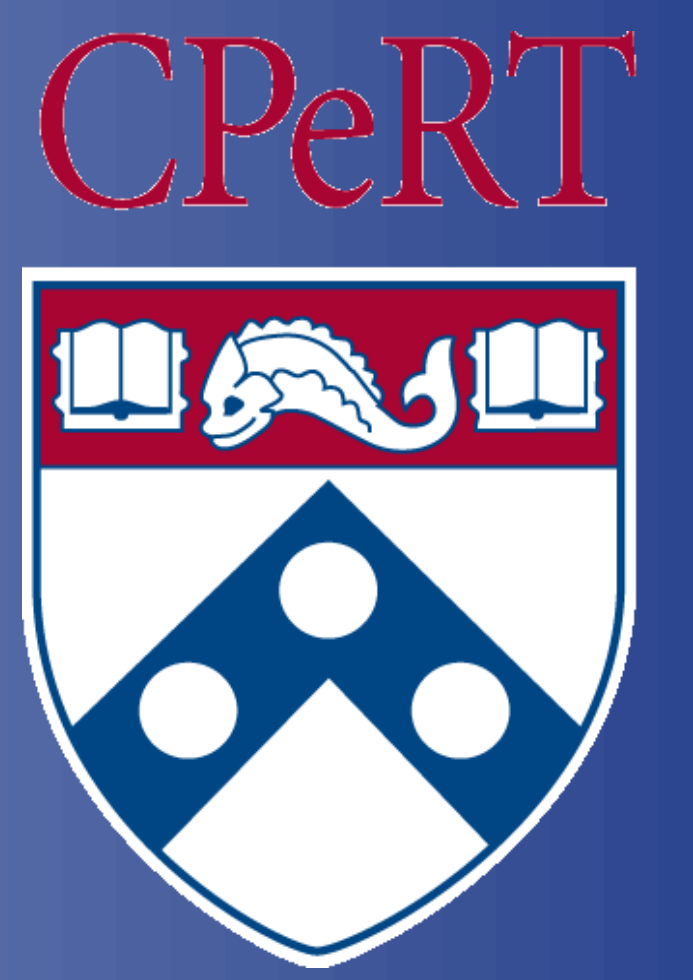


# Pilot Test of the Sentinel Modular Program for Propensity Score Matched Cohort Analyses: Application to Glyburide, Glipizide, and Severe Hypoglycemia



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## BACKGROUND

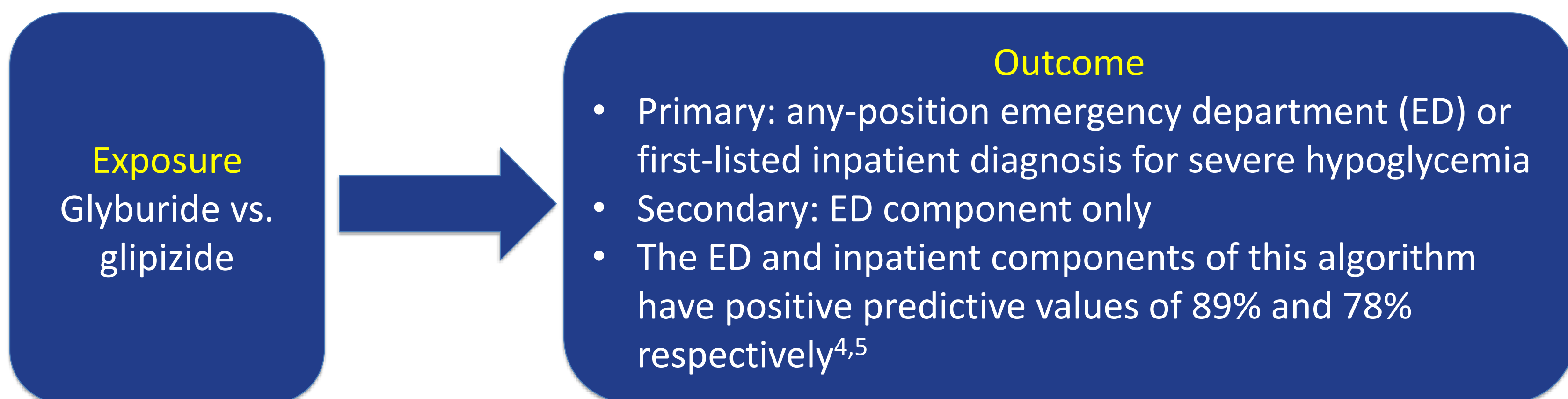
- Sentinel is a program sponsored by the US Food and Drug Administration to monitor the safety of medical products
- Prior epidemiologic studies reported a 67-90% greater risk of severe hypoglycemia associated with glyburide vs. glipizide<sup>1,2</sup>
- A systematic review of clinical trials found higher risk for glyburide compared to other secretagogues<sup>3</sup>

