CIDA Report Interpretation

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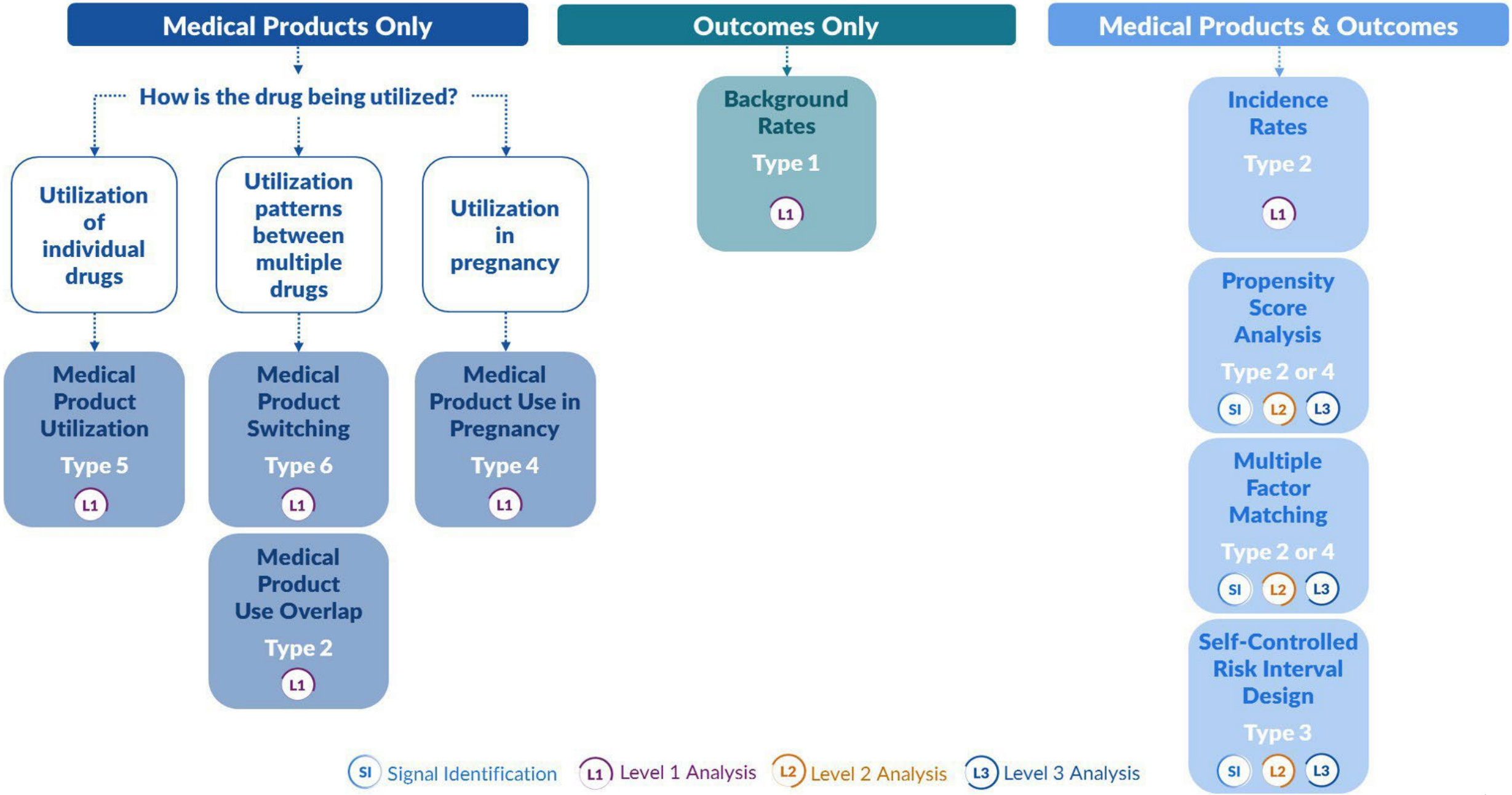
Active Risk Identification and Analysis (ARIA)

- Template computer programs with standardized questions
- Parameterized at program execution
- Pre-tested and quality-checked
- Standard output

https://www.sentinelinitiative.org/active-risk-identification-and-analysis-aria

What are you investigating?

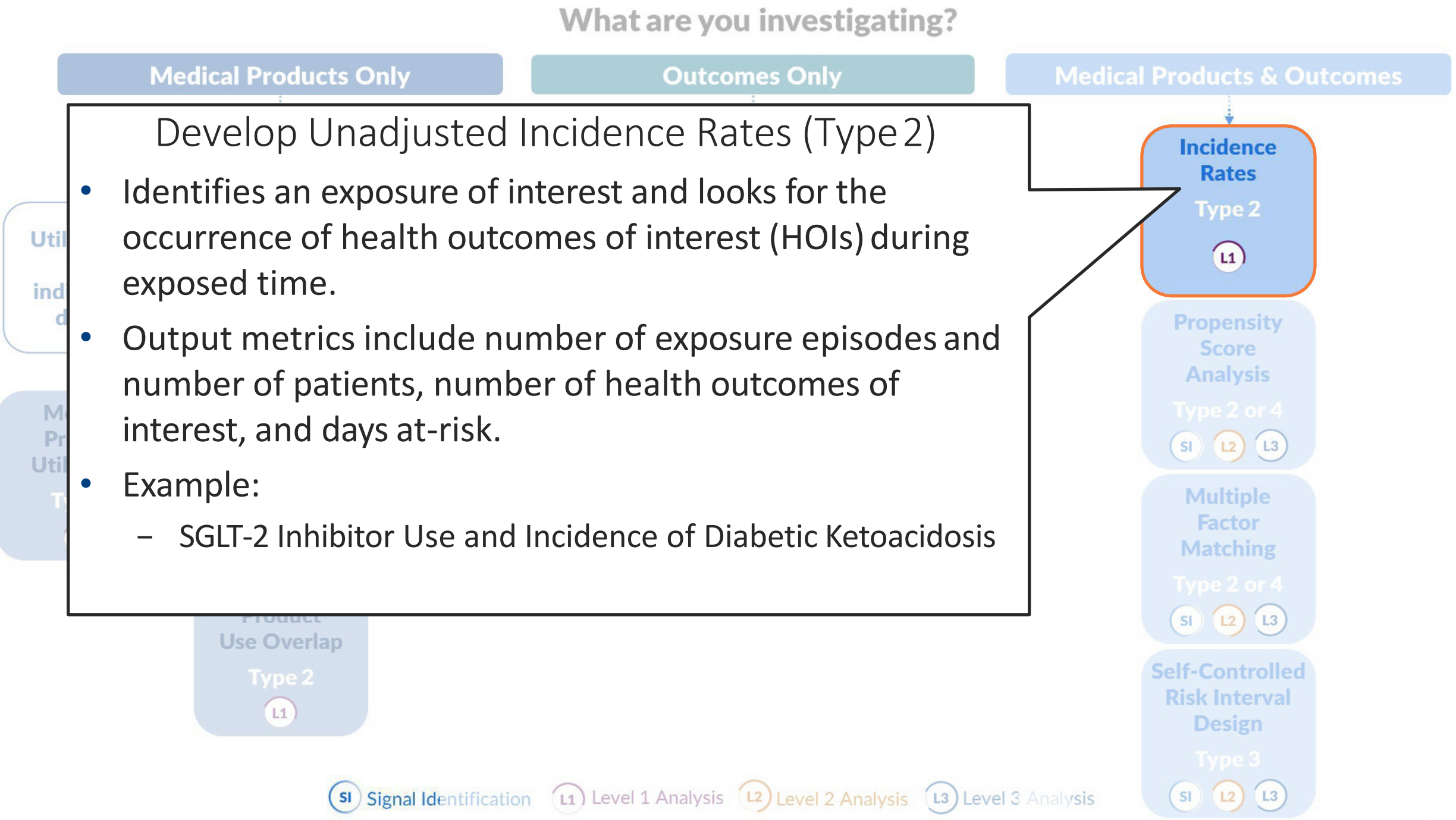


Agenda

- Review of Query Design
- Interpretation of Report Contents

Topics

- Baseline Characteristics
- Type 2 Report
- Propensity Score Analysis


What are you investigating?
Medical Products Only
Outcomes Only
Medical Products & Outcomes
Develop Unadjusted Incidence Rates (Type 2)
• Identifies an exposure of interest and looks for the occurrence of health outcomes of interest (HOIs) during exposed time.
• Output metrics include number of exposure episodes and number of patients, number of health outcomes of interest, and days at-risk.
• Example:
– SGLT-2 Inhibitor Use and Incidence of Diabetic Ketoacidosis
Incidence Rates
Type 2
L1
Propensity Score Analysis
Type 2 or 4
SI L2 L3
Multiple Factor Matching
Type 2 or 4
SI L2 L3
Self-Controlled Risk Interval Design
Type 3
SI L2 L3
Use Overlap
Type 2
L1
SI Signal Identification
L1 Level 1 Analysis
L2 Level 2 Analysis
L3 Level 3 Analysis

Recap of this Morning's Session

- Introduced our case study problem
  - Stroke following antipsychotics use
- Evaluated medical product utilization data
  - Sentinel Query Builder (Simplified Type 5 CIDA) Analysis Tool
- Introduced design diagram and query specifications for an incidence rates query with associated propensity score matching analysis
  - How to parameterize the regulatory question

Query Design

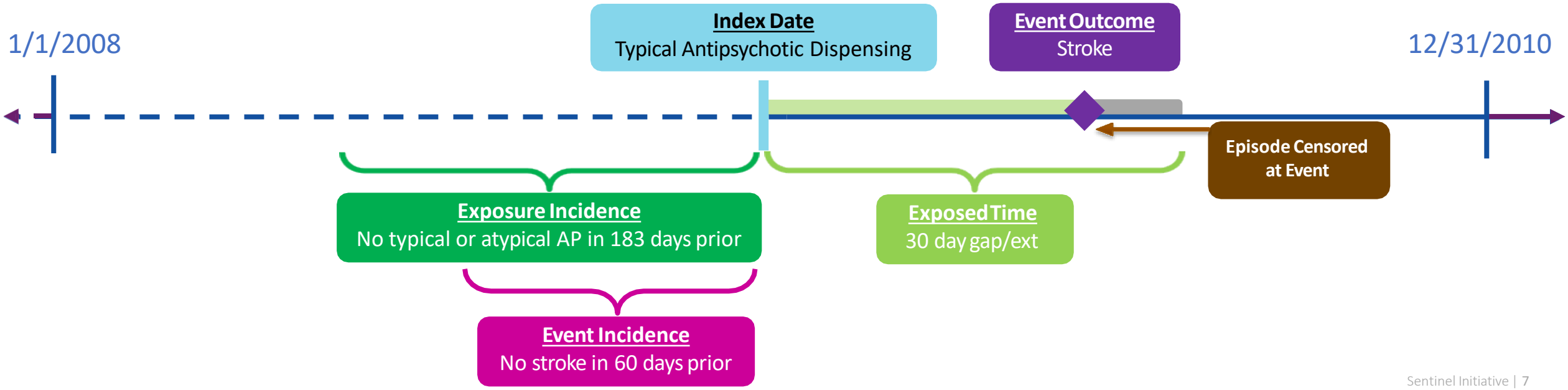
Covariate Evaluation Window
183 days to 1 day prior to index

Exclusion
Dementia 183 days to 0 day prior to index

Enrollment
183 day Enrollment
45 day Enrollment Gap
Medical and Drug Coverage

Cohort Definition
First valid exposure episode; no cohort re-entry

Cohort Characteristics
- Include adults ages 18-65 at index
- Do not restrict sex or race
- No chart availability restrictions



Baseline Output

- Default output table characterizes each exposure/outcome scenario for:
  - Age
  - Sex
  - Race
  - Year of exposure
  - User-defined conditions
  - Medical and drug utilization metrics
  - Comorbidity score
- Evaluation for conditions occurs in flexible periods of time relative to the index date

Baseline Table

User specified age categories

Sex

Year

Covariates

Table 1a. Baseline table for Typical Antipsychotics		
	Typical Antipsychotics	
Characteristic[1]	N/Mean	%/Std Dev[2]
Number of episodes	18,997	
Number of unique patients	18,997	
Demographics		
Mean Age	51.5	10.6
Age: 18-39	3,243	17.1%
Age: 40-54	7,359	38.7%
Age: 55-65	8,395	44.2%
Gender (Female)	10,041	52.9%
Gender (Male)	8,956	47.1%
Race (Unknown)	1,378	7.3%
Race (Black or African American)	3,595	18.9%
Race (White)	14,024	73.8%
Hispanic Origin	657	3.5%
Year (2008)	5,499	28.9%
Year (2009)	8,782	46.2%
Year (2010)	4,716	24.8%
Recorded history of:		
AMI	2,183	11.5%
Anxiety	2,679	14.1%
Bipolar	4,645	24.5%
Depression	4,956	26.1%
Diabetes	10,065	53.0%
Heart failure	4,534	23.9%
Hypercholesterolemia	9,545	50.2%
Hypertension	12,206	64.3%
Kidney failure	4,887	25.7%
Schizophrenia/psychotic	4,103	21.6%
Substance abuse	1,600	8.4%
Transient ischemic attack	601	3.2%

- Table 1s show baseline characteristics
- Baseline table created for each exposure/outcome scenario (Tables 1a – 1d)

Type 2 Report - Overall Summary Counts

Table 2. Summary of Typical and Atypical Antipsychotics and Stroke in the Sentinel Distributed Database between January 1, 2008 and December 31, 2010 Overall

	New Users	Eligible Members[1]	New Episodes	Days At Risk	Years at Risk	Adjusted Dispensings	Raw Dispensings	Days Supplied	Amount Supplied	New Episodes with an Event	Eligible Member-Days[1]	Eligible Member Years[1]
Ischemic Stroke												
Typical Antipsychotics	18,997	271,138	18,997	1,121,282	3,069.9	19,916	19,917	596,944	933,469	13	119,772,697	327,919.8
Atypical Antipsychotics	15,390	271,138	15,390	906,822	2,482.7	15,773	15,773	488,156	802,324	8	120,371,621	329,559.5
Intracranial Hemorrhage												
Typical Antipsychotics	18,572	270,909	18,572	1,096,655	3,002.5	19,470	19,471	583,672	912,526	3	117,763,483	322,418.8
Atypical Antipsychotics	15,030	270,909	15,030	885,616	2,424.7	15,404	15,404	476,898	784,264	1	118,344,042	324,008.3

[1]Eligible Members, Member-Days, and Member-Years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period

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Who are Eligible Members?

- Eligible Members, Member-Days, and Member-Years
  - Reflective of the number of members that met all cohort entry criteria on at least one day during the query period (*i.e., those eligible for an index event)*
  - Restricted to health plan members at participating Data Partners and may not be nationally representative
- In this query:
  - 18-65 years
  - Medical and drug coverage for 183 days
  - No exposure in -183 days (washout for exposure)
  - No stroke in -60 days (washout for outcome)
  - No dementia in -183 days (exclusion)

Who are Eligible Members? continued

Lymphoma HOI* validation project, CIDA workplan to id cases chart review

- Algorithm to validate: 2 lymphoma dx codes within 183 days, first is index and incident, have biopsy and imaging px codes within +/- 90 days of index

❼ Eligible Members:

- ≥15 years
- Medical and drug coverage for 365 days
- No lymphoma is -183 days (washout for cohort)
- Biopsy px code in +/- 90 days
- Imaging px code in +/- 90 days

*Health outcome of interest

CIDA Denominators – for Types 1 and 2

- Eligible members
  - Number of members eligible for an index date
  - Must meet enrollment requirements, washout criteria, and inclusion/exclusion criteria for at least one day during the query period
- Eligible member days
  - All the days during the query period that an eligible member is eligible for inclusion in the cohort

- Tool assesses members every day of query period and counts eligible member days
- If you have at least 1 eligible day, you are an eligible member

