ENGELBERG CENTER for Health Care Reform at BROOKINGS

Lessons from the Department of Veterans Affairs Active Surveillance Activities

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June 20, 2011

Brookings Roundtable on Active Medical Product Surveillance

Some Initial Housekeeping

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Lessons from the Department of Veterans Affairs Active Surveillance Activities

Brookings Institution Webinar
June 20, 2011

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Review

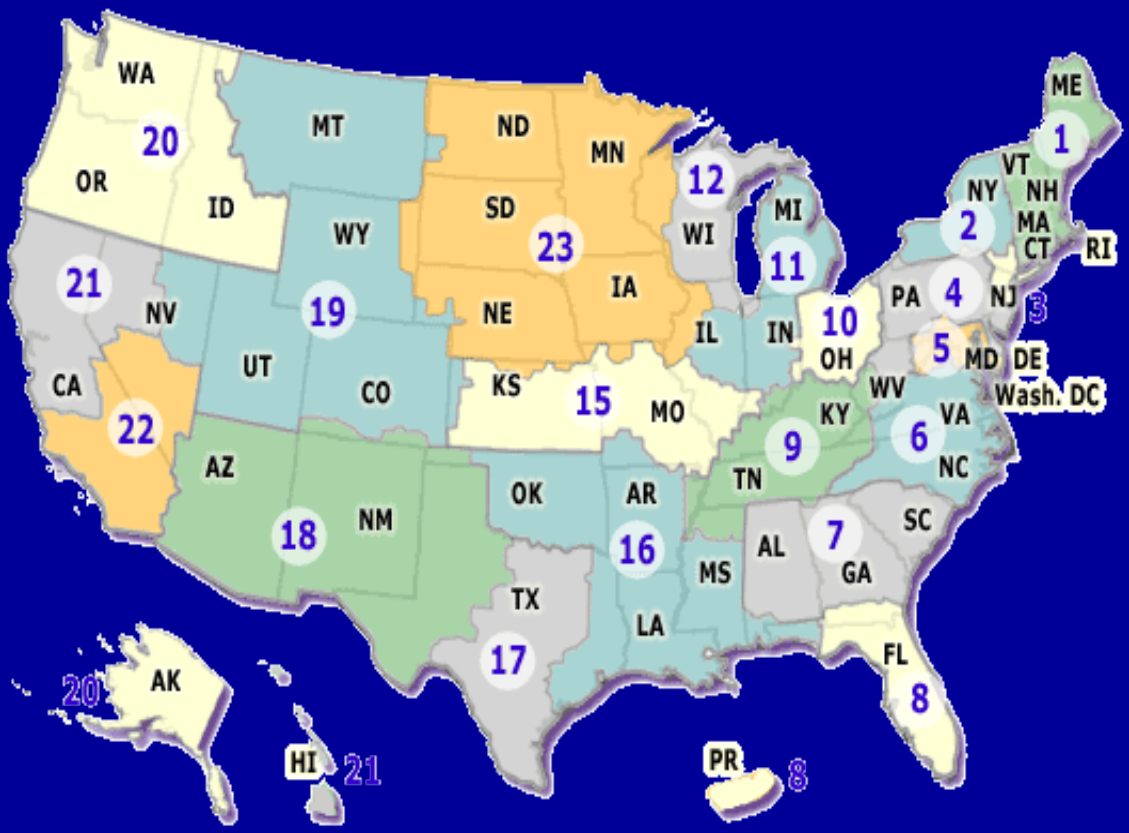
- Overview of VA Healthcare System
- Pharmacovigilance and Drug Surveillance in VA Healthcare
- Databases Used for Surveillance in VA
- Drug Surveillance/ Rapid Cycle Evaluations
- Risk Reduction and Intervention Assessment
- FDA Collaboration
- OMOP CDM in VA