## OBJECTIVE

- To evaluate the ability of the semi-automated, customizable Sentinel Propensity Score Matching (PSM) Tool to reproduce the increased risk of severe hypoglycemia seen in users of glyburide vs. glipizide in an expedited fashion

## METHODS

- Study Design:** Retrospective cohort study
- Data Source:**
  - Sentinel Distributed Database (SDD)
  - Thirteen Data Partners (DPs) participated in this assessment
- Study Population:**
  - Individuals  $\geq 18$  years of age who initiated glyburide or glipizide between January 1, 2008 and September 30, 2014



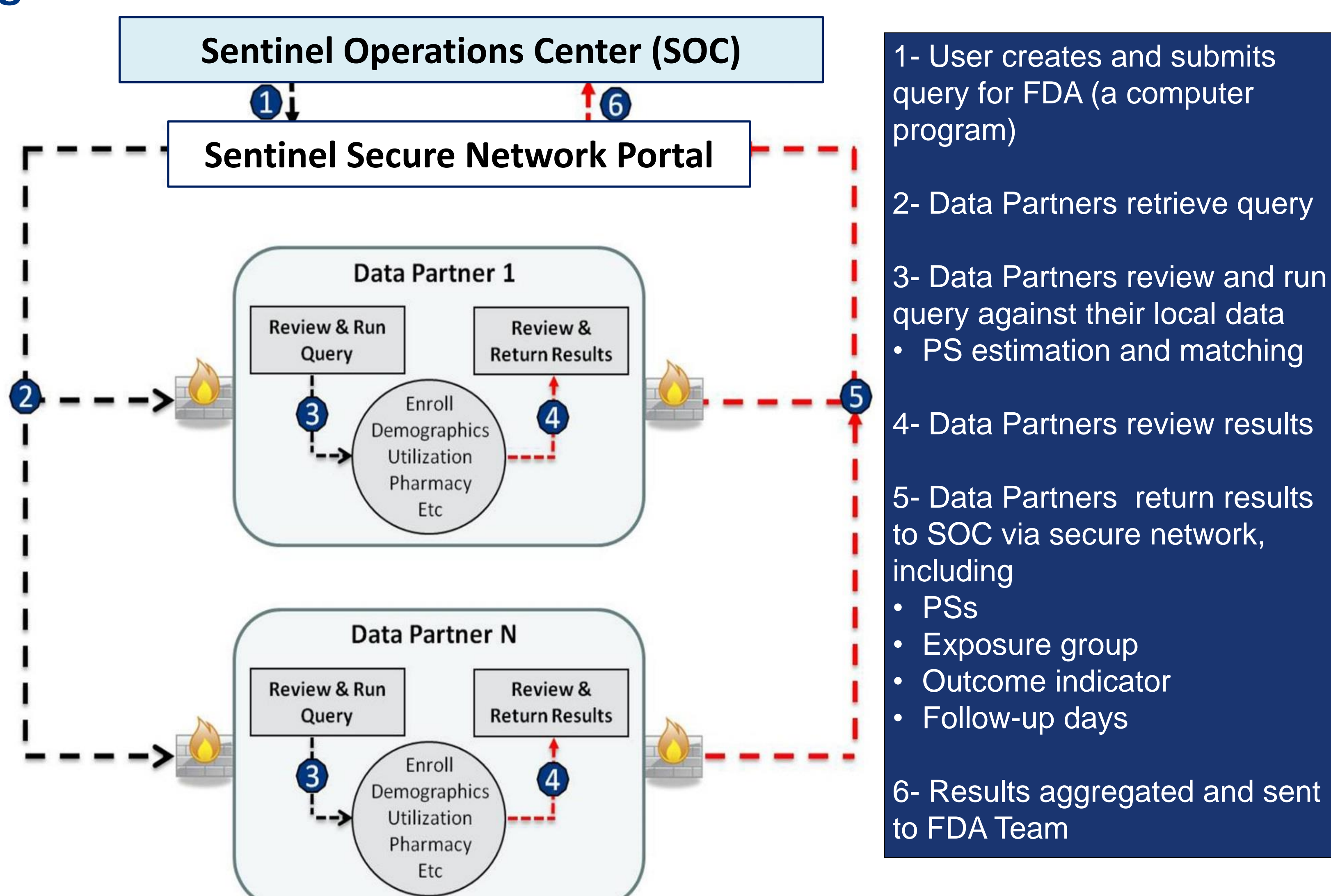
### Predefined covariates:

- The 12 basic covariates for the program included age, gender, time period (monitoring period), year of exposure, combined Charlson/Elixhauser comorbidity score and the seven measures of healthcare utilization intensity
- History of severe hypoglycemia, chronic kidney disease, and use of insulin, metformin, or non-secretagogue antidiabetic drugs
- Assessed in the 183 days before cohort entry

### Statistical analysis:

- The Sentinel Cohort Identification and Descriptive Analysis (CIDA) Tool was used to identify and extract the cohorts
- The Sentinel Propensity Score Matching (PSM) Tool was used to conduct three PS matched analyses that utilized PS that included (1:1 matching with a maximum caliper of 0.025):
  - Predefined covariates only
  - Covariates identified by the automated, high-dimensional propensity score (hdPS) algorithm
  - Both predefined covariates and those selected by hdPS
- All Cox proportional hazard models were stratified by DP
- Conditional models fit to the matched cohorts were further stratified on matched pair

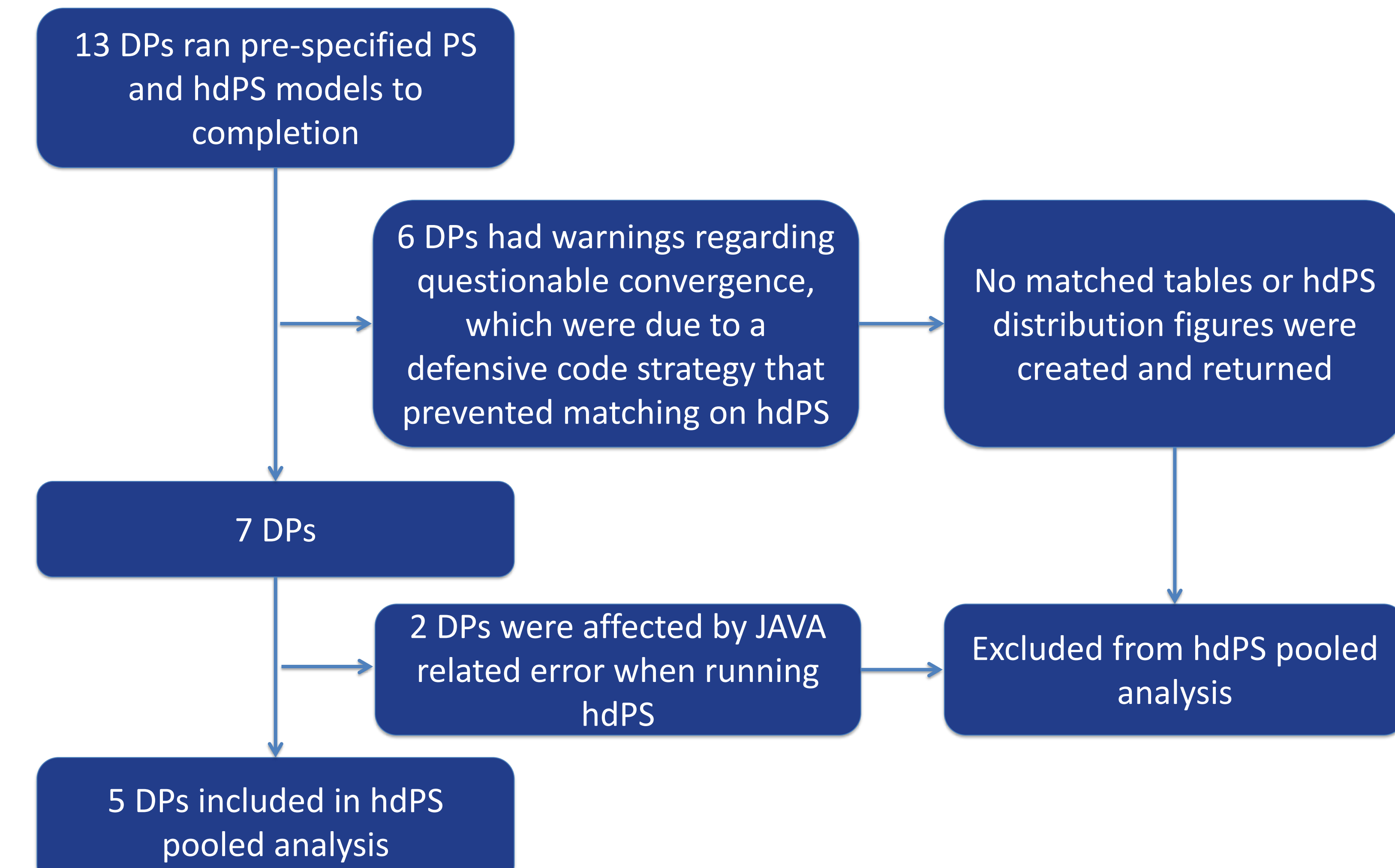
Figure 1. Sentinel Distributed Data Network