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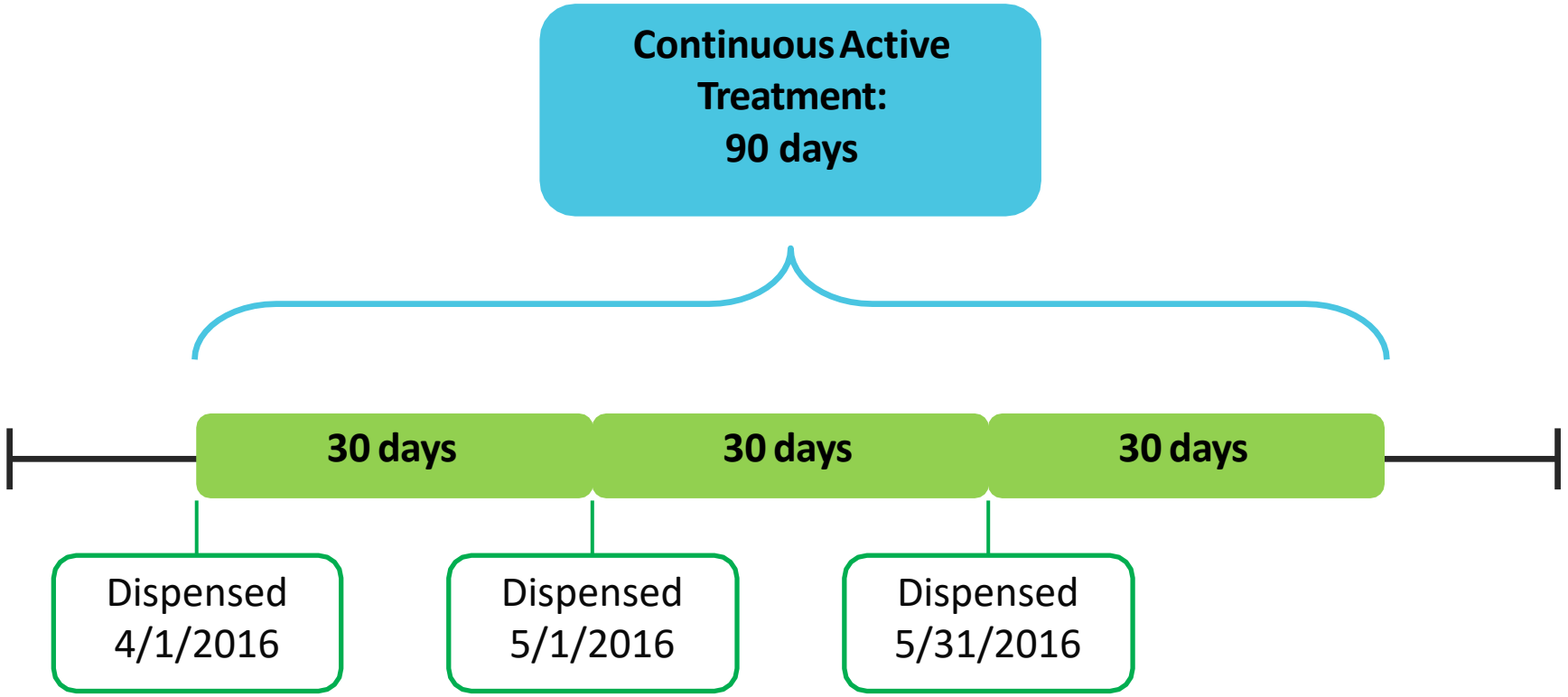
Adjusted vs Raw Code Counts

 # Patients: 1
 # Episodes: 1
Adjusted Code Count: 3
Raw Code Count: 3



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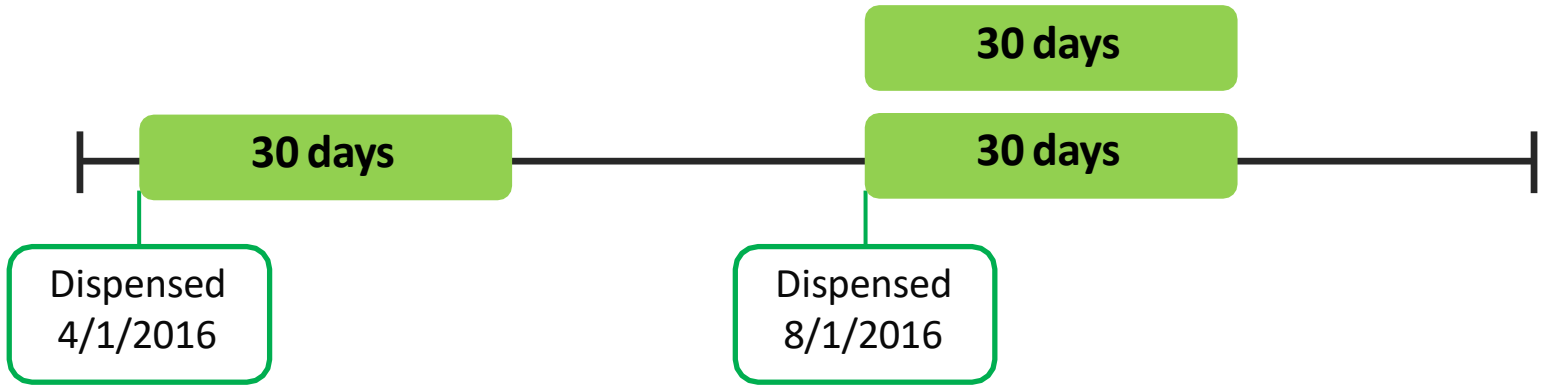

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Stratification of Results

- The CIDA tool can stratify select results from all cohort identification strategies by age, sex, year, month, race, and certain geographic information.
- Stratifications are user-defined.
- Custom strata may be defined in the CIDA tool from lists of valid stratification variables specific to each method of cohort identification.
- Results may also be stratified by defined covariates.

Summary Counts by Year

Table 3. Summary of Typical and Atypical Antipsychotics and Stroke in the Sentinel Distributed Database between January 1, 2008 and December 31, 2010 by Year

Year	New Users	Eligible Members[1]	New Episodes	Days At Risk	Years at Risk	Adjusted Dispensings	Raw Dispensings	Days Supplied	Amount Supplied	New Episodes with an Event	Eligible Member-Days[1]	Eligible Member Years[1]
Ischemic Stroke												
Typical Antipsychotics												
2008	5,499	182,153	5,499	327,097	895.5	5,810	5,810	173,100	274,403	3	25,591,065	70,064.5
2009	8,782	209,925	8,782	524,339	1,435.6	9,231	9,232	278,188	432,663	8	47,780,644	130,816.3
2010	4,716	182,189	4,716	269,846	738.8	4,875	4,875	145,656	226,403	2	46,400,988	127,039.0
Atypical Antipsychotics												
2008	4,223	182,153	4,223	249,875	684.1	4,327	4,327	133,314	225,235	5	25,591,065	70,064.5
2009	7,107	210,858	7,107	425,494	1,164.9	7,302	7,302	227,959	373,196	3	47,929,158	131,222.9
2010	4,060	184,596	4,060	231,453	633.7	4,144	4,144	126,883	203,893	0	46,851,398	128,272.1
Intracranial Hemorrhage												
Typical Antipsychotics												
2008	5,377	181,560	5,377	320,025	876.2	5,680	5,680	169,239	268,753	0	25,122,527	68,781.7
2009	8,562	209,553	8,562	511,614	1,400.7	8,998	8,999	271,271	421,173	1	46,841,799	128,245.9
2010	4,633	182,282	4,633	265,016	725.6	4,792	4,792	143,162	222,600	2	45,799,157	125,391.3
Atypical Antipsychotics												
2008	4,106	181,560	4,106	242,814	664.8	4,209	4,209	129,510	219,188	0	25,122,527	68,781.7
2009	6,938	210,491	6,938	415,603	1,137.9	7,125	7,125	222,702	364,111	0	46,987,489	128,644.7
2010	3,986	184,636	3,986	227,199	622.0	4,070	4,070	124,686	200,966	1	46,234,026	126,581.9

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Summary Counts by Sex

Table 4. Summary of Typical and Atypical Antipsychotics and Stroke in the Sentinel Distributed Database between January 1, 2008 and December 31, 2010 by Sex

Sex	New Users	Eligible Members[1]	New Episodes	Days At Risk	Years at Risk	Adjusted Dispensings	Raw Dispensings	Days Supplied	Amount Supplied	New Episodes with an Event	Eligible Member-Days[1]	Eligible Member Years[1]
Ischemic Stroke												
Typical Antipsychotics												
Female	10,041	138,335	10,041	591,598	1,619.7	10,491	10,491	314,010	494,770	9	61,147,468	167,412.6
Male	8,956	132,803	8,956	529,684	1,450.2	9,425	9,426	282,934	438,700	4	58,625,229	160,507.1
Other	0	0	0	0	0.0	0	0	0	0	0	0	0.0
Atypical Antipsychotics												
Female	8,204	138,335	8,204	483,786	1,324.5	8,398	8,398	260,758	425,634	2	61,428,903	168,183.2
Male	7,186	132,803	7,186	423,036	1,158.2	7,375	7,375	227,398	376,690	6	58,942,718	161,376.4
Other	0	0	0	0	0.0	0	0	0	0	0	0	0.0
Intracranial Hemorrhage												
Typical Antipsychotics												
Female	9,804	138,226	9,804	578,112	1,582.8	10,243	10,243	306,725	482,778	2	60,098,752	164,541.4
Male	8,768	132,683	8,768	518,543	1,419.7	9,227	9,228	276,947	429,748	1	57,664,731	157,877.4
Other	0	0	0	0	0.0	0	0	0	0	0	0	0.0
Atypical Antipsychotics												
Female	8,016	138,226	8,016	472,691	1,294.2	8,204	8,204	254,930	416,227	0	60,373,156	165,292.7
Male	7,014	132,683	7,014	412,925	1,130.5	7,200	7,200	221,968	368,038	1	57,970,886	158,715.6
Other	0	0	0	0	0.0	0	0	0	0	0	0	0.0

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Summary Counts by Age Group

Table 5. Summary of Typical and Atypical Antipsychotics and Stroke in the Sentinel Distributed Database between January 1, 2008 and December 31, 2010 by Age Group

Age Group	New Users	Eligible Members[1]	New Episodes	Days At Risk	Years at Risk	Adjusted Dispensings	Raw Dispensings	Days Supplied	Amount Supplied	New Episodes with an Event	Eligible Member-Days[1]	Eligible Member Years[1]
Ischemic Stroke												
Typical Antipsychotics												
18-39	3,243	35,407	3,243	192,325	526.6	3,432	3,432	102,957	160,840	3	16,494,897	45,160.6
40-54	7,359	91,944	7,359	436,787	1,195.9	7,736	7,737	233,037	360,593	4	42,162,483	115,434.6
55-65	8,395	159,963	8,395	492,170	1,347.5	8,748	8,748	260,950	412,035	6	61,115,317	167,324.6
Atypical Antipsychotics												
18-39	2,513	35,407	2,513	146,204	400.3	2,573	2,573	78,517	128,436	4	16,614,705	45,488.6
40-54	5,799	92,017	5,799	340,605	932.5	5,973	5,973	183,444	298,044	2	42,431,333	116,170.7
55-65	7,078	160,073	7,078	420,013	1,149.9	7,227	7,227	226,195	375,845	2	61,325,583	167,900.3
Intracranial Hemorrhage												
Typical Antipsychotics												
18-39	3,178	35,389	3,178	188,407	515.8	3,361	3,361	100,697	157,820	1	16,226,427	44,425.5
40-54	7,195	91,876	7,195	427,285	1,169.8	7,561	7,562	227,889	351,963	2	41,454,712	113,496.8
55-65	8,199	159,795	8,199	480,963	1,316.8	8,548	8,548	255,086	402,743	0	60,082,344	164,496.5
Atypical Antipsychotics												
18-39	2,455	35,389	2,455	143,001	391.5	2,515	2,515	76,845	125,245	0	16,339,859	44,736.1
40-54	5,665	91,954	5,665	332,670	910.8	5,835	5,835	179,167	292,195	0	41,717,901	114,217.4
55-65	6,910	159,906	6,910	409,945	1,122.4	7,054	7,054	220,886	366,825	1	60,286,282	165,054.8

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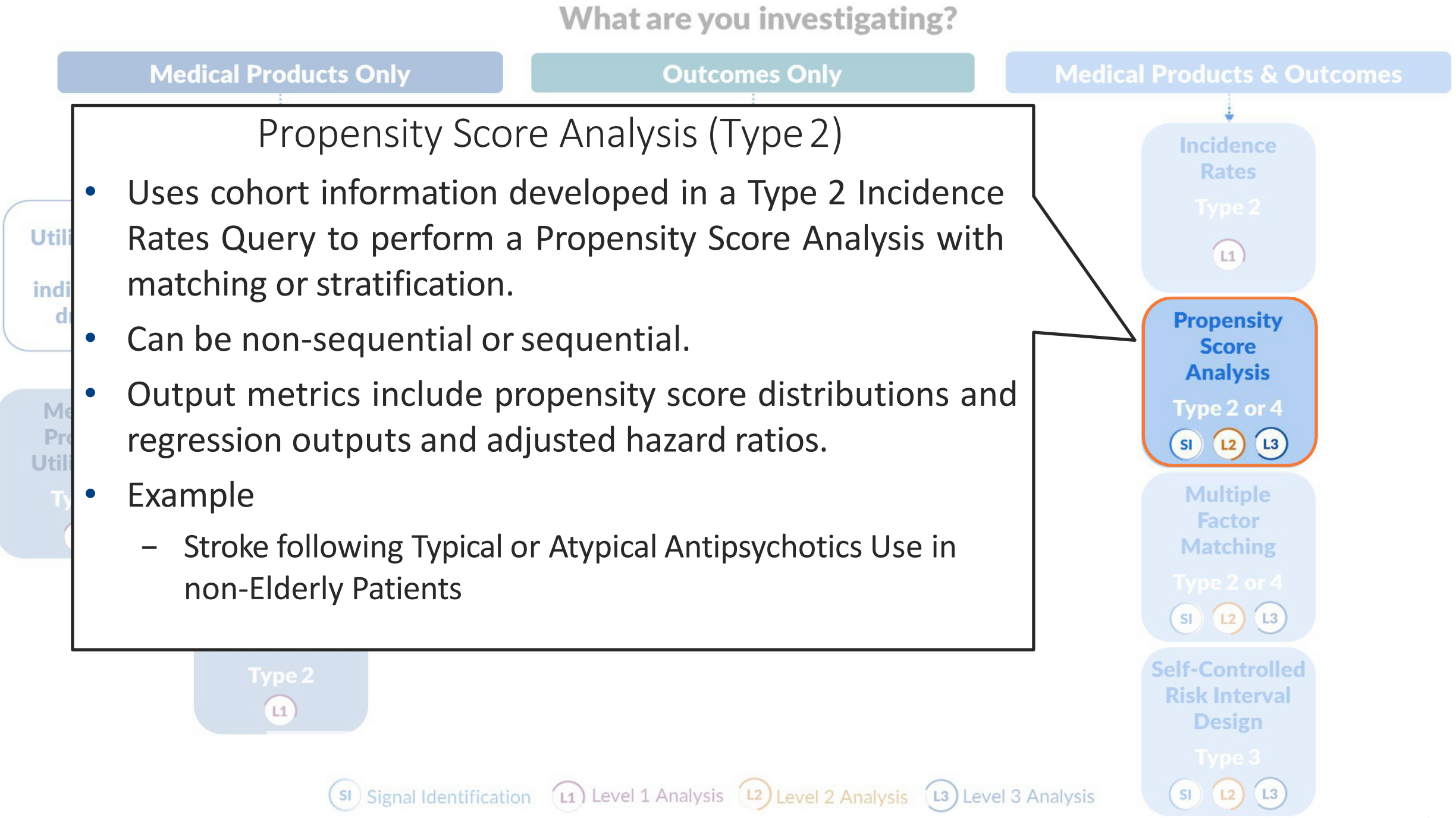
Propensity Score Analysis



Propensity Score Analysis (Type 2)

- Uses cohort information developed in a Type 2 Incidence Rates Query to perform a Propensity Score Analysis with matching or stratification.
- Can be non-sequential or sequential.
- Output metrics include propensity score distributions and regression outputs and adjusted hazard ratios.
- Example
  - Stroke following Typical or Atypical Antipsychotics Use in non-Elderly Patients

Propensity Score Match Design Diagram

Propensity Score
- 1:1 Matching
- Caliper: 0.05
- Age, Sex
- Recorded History Parameters

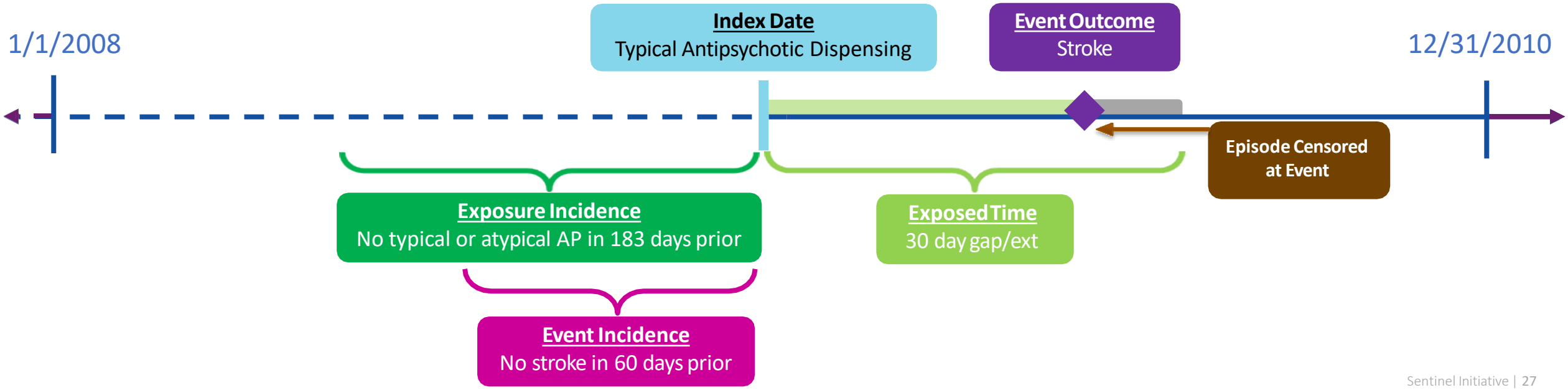
Covariate Evaluation Window
183 days to 1 day prior to index

Exclusion
Dementia 183 days to 0 day prior to index

Enrollment
183 day Enrollment
45 day Enrollment Gap
Medical and Drug Coverage

Cohort Definition
First valid exposure episode; no cohort re-entry

Cohort Characteristics
- Include adults ages 18-65 at index
- Do not restrict sex or race
- No chart availability restrictions



