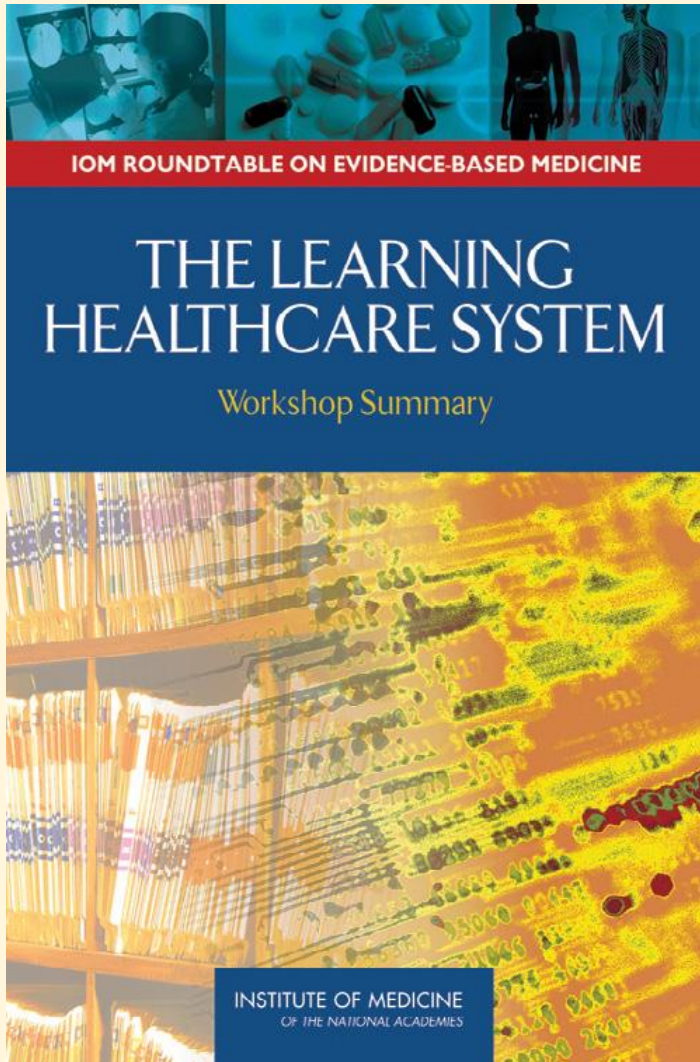


# The Sentinel System: the Case for Analysis Ready Data

Richard Platt MD, MS, and Jeff Brown, PhD.  
Harvard Pilgrim Health Care Institute and  
Harvard Medical School  
for the Sentinel Investigators  
June 23, 2017

# Learning Healthcare System



INSTITUTE OF MEDICINE  
OF THE NATIONAL ACADEMIES

Advising the nation / Improving health

“The increased complexity of health care requires a sustainable system that gets the right care to the right people when they need it, and then captures the results for improvement. **The nation needs a healthcare system that learns.**”



- Data collected for one purpose aren't reliably useful for other purposes

# Platelet count units of measure

*Platelet count original result units<sup>‡</sup>*

|         |             |             |            |
|---------|-------------|-------------|------------|
| Blank   | FL          | TH/UL       | X10(3)     |
| %       | K/CMM       | THOU/CMM    | 1000/UL    |
| /100 W  | k/cmm       | thou/cmm    | X10(3)/MCL |
| /CMM    | K/CU MM     | thou/mm3    | X10(3)/UL  |
| CMM     | K/CUMM      | THOU/UL     | X10(6)/MCL |
| 10 3 L  | K/MCL       | THOUS/CU.MM | X10*9/L    |
| 10X3UL  | K/mcL       | THOUS/MCL   | X10E3/UL   |
| 10^3/UL | K/UL        | THOU/mcL    | X1000      |
| 10*3/uL | k/uL        | THOUS/UL    | X10X3      |
| 10?3/uL | KU/L        | Thou/uL     | X10^3/UL   |
| 10E3/uL | K/MM3       | THOUSA      | x10        |
| 10e3/uL | K/mm3       | THOUSAND    | X10?3/ul   |
| 10e9/L  | LB          | THOUSAND/UL | X10E3/UL   |
| E9/L    | PLATELET CO | U           | X10E3      |
| BIL/L   | T/CMM       | X 10-3/UL   | K/A?L      |
| bil/L   | TH/MM3      | X 10(3)/UL  | K/B5L      |
| CU MM   | th/mm3      | X10 3       |            |

# Data must be fit for intended purpose

- Accuracy
  - Identifying potential candidates for a clinical trial
  - Making a regulatory decision affecting a widely used drug

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  - Identifying potential candidates for a clinical trial
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- Time required to be ready for analysis

# Data must be fit for intended purpose

- Accuracy
  - Identifying potential candidates for a clinical trial
  - Making a regulatory decision affecting a widely used drug
- Time required to be ready for analysis
- Need to use all data vs a subset



# Sentinel is a National Medical Product Monitoring System

[LEARN MORE](#)

## ABOUT

- Background
- Coordinating Center
- Privacy and Security
- The Sentinel System Story



## SAFETY ASSESSMENTS

- Active Risk Identification and Analysis System
- Assessments of Drugs
- Assessments of Vaccines, Blood, & Biologics



## DATA & SURVEILLANCE TOOLS

- Distributed Database and Common Data Model
- Complementary Data Sources
- Routine Querying Tools
- Validations and Literature Reviews



## COMMUNICATIONS

- FDA Safety Communications
- Publications and Presentations
- Sentinel Initiative Events
- Report Finder

## Latest Postings

### SPOTLIGHT

- Sentinel Initiative Public Workshop - Ninth Annual  
*Tue, 11/08/2016*

### STUDY PROTOCOLS & SURVEILLANCE PLANS

- Influenza Vaccines and Birth Outcomes Protocol (PRISM)  
*Fri, 01/20/2017*
- Identify and Evaluate Manufacturer-Level Drug Utilization and Switching Patterns in Sentinel  
*Mon, 12/12/2016*

### MODULAR PROGRAMS

- Querying Tools: Overview of Functionality and Technical Documentation  
*Tue, 12/27/2016*
- Influenza antiviral drug use 2010-2015  
*Mon, 10/31/2016*



# Sentinel's charge

Assess the use, safety, and effectiveness of regulated medical products by using electronic healthcare data plus other resources

Create data, informatics, and methodologic capabilities to support these activities

# Sentinel partner organizations

## Lead – HPHC Institute

DEPARTMENT OF POPULATION MEDICINE



**HARVARD**  
MEDICAL SCHOOL



Harvard Pilgrim  
Health Care Institute

## Data and scientific partners



## Scientific partners

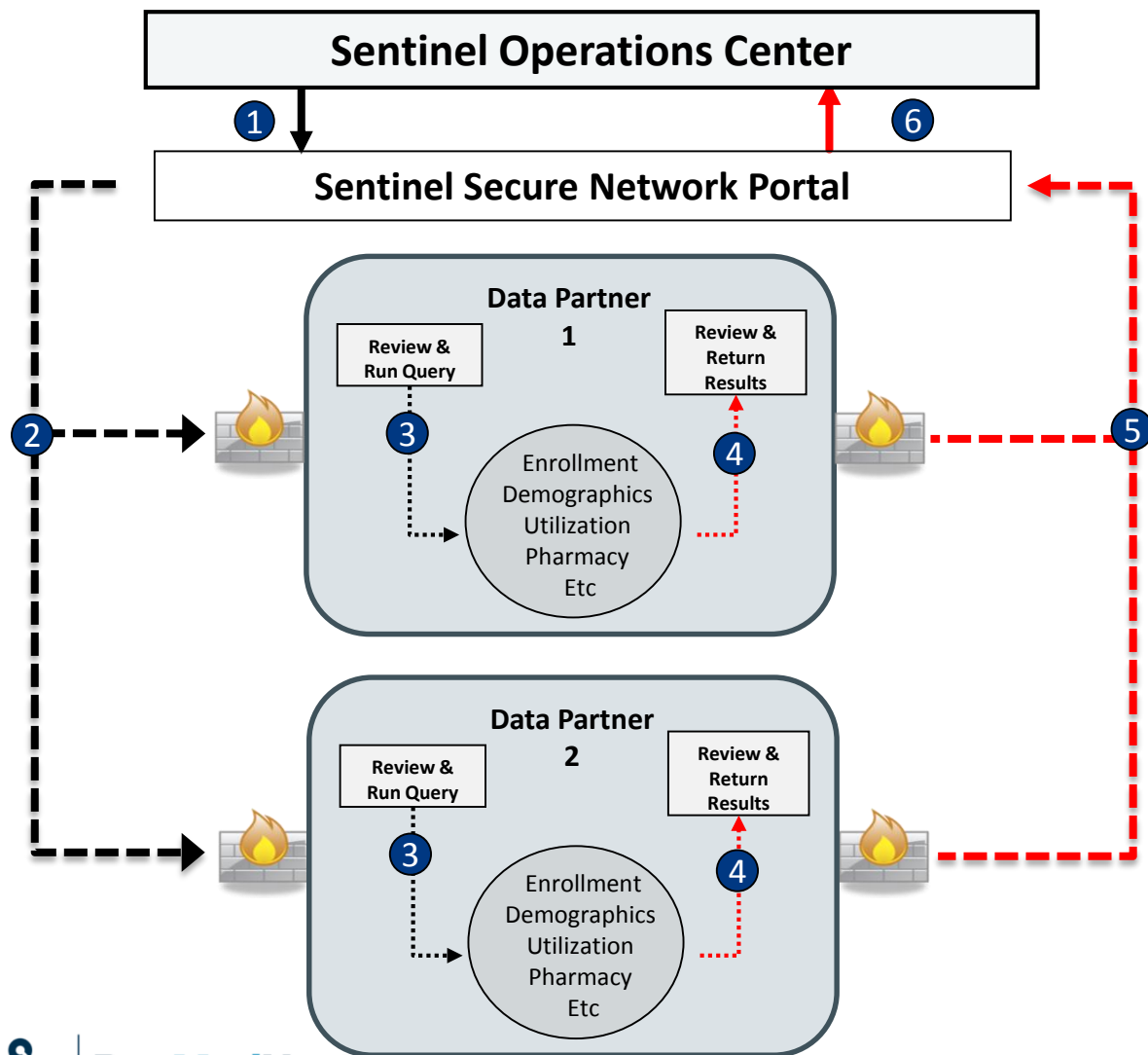


# Sentinel distributed database\*

- ❑ Populations with well-defined person-time for which most medically-attended events are known
- 223 million unique member IDs
- 425 million person-years of observation time
- 43 million people currently accruing new data
- 5.9 billion dispensings
- 7.2 billion unique encounters
- 42 million people with  $\geq 1$  laboratory test result

\* As of January 2017

# Sentinel distributed analysis



- 1- User creates and submits query
- 2- Data Partners retrieve 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

# Three ways to address questions

## Routine Analytic Framework (RAF)



- Off-the-shelf query “templates”
- Standard inputs, standard output
- Quick execution

## RADaR: Rapid Analytic Development and Response: RAF + custom code



- Hybrid approach: custom code leveraging RAF
- Standard inputs, custom output

## Custom Programs



- Analysis as specified
- Custom inputs, custom output
- Longer execution

# Selected protocol based assessments

## ■ CDER

- Dabigatran and several outcomes
- Metabolic effects of 2<sup>nd</sup> generation antipsychotics in youth
- Diabetes drugs and acute myocardial infarction
- IV Iron and anaphylaxis

## ■ CBER

- IV Immune Globulin and thromboembolic events
- Gardasil and venous thromboembolism
- Influenza vaccines and pregnancy outcomes
- Gardasil 9 and Pregnancy Outcomes
- Prevnar 13 and Kawasaki disease
- Blood components and Transfusion-Related Lung Injury (TRALI)

# Three ways to address questions

## Rapid Analyses

### Routine Analytic Framework (RAF)



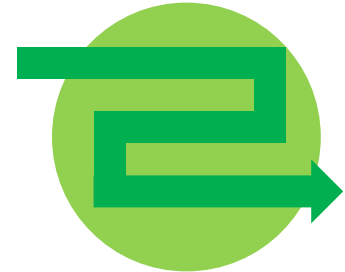
- Off-the-shelf query “templates”
- Standard inputs, standard output
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### RADaR: Rapid Analytic Development and Response: RAF + custom code