## RESULTS

- All 13 DPs returned results for unmatched pre-defined PS and hdPS models and results for matched pre-defined PS models
- Seven DPs returned results for matched hdPS models

Figure 2. Summary of results



- In the unmatched cohorts, we identified 198,550 and 379,507 new users of glyburide and glipizide, respectively
- Median length of follow-up:
  - Glyburide vs. glipizide users: 79 days vs. 114 days

Table 1. Incidence rate (IR) and hazard ratios (HR) of ED visits and hospital admissions for hypoglycemia

Exposure	New users	Person years at risk	Events	IR per 1,000 person years	HR (95% CI)
<b>Data from 13 Data Partners</b>					
Unmatched <sup>a</sup>					
Glyburide	198,550	89,719	1,685	18.8	1.11 (1.05-1.18)
Glipizide	379,507	244,094	5,406	22.2	
Matched on predefined covariates – Unconditional model <sup>b</sup>					
Glyburide	173,655	83,108	1,633	19.65	1.35 (1.26, 1.45)
Glipizide	173,656	99,834	1,393	13.95	
Matched on predefined covariates – Conditional model <sup>c</sup>					
Glyburide	173,655	38,986	1,064	27.3	1.36 (1.24, 1.49)
Glipizide	173,656	38,986	784	20.1	
<b>Data from 5 Data Partners in which the hdPS model converged and completed without errors</b>					
Unmatched <sup>a</sup>					
Glyburide	139,113	58,075	905	15.6	1.26 (1.16, 1.38)
Glipizide	181,911	94,941	1,079	11.4	
Matched on predefined covariates - Unconditional model <sup>b</sup>					
Glyburide	120,334	53,366	859	16.1	1.41 (1.27, 1.56)
Glipizide	120,335	61,552	666	10.8	
Matched on predefined covariates – Conditional model <sup>c</sup>					
Glyburide	120,334	24,708	568	23.0	1.42 (1.25, 1.62)
Glipizide	120,335	24,708	399	16.2	
Matched on hdPS – Unconditional model <sup>b</sup>					
Glyburide	116,930	52,816	870	16.5	1.50 (1.36, 1.66)
Glipizide	116,931	62,526	644	10.3	
Matched on hdPS – Conditional model <sup>c</sup>					
Glyburide	116,930	24,494	581	23.7	1.49 (1.31, 1.70)
Glipizide	116,931	24,498	389	15.9	
Matched on predefined covariates and hdPS – Unconditional model <sup>b</sup>					
Glyburide	116,639	52,713	868	16.5	1.49 (1.34, 1.65)
Glipizide	116,641	61,778	644	10.4	
Matched on predefined covariates and hdPS – Conditional model <sup>c</sup>					
Glyburide	116,639	24,332	575	23.6	1.51 (1.32, 1.71)
Glipizide	116,641	24,333	382	15.7	

<sup>a</sup> Site adjusted only, <sup>b</sup> Cox model not stratified by matched pair, <sup>c</sup> Cox model stratified by matched pair.

## CONCLUSIONS

- Our findings are consistent with the known higher rate of serious hypoglycemia with glyburide, and demonstrated the ability of the Sentinel PSM Tool to reproduce this known association in Sentinel
- This study supports the utility of Sentinel to actively examine the safety of medical products

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