Propensity Score Analysis

- By assigning an exposure of interest and comparator, the type 2 output can be leveraged in an inferential analysis to:
  - Assign members a propensity score, based on user-defined criteria
  - Calculate adjusted risk estimates using matching or stratification

- For each comparison, Cox proportional hazards regression models is used to estimate hazard ratios and corresponding 95% confidence intervals

- There is an option for risk-set level return, and patient-level return

Baseline Characteristics

Table 1a. Cohort of New Initiators of Typical Antipsychotics and Typical Antipsychotics, Ischemic Stroke (Unmatched, Aggregated), Ratio: 1:1, Caliper: 0.05

	Medical Product				Covariate Balance	
Characteristic[2]	**Typical Antipsychotics**		**Typical Antipsychotics**			
	N/Mean	**%/Std Dev[1]**	**N/Mean**	**%/Std Dev[1]**	**Absolute Difference**	**Standardized Difference**
Patients (N)	18,094	100.0%	14,370	100.0%	-	-
Demographics						
Mean age	51.6	10.6	52.0	10.6	-0.438	-0.041
Age: 18-39	3,075	17.0%	2,319	16.1%	0.857	0.023
Age: 40-54	6,984	38.6%	5,365	37.3%	1.264	0.026
Age: 55-65	8,035	44.4%	6,686	46.5%	-2.121	-0.043
Gender (Female)	9,560	52.8%	7,667	53.4%	-0.519	-0.010
Gender (Male)	8,534	47.2%	6,703	46.6%	0.519	0.010
Race (Black or African American)	3,425	18.9%	2,749	19.1%	-0.201	-0.005
Race (Unknown)	1,316	7.3%	1,126	7.8%	-0.563	-0.021
Race (White)	13,353	73.8%	10,495	73.0%	0.764	0.017
Hispanic Origin	625	3.5%	558	3.9%	-0.429	-0.023
Year (2008)	5,499	30.4%	4,223	29.4%	1.004	0.022
Year (2009)	8,420	46.5%	6,702	46.6%	-0.104	-0.002
Year (2010)	4,175	23.1%	3,445	24.0%	-0.900	-0.021
Recorded History of:						
AMI	2,090	11.6%	1,614	11.2%	0.319	0.010
Anxiety	2,555	14.1%	1,826	12.7%	1.414	0.041
Bipolar	4,388	24.3%	2,914	20.3%	3.973	0.096
Depression	4,696	26.0%	3,186	22.2%	3.782	0.089
Diabetes	9,635	53.2%	7,524	52.4%	0.891	0.018
Heart failure	4,360	24.1%	3,404	23.7%	0.408	0.010
Hypercholesterolemia	9,142	50.5%	7,157	49.8%	0.720	0.014
Hypertension	11,665	64.5%	9,064	63.1%	1.393	0.029
Kidney failure	4,664	25.8%	3,559	24.8%	1.010	0.023
Schizophrenia/psychotic	3,844	21.2%	2,452	17.1%	4.181	0.106
Substance abuse	1,511	8.4%	1,029	7.2%	1.190	0.045
Transient ischemic attack	577	3.2%	444	3.1%	0.099	0.006

[1]Value represents standard deviation where no % follows the value
[2]Covariates in blue show a standardized difference greater than 0.1

Baseline Characteristics

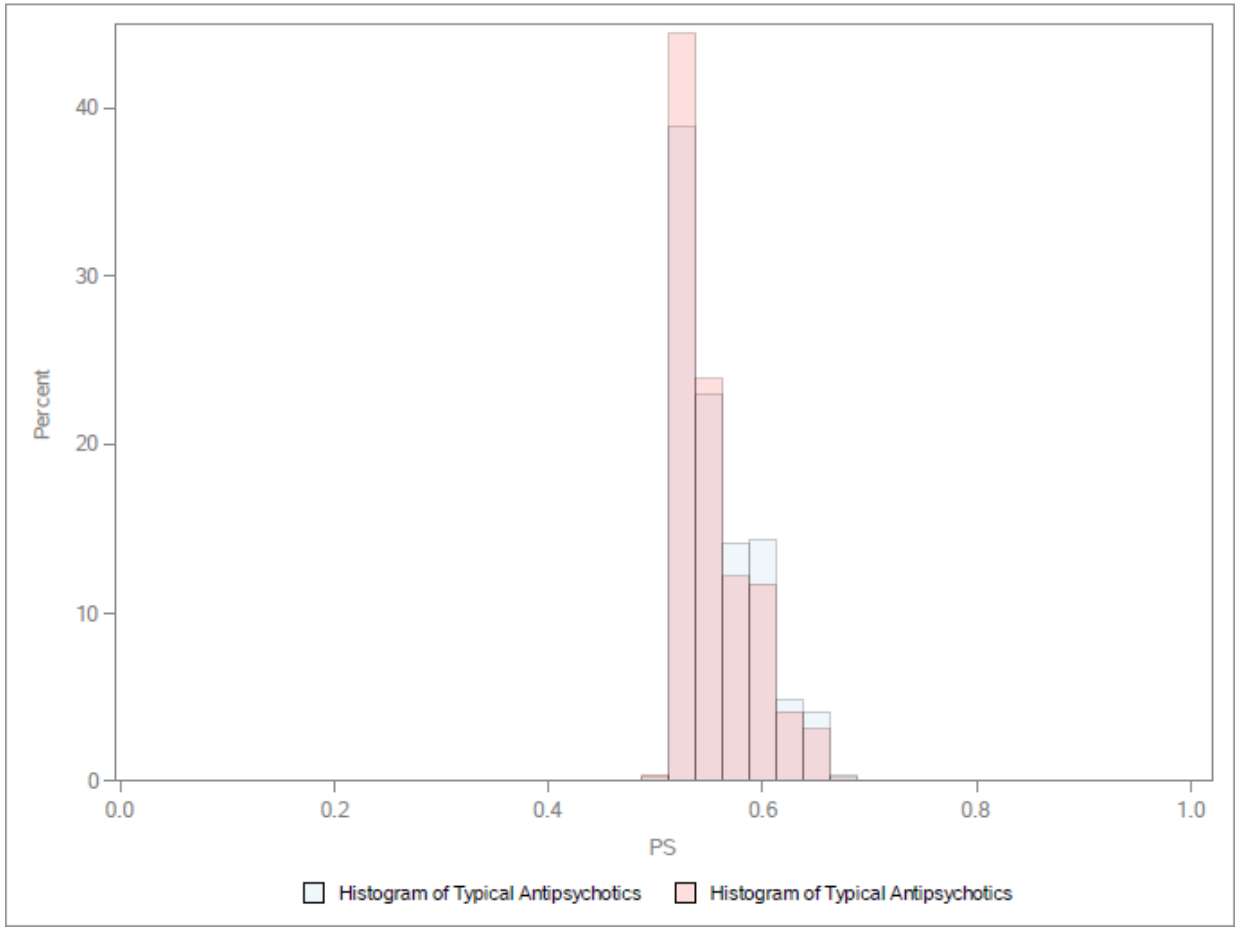
Table 1b. Cohort of New Initiators of Typical Antipsychotics and Typical Antipsychotics, Ischemic Stroke (Matched, Aggregated), Ratio: 1:1, Caliper: 0.05

	Medical Product				Covariate Balance	
Characteristic[2]	**Typical Antipsychotics**		**Typical Antipsychotics**			
	N/Mean	**%/Std Dev[1]**	**N/Mean**	**%/Std Dev[1]**	**Absolute Difference**	**Standardized Difference**
Patients (N)	14,370	79.4%	14,370	100.0%	-	-
Demographics						
Mean age	52.1	10.5	52.0	10.6	0.107	0.010
Age: 18-39	2,269	15.8%	2,319	16.1%	-0.348	-0.009
Age: 40-54	5,386	37.5%	5,365	37.3%	0.146	0.003
Age: 55-65	6,715	46.7%	6,686	46.5%	0.202	0.004
Gender (Female)	7,680	53.4%	7,667	53.4%	0.090	0.002
Gender (Male)	6,690	46.6%	6,703	46.6%	-0.090	-0.002
Race (Black or African American)	2,723	18.9%	2,749	19.1%	-0.181	-0.005
Race (Unknown)	1,051	7.3%	1,126	7.8%	-0.522	-0.020
Race (White)	10,596	73.7%	10,495	73.0%	0.703	0.016
Hispanic Origin	501	3.5%	558	3.9%	-0.397	-0.021
Year (2008)	4,344	30.2%	4,223	29.4%	0.842	0.018
Year (2009)	6,654	46.3%	6,702	46.6%	-0.334	-0.007
Year (2010)	3,372	23.5%	3,445	24.0%	-0.508	-0.012
Recorded History of:						
AMI	1,612	11.2%	1,614	11.2%	-0.014	-0.000
Anxiety	1,825	12.7%	1,826	12.7%	-0.007	-0.000
Bipolar	2,876	20.0%	2,914	20.3%	-0.264	-0.007
Depression	3,137	21.8%	3,186	22.2%	-0.341	-0.008
Diabetes	7,470	52.0%	7,524	52.4%	-0.376	-0.008
Heart failure	3,373	23.5%	3,404	23.7%	-0.216	-0.005
Hypercholesterolemia	7,094	49.4%	7,157	49.8%	-0.438	-0.009
Hypertension	8,974	62.4%	9,064	63.1%	-0.626	-0.013
Kidney failure	3,524	24.5%	3,559	24.8%	-0.244	-0.006
Schizophrenia/psychotic	2,510	17.5%	2,452	17.1%	0.404	0.011
Substance abuse	1,044	7.3%	1,029	7.2%	0.104	0.004
Transient ischemic attack	432	3.0%	444	3.1%	-0.084	-0.005

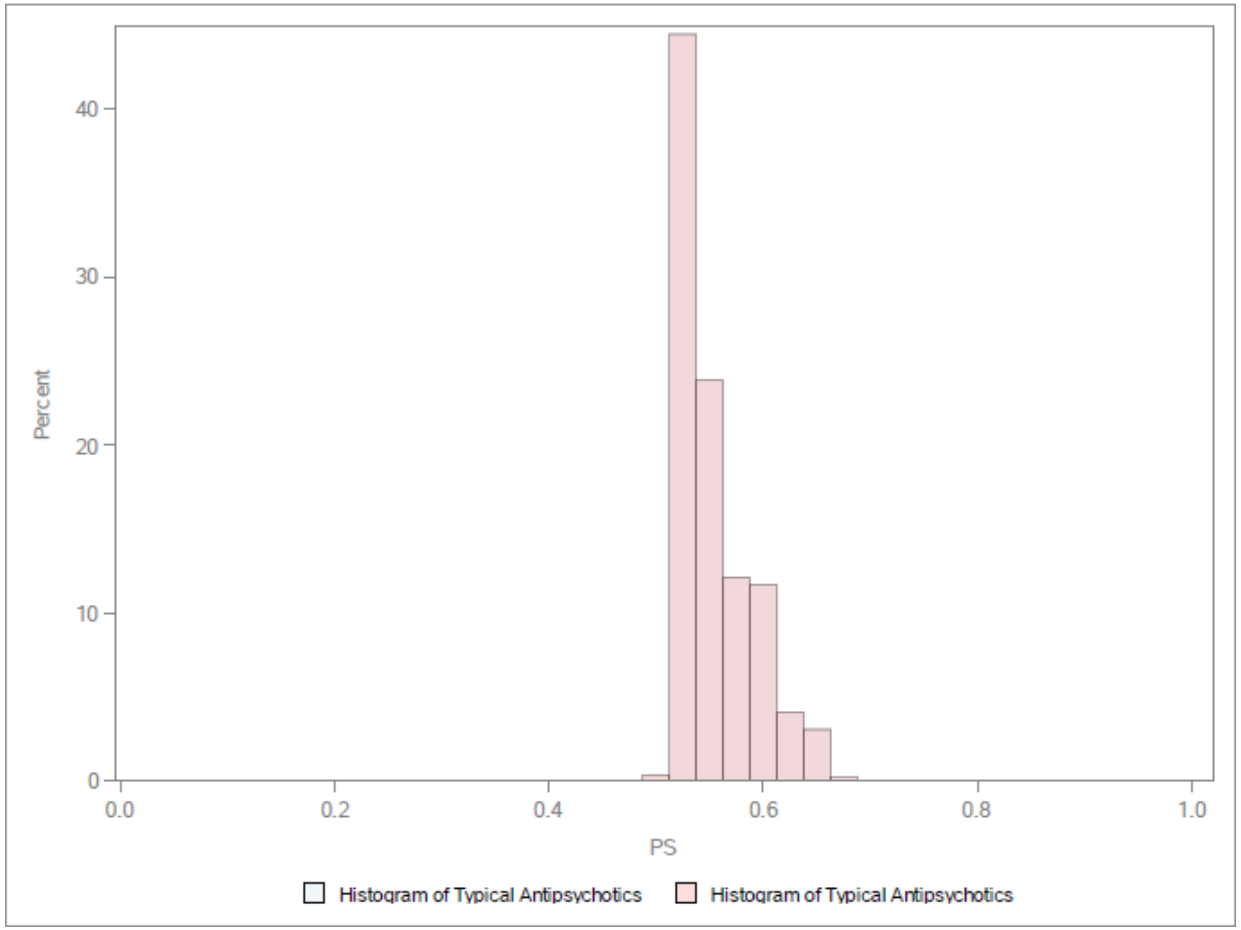
[1]Value represents standard deviation where no % follows the value
[2]Covariates in blue show a standardized difference greater than 0.1

Propensity Score Distribution

Histograms of Propensity Score Distribution Aggregated



Propensity score 1:1 Aggregated Matched Cohort, Matched Caliper = 0.05



Risk Estimates

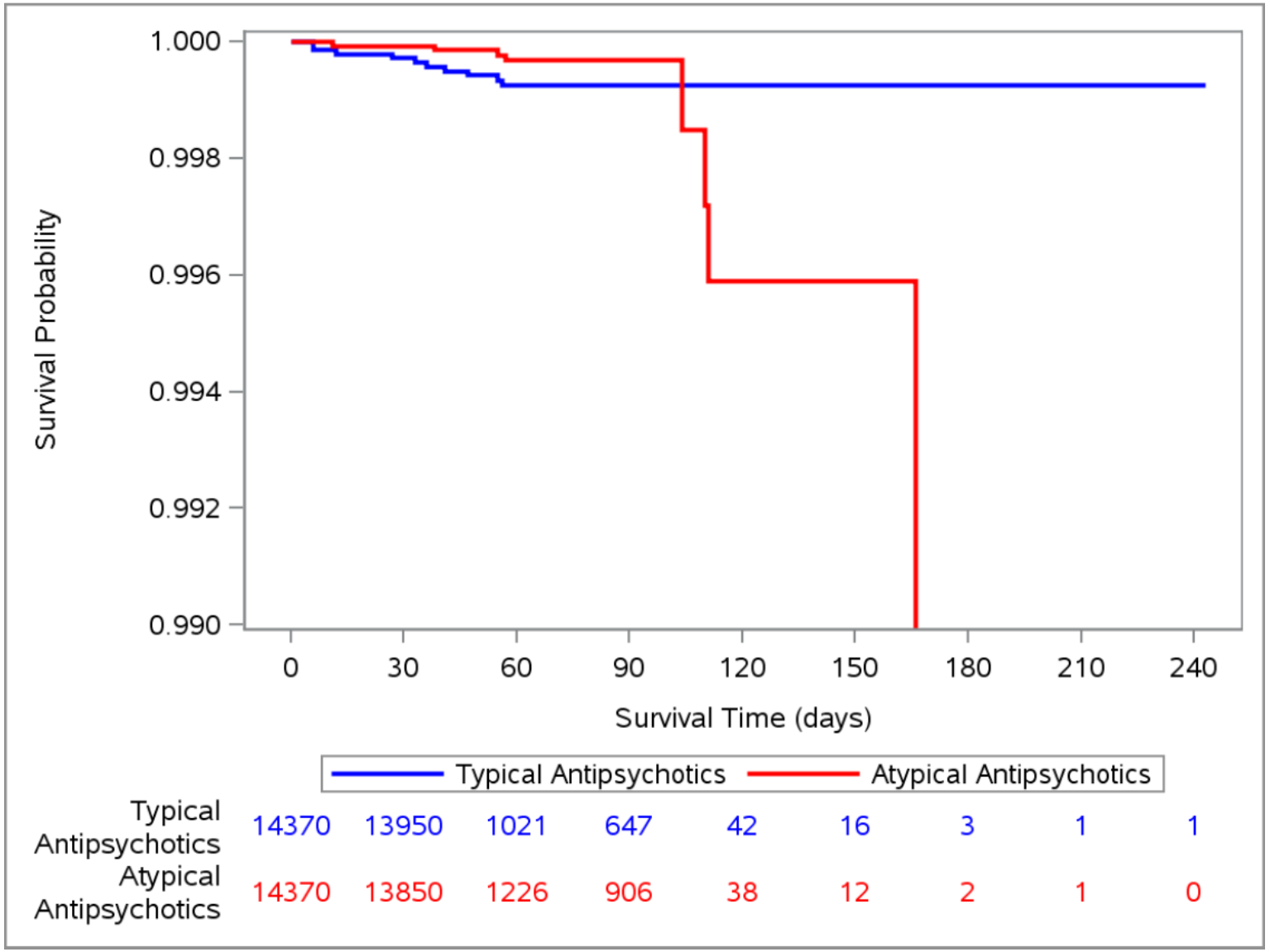
Table 2: Effect Estimates for Ischemic Stroke by Analysis Type

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% CI)	Wald P-Value
Unmatched Analysis (Site-adjusted only)											
Typical Antipsychotics	18,094	2,925.80	59.06	0.16	13	4.44	0.72	1.00	0.16	1.33 (0.55, 3.23)	0.529
Atypical Antipsychotics	14,370	2,324.53	59.08	0.16	8	3.44	0.56				
1:1 Matched Conditional Analysis; Caliper= 0.05[1]											
Typical Antipsychotics	14,370	2,067.32	52.55	0.14	10	4.84	0.70	2.42	0.35	2.00 (0.68, 5.85)	0.206
Atypical Antipsychotics	14,370	2,067.32	52.55	0.14	5	2.42	0.35				
1:1 Matched Unconditional Analysis; Caliper= 0.05											
Typical Antipsychotics	14,370	2,320.71	58.99	0.16	10	4.31	0.70	0.87	0.14	1.30 (0.51, 3.32)	0.583
Atypical Antipsychotics	14,370	2,324.53	59.08	0.16	8	3.44	0.56				

[1]Conditional analysis includes informative events and person-time.

