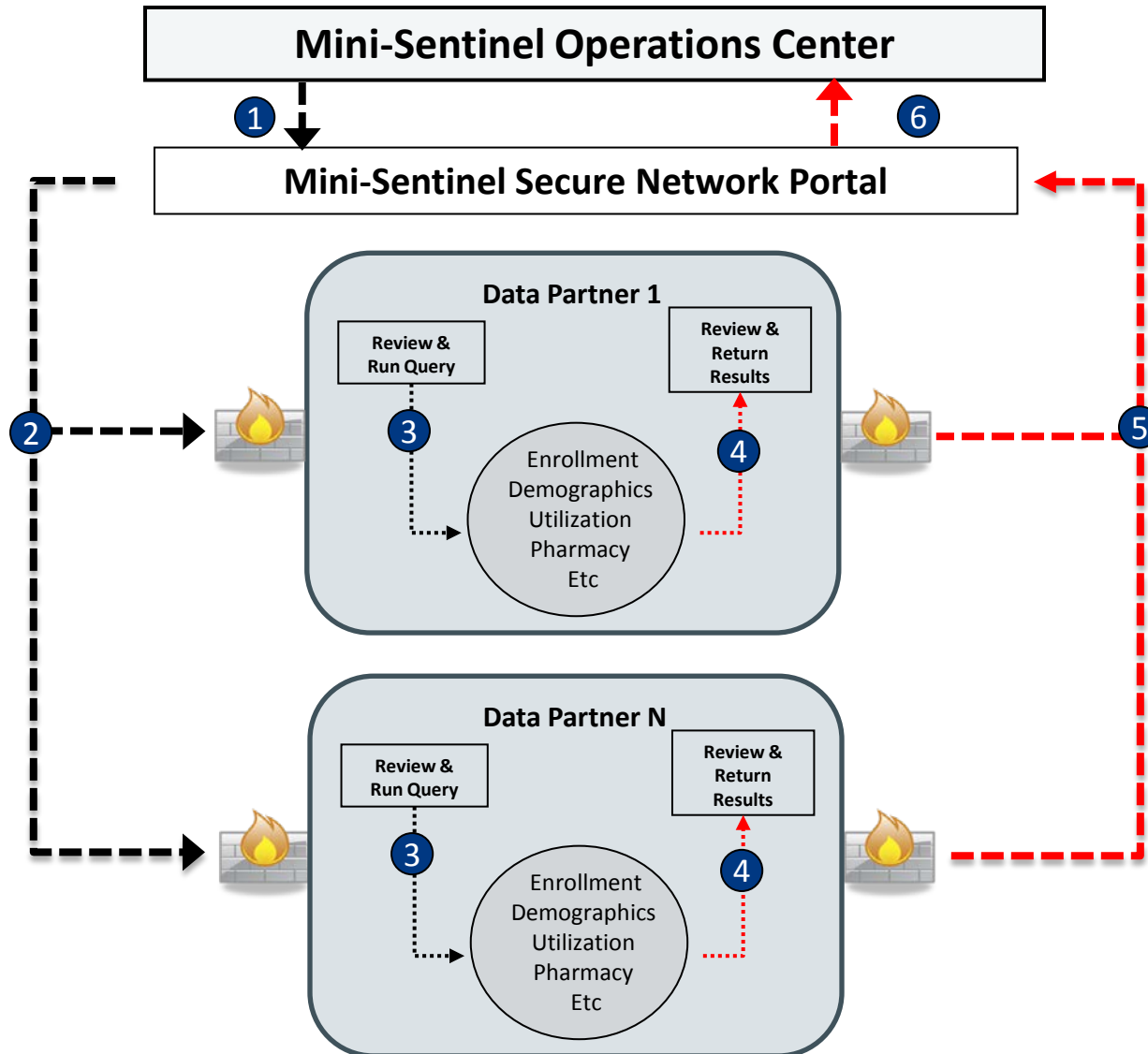


## Process to conducting a MS protocol-based assessment

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**FDA identifies topic**