VA HEALTH CARE SYSTEM

- U.S. Veteran Population: Approx. 23.5 M
- U.S. integrated health care system
  - Over 8 million enrollees
    - 5.5 M obtain health care
    - > 5 M obtain prescriptions
- Veteran Population (approx)
  - White – 80 %
  - Black Non-Hispanic 11%
  - Hispanic 6%
  - Women 8%

VA HEALTH CARE SYSTEM

- VA Medical Centers: 153
  - Affiliations with 107 medical schools
- VA Outpatient Clinics: Over 1000
- VA patients have complex health care needs
  - multiple morbidities
  - disabilities
  - mental health problems



Over 150 medical facilities distributed among 21 VISNS

VAMedSAFE – VA's Comprehensive Pharmacovigilance Program

ADVERSE EVENT SIGNAL DETECTION, EVALUATION & PREVENTION in VA

- *Signal Generation*
- Signal Refinement
- Signal Evaluation/Confirmation
- Risk Reduction/Mitigation
- Intervention Assessment

GOAL of VAMedSAFE PHARMACOVIGILANCE PROGRAM

- Track and evaluate high risk agents, high volume agents, and NMEs with potential risks in the Veteran population
- Determine rates and risks of ADEs associated with specific agents
- Maintain VA's national drug safety program with emphasis on:
  - Utilizing integrated databases as the foundation of the VA comprehensive pharmacovigilance program
  - Enhancing spontaneous ADE reporting for system based changes and enhancement of drug safety efforts
  - Communicating drug safety information throughout VA healthcare system

Surveillance in VA

- The VA as a resource for active surveillance and adverse event evaluation
  - Older/Sicker patients
  - High medication use
  - Penetration of new agents is fairly rapid
  - Small turnover of Beneficiaries
  - Good Information Systems
  - Ongoing monitoring of outcomes in place

Surveillance Using VA Databases

- Prescription Databases
- Treatment Files
- Mortality
- Disease State Registries
- Other
- Validation

VA Databases as a Tool

- An effective tool in VA
  - Monitoring exposure rate and ADEs
    - High risk agents
    - New agents
    - Agents with newly identified safety information
- VA databases provide the mechanism for
  - Active Surveillance initiatives
  - Clinical decisions
  - Research

Surveillance/Evaluations

- Databases linked at patient level to monitor agents
- Patients followed for specified period
- Control agent, baseline rate
- Rates of exposure and suspected adverse outcomes assessed
- Cohort Analysis
  - Unadjusted
  - Adjusted pre-identified covariates
  - Other
- Full study recommended when required

SELECTED EXAMPLES OF VA PHARMACOVIGILANCE / SURVEILLANCE PROJECTS

- Antipsychotics
- High Dose Statins
- PPIs
- Opioids
- Prasugrel
- Natalizumab
- TZDs
- Dronedarone
- Varenicline
- Dabigatran
- Vaccines
- Bisphosphonates

EXAMPLE

Surveillance, Evaluation and Formulary Decision

- Rapid Cycle Evaluation was developed and completed, and results served as a preliminary marker for full pharmacoepidemiologic study

- Subsequent analysis was designed and conducted -- Formulary Decision

- Detailed analysis using Registry data and more sophisticated analytic methods conducted

CONCLUSION

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- Consistent with VA Criteria for Use, rosiglitazone and pioglitazone were most commonly prescribed as 3rd line agents
- Health risk for rosiglitazone did not support the high percentage level identified in the meta analysis

CONCLUSION

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- A slight but consistently lower risk was found for pioglitazone compared to rosiglitazone particularly when rosiglitazone was used as third line agent or in combination with insulin

VA Decision

- Rosiglitazone was removed from Formulary but remained available in the VA healthcare system
- Pioglitazone became VA's preferred TZD
- Criteria for Drug Use updated

Dronedarone

- Patients prescribed dronedarone through 2nd quarter of fiscal year 2011
  - # patients exposed
- Evaluation
  - Inappropriate prescribing in HF pts
  - Exacerbation of HF
  - *New Onset HF*

Dronedarone

All users Dronedarone	Incident Users	HF Dx Post Dronedarone Initiation		
Evaluation period:	**Cohort**	**within 30 days N(%)**	**within 90 days N(%)**	**within 180 days N(%)**
	No Hx of HF			
	Mild Heart Failure			
	Recent Decompensated HF (Risk Reduction)			

RISK REDUCTION PROJECTS

Risk Reduction and Intervention Assessment

- Risk Reduction Program was initiated to:
  - Identify patients receiving medications with a true contraindication for a given disease state or patients requiring a change in medication regimen to enhance patient safety and prevent potential untoward outcomes.