Kaplan Meyer Survival Curve

Kaplan Meier Survival Curves of Events and Followup Time for Ischemic Stroke, Unconditional Matched Cohort.



Attrition Table – Proposed revision

- Reports the initial member count in a population
- Reports the loss in eligible members due to required enrollment coverage, inclusion and exclusion criteria, incidence washout, etc.

	Remaining	*Excluded*
Members meeting enrollment and demographic requirements		
Enrolled at any point during the query period		
Had required coverage type(s)		
Enrolled during specified age range		
Had requestable medical charts		
Met demographic requirements		
Members with a valid index event		
Had any cohort-defining claim		
Claim recorded during specified age range		
Met all episode definitions		
Met episode incidence requirement		
Had single NDC on index date		
Members with required pre-index history		
Had sufficient pre-index continuous enrollment		
Met event incidence criteria		
Had no recorded history of exclusion condition(s)		
Had recorded history of inclusion condition(s)		

Questions?

info@sentinelsystem.org

Sentinel

Case Study: Antipsychotics and Stroke
A Journey from Summary Table to Propensity Score Analysis

Ting-Ying Jane Huang, PhD

Sentinel Operations Center

August 29, 2019

THE JOURNAL OF CLINICAL PSYCHIATRY

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Antipsychotic Use and Stroke: A Retrospective Comparative Study in a Non-Elderly Population

Lockwood G. Taylor, PhD; Genna Panucci, MS; Andrew D. Mosholder, MD; Sengwee Toh, ScD; and Ting-Ying Huang, PhD

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DEPARTMENT OF POPULATION MEDICINE

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- Andy Mosholder
- Michael Nguyen

Sentinel

Many thanks are due to the Data Partners who provided the data used in these analyses

Outline

- Safety question
- Background rate: drug utilization
- Feasibility assessment: incidence rate in target population
- Comparative assessment: propensity score analysis
- Regulatory actions and publications

Safety Question

- In 2016, the FDA considered a proposed label change for warning/precaution regarding cerebrovascular events associated with antipsychotic use

Typical Antipsychotics
1. Prochlorperazine (Compazine)
2. Haloperidol (Haldol)
3. Loxapine (Loxitane)
4. Thioridazine (Mellaril)
5. Molindone (Moban)
6. Thiothixene (Navane)
7. Pimozide (Orap)
8. Fluphenazine (Prolixin)
9. Trifluoperazine (Stelazine)
10. Chlorpromazine (Thorazine)
11. Perphenazine (Trilafon)

Atypical Antipsychotics
1. Aripiprazole (Abilify)
2. Asenapine (Saphris)
3. Clozapine (Clozaril)
4. Iloperidone (Fanapt)
5. Lurasidone (Latuda)
6. Olanzapine (Zyprexa)
7. Olanzapine/fluoxetine (Symbyax)
8. Paliperidone (Invega)
9. Quetiapine (Seroquel)
10. Risperidone (Risperdal)
11. Ziprasidone (Geodon)

Existing language in safety label regarding cerebrovascular risk among elderly patients with dementia

Study	Population	Risk estimate (95% CI), stroke	Comparison
Cohort studies			
Barnett (2007)	Dementia	1.29 (0.48-3.47)	FGAs: unexposed
Gill (2005)	Dementia	1.01 (0.81-1.26)	Atypical:Typical
Hermann (2004)	65+ years old	1.1 (0.5-2.3)	Olanzapine: Typical
"	"	1.4(0.7-2.8)	Risperidone:Typical
Sacchetti (2008)	65+ years old	**2.34 (1.01-5.41)**	Phenothiazines:Atypical
Shin (2015a)	65+ years old	**3.47 (1.97-5.48)**	Chlorpromazine:Risperidone
Vasilyeva (2013)	65+ years old	1.14 (0.96-1.34)	SGA:FGA
Wang (2007)	Medicare	**1.09 (1.02-1.16)**	Typical:Atypical
Case-control			
Liperoti (2005)	Dementia	1.24 (0.95-1.63)	Conventional:unexposed
Hsieh (2013)	Schizophrenia	**2.75 (1.34-5.64)**	FGA:unexposed
Kleijer (2009)	50+ years old	**2.6 (1.3-5.0)**	Conventional:atypical
Laredo (2011)	Dementia	**1.46 (1.30-1.64)**	Typical: unexposed
Self-controlled			
Douglas (2008)	Stroke patients	**1.69 (1.55-1.84)**	Typical:unexposed
Pratt (2010)	65+ y.o. with stroke	**2.7 (1.8-4.0)**	Typical:unexposed
Wu (2013)	Stroke patients	**1.91 (1.67-2.18)**	SGA:FGA
"	"	**1.43 (1.34-1.51)**	FGA: unexposed
"	"	**2.3 (2.2-2.5)**	Prochlorperazine:unexposed

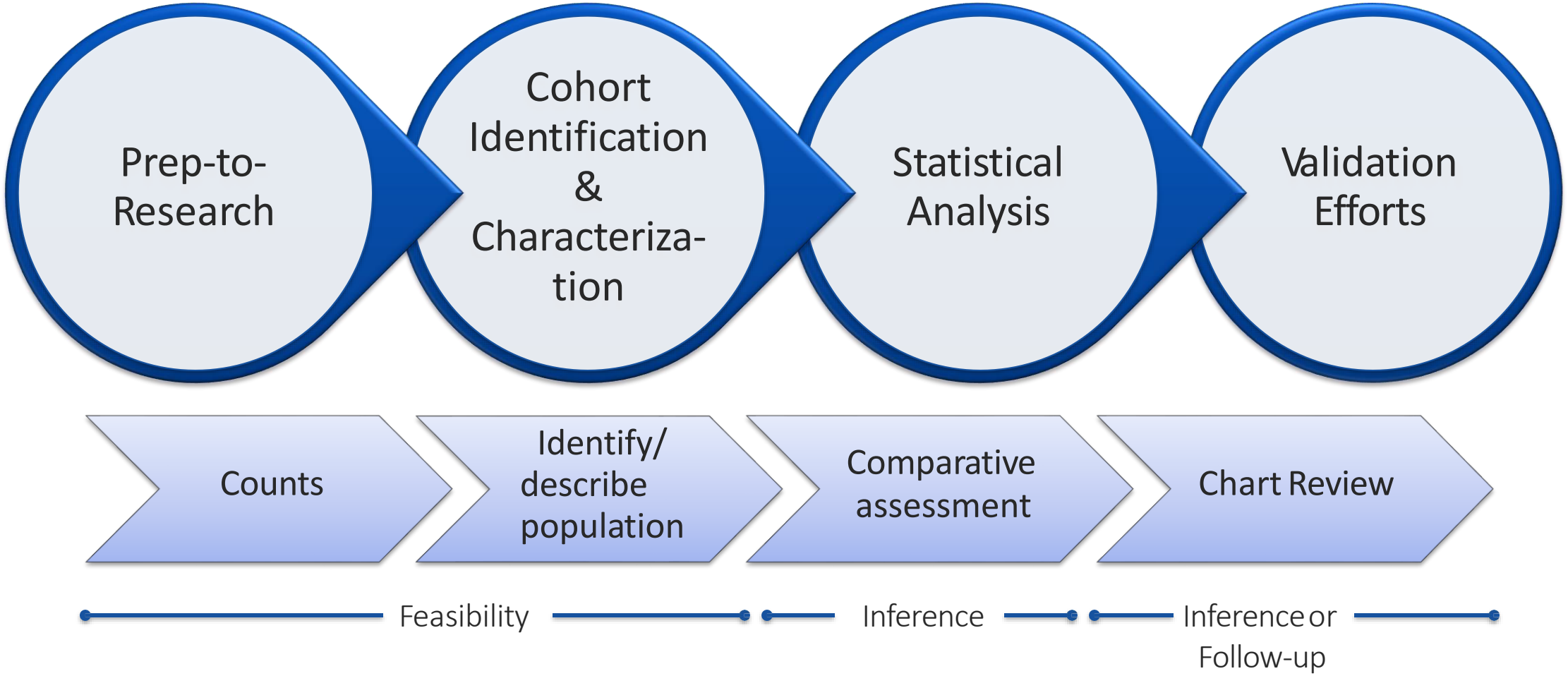
FGA first generation antipsychotics, SGA second generation antipsychotics

Study Questions

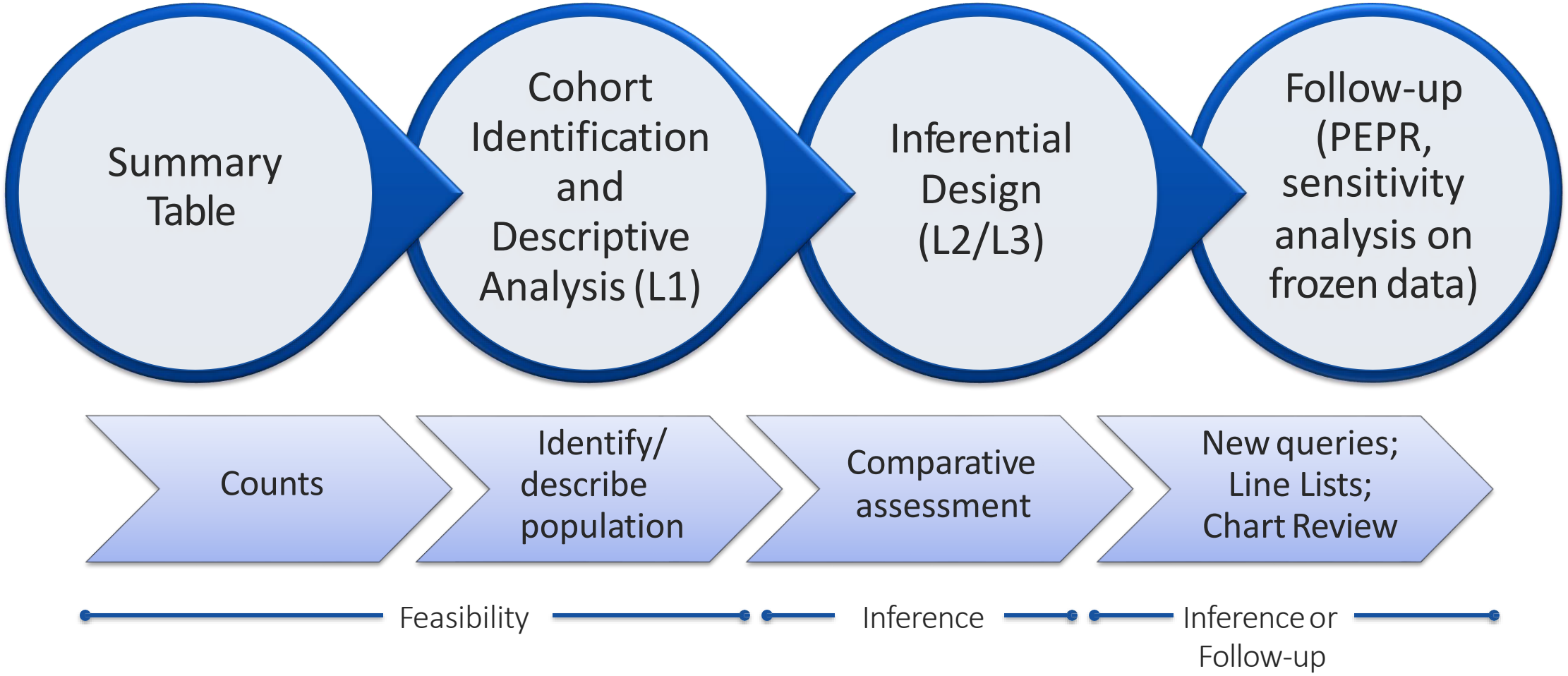
- Do younger (<65 years), non-demented users of typical antipsychotics (APs) have a higher risk of stroke, compared to users of atypical APs?
- Does AP dose modify this risk, haloperidol in particular?
- Is the risk highest in the first few days/weeks after initiating APs?

- Do concomitant users of atypical APs and antidepressants have a higher risk of stroke, compared to users of only antidepressants?