# Mini-Sentinel distributed analysis



1 Workgroup creates and submits query (a computer program)

2 Data partners retrieve the query

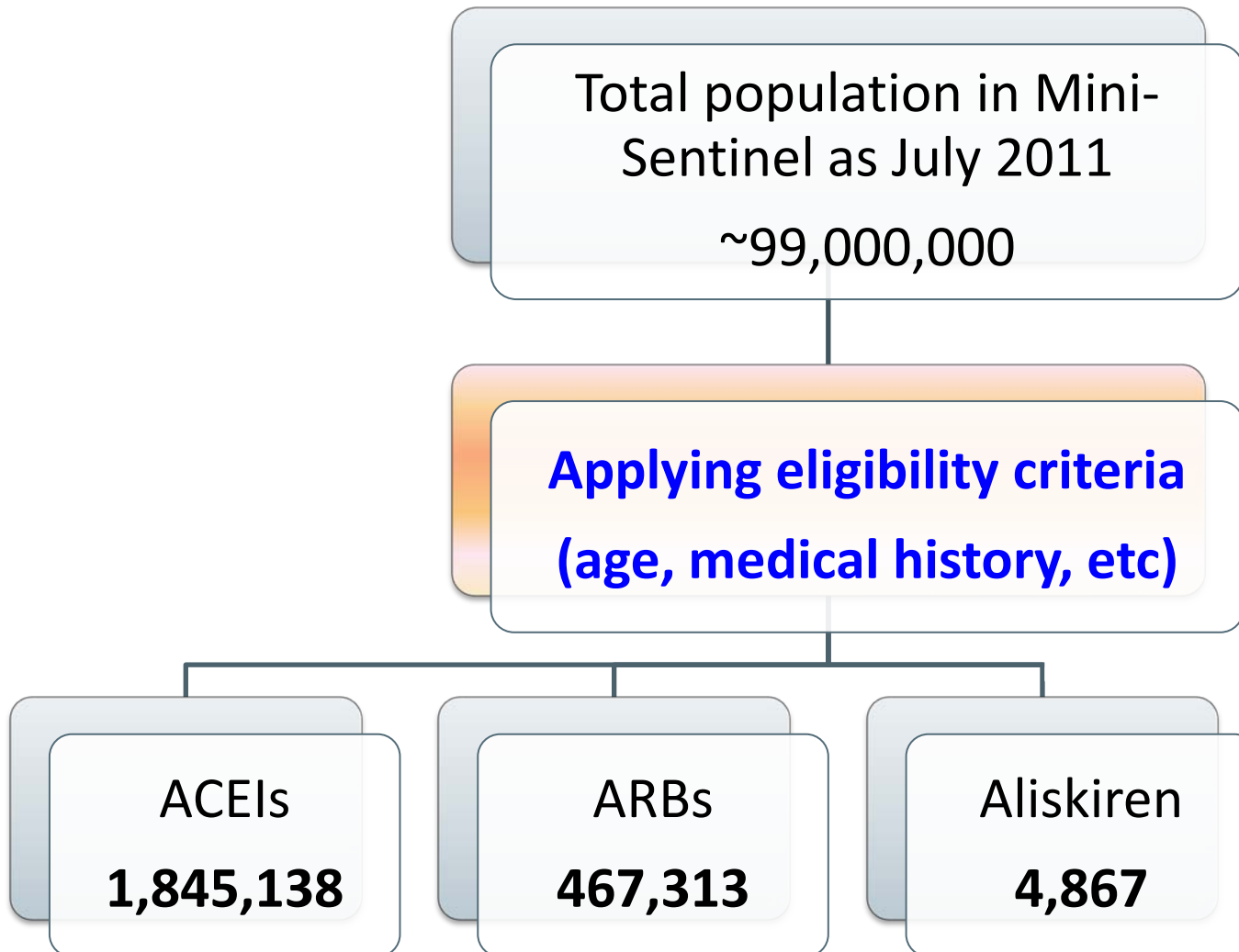
3 Data partners review and run query against their local data