- Intervention Assessment
  - Evaluation designed to assess the outcome of a specific intervention (ie, safety intervention, formulary decision)

Risk Reduction Projects (Selected Example)

- *Nifedipine (short Acting) – Prototype*
- High Dose Vitamin E
- Alpha Blocker Monotherapy
- LABA Monotherapy
- Ketoconazole/Simvastatin
- High Dose Zolpidem
- Glyburide in Elderly with RI

Glyburide Risk Reduction

- Goal – Decrease risk of hypoglycemia
- Identify elderly patients with renal insufficiency
  - >/=65
  - SCr > 2
- Recommend switch to glipizide

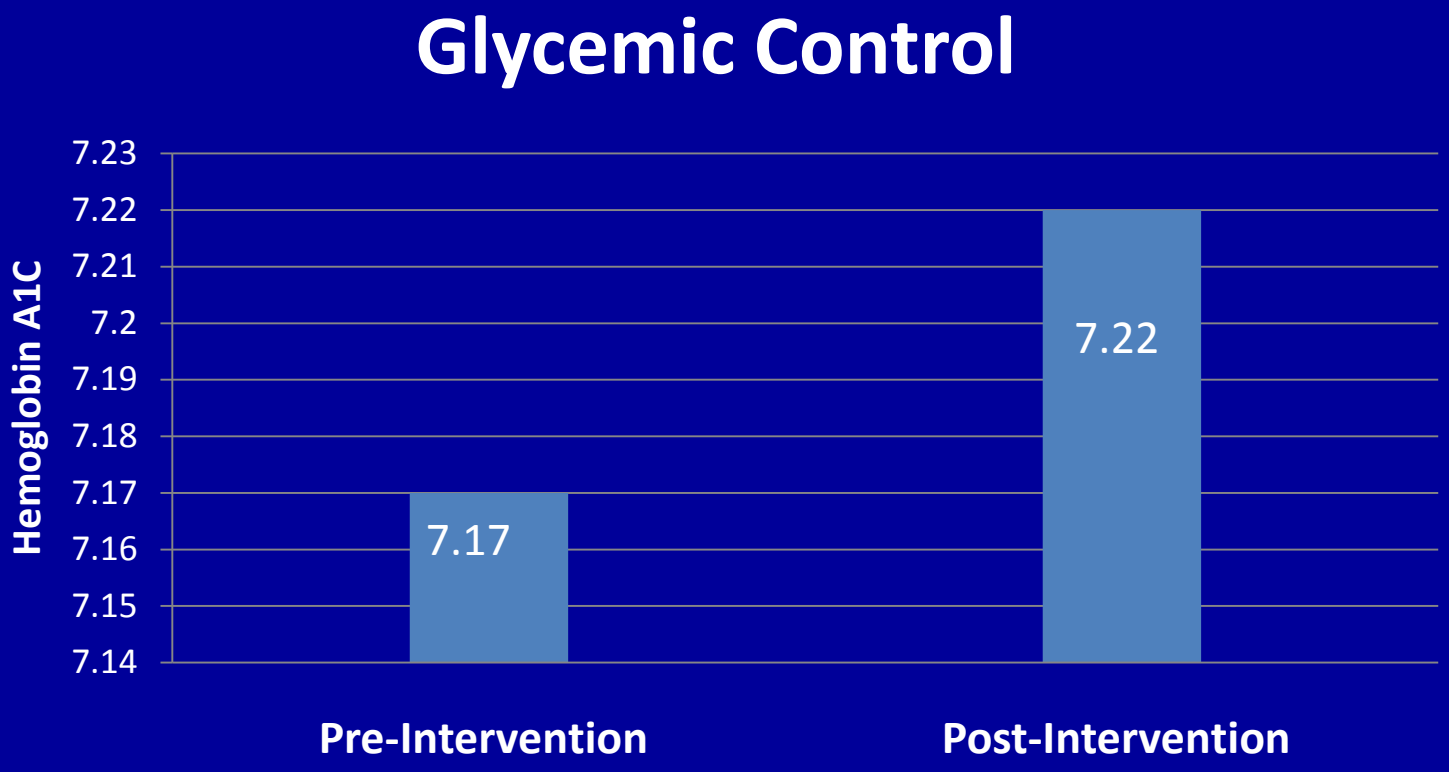
Glyburide Risk Reduction

Data on this slide will be presented during the live webinar, but cannot be distributed publically

Glyburide Intervention Assessment

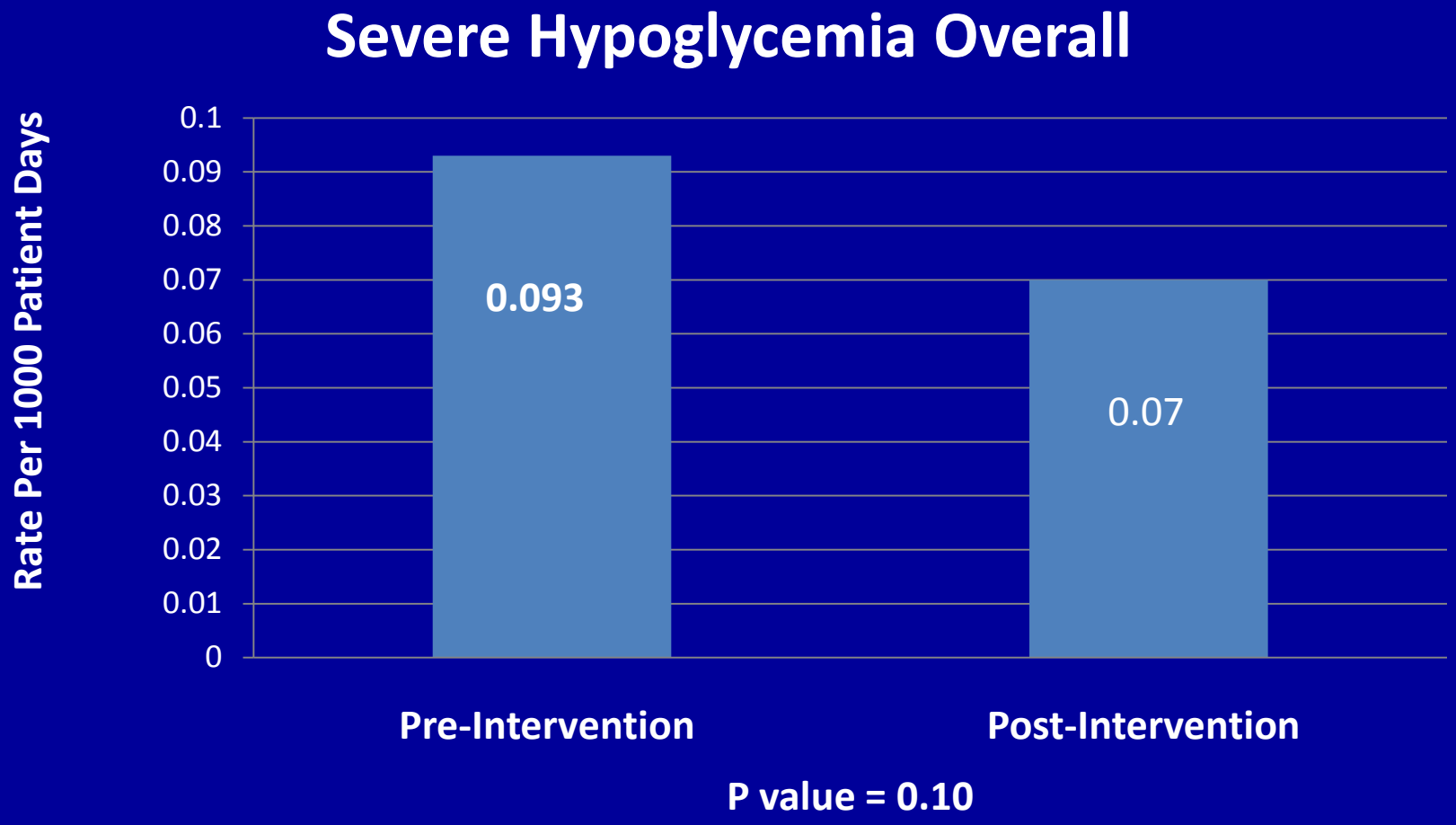
- Goal
  - To assess outcomes secondary to intervention
- Outcomes
  - Glycemic Control
  - Severe Hypoglycemia
  - Subgroup Analysis (severe RI)