Typical Pharmacoepidemiologic Evaluation

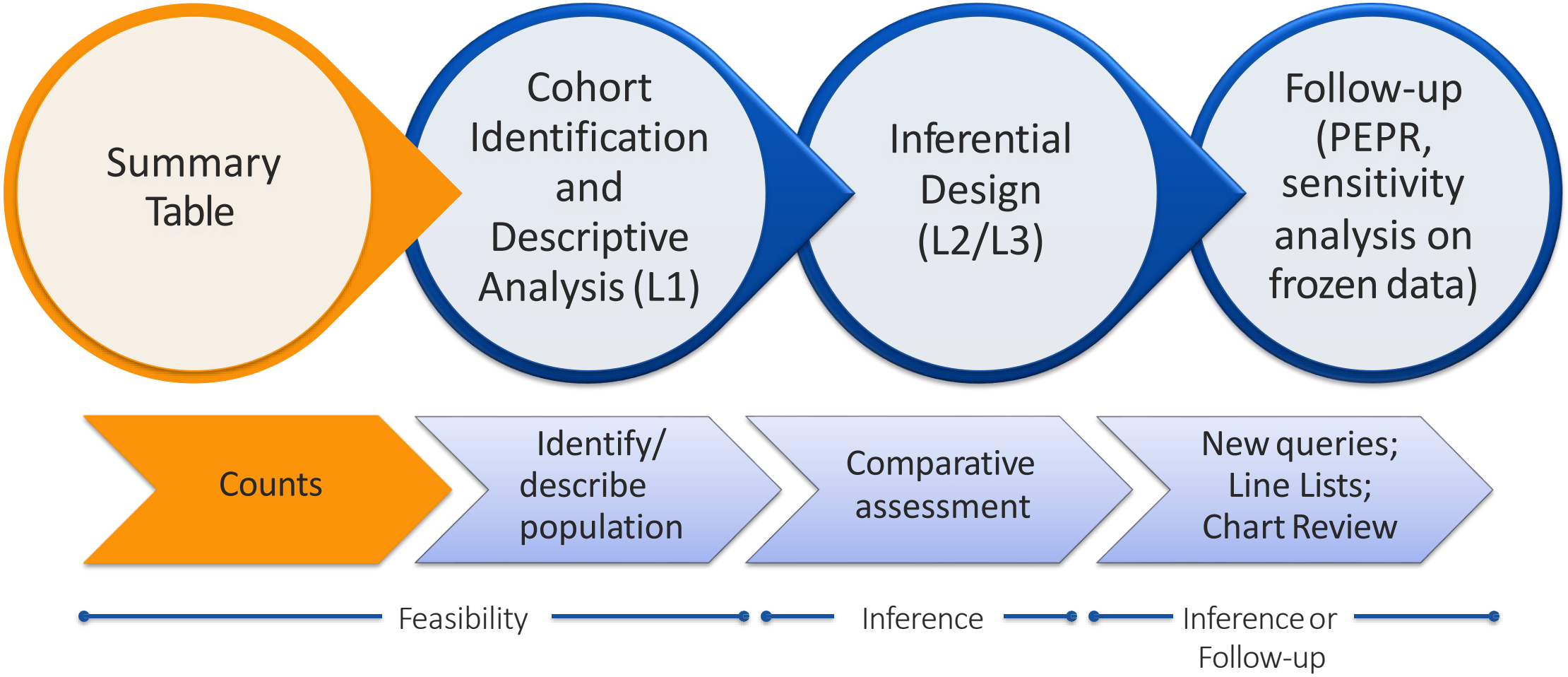


Safety Assessment in Sentinel



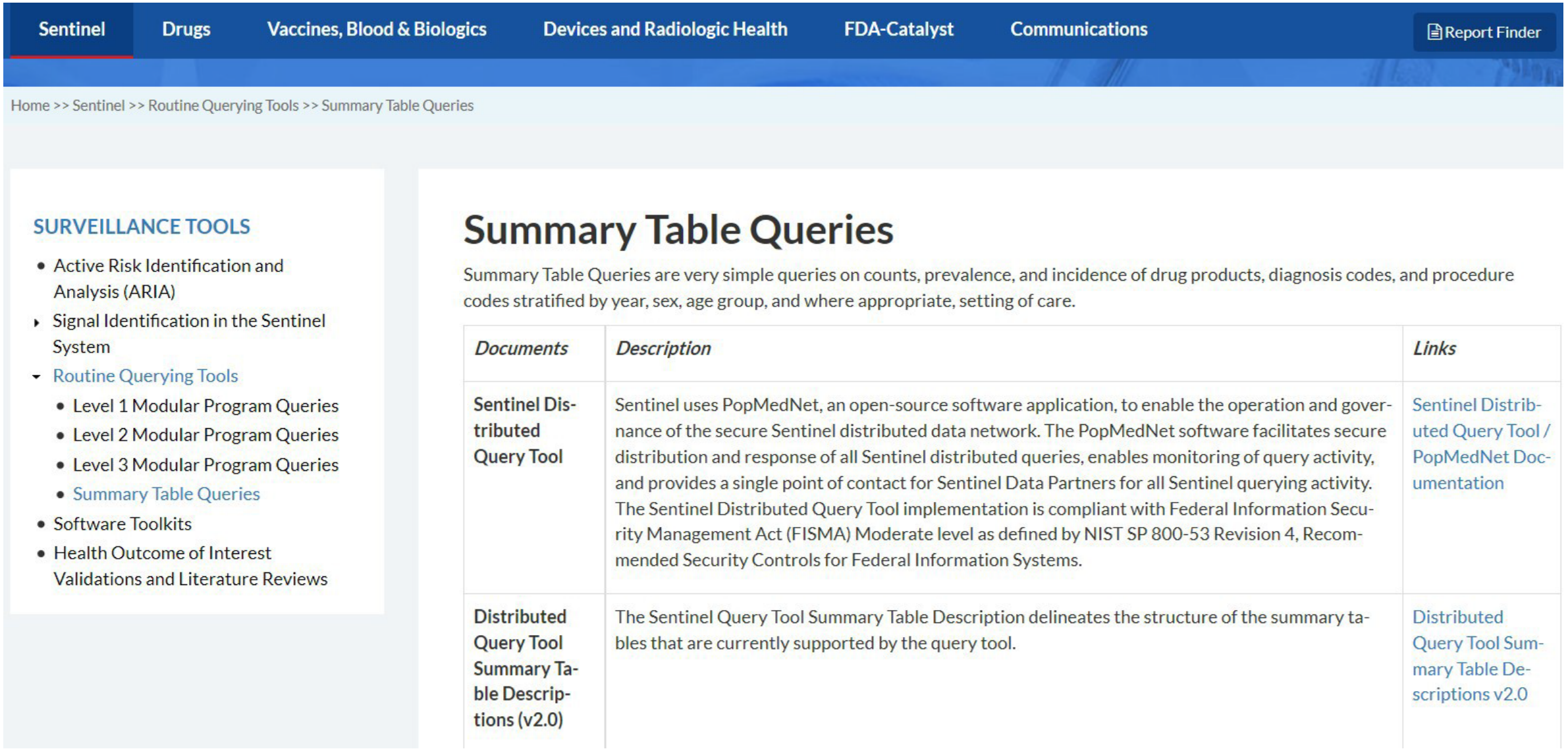
PEPR: Patient Episode Profile Retrieval

Safety Assessment in Sentinel



PEPR: Patient Episode Profile Retrieval

Summary Table



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Home >> Sentinel >> Routine Querying Tools >> Summary Table Queries

SURVEILLANCE TOOLS

- Active Risk Identification and Analysis (ARIA)
- Signal Identification in the Sentinel System
- Routine Querying Tools
  - Level 1 Modular Program Queries
  - Level 2 Modular Program Queries
  - Level 3 Modular Program Queries
  - Summary Table Queries
- Software Toolkits
- Health Outcome of Interest Validations and Literature Reviews

Summary Table Queries

Summary Table Queries are very simple queries on counts, prevalence, and incidence of drug products, diagnosis codes, and procedure codes stratified by year, sex, age group, and where appropriate, setting of care.

Documents	*Description*	*Links*
Sentinel Distributed Query Tool	Sentinel uses PopMedNet, an open-source software application, to enable the operation and governance of the secure Sentinel distributed data network. The PopMedNet software facilitates secure distribution and response of all Sentinel distributed queries, enables monitoring of query activity, and provides a single point of contact for Sentinel Data Partners for all Sentinel querying activity. The Sentinel Distributed Query Tool implementation is compliant with Federal Information Security Management Act (FISMA) Moderate level as defined by NIST SP 800-53 Revision 4, Recommended Security Controls for Federal Information Systems.	Sentinel Distributed Query Tool / PopMedNet Documentation
Distributed Query Tool Summary Table Descriptions (v2.0)	The Sentinel Query Tool Summary Table Description delineates the structure of the summary tables that are currently supported by the query tool.	Distributed Query Tool Summary Table Descriptions v2.0

Summary Table

Sentinel Distributed Query Tool Summary Table Descriptions

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II. SUMMARY TABLE OVERVIEW 1

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IV. DESCRIPTION OF SUMMARY TABLES 2

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B. Enrollment Summary Table 3
C. ICD-9-CM Diagnosis Summary Table (3 digit) 4
D. ICD-9-CM Diagnosis Summary Table (4 digit) 5
E. ICD-9-CM Diagnosis Summary Table (5 digit) 6
F. HCPCS Summary Table 6
G. ICD-9-CM Procedure Summary Table (3 digit) 7
H. ICD-9-CM Procedure Summary Table (4 digit) 8
I. Ingredient Name Summary Table 9
J. Drug Category Summary Table 10
K. Incident ICD-9-CM Diagnosis Summary Table (3 Digit) 10
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Summary Table

Sentinel Distributed Query Tool Summary Table Descriptions

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I. QUERY TOOL OVERVIEW 1

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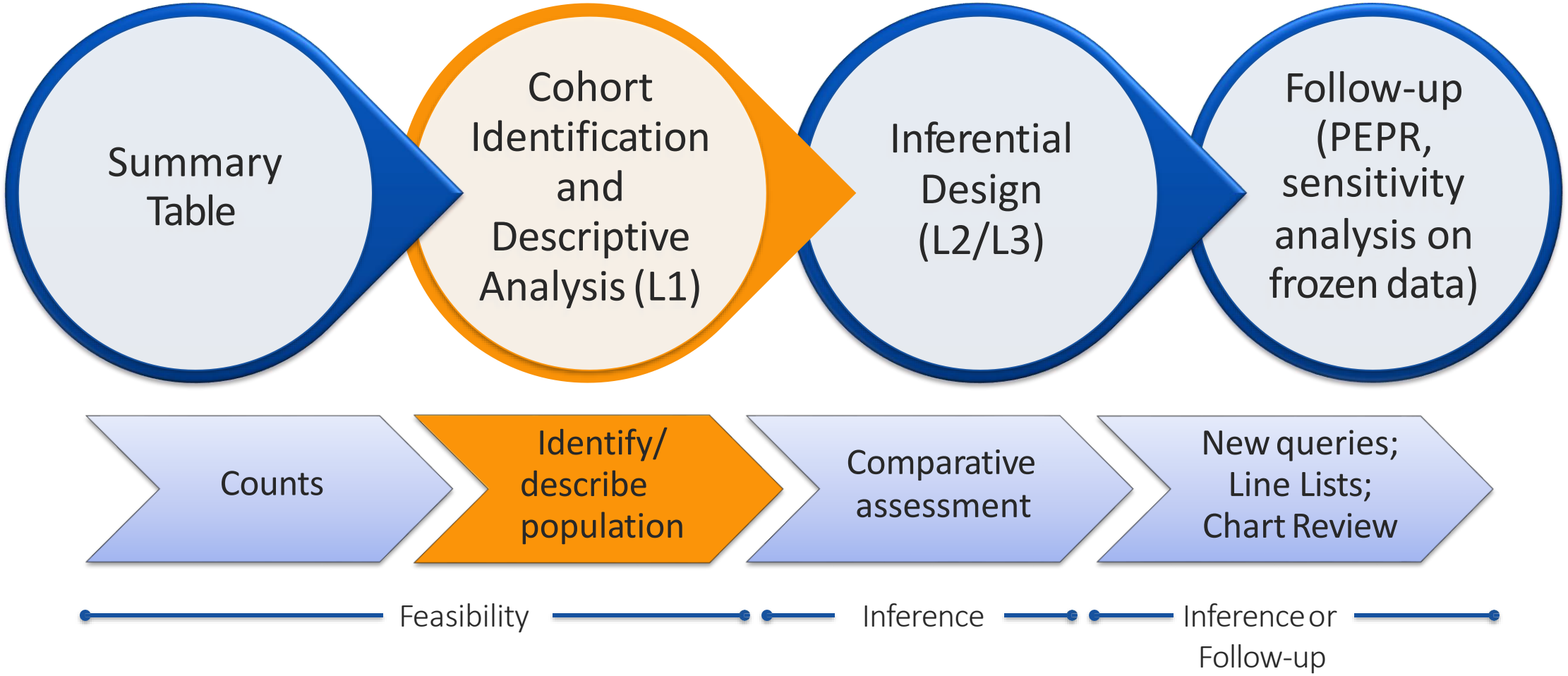
L. Incident Drug Category Summary Table 11
M. Incident Ingredient Name Summary Table 13

Table 1. Number of Prevalent OLANZAPINE Users, Number of Dispensings, and Total Days Supplied by Year, Sex, and Age Group

Generic Name	OLANZAPINE	Selecting generic name here will update table below. Select only one generic name.

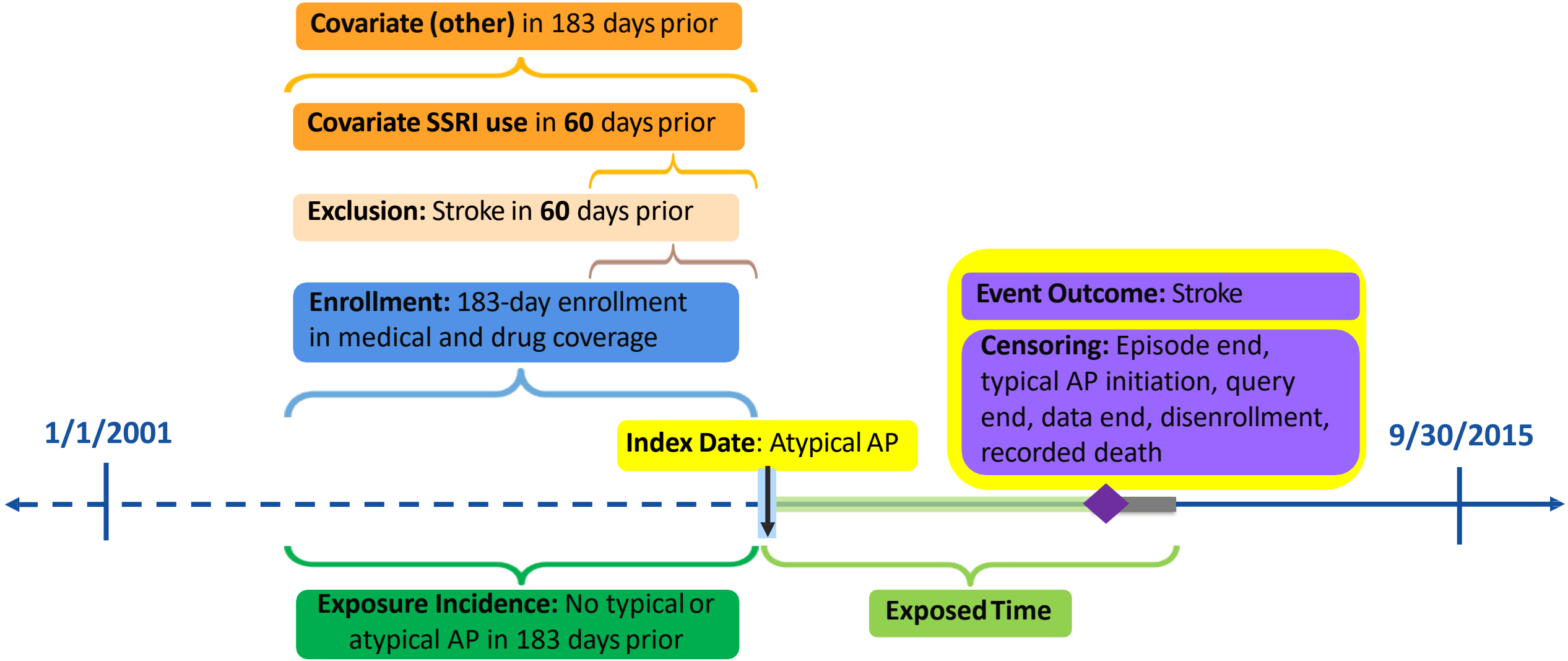
			Data		
Year	Sex	Age Group	Number of Users	Number of Dispensings	Days Supplied
2010	M	19-21	1,286	5,289	169,115
		22-44	7,150	34,822	1,170,166
		45-64	7,400	39,889	1,406,770
		65-74	1,528	7,747	287,870
		75+	1,900	8,751	300,611
	F	19-21	624	2,040	63,607
		22-44	6,970	27,797	918,213
		45-64	9,477	47,545	1,710,644
		65-74	2,548	13,923	506,209
		75+	4,449	24,823	853,600
2011	M	19-21	1,436	5,830	183,938
		22-44	7,146	35,540	1,196,473

Safety Assessment in Sentinel



PEPR: Patient Episode Profile Retrieval

L1: Feasibility Assessment (CIDA Type 2)



L1 Results

Table 1: Baseline Characteristics of Patients Exposed to Atypical or Typical Antipsychotics, Scenarios with Outcome = Ischemic Stroke

	Atypical		Typical		Haloperidol	
	N | Mean	% | Std	N | Mean	% | Std	N | Mean	% | Std
Number of patients	1,241,864		148,229		81,883	
Age	48.6	19	62.4	18.3	70	17.9
Age: 18-39	474,808	38.2%	24,654	16.6%	8,590	10.5%
Age: 40-54	348,067	28.0%	29,237	19.7%	9,914	12.1%
Age: 55+	418,989	33.7%	94,338	63.6%	63,379	77.4%
Female	756,054	60.9%	71,550	48.3%	45,671	55.8%
Haloperidol Low (0.5-2 mg)					55,087	67.3%
Haloperidol Medium (5-10 mg)					11,749	14.3%
Haloperidol High (20 mg)					104	0.1%
Haloperidol Liquid					15,314	18.7%
Stroke in prior 3-6 months	16,549	1.3%	3,218	2.2%		
SSRI in prior 3-6 months	412,230	33.2%	29,677	20.0%		
					15,586	19.0%
					27,506	33.6%
Hypertension	383,517	30.9%	70,546	47.6%	44,579	54.4%
Kidney Failure	71,968	5.8%	23,285	15.7%	18,059	22.1%
Transient Ischemic Attack	14,457	1.2%	2,864	1.9%	2,135	2.6%

1. Product strength, but not daily dose, of index exposure is readily available in SCDM
2. Comparative analyses stratified by index exposure product strength may experience sample size issue

How many concomitant SSRI users do we gain if we extend the concomitancy definition from 2 to 6 months prior to index date?

How many AP users with stroke history do we lose if we extend stroke exclusion from 2 to 6 months prior to index date?

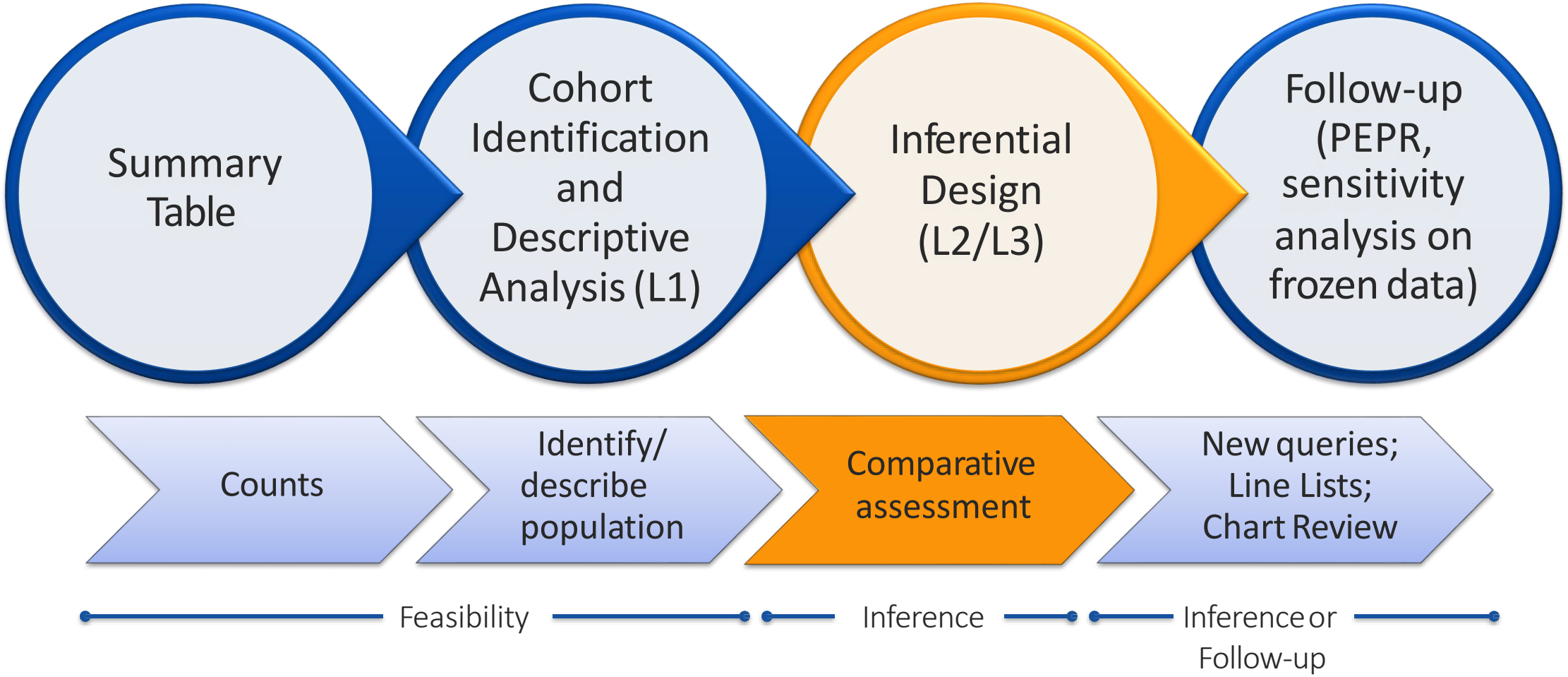
L1 Results

Table 4: Summary of Stroke following Treatment with Atypical or Typical Antipsychotics, with or without Selective Serotonin Reuptake Inhibitors (SSRIs) in the Sentinel Distributed Database between January 1, 2001 and September 30,

Scenarios with Outcome = Ischemic Stroke

	New Users	Years at Risk	New Users w/ Outcome	New Users w/ Outcome / 10K Years at Risk
Atypical Antipsychotics and Ischemic Stroke				
	1,241,864	631,084.5	2,669	42.29
Typical Antipsychotics and Ischemic Stroke				
	148,229	35,356.6	339	95.88
Haloperidol and Ischemic Stroke				
	81,883	17,602.5	247	140.32

Safety Assessment in Sentinel



PEPR: Patient Episode Profile Retrieval

Study Questions

- Do younger (<65 years), non-demented users of typical antipsychotics (APs) have a higher risk of stroke, compared to users of atypical APs?
- Does AP dose modify this risk, haloperidol in particular?
- Is the risk highest in the first few days/weeks after initiating APs?