- Hybrid approach: custom code leveraging RAF
- Standard inputs, custom output

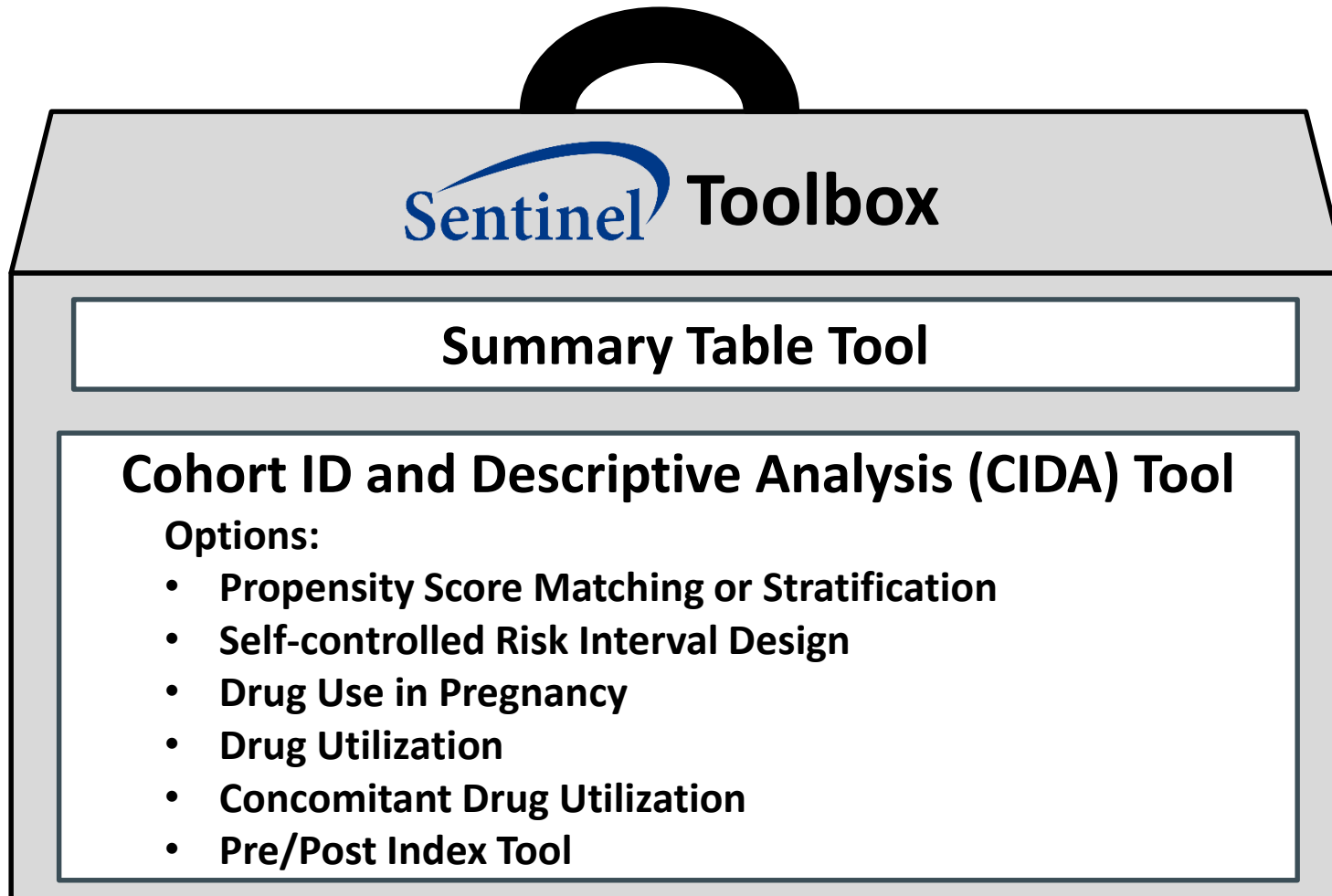
### Custom Programs



- Analysis as specified
- Custom inputs, custom output
- Longer execution



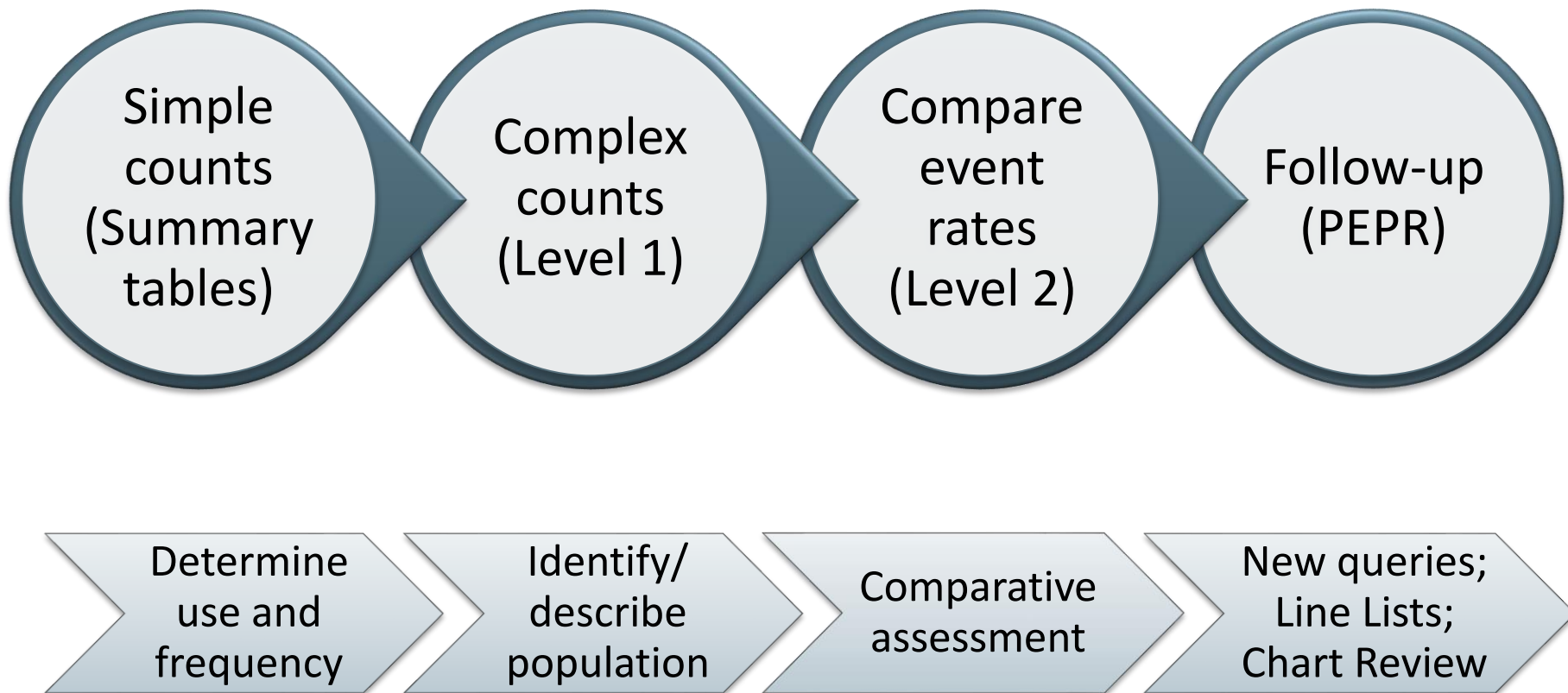
# Sentinel's tools



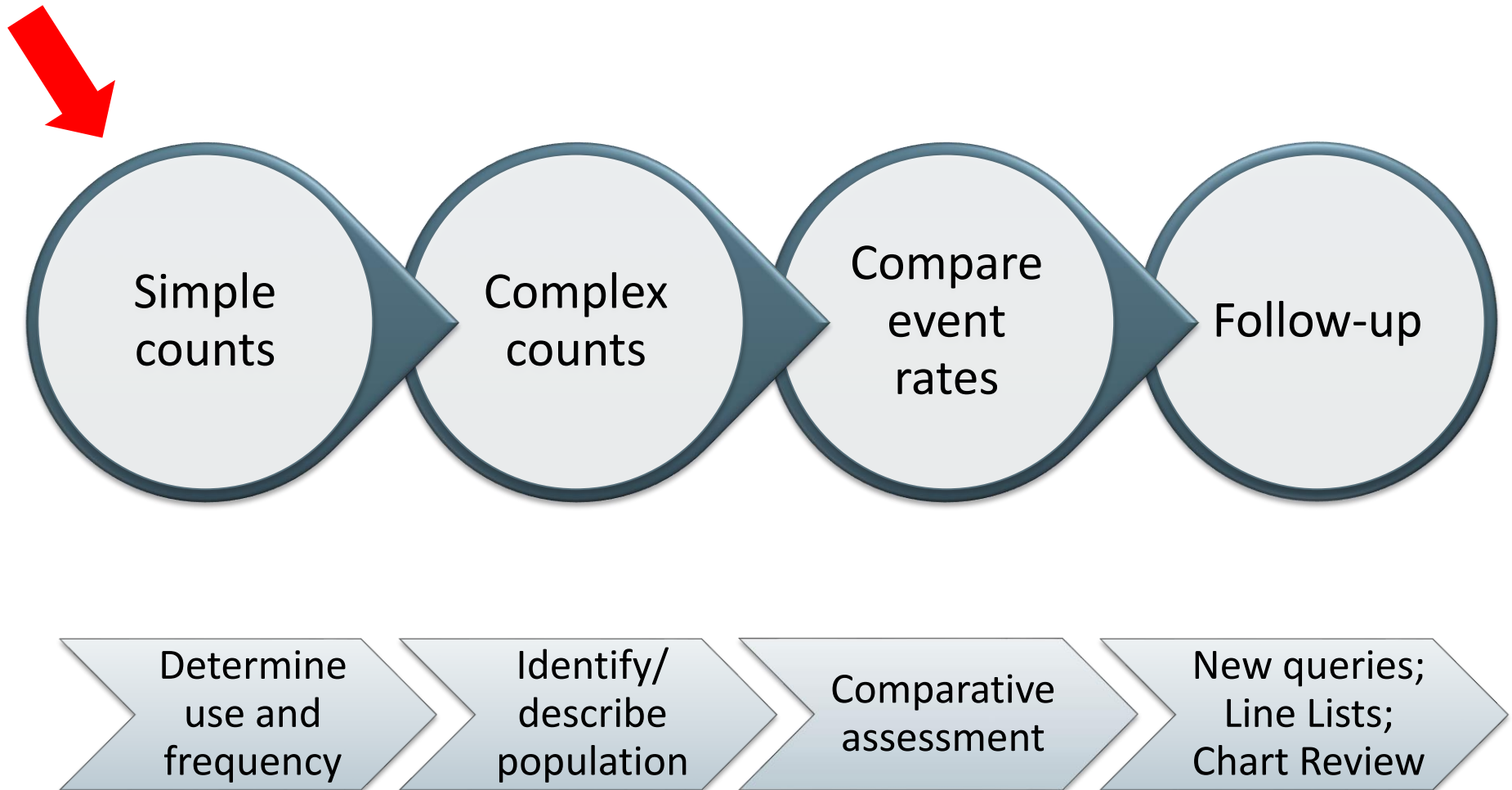
# Routine Analytic Framework tools

- Validated, flexible, and reusable analytic programs
- Run efficiently against the Sentinel CDM and generate standardized output
- Optimized to meet FDA's needs for responsiveness, data quality, reproducibility, and transparency
- Meets needs of Data Partners with diverse technical, data governance, security, and confidentiality requirements

# Rapid analysis querying sequence



# Querying sequence



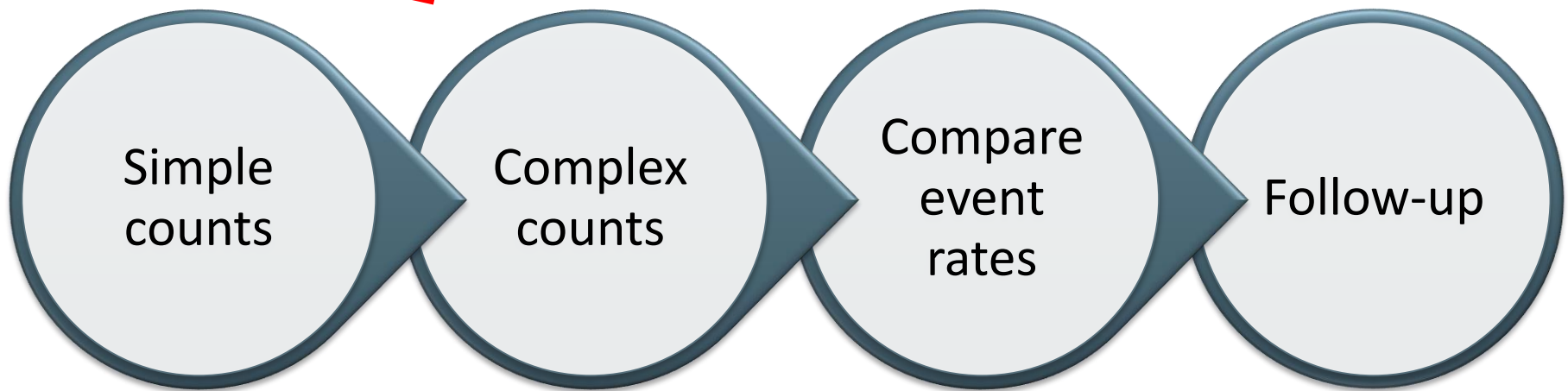
# Simple counts (summary table queries)

- Counts of (new) users with exposure or condition
- Example: Dispensing of evolocumab (PCSK9 inhibitor) without prior dispensing during preceding 180 days, by age, sex, and year

| Age          | 2015       |        | 2016 (partial) |        |
|--------------|------------|--------|----------------|--------|
|              | Male       | Female | Male           | Female |
| <44          | 5          | 2      | 55             | 17     |
| 45-64        | 85         | 61     | 424            | 230    |
| 65-74        | 42         | 35     | 171            | 169    |
| 75+          | 11         | 20     | 72             | 117    |
| <b>TOTAL</b> | <b>261</b> |        | <b>1,255</b>   |        |

- 49 such queries / 291 scenarios in 2016

# Querying sequence

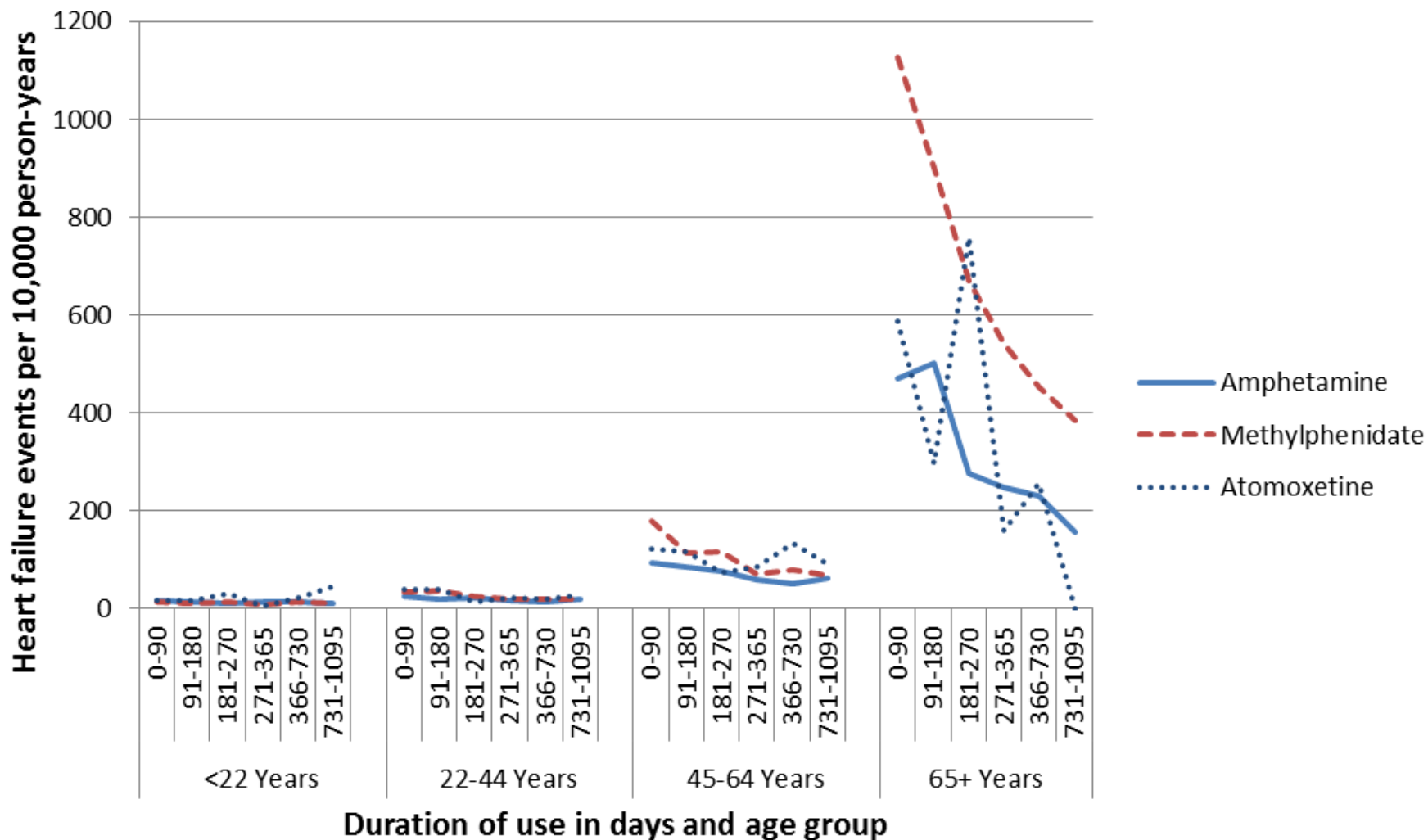


# Complex count queries (Level 1 / 1+)

- Counts and rates of events within user specified times, among populations identified using complex “and/or/not” relationships.
  - Example: Rates of first diagnosis of heart failure or cardiomyopathy among new users of different drugs used to treat ADHD, by age and duration of exposure
- 53 queries, 800+ scenarios in 2016