4 Data partners review results

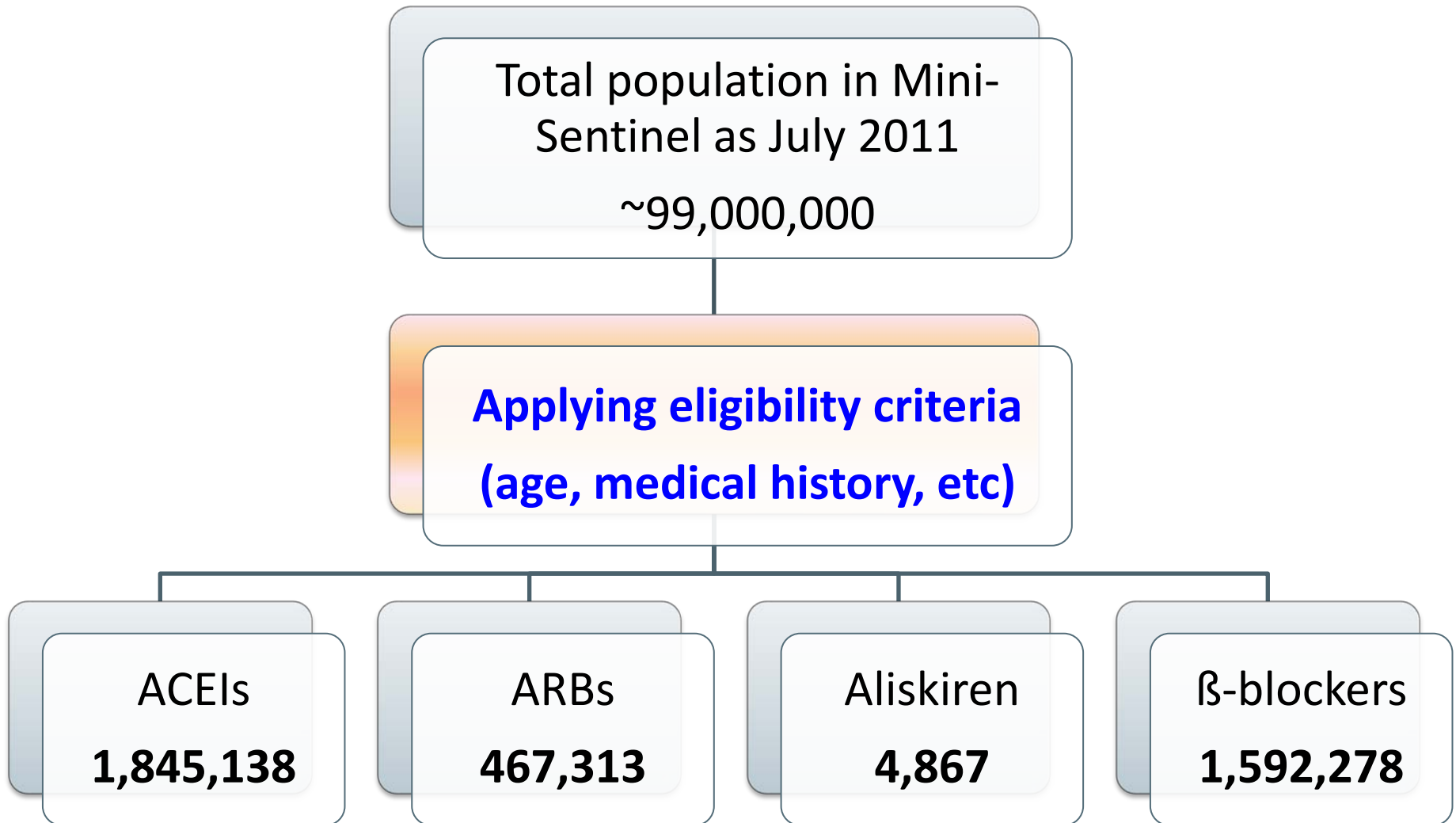
5 Data partners return results via secure network