- Do concomitant users of atypical APs and antidepressants have a higher risk of stroke, compared to users of only antidepressants?

Study Questions

- Do younger (<65 years), non-demented users of typical antipsychotics (APs) have a higher risk of stroke, compared to users of atypical APs?
- Does AP dose modify this risk, haloperidol in particular?
- Is the risk highest in the first few days/weeks after initiating APs?

Study Questions

- Do younger (<65 years), non-demented users of typical antipsychotics (APs) have a higher risk of stroke, compared to users of atypical APs?
- Is the risk highest in the first few days/weeks after initiating APs?

Study Questions

Specifications for Request ID cder_mpl2p_wp004

The Center for Drug Evaluation and Research has requested execution of the Cohort Identification and Descriptive Analysis (CIDA) tool with Propensity Score Matching (PSM) to investigate the risk of ischemic and hemorrhagic stroke among new users of typical antipsychotics compared to new users of atypical antipsychotics with varying risk windows.

Query Period: January 1, 2001 - September 30, 2015
Coverage Requirement: Medical and Drug Coverage
Enrollment Requirement: 183 days
Enrollment Gap: 45 Days
Age Group(s): 18-64 years

	Exposure/Comparator Pair 1		Exposure/Comparator Pair 2		Exposure/Comparator Pair 3		Exposure/Comparator Pair 4	
Drug/Exposure								
Incident Exposure/Comparator	All typical antipsychotics	All atypical antipsychotics	All typical antipsychotics (risk window = 1-15 days)	All atypical antipsychotics (risk window = 1-15 days)	All typical antipsychotics (risk window = 16-90 days)	All atypical antipsychotics (risk window = 16-90 days)	Haloperidol	All atypical antipsychotics
Incident w/ Respect to:	All atypical and typical antipsychotics	All atypical and typical antipsychotics	All atypical and typical antipsychotics	All atypical and typical antipsychotics	All atypical and typical antipsychotics	All atypical and typical antipsychotics	All atypical and typical antipsychotics	All atypical and typical antipsychotics
Washout	183 days	183 days	183 days	183 days	183 days	183 days	183 days	183 days
Cohort Definition	Cohort includes only the first valid incident treatment episode during the query period	Cohort includes only the first valid incident treatment episode during the query period	Cohort includes only the first valid incident treatment episode during the query period	Cohort includes only the first valid incident treatment episode during the query period	Cohort includes only the first valid incident treatment episode during the query period	Cohort includes only the first valid incident treatment episode during the query period	Cohort includes only the first valid incident treatment episode during the query period	Cohort includes only the first valid incident treatment episode during the query period
Episode Gap	30 days	30 days	30 days	30 days	30 days	30 days	30 days	30 days
Episode Extension Period	None	None	None	None	None	None	None	None
Minimum Episode Duration	1 day	1 day	1 day	1 days	16 days	16 days	1 day	1 day
Maximum Episode Duration	None	None	15 days	15 days	90 days	90 days	None	None
Episode Truncation for Exposure	All atypical antipsychotics	All typical antipsychotics	All atypical antipsychotics	All typical antipsychotics	All atypical antipsychotics	All typical antipsychotics	All atypical and typical antipsychotics (except Haloperidol)	All typical antipsychotics
Inclusion/Exclusion								
Pre-Existing Condition	Dementia	Dementia	Dementia	Dementia	Dementia	Dementia	Dementia	Dementia
Include/Exclude	Exclude	Exclude	Exclude	Exclude	Exclude	Exclude	Exclude	Exclude
Care Settings/PDX	Any	Any	Any	Any	Any	Any	Any	Any

Study Questions

- Do younger (<65 years), non-demented users of typical antipsychotics (APs) have a higher risk of stroke, compared to users of atypical APs?
- Does AP dose modify this risk, haloperidol in particular?
- Is the risk highest in the first few days/weeks after initiating APs?

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Study Questions

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Comparative Assessment

- Do concomitant users of atypical APs and antidepressants have a higher risk of stroke, compared to users of only antidepressants?

Comparative Assessment

Compare AP users to whom?

- Do concomitant users of atypical APs and antidepressants have a higher risk of stroke, compared to users of only antidepressants?

Comparative Assessment

Options for the comparator group

1. AP users themselves: self-controlled design
2. Non-users: exact match on age, sex, and/or calendar time
3. Antidepressant users: prevalent new user design
4. Negative controls: users of another drug class with similar indications but no known associated risk for stroke

Comparative Assessment

Options for the comparator group

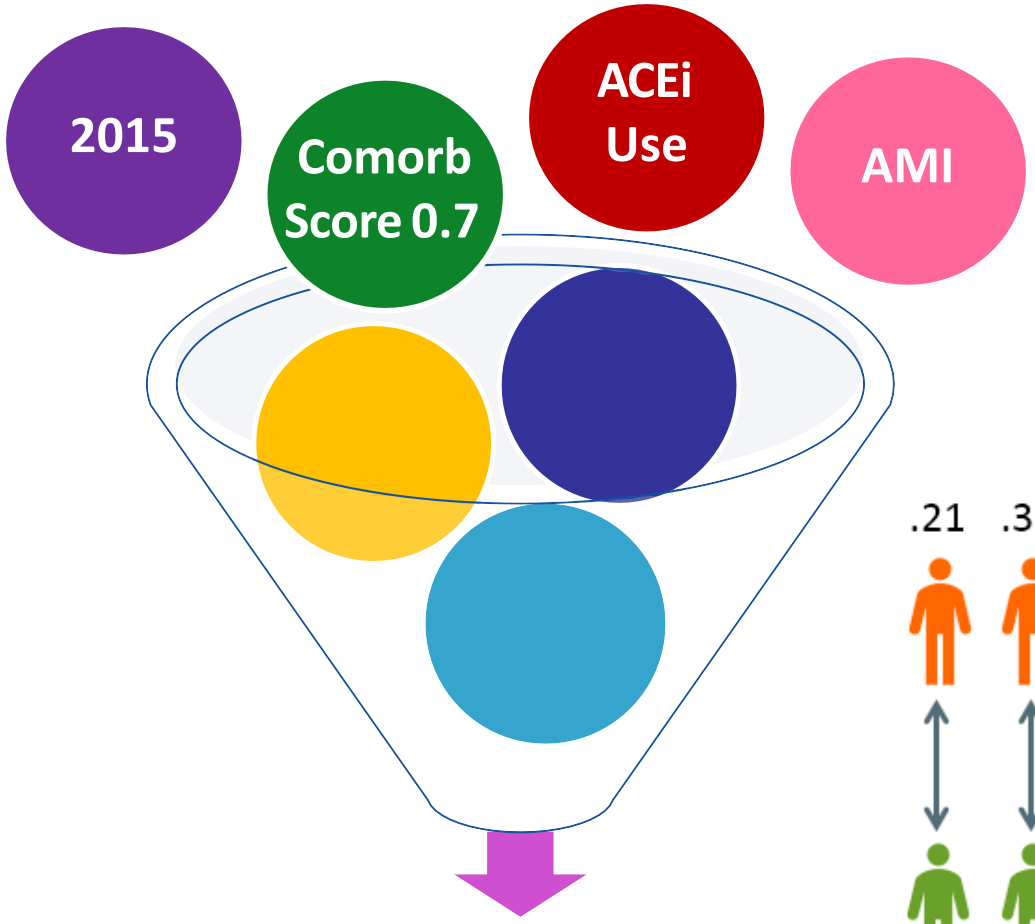
1. AP users themselves: self-controlled design
2. Non-users: exact match on age, sex, and/or calendar time
3. Antidepressant users: prevalent new user design

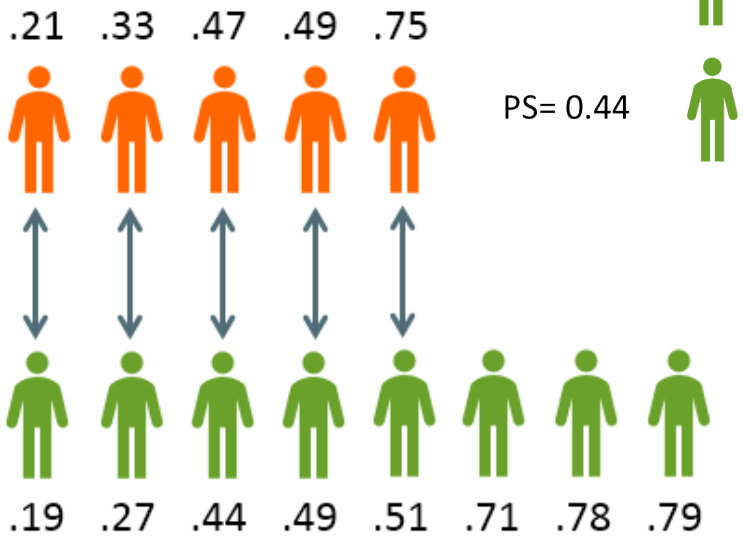
4.Negative controls: users of another drug class with similar indications but no known associated risk for stroke

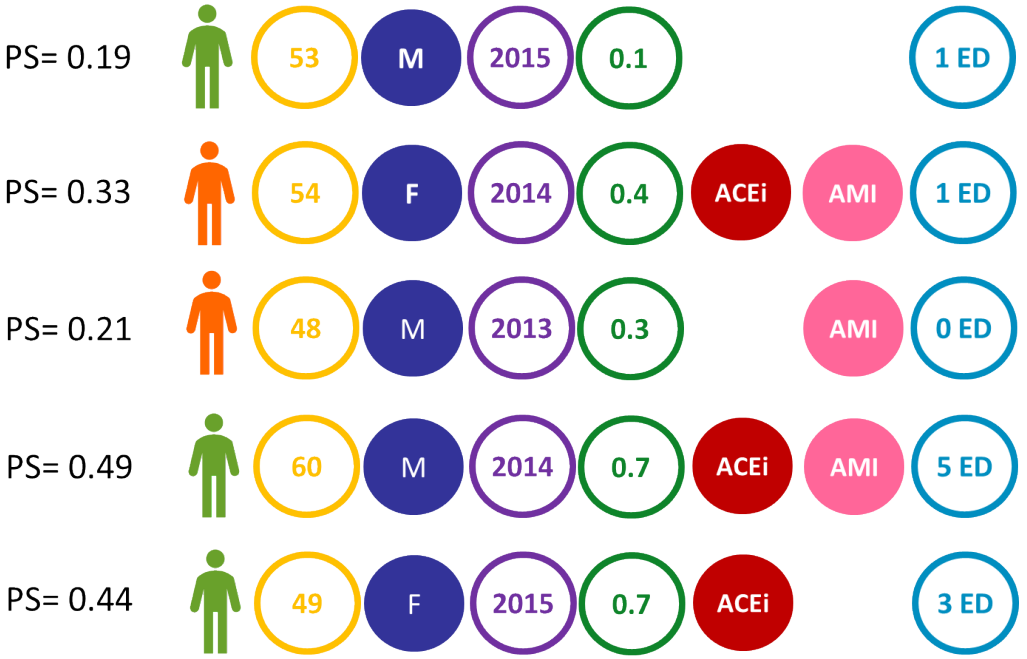
- Z-hypnotics: non-benzodiazepine hypnotics zolpidem, eszoplicone, zaleplon, used in treatment of insomnia

→ Final comparison: AP users vs z-hypnotic users, with existing SSRI use at baseline

1:1 Propensity Score Matching







https://www.sentinelinitiative.org/communications/sentinel-initiative-events/sentinel-initiative-public-workshop-tenth-annual-day-2

L2 Results: Typical vs Atypical APs

Baseline Characteristics
Unmatched & Matched Cohorts

	Unmatched			Matched		
Selected characteristics	**Typical AP N (%/SD*)**	**Atypical AP N (%/ SD*)**	**Std Diff**	**Typical AP N (%/ SD*)**	**Atypical AP N (%/ SD*)**	**Std Diff**
Total	45,576	806,611		45,495	45,495	
Mean age	44.0 (12.6*)	39.9 (12.8*)	0.324	44.0 (12.6*)	44.2 (12.7*)	-0.020
Female	21,206 (46.5)	489,469 (60.7)	-0.287	21,194 (46.6)	20,987 (46.1)	0.009
Afib/flutter	648 (1.4)	4,745 (0.6)	0.084	620 (1.4)	660 (1.5)	-0.007
AMI	899 (2.0)	7,789 (1.0)	0.084	879 (1.9)	928 (2.0)	-0.008
Diabetes	5,226 (11.5)	52,950 (6.6%)	0.172	5,182 (11.4)	5,393 (11.9)	-0.014
HTN	9,800 (21.5)	120,258 (14.9)	0.171	9,754 (21.4)	9,886 (21.7)	-0.007
Renal failure	1,869 (4.1)	11,495 (1.4)	0.164	1,817 (4.0)	1,855 (4.1)	-0.004
Depression	10,603 (23.3)	324,387 (40.2)	-0.370	10,586 (23.3)	10,860 (23.9)	-0.014
Schizophrenia	5,687 (12.5)	56,550 (7.0)	0.185	5,676 (12.5)	5,998 (13.2)	-0.021
ACE-inhibitor	6,152 (13.5)	75,035 (9.3)	0.132	6,125 (13.5)	6,228 (13.7)	-0.007
Beta-blockers	5,786 (12.7)	76,471 (9.5)	0.103	5,753 (12.6)	5,857 (12.9)	-0.007
Oral anti-coagulants	1,025 (2.2)	9,540 (1.2)	0.082	993 (2.2)	981 (2.2)	0.002
Statins	6,787 (14.9)	91,915 (11.4)	0.104	6,762 (14.9)	6,928 (15.2)	-0.010

L2 Results

Stroke Risk for Antipsychotics (AP):

Overall, 1-15 days, 16-90 days, Haloperidol only

	Unmatched (site adjusted-only)				1:1 matched			
	# Exposed	Person years	# Events	HR (95% CI)	# Exposed	Person years	# Events	HR (95% CI)
Overall								
Typical AP	45,576	10,125.82	25	1.75 (1.17-2.63)	45,495	10,113.92	25	**0.87 (0.54-1.41)**
Atypical AP	806,611	338,987.22	396	1 (Ref)	45,495	20,646.19	53	1 (Ref)
1-15 days after exposure								
Typical AP	45,576	1,534.75	7	3.06 (1.37-6.83)	45,495	1,532.82	7	**1.16 (0.41-3.32)**
Atypical AP	806,611	32,431.81	42	1 (Ref)	45,495	1,829.06	7	1 (Ref)
16-90 days after exposure								
Typical AP	30,204	3,109.76	6	1.23 (0.54-2.80)	30,186	3,107.76	6	**0.52 (0.20-1.36)**
Atypical AP	757,812	96,228.27	124	1 (Ref)	30,186	3,885.00	14	1 (Ref)
Haloperidol only								
Haloperidol	13,882	3,369.51	9	1.80 (0.93-3.48)	13,841	3,366.33	9	**1.31 (0.54-3.21)**
Atypical AP	801,275	336,212.38	397	1 (Ref)	13,841	6,482.65	11	1 (Ref)

Survival Probability

Typical
Atypical

L2 Results:
Atypical APs + SSRI vs Z-Hypnotics + SSRI

Stroke Risk for Atypical Antipsychotics (APs) vs. z-hypnotics, adjusted for duration of SSRI use