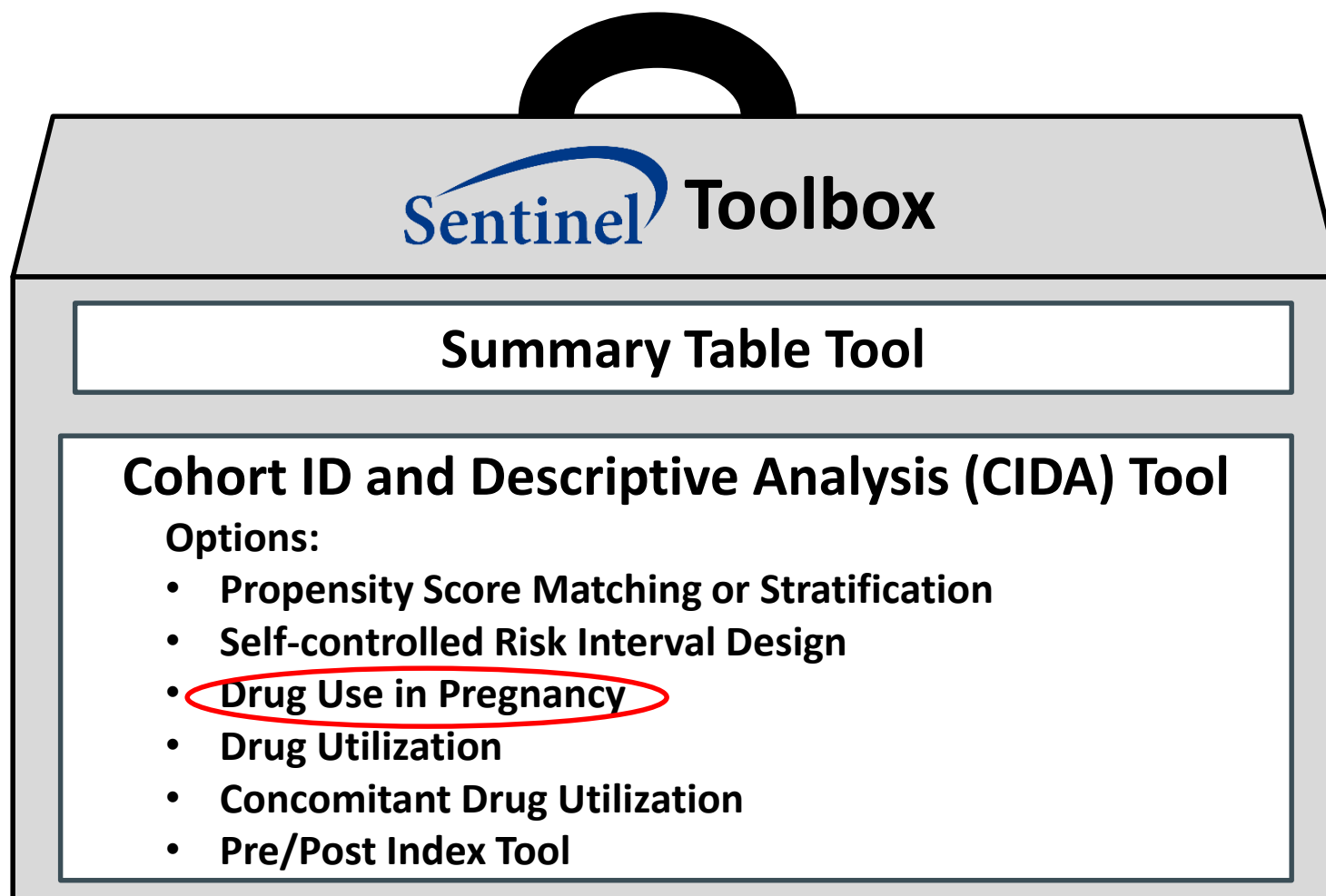
**Figure 1. Rate of heart failure events (per 10,000 person years) by age group, medication, and duration of use**



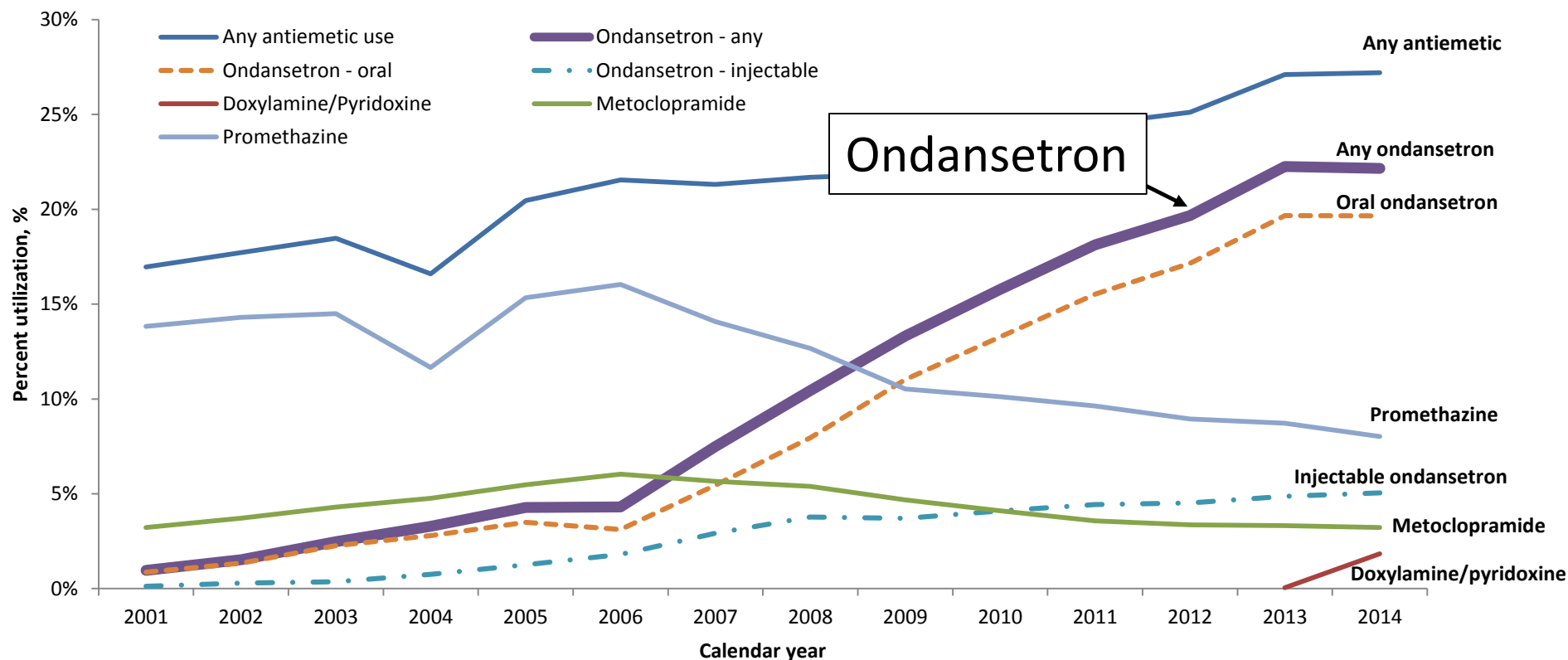
# Complex count queries (Level 1 / 1+)

- Counts and rates of events within user specified times, among populations identified using complex “and/or/not” relationships.
  - Example: Rates of first diagnosis of heart failure or cardiomyopathy among new users of different drugs used to treat ADHD, by age and duration of exposure
- 53 queries, 800+ scenarios in 2016
- *New uses*
  - *Medications errors (name confusion, dosing errors)*
  - *Geographic location stratification*

# Sentinel's tools



# Use of antiemetic drugs among live birth pregnancies in the Sentinel Distributed Database, 2001-2014<sup>a,b</sup>



<sup>a</sup> Dashed lines for oral and injection ondansetron form represent a portion of all total ondansetron use as shown by the solid purple line. Summation of oral and injection utilization sums to greater than total ondansetron use since some women received both products.

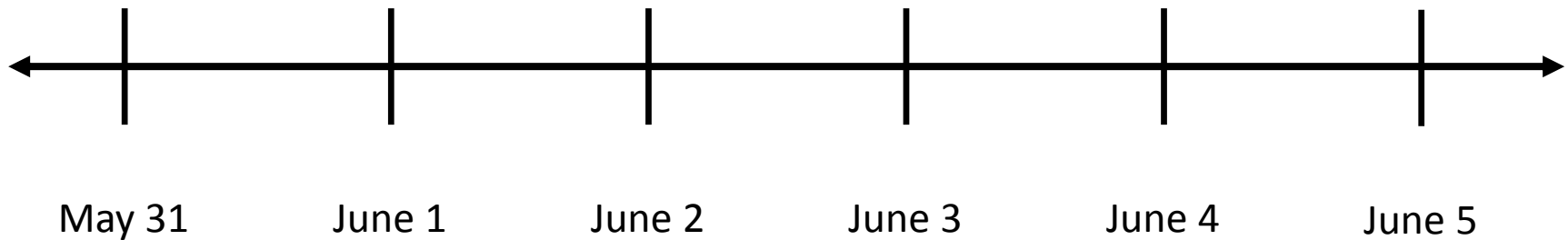
<sup>b</sup> Not all Mini-Sentinel data partners contributed data for the entire study period

Taylor. Pharmacoepidemiology and Drug Safety 2017;26:592

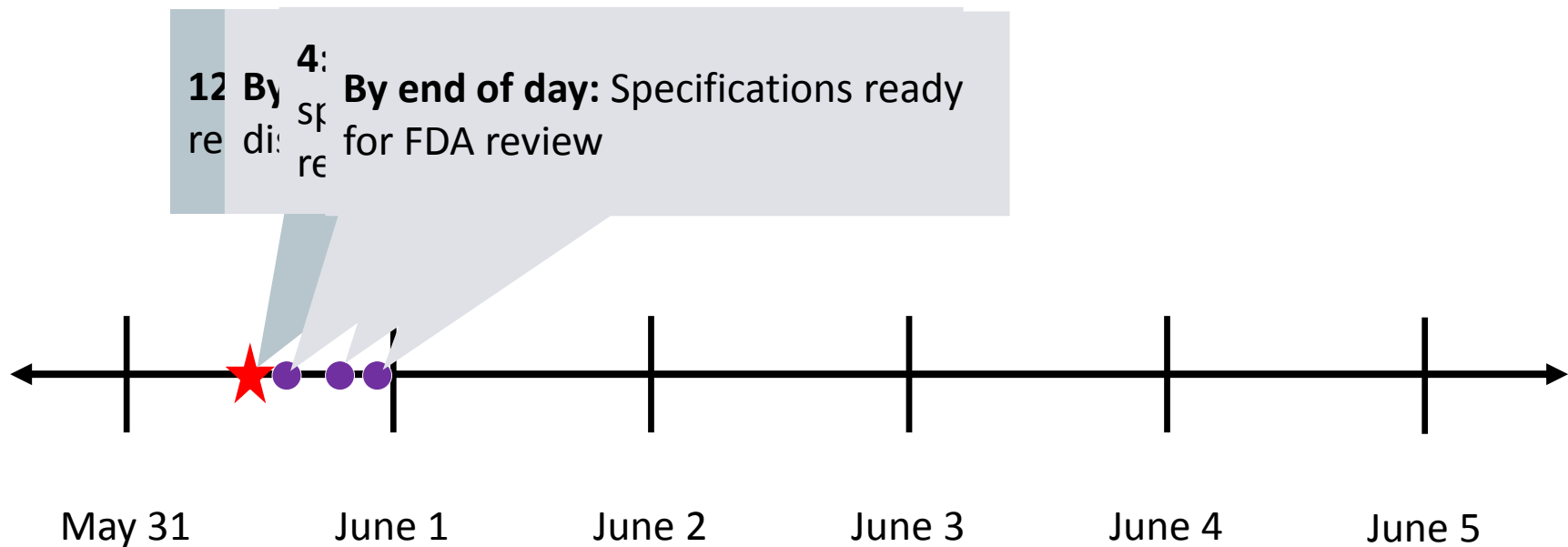
# Recent urgent request

- Issue related to concomitant drug use
- Two similar drugs
  - Drug A has known interaction with Drug Class X
  - Drug B does not have known interaction with Drug Class X
- Goal: Estimate the proportion of concomitant use of Drug A and Drug Class X compared to proportion of concomitant use of Drug B and Drug Class X