Glyburide Intervention Assessment Results

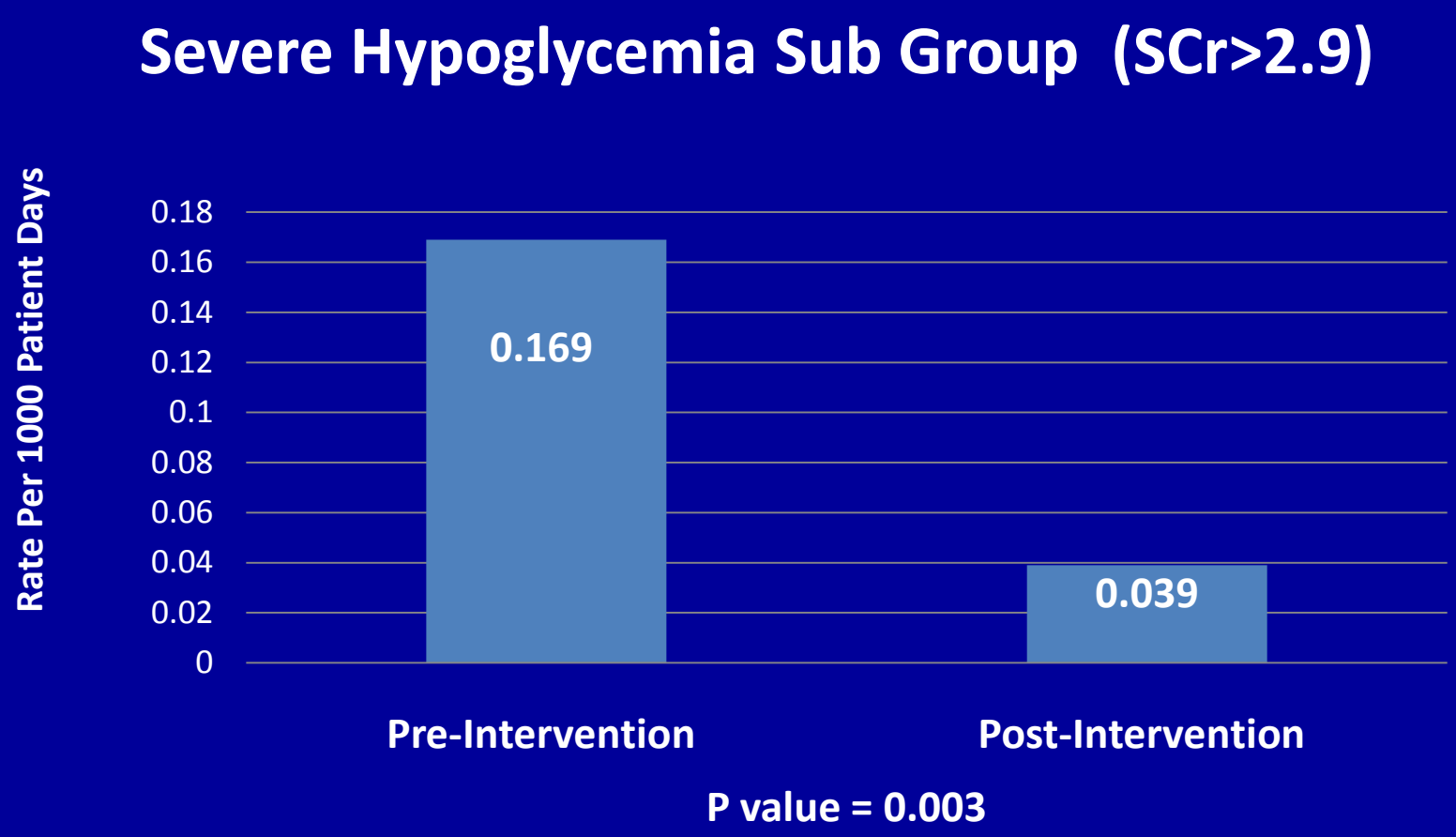


Note: Some patients simply had glyburide discontinued accounting for some rise in Hemoglobin A1C

Glyburide Intervention Assessment Results



Glyburide Intervention Assessment Results



Glyburide Intervention Assessment Conclusions

- The Risk Reduction successfully switched high-risk patients to safer medication alternatives
- Glycemic control was not significantly impacted
- Lower rates of severe hypoglycemia in patients at greatest risk (e.g. sCr > 2.9)

Collaboration with Food and Drug Administration

- FDA–VA–DoD – Memorandum of Understanding – 2008
- Collaboration
  - Drug Safety Oversight Board
  - CDER/CBER
  - Sentinel – Federal Partners Collaboration

VAMedSAFE and Observational Medical Outcomes Partnership (OMOP): Focus on Development of Common Data Model