	Unmatched (site-adjusted only)				1:1 matched			
	# Exposed	Person years	# Events	HR (95% CI)	# Exposed	Person years	# Events	HR (95% CI)
Overall								
Atypical AP + SSRI	303,428	121,662.27	147	0.89 (0.70-1.13)	214,453	85,129.30	112	**1.31 (0.93-1.84)**
Z-hyp + SSRI	516,456	131,308.61	144	1 (Ref)	214,453	52,090.92	49	1 (Ref)
1-15 days								
Atypical AP + SSRI	303,428	12,156.06	11	0.74 (0.35-1.56)	214,453	8,600.55	5	**0.71 (0.23-2.25)**
Z-hyp + SSRI	516,456	20,055.07	20	1 (Ref)	214,453	8,297.13	7	1 (Ref)
16-90 days								
Atypical AP + SSRI	286,586	36,596.09	45	0.88 (0.58-1.32)	192,817	24,316.00	32	**1.33 (0.76-2.33)**
Z-hyp + SSRI	438,894	43,234.33	51	1 (Ref)	192,817	19,349.82	20	1 (Ref)

Discussion

- No significant associations found in either analysis
  - Typical vs atypical APs: crude increased HR adjusted away with 1:1 propensity-score matching
  - Atypical vs z-hypnotics: modestly, but non-significant, increased HRs
  - Increased risk not ruled out completely
- Event rates low in non-elderly population
- 1:1 propensity-score matching reduced sample size and precision of estimates
  - Trade-off with improved confounding adjustment
- Did not assess subgroup risk by age group, dose

https://www.sentinelinitiative.org/sites/default/files/communications/publications-presentations/Sentinel-ICPE-2017-Symposium-Snapshot-of-the-First-Year_Antipsychotic_stroke.pdf

Regulatory Actions and Publications

- FDA decided that no action was necessary
  - Study results did not warrant labeling stroke risk for non-elderly/non-demented patients taking APs
- Presentation at the 2017 International Conference on Pharmacoepidemiology & Therapeutic Risk Management
- Taylor LG, Panucci G, Mosholder AD, Toh S, Huang TY, 2019. Antipsychotic Use and Stroke: A Retrospective Comparative Study in a Non-Elderly Population. The Journal of Clinical Psychiatry, 80(4).

https://www.sentinelinitiative.org/communications/publications/2017-icpe-symposium-integrating-sentinel-routine-regulatory-drug-review

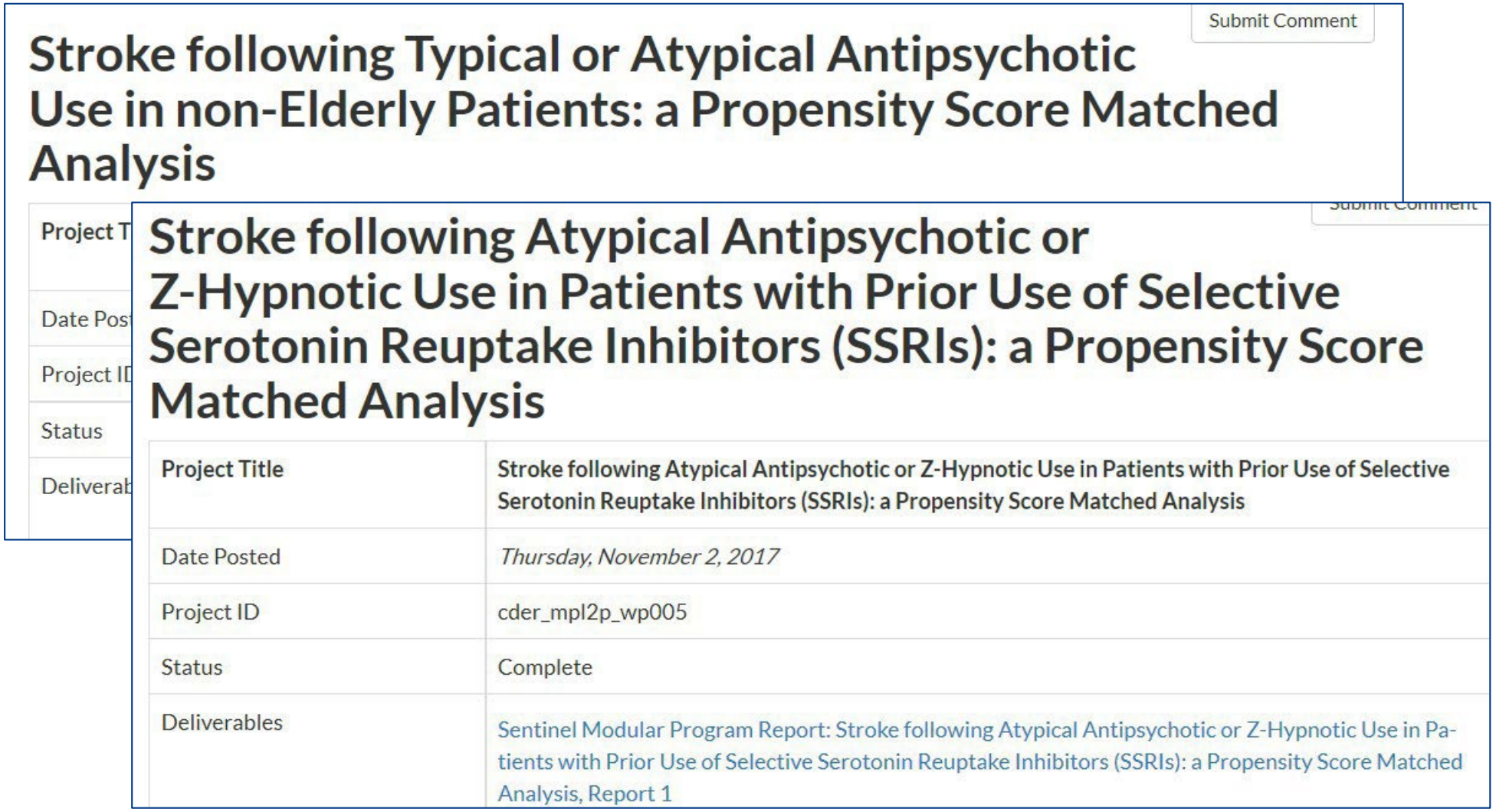
For More Information …

Submit Comment

Stroke following Typical or Atypical Antipsychotic Use in non-Elderly Patients: a Propensity Score Matched Analysis

Project Title	**Stroke following Typical or Atypical Antipsychotic Use in non-Elderly Patients: a Propensity Score Matched Analysis**
Date Posted	*Thursday, November 2, 2017*
Project ID	cder_mpl2p_wp004
Status	Complete
Deliverables	Sentinel Modular Program Report: Stroke following Typical or Atypical Antipsychotic Use in non-Elderly Patients: a Propensity Score Matched Analysis, Report 1

For More Information …



For More Information …

Sentinel

Sentinel Analytic Packages

https://dev.sentinelsystem.org/projects/AP/repos/sentinel-analytic-packages/browse

Overview

A Sentinel analytic package is a standard folder structure containing detailed user-defined specifications, input files, SAS® macros, and SAS programs used to c
the user to select the cohort(s) of interest in order to examine their health profile and outcomes.

Sentinel's analytic request packages are intended to run on data formatted in accordance with the Sentinel Common Data Model (SCDM). Note that data must b

Analytic Request Packages Available for Download

Request ID	Summary
cder_mpl2r_wp008	Acute Myocardial Infarction and Hospitalized Heart Failure following Saxagliptin or Sitagliptin Use: a Propensity Score Matched Analysis
cder_mpl2p_wp009	Stroke, Gastrointestinal Bleeding, and Intracranial Hemorrhage following Apixaban or Warfarin Use in Patients with Non-Valvular Atrial F
cder_mpl2p_wp006	Seizure following Ranolazine Use: a Self-Controlled Risk Interval Analysis (an update to cder_mpl2p_wp002)
cder_mpl2p_wp005	Stroke following Atypical Antipsychotic or Z-Hypnotic Use in Patients with Prior Use of Selective Serotonin Reuptake Inhibitors (SSRIs): a
cder_mpl2p_wp001	Venous Thromboembolism following Continuous or Extended Cycle Contraceptive Use: a Propensity Score Matched Analysis
cder_mpl2p_wp004	Stroke following Typical or Atypical Antipsychotic Use in non-Elderly Patients: a Propensity Score Matched Analysis

Questions?

info@sentinelsystem.org

Coffee Break

2:15pm – 2:30pm

If you are not attending the CIDA Lab, please remember to complete and return the survey at this time.

Sentinel

Overview of Cohort Identification and Descriptive Analysis (CIDA) SAS Analytic Package Creation

Judith C. Maro, PhD

Sentinel Operations Center

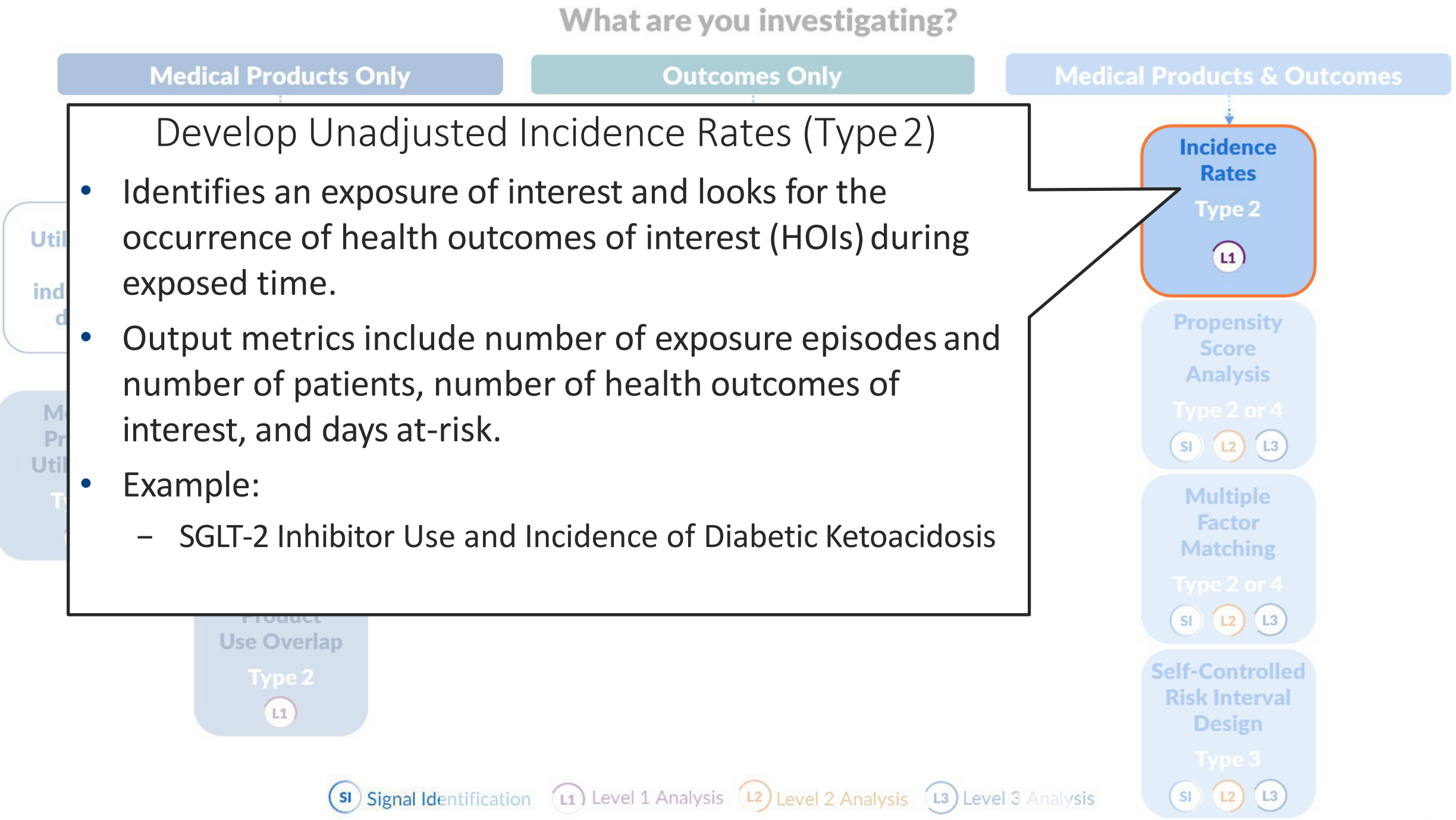
August 29, 2019

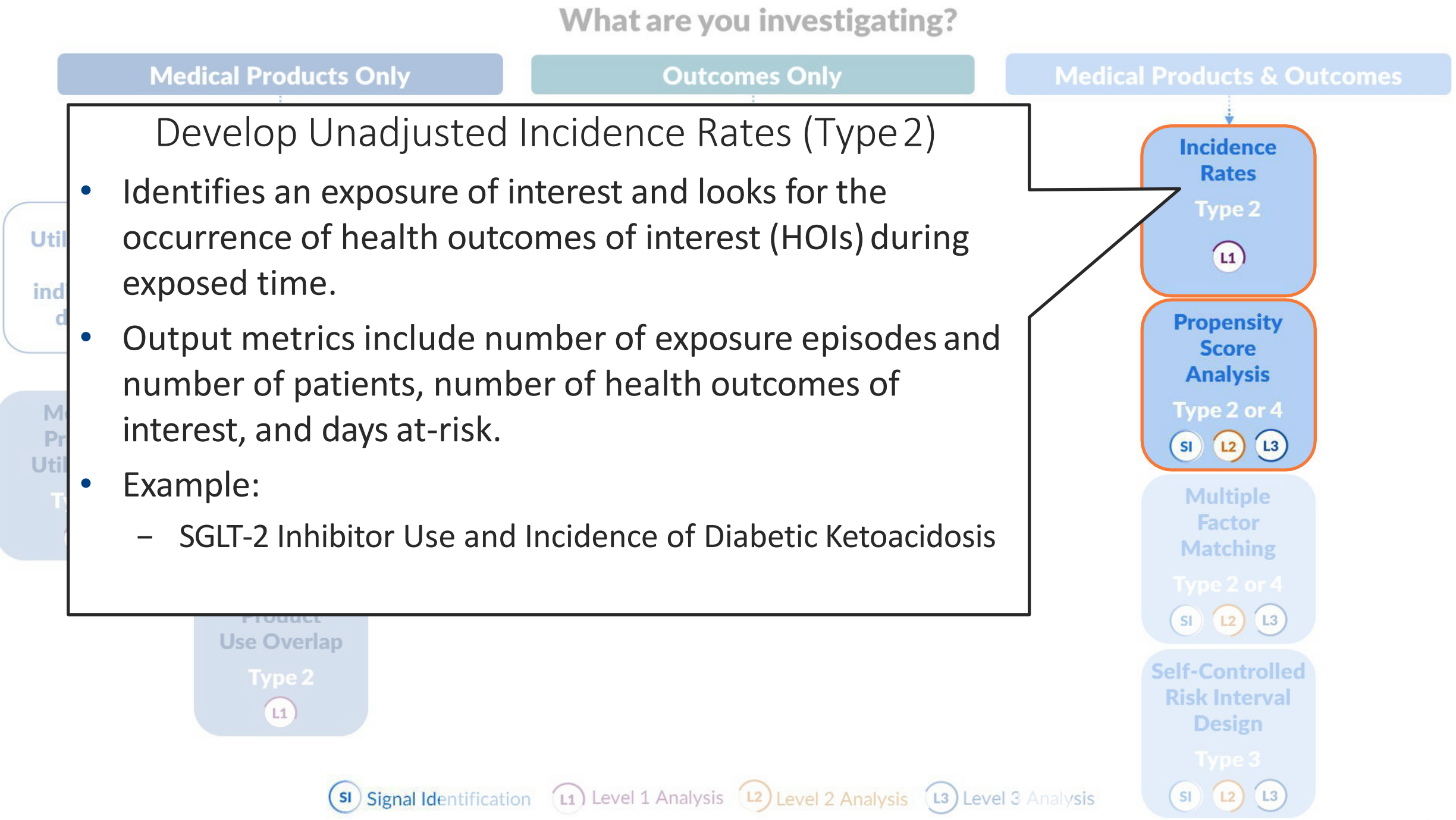
Agenda

- Review Sentinel Operations Center Process Flow
- Create a CIDA SAS Package
    1. Complete Specifications and Compile Code Lists
    2. Input Files
    3. RUN_PROGRAMS (Main Program)
    4. SASPROGRAM (Master Program)

Recap of this Morning's Session

- Introduced our case study problem
  - Stroke following antipsychotics use
- Evaluated medical product utilization data
  - Sentinel Query Builder (Simplified Type 5 CIDA) Analysis Tool
- Introduced design diagram and query specifications for an incidence rates query with associated propensity score matching analysis
  - How to parameterize the regulatory question