# Query Timeline

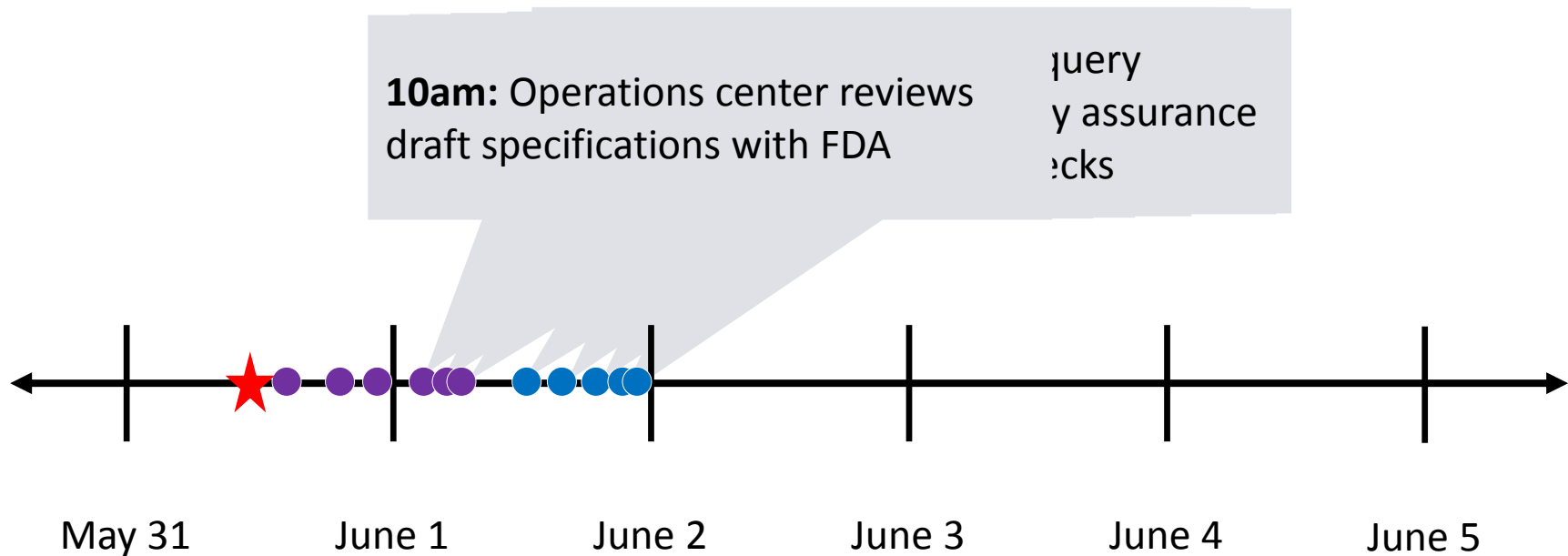


# Query Timeline: May 31

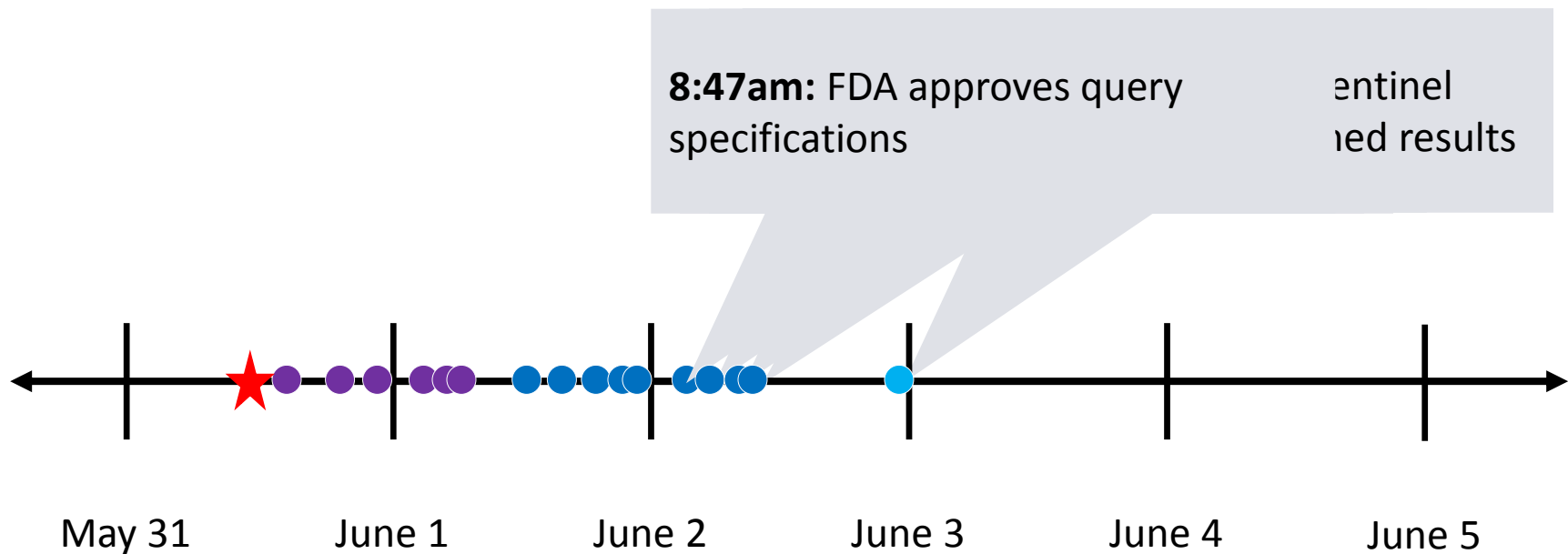




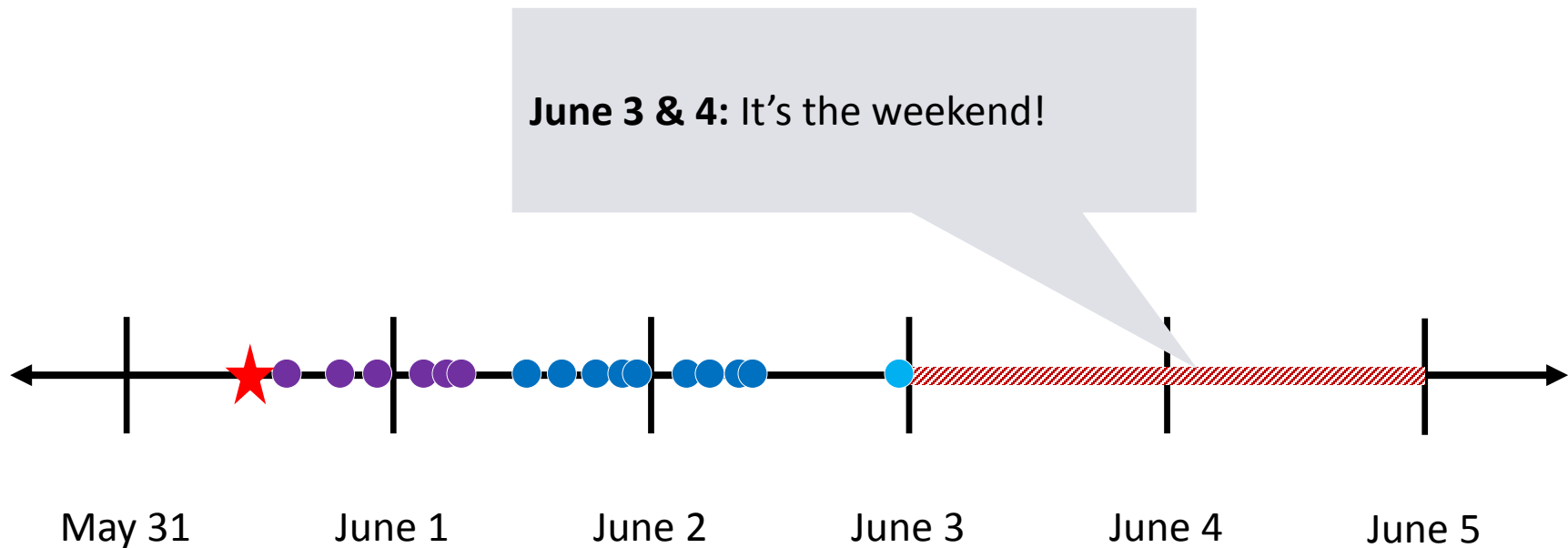
# Query Timeline: June 1



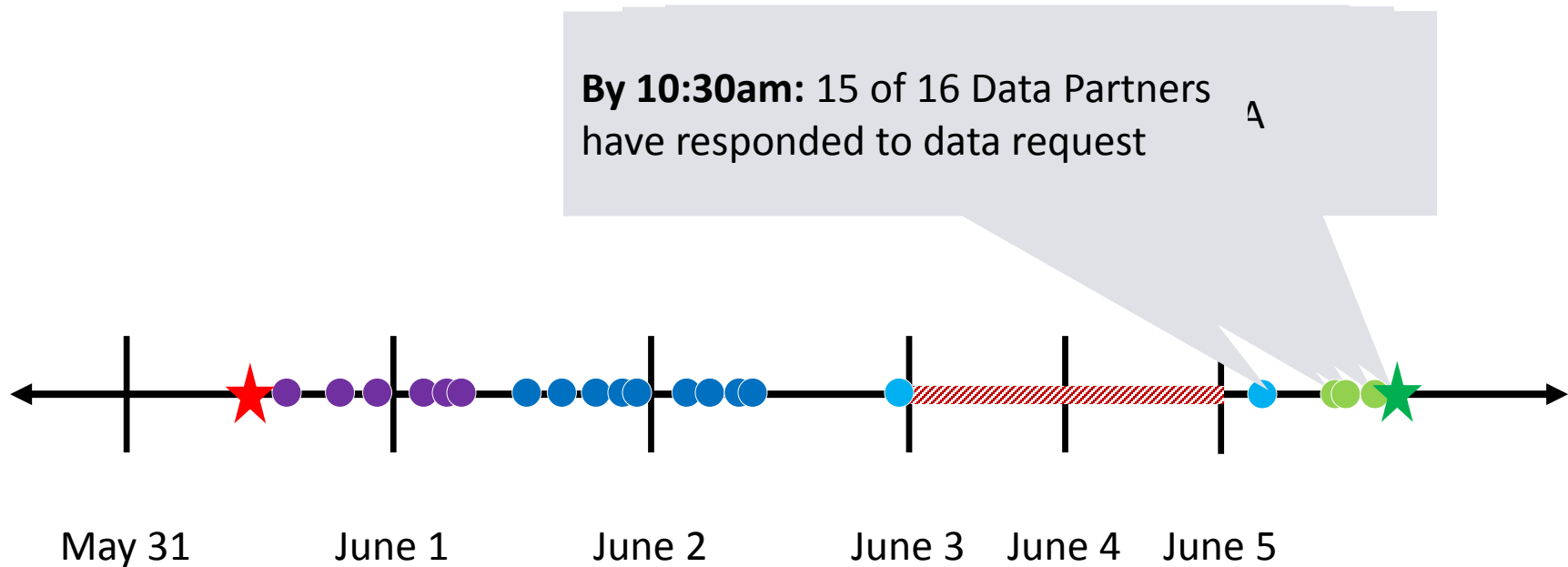
# Query Timeline: June 2



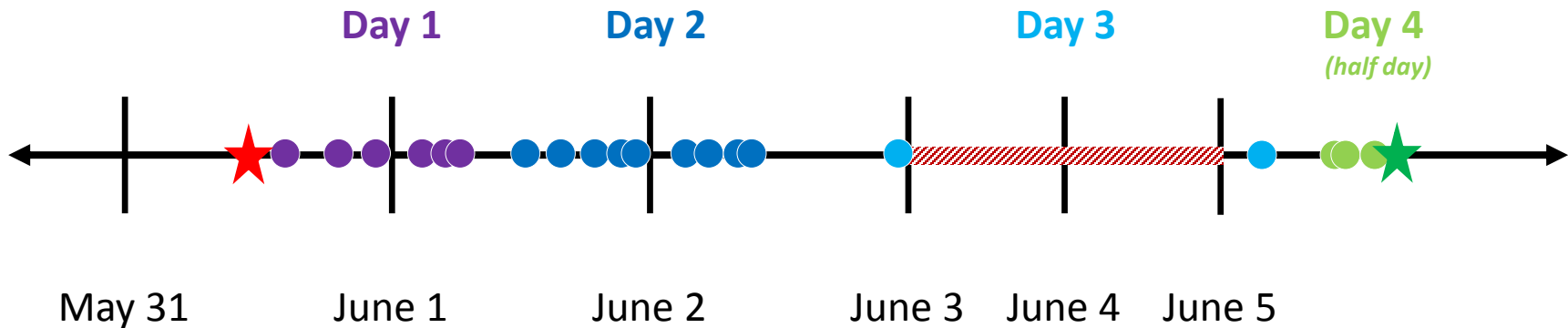
# Query Timeline: June 3 & 4



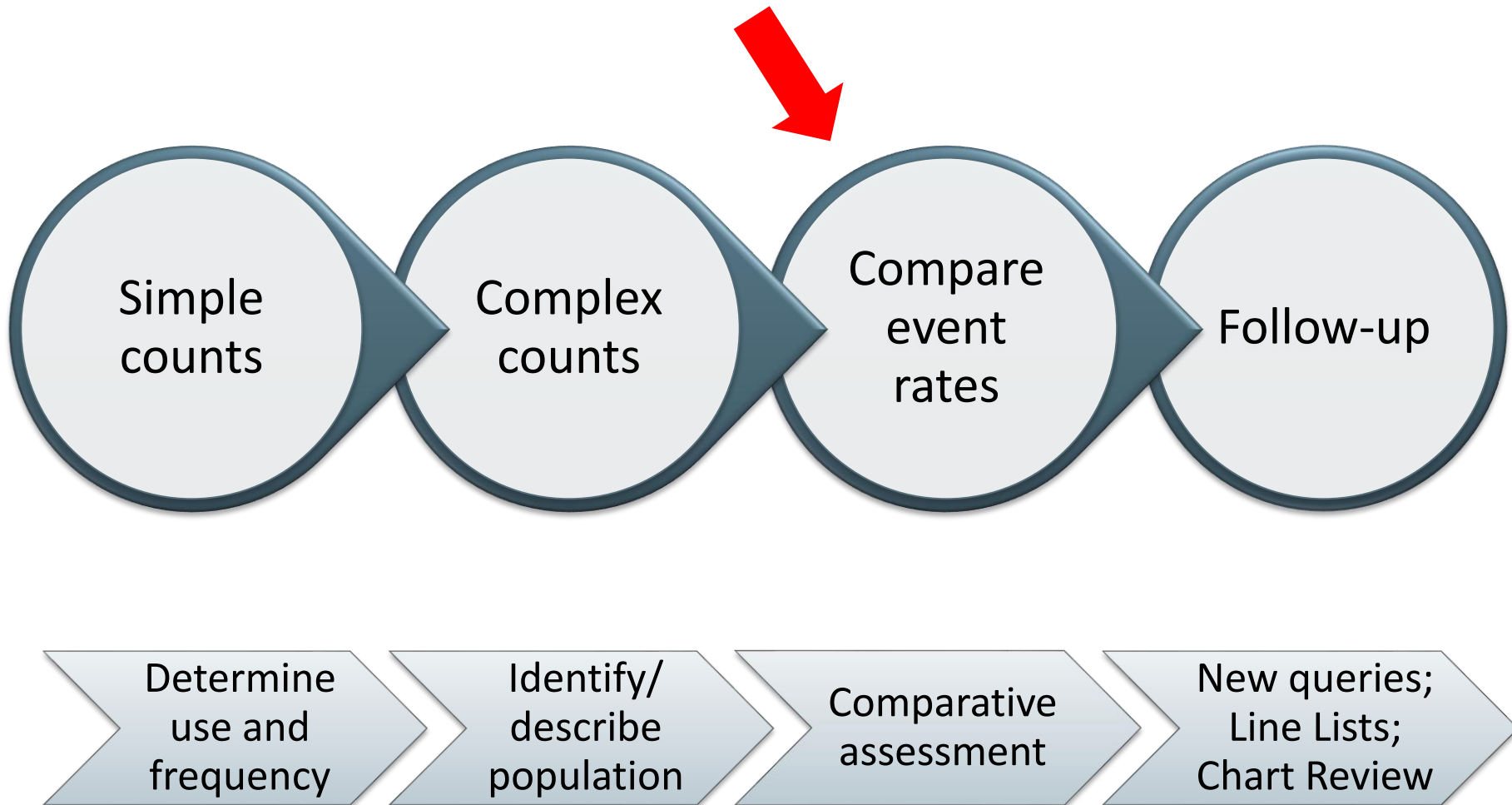
# Query Timeline: June 5



# Query Timeline = 3.5 business days



# Querying sequence

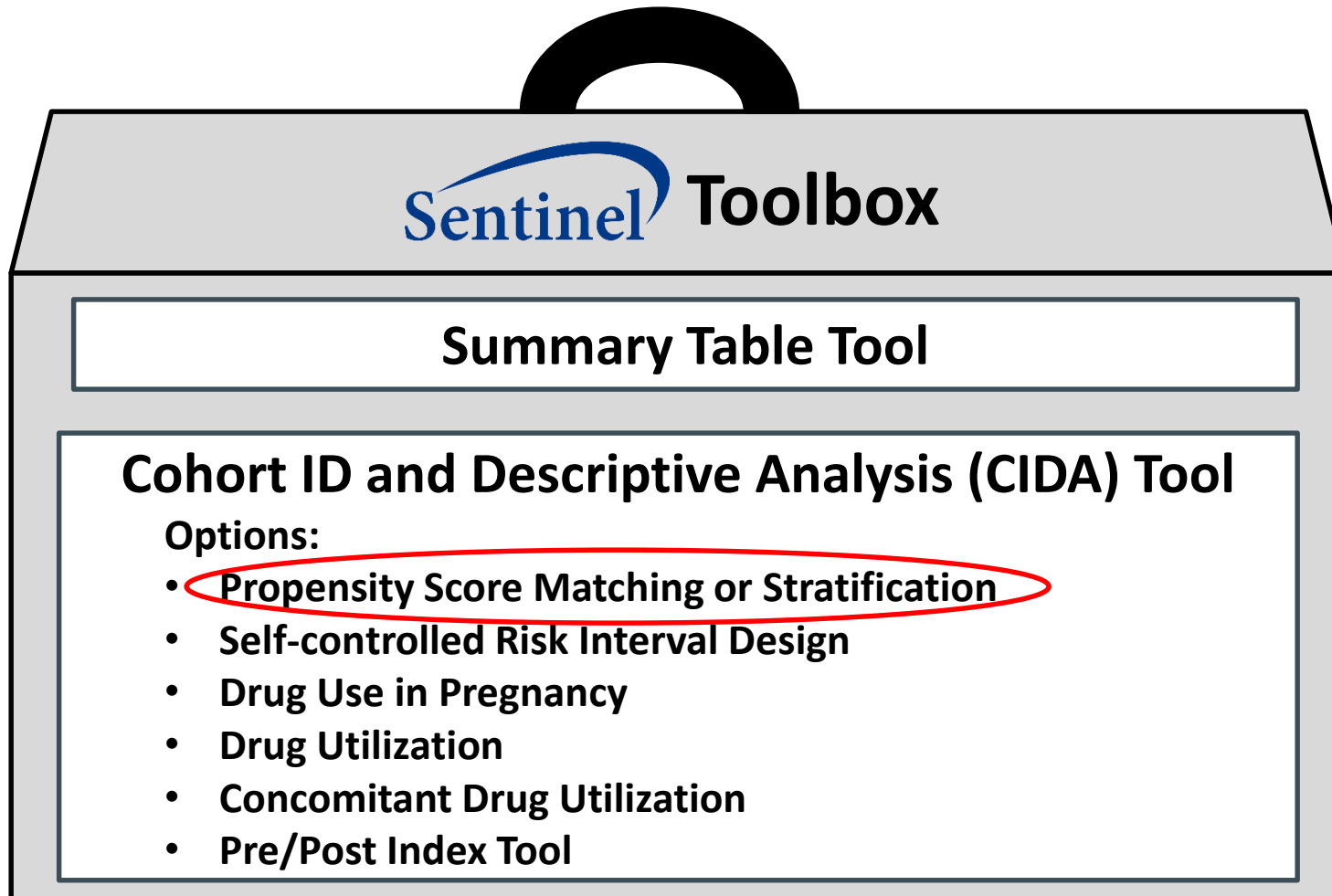


## Comparison of rates (Level 2 / 2+)

- Adjusted relative rates or hazard ratios comparing outcomes among two cohorts identified by complex count program
  - or
- Adjusted self-controlled risk interval analysis
  - Example: Risk of seizures associated with new use of ranolazine
- 11 queries / 100+ scenarios in 2016



# Sentinel's tools



# Angioedema: Table 1. Unmatched cohort

Table 1. Cohort of New Initiators of ACE Inhibitors and Beta Blockers (Unmatched)

| Characteristics                                   | Primary Analysis |         |               |        | Covariate Balance   |                         |
|---|------------------|---------|---------------|--------|---------------------|-------------------------|
|   | ACE Inhibitors   |         | Beta Blockers |        | Absolute Difference | Standardized Difference |
|   | N                | %       | N             | %      |                     |                         |
| Patients  | 2,211,215        | 100%    | 1,673,682     | 100%   | 0.0                 | -                       |
| Events while on therapy                           | 5,158            | 0.2%    | 1,292         | 0.1%   | 0.1                 | 0.0                     |
| Person-time at risk (days)                        | 186.9            | 266.6   | 149.2         | 235.1  | 37.7                | 0.2                     |
| <b>Patient Characteristics</b>                    |                  |         |               |        |                     |                         |
| Gender (F)  | 997,962          | 45.10%  | 946,344       | 56.50% | -11.4               | -0.2                    |
| Mean age (std dev)                                | 54.6             | 12.7    | 53.7          | 15.6   | 0.9                 | 0.1                     |
| <b>Recorded History of:</b>                       |                  |         |               |        |                     |                         |
| Allergic reactions                                | 207,344          | 9.4%    | 190,387       | 11.4%  | -2.0                | -0.1                    |
| Diabetes  | 471,661          | 21.3%   | 173,083       | 10.3%  | 11.0                | 0.3                     |
| Heart failure                                     | 41,060           | 1.9%    | 74,897        | 4.5%   | -2.6                | -0.1                    |
| Ischemic heart diseases                           | 109,948          | 5.0%    | 224,681       | 13.4%  | -8.4                | -0.3                    |
| NSAID use   | 318,298          | 14.4%   | 250,697       | 15.0%  | -0.6                | 0.0                     |
| <b>Health Service Utilization Intensity:</b>      |                  |         |               |        |                     |                         |
|   | Mean             | Std Dev |               |        |                     |                         |
| Number of generics                                | 3.4              | 3.5     |               |        |                     |                         |
| Number of filled prescriptions                    | 7.5              | 9.6     |               |        |                     |                         |
| Number of inpatient hospital encounters (IP)      | 0.1              | 0.4     |               |        |                     |                         |
| Number of non-acute institutional encounters (IS) | 0.0              | 0.6     | 0.1           | 0.9    | -0.1                | -0.1                    |
| Number of emergency room encounters (ED)          | 0.2              | 0.7     | 0.4           | 1.0    | -0.2                | -0.2                    |
| Number of ambulatory encounters (AV)              | 4.8              | 6.3     | 6.9           | 8.4    | -2.1                | -0.3                    |
| Number of other ambulatory encounters (OA)        | 1.1              | 2.6     | 1.5           | 3.6    | -0.4                | -0.1                    |

3.9 million new users

**Diabetes** 21% vs 10%  
**Heart failure** 2% vs 4%  
**Ischemic heart disease** 5% vs 13%

# Angioedema: Table 2. Matched cohort

Table 2. Cohort of New Initiators of ACE Inhibitors and Beta Blockers (Matched Predefined PS, Caliper = .025)

| Characteristics                                   | Primary Analysis |               |           |       | Covariate Balance   |                         |
|---|------------------|---------------|-----------|-------|---------------------|-------------------------|
|   | ACE Inhibitors   | Beta Blockers |           |       | Absolute Difference | Standardized Difference |
|   |                  | %             | N         | %     |                     |                         |
| Patients  | 1,309,104        | 59.2%         | 1,309,104 | 78.2% | 0.0                 | -0.4                    |