6 Results are aggregated and returned

# Cohort creation



# Cohort creation





# Statistical analysis

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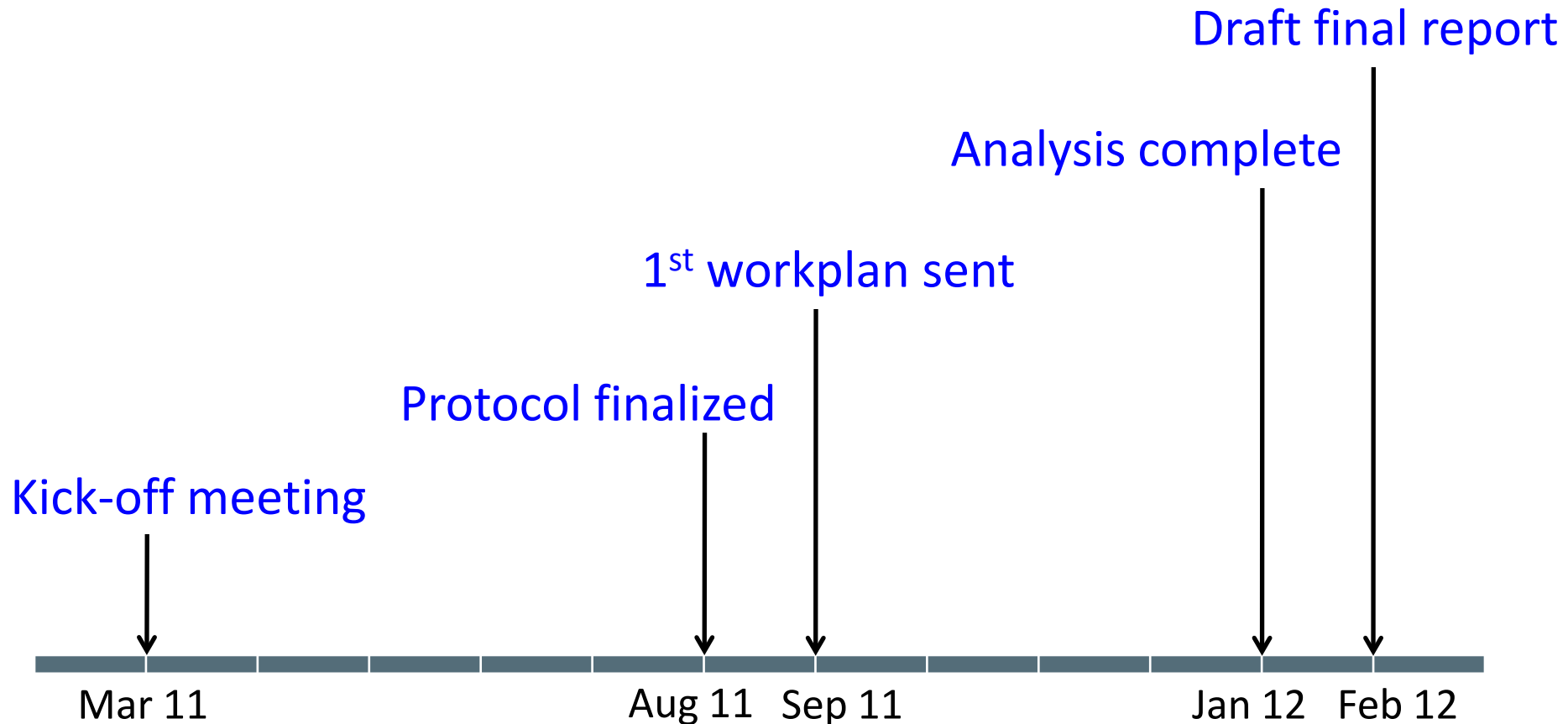
## ❑ Propensity score approach