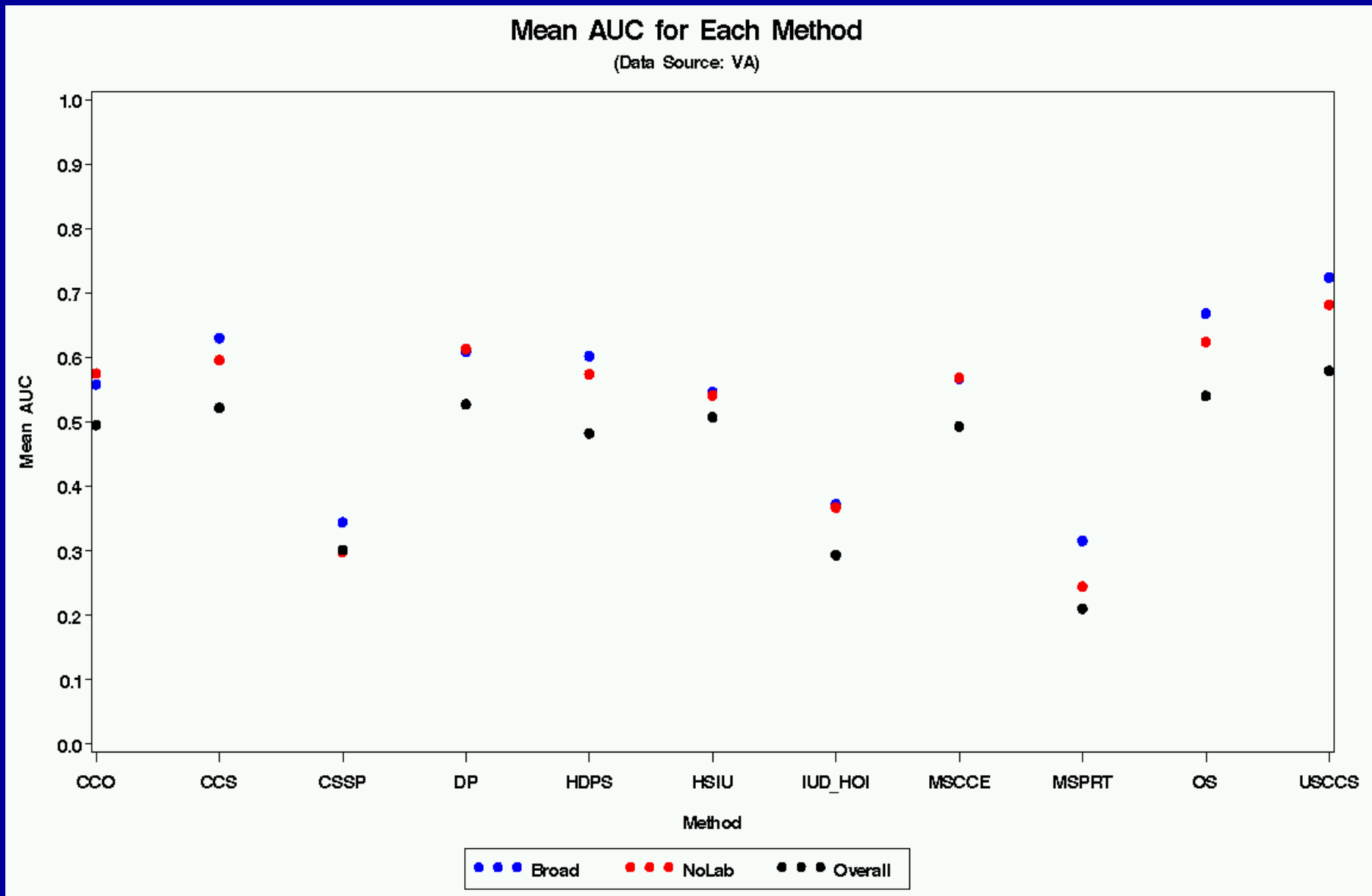
Background

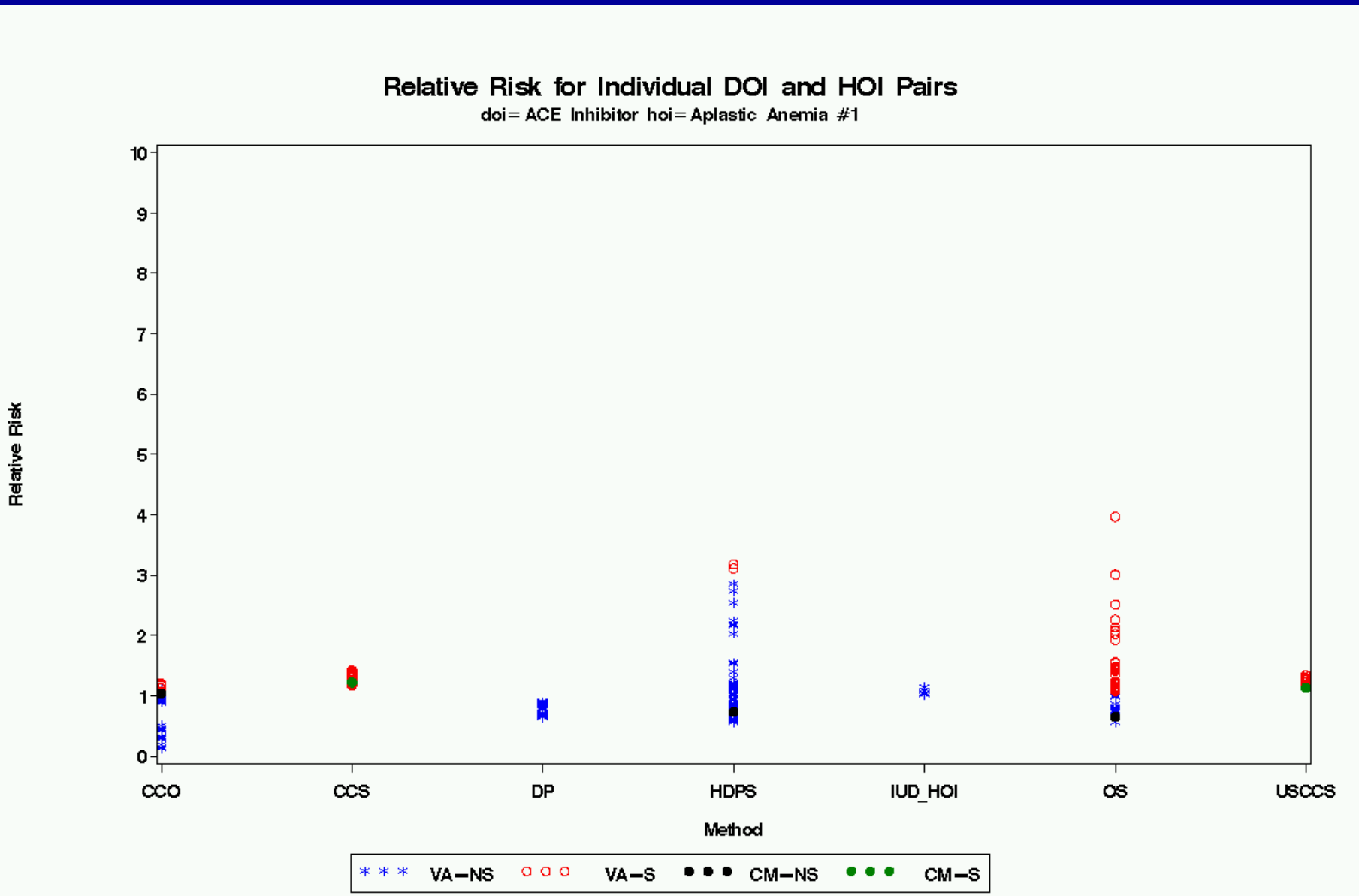
- Goal
  - To identify optimal automated methodologies for signal strengthening/refinement for large number of drugs

- Common Data Model Development
  - To evaluate drug-outcome association using analytic methods provided by OMOP

Conversion to VA CDM

- VA data – identified, extracted and cleaned
- Data were mapped using mapping tables
  - LOINC code (lab data)
  - Conditions (ICD9 codes, CPT codes, HCPCS Codes)
  - VA product (drugs)
- Various programs written to convert data to CDM
- Upon completion of basic CDM tables, drug and condition ERA tables were created