| Events while on therapy                           | 3,311            | 0.3%          | 988       | 0.1%  | 0.2                 | 0.0                     |
| Person-time at risk (days)                        | 183.8            | 263.7         | 151.8     | 238.9 | 31.9                | 0.1                     |
| <b>Patient Characteristics</b>                    |                  |               |           |       |                     |                         |
| Gender (F)  | 723,955          | 55.3%         | 689,617   | 52.7% | 2.6                 | 0.1                     |
| Mean age (std dev)                                | 54.1             | 13.1          | 54.4      | 14.9  | -0.3                | 0.0                     |
| <b>Recorded History of:</b>                       |                  |               |           |       |                     |                         |
| Allergic reactions                                | 137,920          | 10.5%         | 134,933   | 10.3% | 0.2                 | 0.0                     |
| Diabetes  | 150,036          | 11.5%         | 150,551   | 11.5% | 0.0                 | 0.0                     |
| Heart failure                                     | 35,302           | 2.7%          | 38,966    | 3.0%  | -0.3                | 0.0                     |
| Ischemic heart diseases                           | 102,200          | 7.8%          | 106,786   | 8.2%  | -0.4                | 0.0                     |
| NSAID use   | 191,798          | 14.7%         | 189,612   | 14.5% | 0.2                 | 0.0                     |
| <b>Health Service Utilization Intensity:</b>      |                  |               |           |       |                     |                         |
|   | Mean             | Std Dev       |           |       |                     |                         |
| Number of generics                                | 3.7              | 3.7%          |           |       |                     |                         |
| Number of filled prescriptions                    | 8.1              | 10.2%         |           |       |                     |                         |
| Number of inpatient hospital encounters (IP)      | 0.1              | 0.5%          |           |       |                     |                         |
| Number of non-acute institutional encounters (IS) | 0.1              | 0.7%          | 0.1       | 0.7%  | 0.0                 | 0.0                     |
| Number of emergency room encounters (ED)          | 0.3              | 0.8%          | 0.3       | 0.8%  | 0.0                 | 0.0                     |
| Number of ambulatory encounters (AV)              | 5.6              | 7.3%          | 5.6       | 6.6%  | 0.0                 | 0.0                     |
| Number of other ambulatory encounters (OA)        | 1.2              | 2.9%          | 1.3       | 3.0%  | 0.0                 | 0.0                     |

2.6 million new users

**Diabetes** 10% vs 10%  
**Heart failure** 3% vs 3%  
**Ischemic heart disease** 8% vs 8%

# Angioedema: Table 3. Results

ACEI vs  $\beta$ -blocker  
1:1 matched  
analysis:

- **HR = 3.1**  
(95% CI, 2.9-3.4)

Toh *et al* findings:

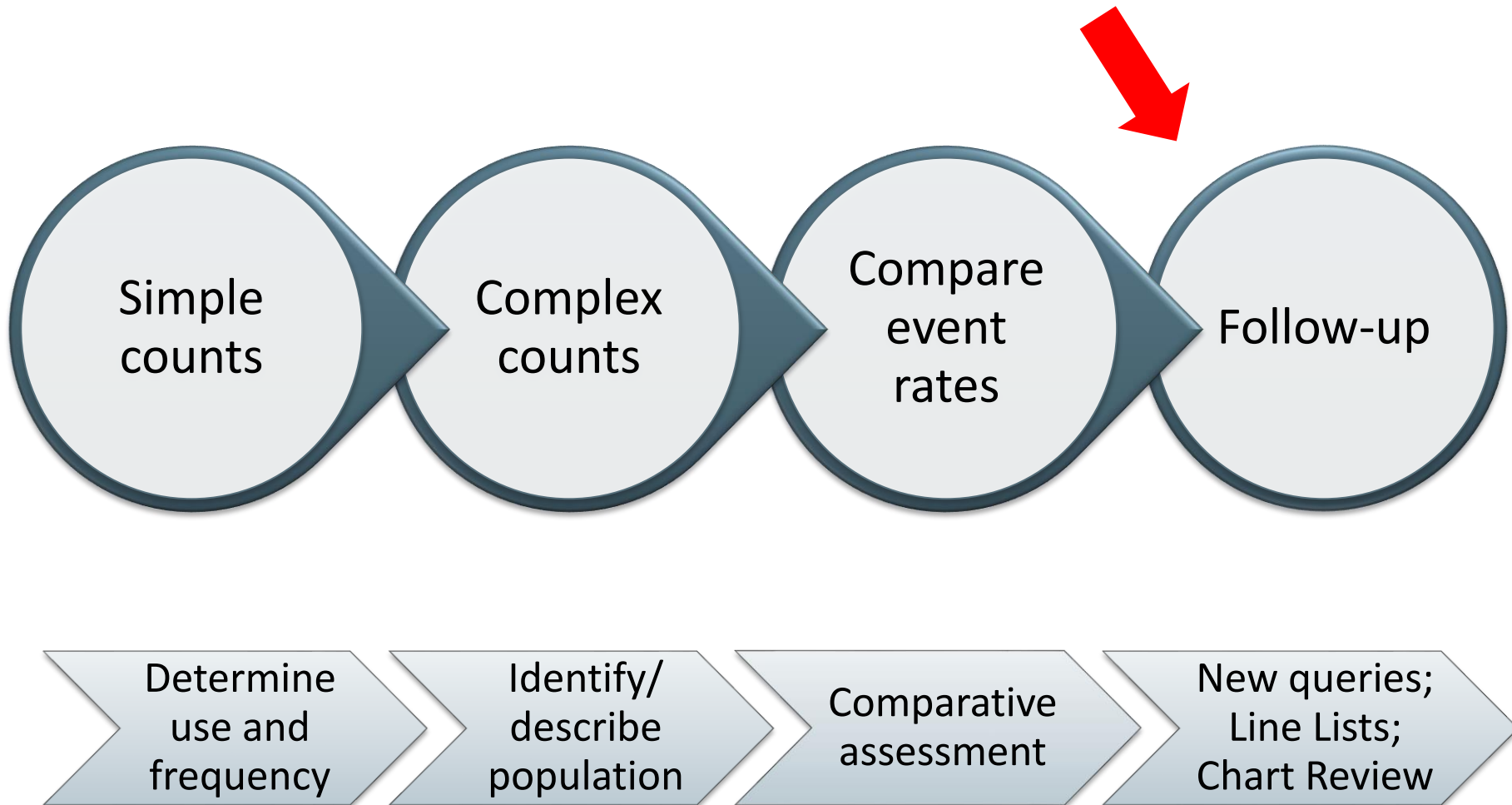
- **HR = 3.0**  
(95% CI, 2.8-3.3)

| Exposure Definition                     | Monitoring Period | New Users | Person Years at Risk | Average Person Years at Risk | Number of Events |
|---|-------------------|-----------|----------------------|------------------------------|------------------|
| Unmatched Analysis (Site-adjusted only) |                   |           |                      |                              |                  |
| ACE Inhibitors                          | 1                 | 2,211,215 | 1,131,526            | 0.51                         | 5,158            |
| Beta Blockers                           |                   | 1,673,682 | 683,614              | 0.41                         | 1,292            |
| 1:1 Matched Analysis; Caliper=0.025     |                   |           |                      |                              |                  |
| ACE Inhibitors                          | 1                 | 1,309,104 | 658,700              | 0.50                         | 3,311            |
| Beta Blockers                           |                   | 1,309,104 | 544,285              | 0.42                         | 988              |

| Incidence Rate per 1000 Person Years | Risk per 1000 New Users | Difference per 1000 Person Years | Difference in Risk per 1000 New Users | Hazard Ratio (95% CI) | Wald P-Value |
|--------------------------------------|-------------------------|----------------------------------|---------------------------------------|-----------------------|--------------|
| 4.558                                | 2.33                    | 2.67                             | 1.56                                  | 2.55 ( 2.40, 2.71)    | <.0001       |
| 1.890                                | 0.77                    |                                  |                                       |                       |              |
| 5.027                                | 2.53                    | 3.21                             | 1.77                                  | 3.14 ( 2.86, 3.44)    | <.0001       |
| 1.815                                | 0.75                    |                                  |                                       |                       |              |