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

## ❑ Case-centered approach and meta-analysis

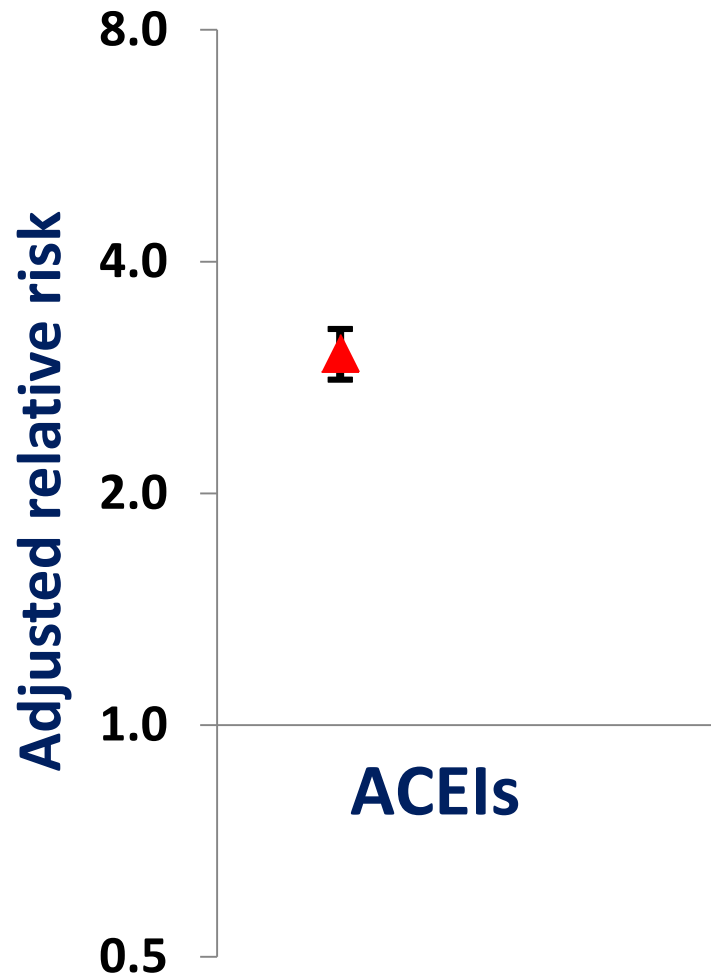
- Needing only aggregated data to complete the analysis

# Timeline



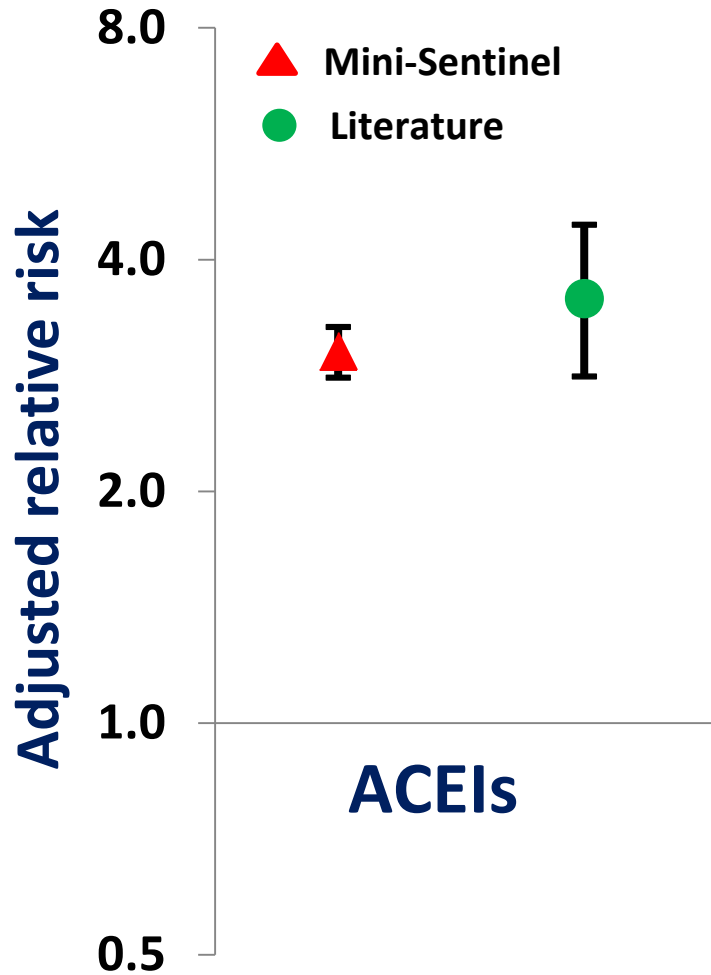
**Total time from start to completion: ~11 months**