- HOI and DOI tables developed


Mean AUC for Each Method
(Data Source: VA)
Mean AUC
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
CCO
CCS
CSSP
DP
HDPS
HSIU
IUD_HOI
MSCCE
MSPRT
OS
USCCS
Method
Broad
NoLab
Overall


Relative Risk for Individual DOI and HOI Pairs
doi= ACE Inhibitor hoi= Aplastic Anemia #1
Relative Risk
10
9
8
7
6
5
4
3
2
1
0
CCO
CCS
DP
HDPS
IUD_HOI
OS
USCCS
Method
VA–NS
VA–S
CM–NS
CM–S

Limitations

- Performance depends on parameterization
- Patterns of utilization
- Method success unknown

What Next?

- Assess models following re-paramaterization
- Identify best methods effective for specific outcomes
- Compare with prior evaluations

Summary

- Surveillance/Rapid Cycle Evaluations
  - Results provide information for:
    - Risk Reduction efforts
    - Formulary decisions
      - Criteria for Drug Use
    - Further Study
- Risk Reduction/Mitigation
  - Enhance patient safety via prevention of potential adverse events
- Intervention Assessment
  - Help determine impact of our decisions and interventions

QUESTIONS

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Roundtable Discussion and Questions

View this and past Active Medical Product Surveillance webinars at:
http://www.brookings.edu/health/Projects/evidence/roundtables.aspx