# Querying sequence



# Patient Episode Profile Retrieval (PEPR)

| Episode Detail  |          |       |               |    |       | ^ Incidence: F = first observed; I = incident; blank = prevalent<br># Primary Dx: P = primary; S = secondary; X = N/A<br>~ Med enroll segment containing the admission date of the encounter<br>or the drug enroll segment containing the dispensing date |            |       |            |                  |                |              |        |            |          |
|-----------------|----------|-------|---------------|----|-------|---|------------|-------|------------|------------------|----------------|--------------|--------|------------|----------|
| Days from expos | Enc type | L O S | Clinical code |    |       | Code description  | Incidence^ | P Dx# | Node (Y/N) | Main expos (Y/N) | Any vacc (Y/N) | Rx days supp | Rx amt | Cov start~ | Cov end~ |
| Cat             | Type     | Code  |               |    |       |   |            |       |            |                  |                |              |        |            |          |
| 0               | AV       |       | DX            | 09 | V0382 | Need Proph Vacc Agnst Strep Pne   |            |       |            |                  | 1              |              |        | -386       | 1260     |
| 0               | AV       |       | DX            | 09 | V068  | Need Proph Vacc Against Oth Comb Dz   | F          |       |            |                  | 1              |              |        | -386       | 1260     |
| 0               | AV       |       | DX            | 09 | V202  | Routine Infant/Child Health Check   |            |       |            |                  |                |              |        | -386       | 1260     |
| 0               | AV       |       | PX            | C4 | 90471 | Immunization Admin  | F          |       |            |                  | 1              |              |        | -386       | 1260     |
| 0               | AV       |       | PX            | C4 | 90472 | Immunization Admin Each Add   | F          |       |            |                  | 1              |              |        | -386       | 1260     |
| 0               | AV       |       | PX            | C4 | 90669 | PCV7 Vaccine Im   |            |       |            |                  | 1              |              |        | -386       | 1260     |
| 0               | AV       |       | PX            | C4 | 90710 | MMRV Vaccine Sc   | F          |       |            | 1                | 1              |              |        | -386       | 1260     |
| 0               | AV       |       | PX            | C4 | 99392 | Prev Visit Est Age 1-4  | F          |       |            |                  |                |              |        | -386       | 1260     |
| 4               | AV       |       | DX            | 09 | 0090  | Inf Colitis Enterit & Gastroenterit   | F          |       |            |                  |                |              |        | -386       | 1260     |
| 4               | AV       |       | PX            | C4 | 99213 | Office/Outpatient Visit Est   | F          |       |            |                  |                |              |        | -386       | 1260     |
| 7               | IP       | 1     | DX            | 09 | 27651 | Dehydration   | I          | P     |            |                  |                |              |        | -386       | 1260     |
| 7               | IP       | 1     | DX            | 09 | 53550 | Uns Gastrit & Gastroduodit No Hemorr  | I          | X     |            |                  |                |              |        | -386       | 1260     |
| 7               | IP       | 1     | DX            | 09 | 7862  | Cough   | I          | X     |            |                  |                |              |        | -386       | 1260     |
| 7               | IP       | 1     | DX            | 09 | 78703 | Vomiting Alone  | I          | S     | 1          |                  |                |              |        | -386       | 1260     |
| 7               | IP       | 1     | PX            | C4 | 71020 | Chest X-Ray 2Vw Frontal & Latl  | F          |       |            |                  |                |              |        | -386       | 1260     |
| 7               | IP       | 1     | PX            | C4 | 74000 | X-Ray Exam Of Abdomen   | F          |       |            |                  |                |              |        | -386       | 1260     |

**In theory there is no difference  
between theory and practice.  
In practice there is.**

**Yogi Berra**



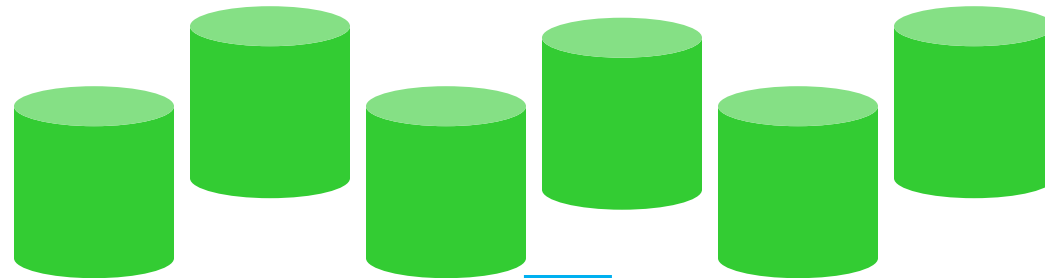
**How does it work?**

**Routine Tools combined with Robust  
Data Quality Assurance Practices**



# Every Data Partner transforms their data into the Sentinel Common Data Model

Unique Data Partner's Source Database Structure



Transformation Program

Data Partner's Database Transformed into SCDM Format (DP ETL)

| Enrollment                   | Demographic | Dispensing               | Encounter                 | Diagnosis                     | Procedure                 |
|------------------------------|-------------|--------------------------|---------------------------|-------------------------------|---------------------------|
| Person ID                    | Person ID   | Person ID                | Person ID                 | Person ID                     | Person ID                 |
| Enrollment start & end dates | Birth date  | Dispensing date          | Service date(s)           | Service date(s)               | Service date(s)           |
| Drug coverage                | Sex         | National drug code (NDC) | Encounter ID              | Encounter ID                  | Encounter ID              |
| Medical coverage             | ZIP code    | Days supply              | Encounter type & provider | Encounter type & provider     | Encounter type & provider |
| Medical record availability  |             | Amount dispensed         | Facility                  | Diagnosis code & type         | Procedure code & type     |
|                              |             |                          |                           | Principal discharge diagnosis |                           |

| Lab Result  | Vital Signs               | Inpatient Pharmacy           | Inpatient Transfusion                        | Death      | Cause of Death |
|---|---------------------------|------------------------------|--|------------|----------------|
| Person ID   | Person ID                 | Person ID                    | Person ID                                    | Person ID  | Person ID      |
| Result and specimen collection dates                      | Measurement date and time | Administration date and time | Blood product code and type                  | Death date | Cause of death |
| Test type, immediacy & location                           | Height and weight         | Encounter ID                 | Encounter ID                                 | Source     | Source         |
| Logical Observation Identifiers Names and Codes (LOINC ®) | Diastolic & systolic BP   | National Drug Code (NDC)     | Blood type                                   | Confidence | Confidence     |
| Test result & unit  | Tobacco use & type        | Route                        | Administration start and end dates and times |            |                |
|   |                           | Dose                         |  |            |                |

# The quality assurance process

Send a standard  
QA checking  
program to check  
DP's ETL in  
waiting



Data Partner



## Compliance Checks

**Level 1:** Completeness,  
validity, accuracy

**Level 2:** Cross-variable and  
cross-table integrity

## Judgment Call Checks

**Level 3:** Trends: consistency

**Level 4:** Logical: plausibility,  
convergence

# QA example: Admission and discharge date

## Completeness

- Admission date (ADate) variable has missing values

## Validity

- ADate variable is not SAS date value of numeric data type
- ADate variable is not of length 4

## Accuracy

- ADate is before DDate (for IP and IS only)
- ADate and DDate variables have values after DP\_MinDate

## Integrity

- Discharge date (DDate) variable is missing for EncType value "IP"
- DDate variable is populated for EncType values other than "IP" or "IS"

\*IP = Inpatient Setting, IS= Institutional Setting like a Skilled Nursing Facility

# The quality assurance process

Send a standard  
QA checking  
program to check  
DP's ETL in  
waiting



Data Partner



## Compliance Checks

**Level 1:** Completeness,  
validity, accuracy

**Level 2:** Cross-variable and  
cross-table integrity

## Judgment Call Checks

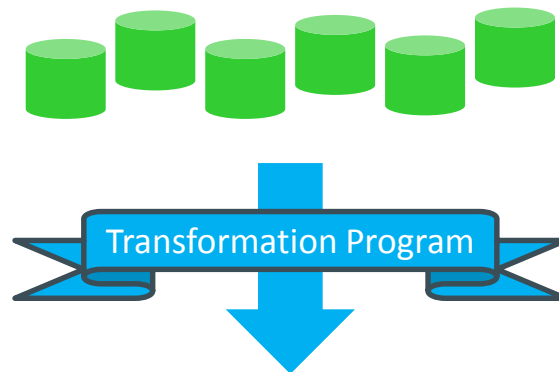
**Level 3:** Trends: consistency

**Level 4:** Logical: plausibility,  
convergence

# The database is dynamic – updates overwrite the preceding data!

Unique Data  
Partner Source  
Database Structure

Data Delivery 1

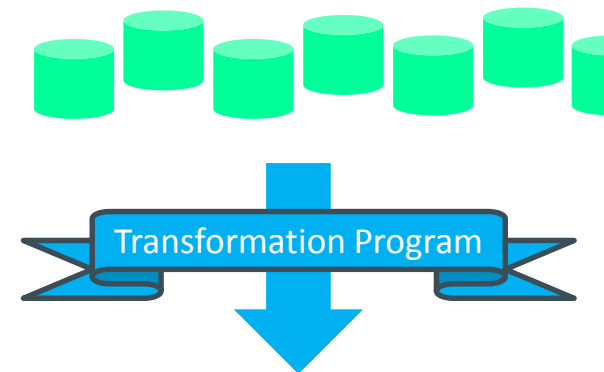


| Enrollment                   | Demographic | Dispensing               | Encounter                 | Diagnosis                     | Procedure                 |
|------------------------------|-------------|--------------------------|---------------------------|-------------------------------|---------------------------|
| Person ID                    | Person ID   | Person ID                | Person ID                 | Person ID                     | Person ID                 |
| Enrollment start & end dates | Birth date  | Dispensing date          | Service (SNOMED)          | Service (SNOMED)              | Service (SNOMED)          |
| Drug coverage                | Sex         | National Drug Code (NDC) | Encounter ID              | Encounter ID                  | Encounter ID              |
| Medical coverage             | ZIP code    | Days supply              | Encounter type & provider | Encounter type & provider     | Encounter type & provider |
| Medical record availability  |             | Amount dispensed         | Facility                  | Diagnosis code & type         | Procedure code & type     |
|                              |             |                          |                           | Principal discharge diagnosis |                           |

| Lab Result   | Vital Signs               | Inpatient Pharmacy           | Inpatient Transition                         | Death      | Cause of Death |
|--|---------------------------|------------------------------|--|------------|----------------|
| Person ID  | Person ID                 | Person ID                    | Person ID                                    | Person ID  | Person ID      |
| Result and specimen collection date                        | Measurement date and time | Administration date and time | Blood product code and type                  | Death date | Cause of death |
| Test type, immediacy & urgency                             | Height and weight         | Encounter ID                 | Encounter ID                                 | Source     | Source         |
| Logical Observation Identifiers Names and Codes (LOINC ID) | Diastolic & systolic BP   | National Drug Code (NDC)     | Blood type                                   | Confidence | Confidence     |
| Test result & unit   | Tobacco use & type        | Route                        | Administration start and end dates and times |            |                |
|  |                           | Dose                         |  |            |                |



Data Delivery 2



| Enrollment                   | Demographic | Dispensing               | Encounter                 | Diagnosis                     | Procedure                 |
|------------------------------|-------------|--------------------------|---------------------------|-------------------------------|---------------------------|
| Person ID                    | Person ID   | Person ID                | Person ID                 | Person ID                     | Person ID                 |
| Enrollment start & end dates | Birth date  | Dispensing date          | Service (SNOMED)          | Service (SNOMED)              | Service (SNOMED)          |
| Drug coverage                | Sex         | National Drug Code (NDC) | Encounter ID              | Encounter ID                  | Encounter ID              |
| Medical coverage             | ZIP code    | Days supply              | Encounter type & provider | Encounter type & provider     | Encounter type & provider |
| Medical record availability  |             | Amount dispensed         | Facility                  | Diagnosis code & type         | Procedure code & type     |
|                              |             |                          |                           | Principal discharge diagnosis |                           |

| Lab Result   | Vital Signs               | Inpatient Pharmacy           | Inpatient Transition                         | Death      | Cause of Death |
|--|---------------------------|------------------------------|--|------------|----------------|
| Person ID  | Person ID                 | Person ID                    | Person ID                                    | Person ID  | Person ID      |
| Result and specimen collection date                        | Measurement date and time | Administration date and time | Blood product code and type                  | Death date | Cause of death |
| Test type, immediacy & urgency                             | Height and weight         | Encounter ID                 | Encounter ID                                 | Source     | Source         |
| Logical Observation Identifiers Names and Codes (LOINC ID) | Diastolic & systolic BP   | National Drug Code (NDC)     | Blood type                                   | Confidence | Confidence     |
| Test result & unit   | Tobacco use & type        | Route                        | Administration start and end dates and times |            |                |
|  |                           | Dose                         |  |            |                |