# Results



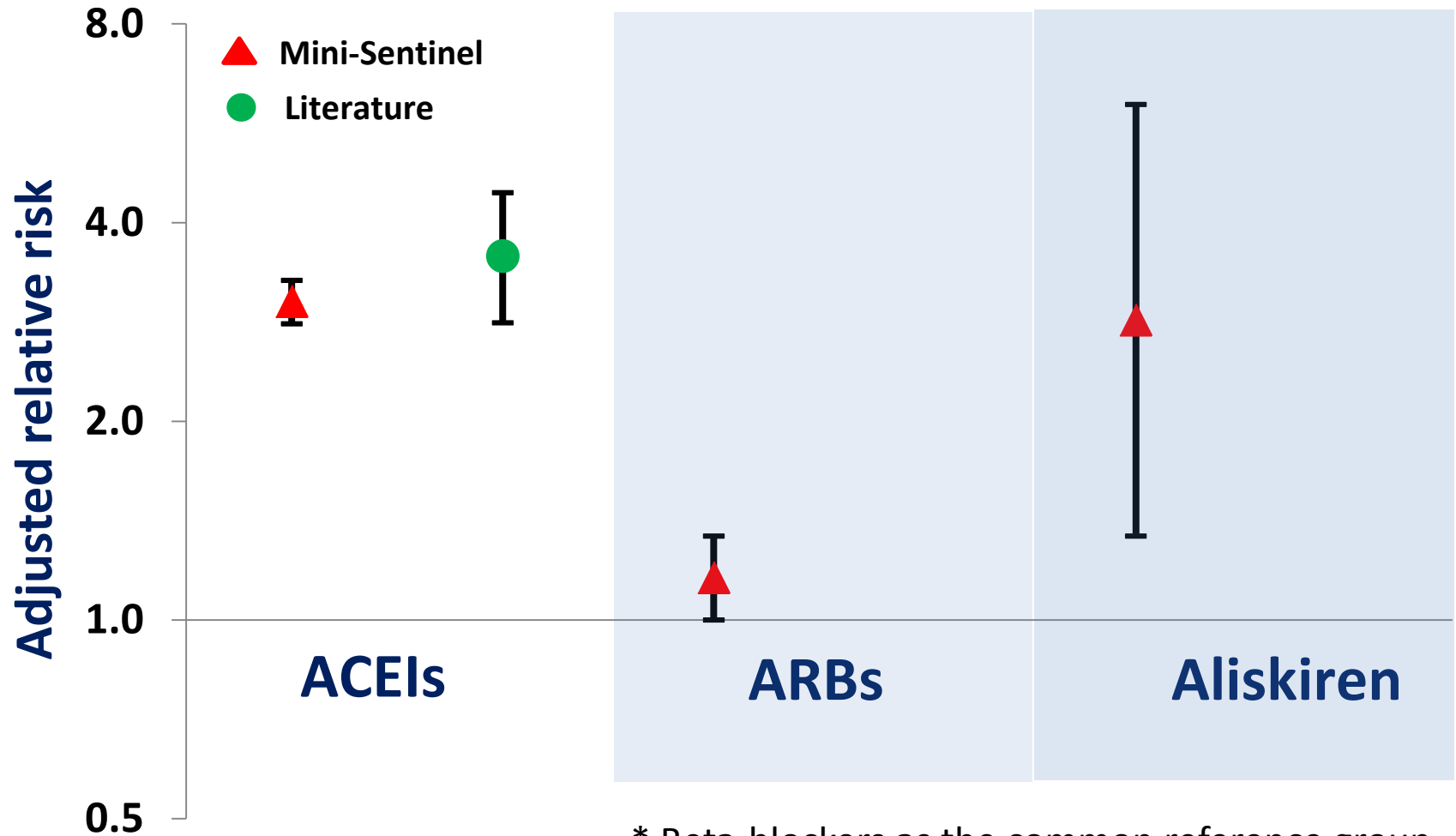
\* Beta-blockers as the common reference group

# Results



\* Beta-blockers as the common reference group

# Results



# More results can be found here

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□ Report:

[http://www.mini-sentinel.org/work\\_products/Assessments/Mini-Sentinel\\_Angioedema-and-RAAS\\_Final-Report.pdf](http://www.mini-sentinel.org/work_products/Assessments/Mini-Sentinel_Angioedema-and-RAAS_Final-Report.pdf)

□ Manuscript:

<http://archinte.jamanetwork.com/article.aspx?articleid=1391058#qundefined>

□ Presentation:

<http://www.brookings.edu/events/2012/10/16-medical-product-assessment-webinar>

# Summary of overarching goal #1

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- ❑ **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

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- ❑ **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**