Data Partner's  
Database  
Transformed into  
SCDM Format

Timeframe of Data  
Available in  
Database

# QA example: Admission / discharge dates

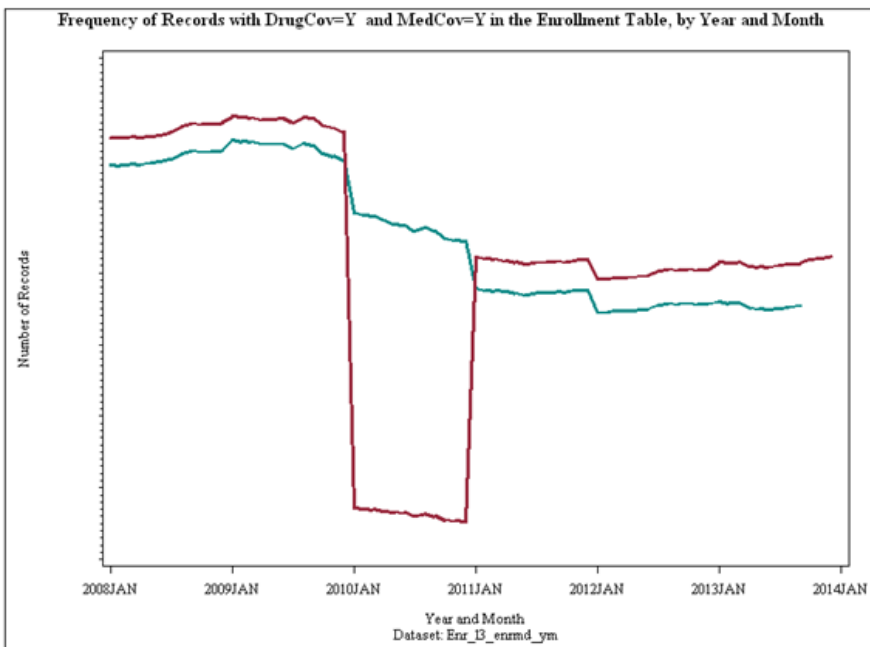
## Check distributions and patterns for notable changes

### Consistency

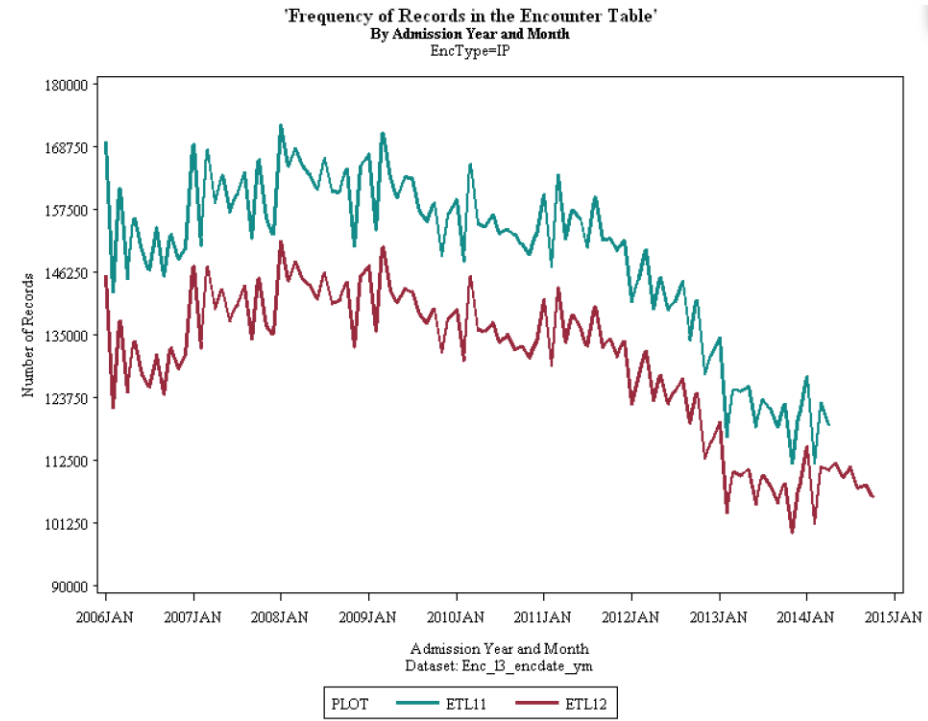
- Problem with distribution of ADate (i.e. total number of records per year) within the ETL
- Problem with distribution of ADate (i.e. total number of records per year-month) within the ETL
- Significant change in number of records per ADate (year) across ETLs
- Significant change in number of records per ADate (year-month) across ETLs
- Problem with distribution of ADate (overall) within the ETL
- Problem with distribution of ADate (overall) across ETLs
- Problem with distribution of DDate variable by EncType per year-month
- Problem with distribution of length of stay by EncType per year

# Sentinel war stories: Consistency checks

Is source of inconsistency clear error or Data Partner changes / improvements?



Incorrect Data Load




Reclassification of Encounter Type

# Sentinel QA statistics

- Annually, the QA team conducts reviews for approximately 50 data deliveries from 17 Data Partners
- Since 1/1/2016, the QA package has had to be re-run in 16 instances to fix an issue
- In the latest data deliveries from the 5 largest DPs, 25 checks were reported in QA that required DP follow-up
  - 22 of the 25 were Level 3 checks



# Data Review Tool – Account of Issues



**Data Review Tool**  
 Manual Review

1) Select MSCDM Table Diagnosis

2) Choose Error Source Dataset To Evaluate dia\_i3\_pdx\_et DISPLAY

3) Select Data Check to Evaluate DIA2.9.2 Status P

MSCDM Item PDX MSCDM Order 263

**Data Check Description**  
 PDX variable is populated for EncType values other than "IP" or "IS"

**Data Check Evaluation Guideline**  
 Should be populated for IP and IS and missing for ED, AV, and OA EncTypes.

Review inappropriately populated values of PDX. If values are populated for EncTypes other than "IP" or "IS", review previous ETL reports to see if the issue has been raised and addressed before. If it has, and MSOC has agreed to allow PDX to be populated for EncTypes other than "IP" or "IS", document this issue on the current ETL report and note that we will continue to monitor. If the issue has not been addressed before, ask the DP to investigate and explain.

4) Describe Issue Here if Check Fails

5) Select Pass, Fail, or Ignore For Selected Check

PASS
FAIL
IGNORE

Problems viewing the dataset? Click on this button to go to the dataset's worksheet

Go To Dataset

6) Click this button to check if you have completed the review

CORE
LABS

| #        | Status |
|----------|--------|
| DIA1.5.1 | P      |
| DIA1.5.2 | P      |
| DIA1.5.3 | P      |
| DIA1.5.4 | P      |
| DIA2.9.2 | P      |
| DIA2.9.1 | P      |
| DIA3.9.2 | P      |

View Selected Error Source Dataset Below
 Convert to Sortable Table

Dia\_i3\_pdx\_et

DPID DIA Freq EncType by PDX

| PDX | ENCTYPE | COUNT4  | COUNT5  | diff_COUNT5_4 | Pcnt_Change |
|-----|---------|---------|---------|---------------|-------------|
|     | AV      | xxxxxxx | xxxxxxx | xxxxxxx       | xxxxxxx     |
|     | ED      | xxxxxxx | xxxxxxx | xxxxxxx       | xxxxxxx     |
|     | IS      | xxxxxxx | xxxxxxx | xxxxxxx       | xxxxxxx     |
|     | OA      | xxxxxxx | xxxxxxx | xxxxxxx       | xxxxxxx     |
| P   | IP      | xxxxxxx | xxxxxxx | xxxxxxx       | xxxxxxx     |
| P   | IS      | xxxxxxx | xxxxxxx | xxxxxxx       | xxxxxxx     |
| S   | IP      | xxxxxxx | xxxxxxx | xxxxxxx       | xxxxxxx     |
| S   | IS      | xxxxxxx | xxxxxxx | xxxxxxx       | xxxxxxx     |
| X   | IP      | xxxxxxx | xxxxxxx | xxxxxxx       | xxxxxxx     |
| X   | IS      | xxxxxxx | xxxxxxx | xxxxxxx       | xxxxxxx     |

Manual\_Review
Report
Master\_Error\_List
Lab\_Result\_Unit\_Lookup
LOGINC\_Lookup

# Sentinel operations center Quality Assurance team

- Refreshes per Year: ~50
- 1 Manager, 2 Programmers, 3 Analysts
- Tasks:
  - Oversight
  - Maintenance and troubleshooting
  - Updating and distribution of quality assurance programs
  - Aggregation and reporting

# Lab Data requires more extensive QA support

PHARMACOEPIDEMIOLOGY AND DRUG SAFETY 2014

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## ORIGINAL REPORT

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### Electronic clinical laboratory test results data tables: lessons from Mini-Sentinel

Marsha A. Raebel<sup>1,2\*</sup>, Kevin Haynes<sup>3</sup>, Tiffany S. Woodworth<sup>4</sup>, Gwyn Saylor<sup>5</sup>, Elizabeth Cavagnaro<sup>4</sup>, Kara O. Coughlin<sup>4</sup>, Lesley H. Curtis<sup>6</sup>, Mark G. Weiner<sup>7†</sup>, Patrick Archdeacon<sup>8</sup> and Jeffrey S. Brown<sup>4</sup>

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<sup>6</sup>*Duke Clinical Research Institute and Department of Medicine, Duke University School of Medicine, Durham, NC, USA*

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<sup>8</sup>*Center for Drug Evaluation and Research, Food and Drug Administration Silver Spring, MD, USA*

# Variations in result units in source data

## *Platelet count original result units<sup>‡</sup>*

|         |             |             |            |
|---------|-------------|-------------|------------|
| Blank   | FL          | TH/UL       | X10(3)     |
| %       | K/CMM       | THOU/CMM    | 1000/UL    |
| /100 W  | k/cmm       | thou/cmm    | X10(3)/MCL |
| /CMM    | K/CU MM     | thou/mm3    | X10(3)/UL  |
| CMM     | K/CUMM      | THOU/UL     | X10(6)/MCL |
| 10 3 L  | K/MCL       | THOUS/CU.MM | X10*9/L    |
| 10X3UL  | K/mcL       | THOUS/MCL   | X10E3/UL   |
| 10^3/UL | K/UL        | THOU/mcL    | X1000      |
| 10*3/uL | k/uL        | THOUS/UL    | X10X3      |
| 10?3/uL | KU/L        | Thou/uL     | X10^3/UL   |
| 10E3/uL | K/MM3       | THOUSA      | x10        |
| 10e3/uL | K/mm3       | THOUSAND    | X10?3/ul   |
| 10e9/L  | LB          | THOUSAND/UL | X10E3/UL   |
| E9/L    | PLATELET CO | U           | X10E3      |
| BIL/L   | T/CMM       | X 10-3/UL   | K/A?L      |
| bil/L   | TH/MM3      | X 10(3)/UL  | K/B5L      |
| CU MM   | th/mm3      | X10 3       |            |



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**National Medical Evidence  
Generation Collaborative (EvGen  
Collaborative)**

# National Medical Evidence Generation Collaborative (EvGen Collaborative)



SHARE



TWEET



LINKEDIN



PIN IT



EMAIL



PRINT

### Resources for You

- [Office of Medical Products and Tobacco](#)



# Medical Product Safety Surveillance

FDA



Biologics & Biosimilars Collective Intelligence Consortium



DISTRIBUTED NETWORK GOVERNANCE

## Payers

- Public
- Private

Common  
Data Model  
Data Standards

## Providers

- Hospitals
- Physicians
- Integrated Systems

## Registries

- Disease-specific
- Product-specific

## Quality of Care

Sponsor(s)



Coordinating  
Center(s)



Public Health Surveillance



Clinical Research



Comparative Effectiveness Research



**Thank you!**

# Summary of query specifications: Overall

|   |   |
|---|---|
| <b>1. Select the Query Type (Level):</b>  | Level 2: Cohort Selection and Analytic Adjustment   |
| <b>2. Select the Analysis Tool:</b>   | Propensity Score Matching Tool  |
| <b>3. Describe Study Objectives:</b>  | <i>To assess the ability of Mini-Sentinel comparative assessment modular programs to reproduce the known association between ACEIs and angioedema</i> |
| <b>4. Define Study Period:</b>  | 01/01/2008 - 09/30/2013   |
| <p><i>If multiple looks are planned (PROMPT), enter the time period for the first look.</i><br/> <i>Look frequency and time period covered should be included in the surveillance plan.</i></p> |   |
| <b>5. List the age group(s) of interest:</b>  | 18 +  |
| <b>6. Specify enrollment requirements:</b>  |   |
| Coverage type:  | Medical and drug coverage   |
| Maximum enrollment gap (days):  | 45  |
| Continuous enrollment before exposure (days):   | 183   |



# Summary of query specifications: Exposures

|   | Exposure of Interest   | Comparator of Interest (1)  |
|---|--|---|
| <b>1. Define exposures (generic/brand names):</b>                                 | ACE inhibitors (benazepril, captopril, enalapril, fosinopril, lisinopril, moexipril, quinapril, perindopril, ramipril, or tranolapril) | Beta-blockers (acebutolol, atenolol, bisoprolol, carvedilol, labetalol, metoprolol, nebivolol, pindolol, propranolol, or timolol) |
| <b>2. Define exposure incidence:</b>  |  |   |
| Washout period (days):  | 183  | 183   |
| Other exposures:<br><i>Incidence defined with respect to additional exposures</i> | Beta-blockers, aliskiren, ARBs (candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, or valsartan)                  | ACE inhibitors, aliskiren, ARBs (candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, or valsartan)            |
| <b>3. Specify exposed time assessment (AT or ITT):</b>                            | As Treated (AT)  | As Treated (AT)   |
| <b>4. Specify follow-up duration (for ITT assessments; in days):</b>              |  |   |
| <i>Leave blank for AT assessments</i>   |  |   |

# Summary of query specifications:

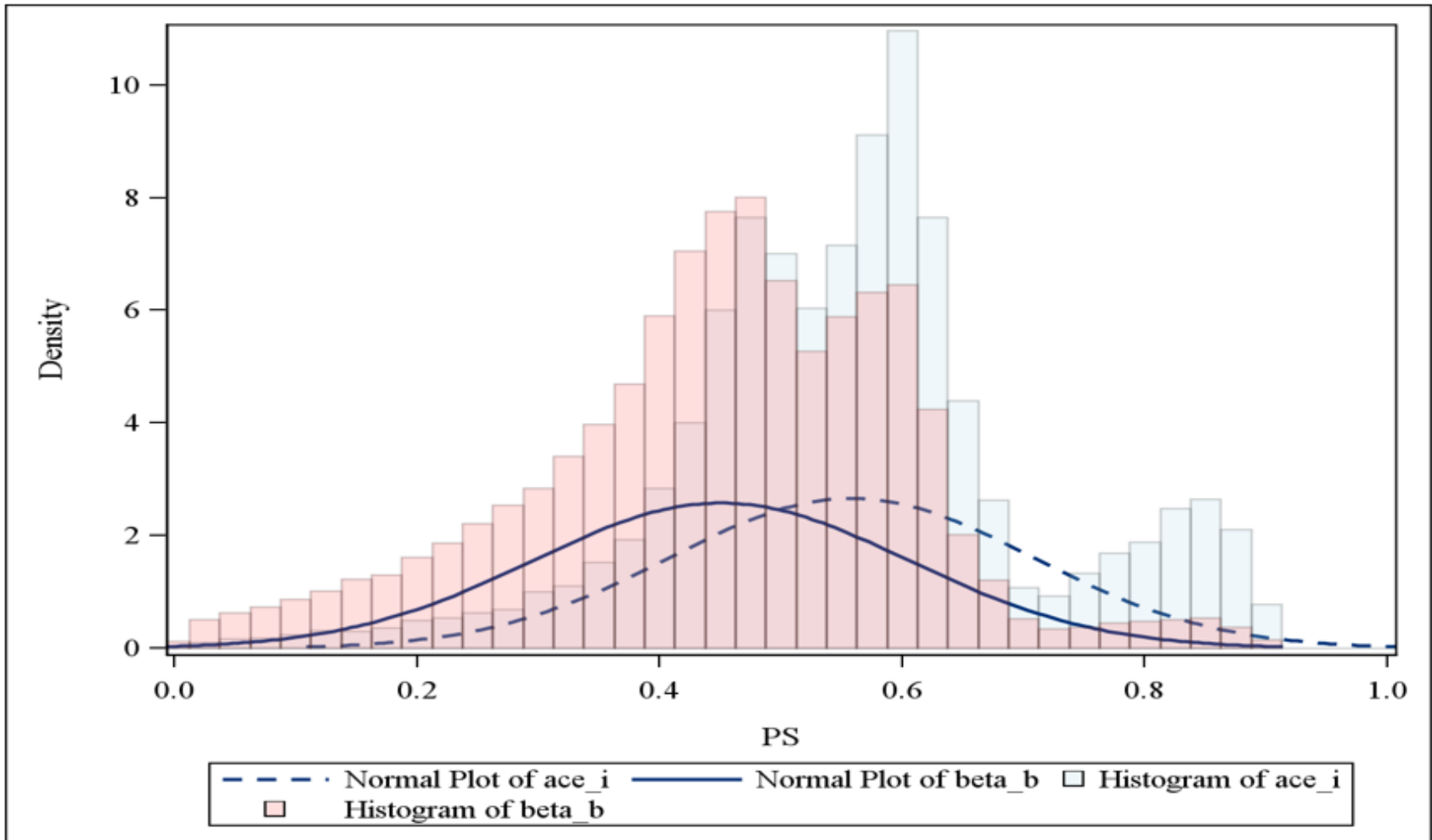
## Additional information

- Outcomes
  - ICD-9-CM code 995.1 in any position during outpatient, inpatient, or emergency department encounter
  - Washout period (days before first dispensing): 183 days
- Inclusion criteria
- Exclusion criteria
- Covariates
- Propensity score matching options
  - Comorbidity, utilization, high dimensional propensity score
  - Matching ratio
  - Caliper size

# Propensity scores before match

Histograms of PS distribution by DP (masked)

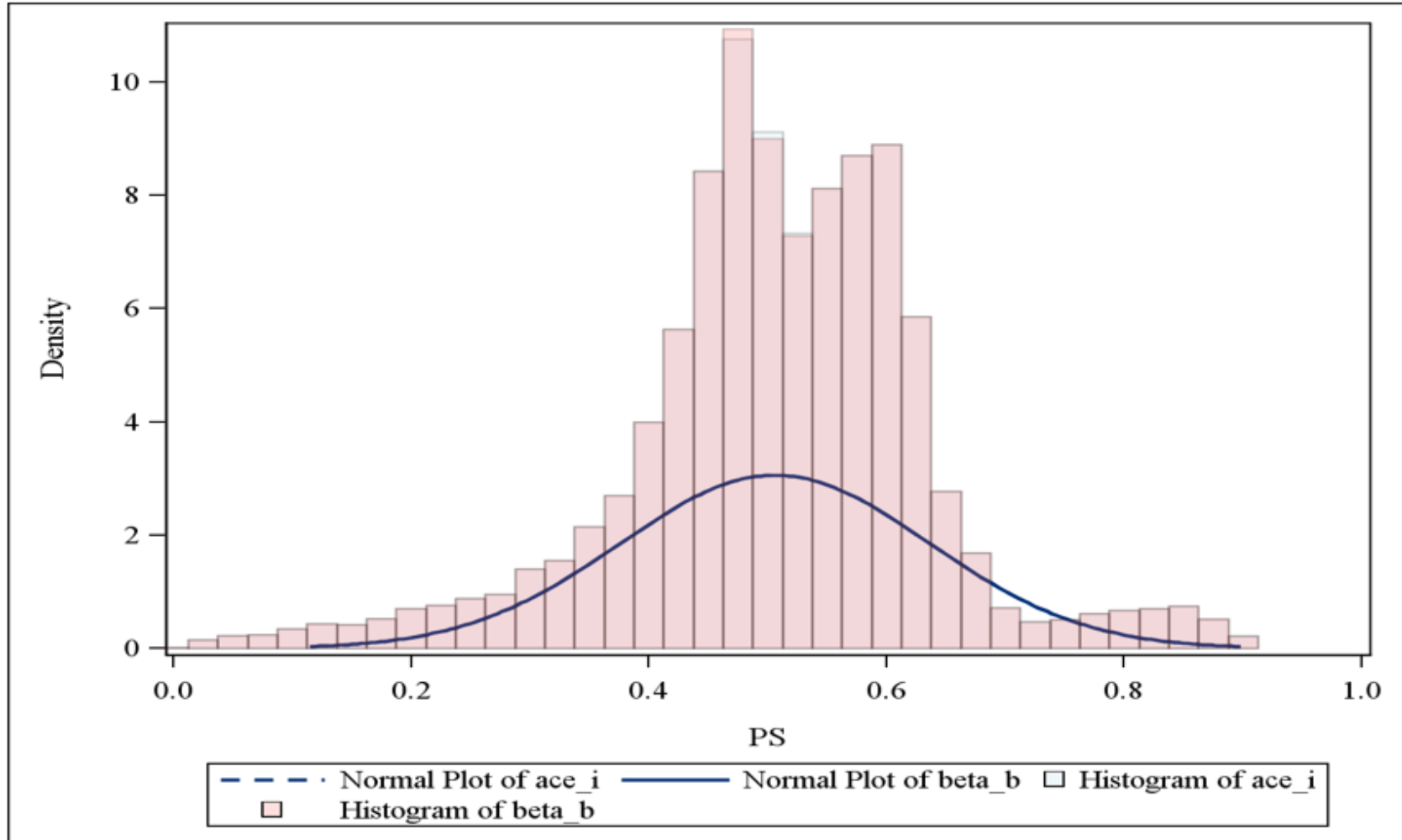
Histogram of Predefined PS, Unmatched Cohort C-Stat for Predefined: 0.695



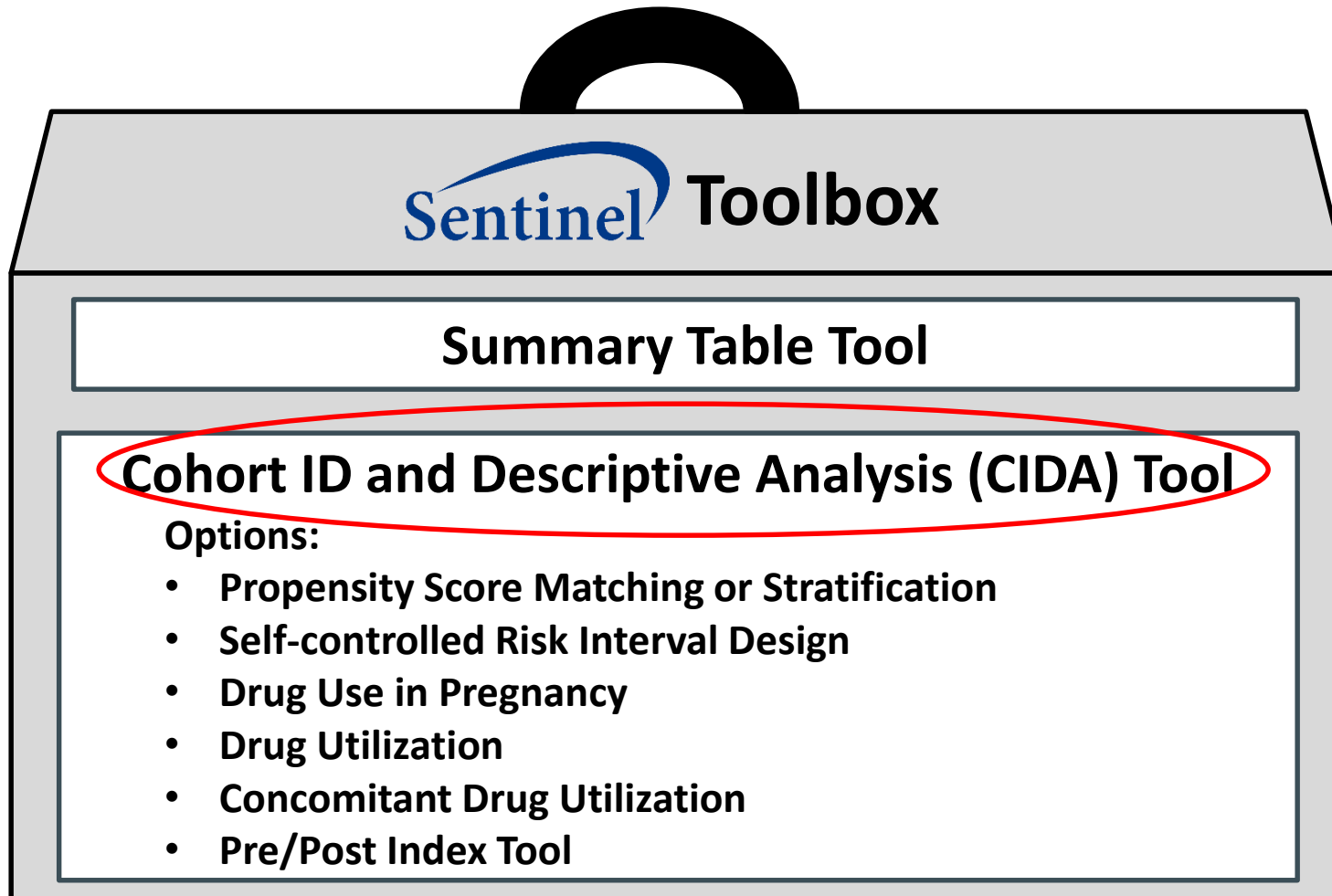
# Propensity scores after match

## Histograms of PS distribution by DP (masked)

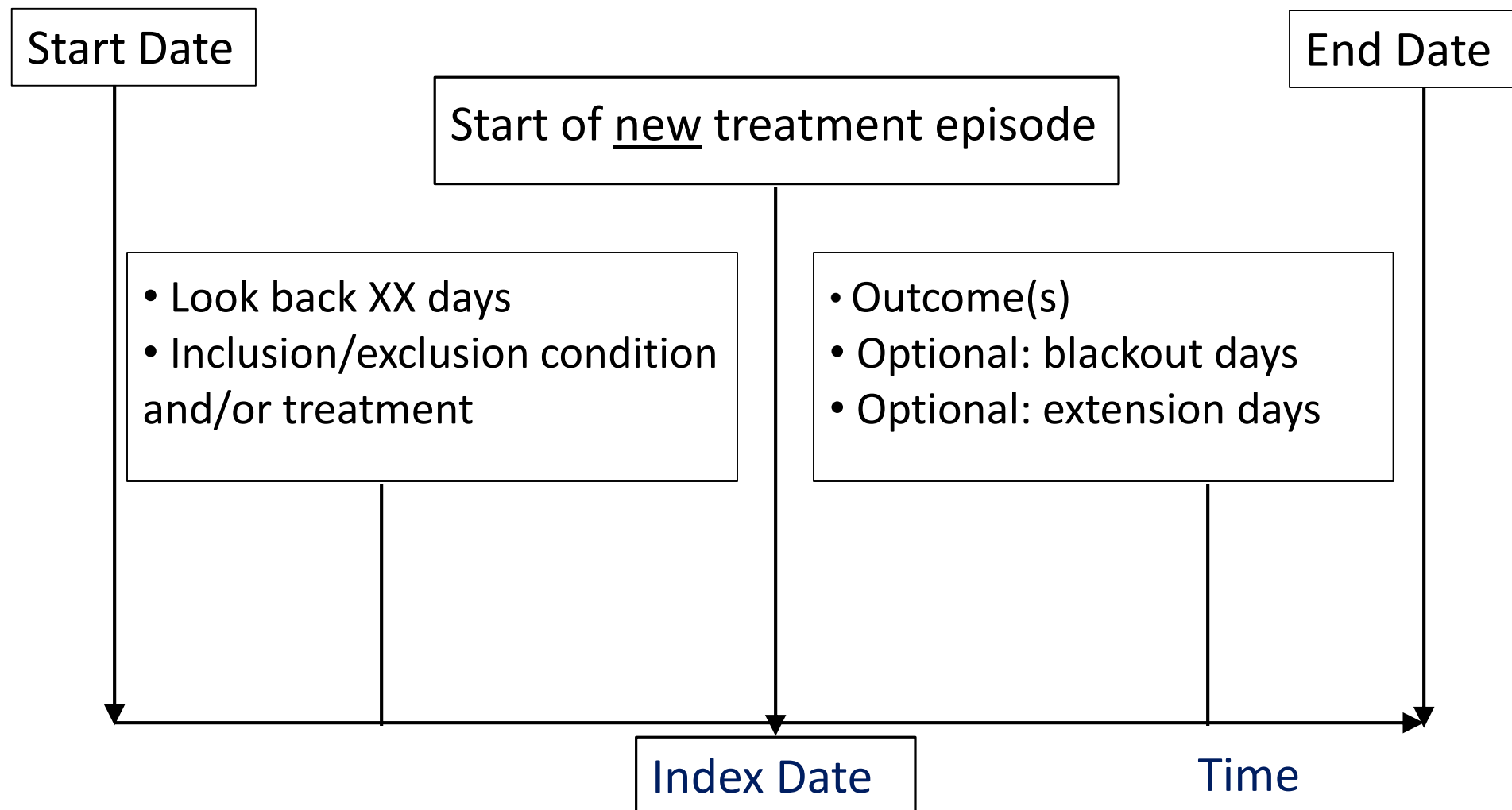
Histogram of Predefined PS among Predefined PS Matched Cohort, Matched Cal = .025 C-Stat for Predefined: 0.695



# Sentinel's tools



# New user cohort design



# Blood transfusion during pregnancy

- Need for rapid assessment of frequency of transfusion during pregnancy
- Sentinel Distributed Dataset identified 1,946,032 deliveries with coverage during entire pregnancy from 2008-2015 (~8% of U.S. deliveries)
- 21,048 (1.1%) pregnancies had blood transfusion
- Report with integrated data from 15 data partners returned to FDA within **3 working days** of final specification