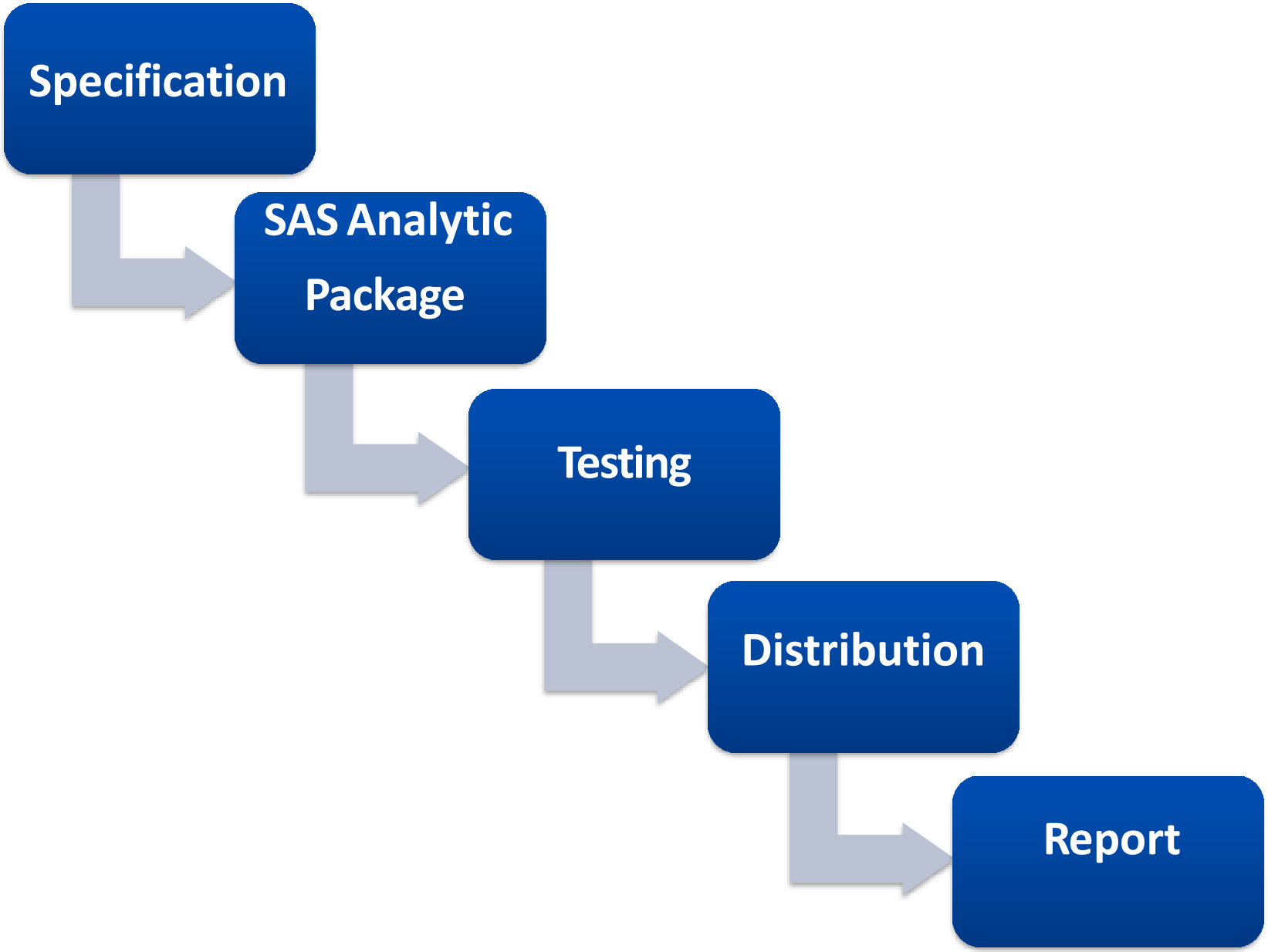

What are you investigating?
Medical Products Only
Outcomes Only
Medical Products & Outcomes
Develop Unadjusted Incidence Rates (Type 2)
• Identifies an exposure of interest and looks for the occurrence of health outcomes of interest (HOIs) during exposed time.
• Output metrics include number of exposure episodes and number of patients, number of health outcomes of interest, and days at-risk.
• Example:
– SGLT-2 Inhibitor Use and Incidence of Diabetic Ketoacidosis
Incidence Rates
Type 2
L1
Propensity Score Analysis
Type 2 or 4
SI L2 L3
Multiple Factor Matching
Type 2 or 4
SI L2 L3
Self-Controlled Risk Interval Design
Type 3
SI L2 L3
Use Overlap
Type 2
L1
SI Signal Identification
L1 Level 1 Analysis
L2 Level 2 Analysis
L3 Level 3 Analysis



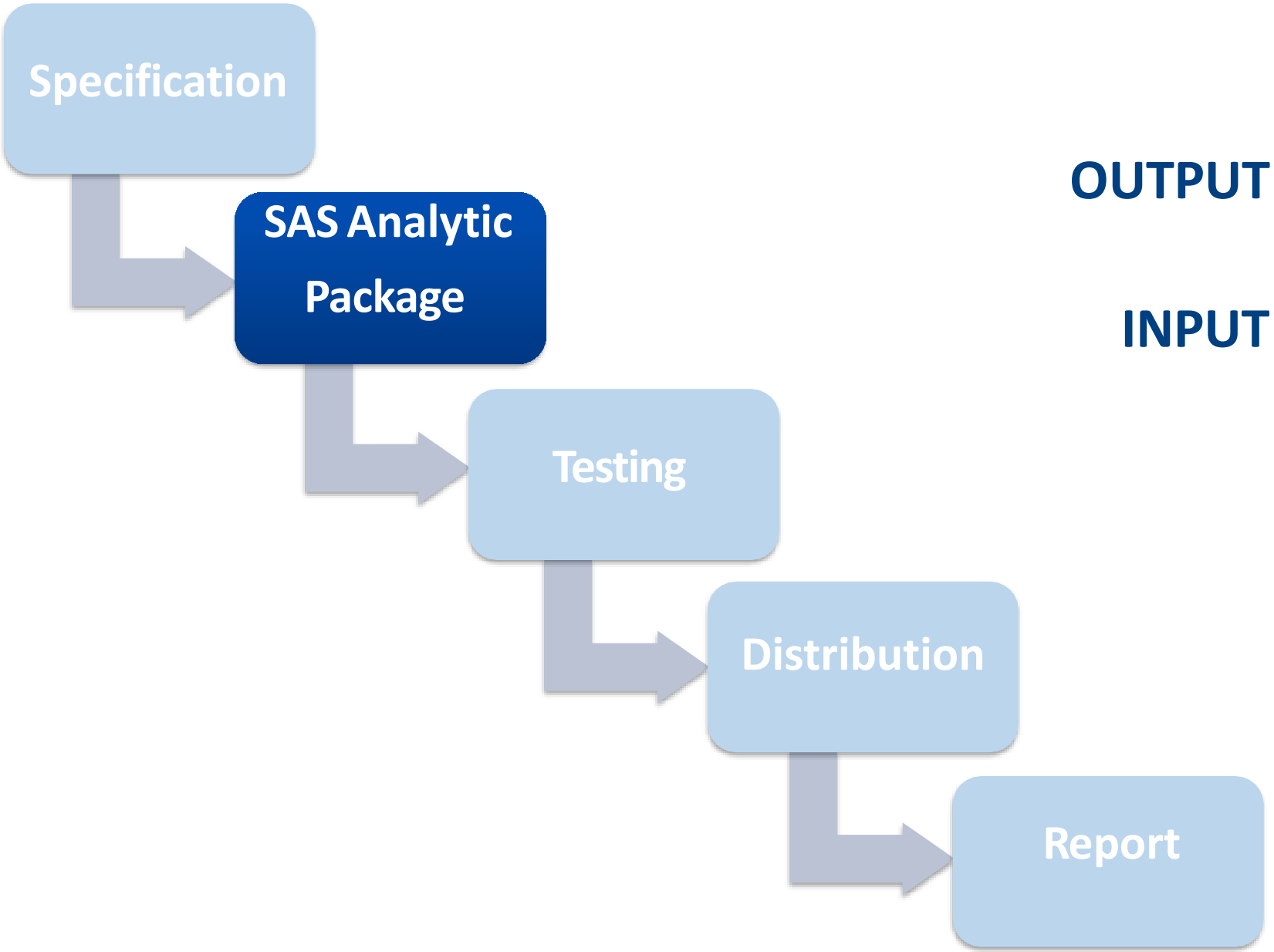
Develop Unadjusted Incidence Rates (Type 2)

- Identifies an exposure of interest and looks for the occurrence of health outcomes of interest (HOIs) during exposed time.
- Output metrics include number of exposure episodes and number of patients, number of health outcomes of interest, and days at-risk.
- Example:
  - SGLT-2 Inhibitor Use and Incidence of Diabetic Ketoacidosis

Operations Center Process Flow



Operations Center Process Flow



OUTPUT

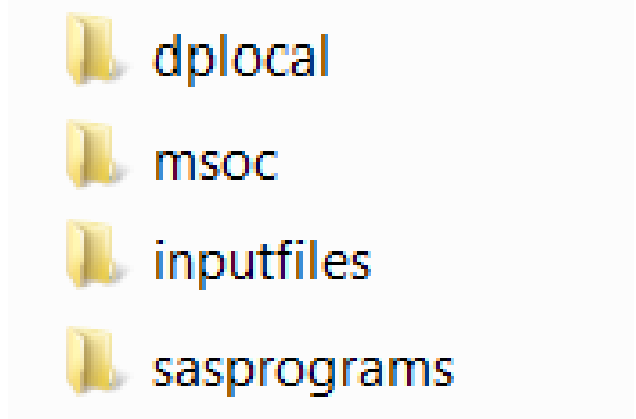
- dplocal
- msoc

INPUT

- inputfiles
- sasprograms

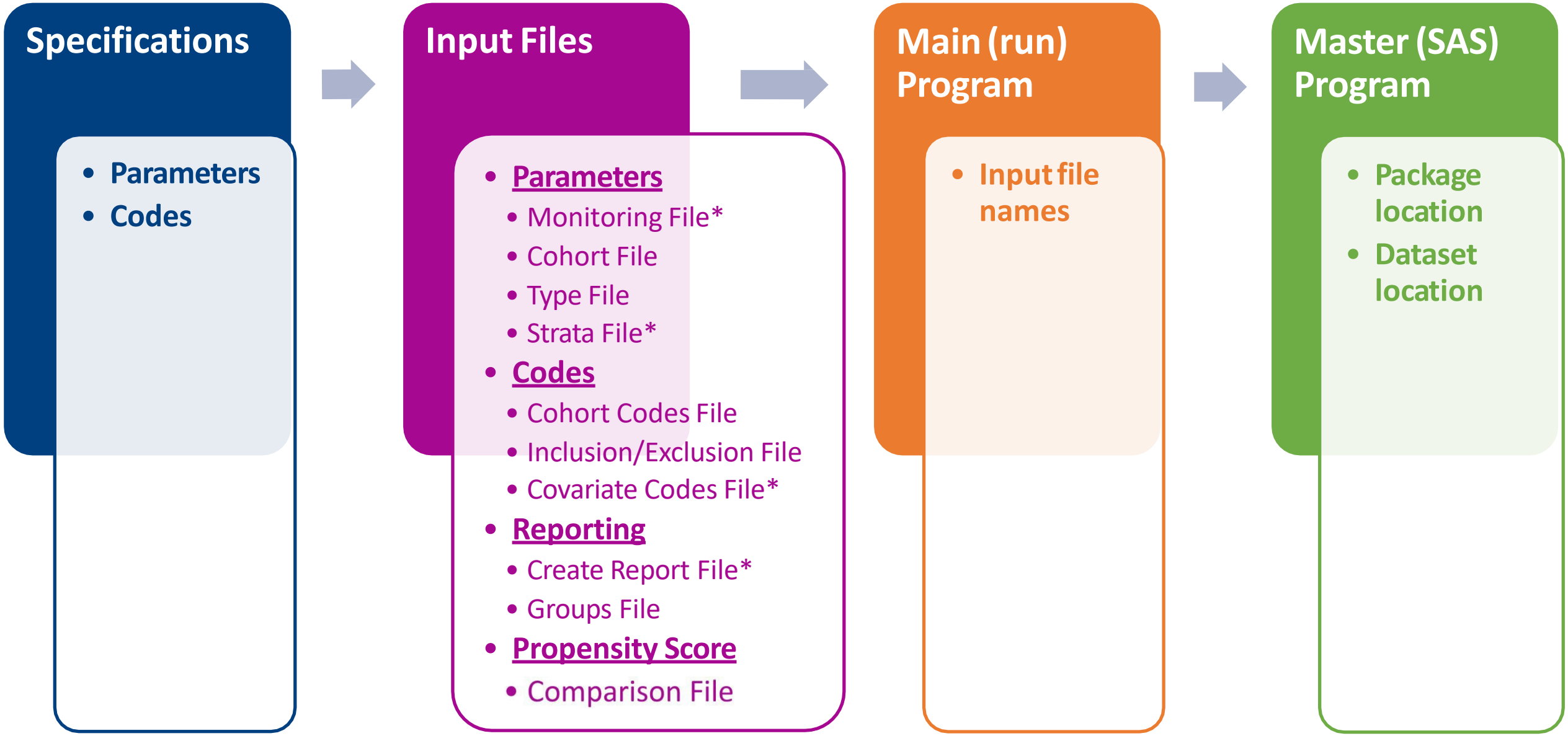
SAS Analytic Package (Program) Runs Against Data

- DPLOCAL (Data Partner Local) – left empty
  - Location for patient-level data output that stays at Data Partner
- MSOC (Mini-Sentinel Operating Center) – left empty
  - Location for aggregate-level data output that is returned



- INPUTFILES contains SAS data sets with necessary parameters, CIDA look-up tables, and CIDA macros
- SASPROGRAMS contains the single SAS macro to be executed in order to run the package

Creating a SAS Analytic Package

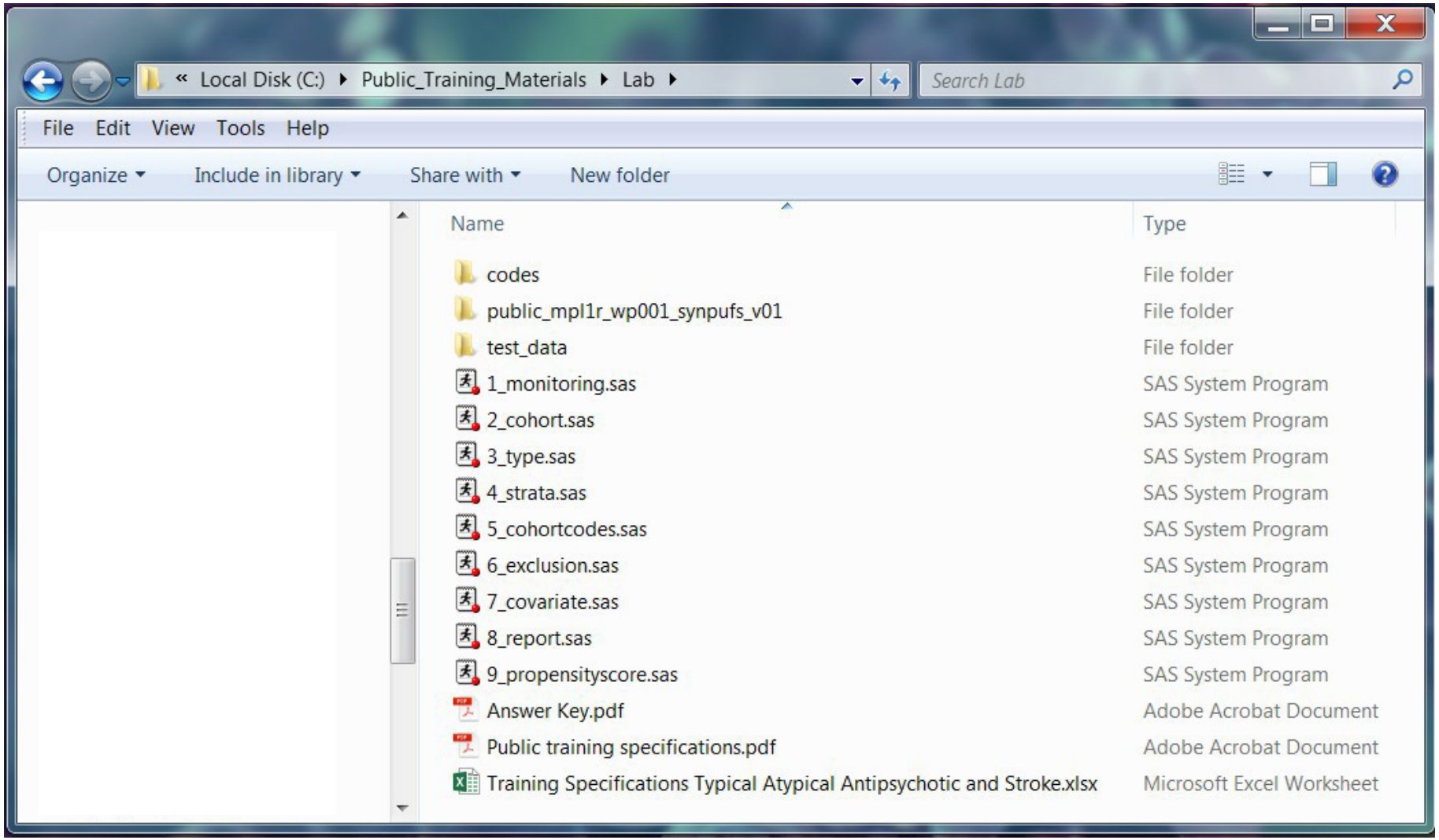


*Global Parameter Files

Making a CIDA SAS Analytic Package: Let's work on the Input Files

Getting Set Up

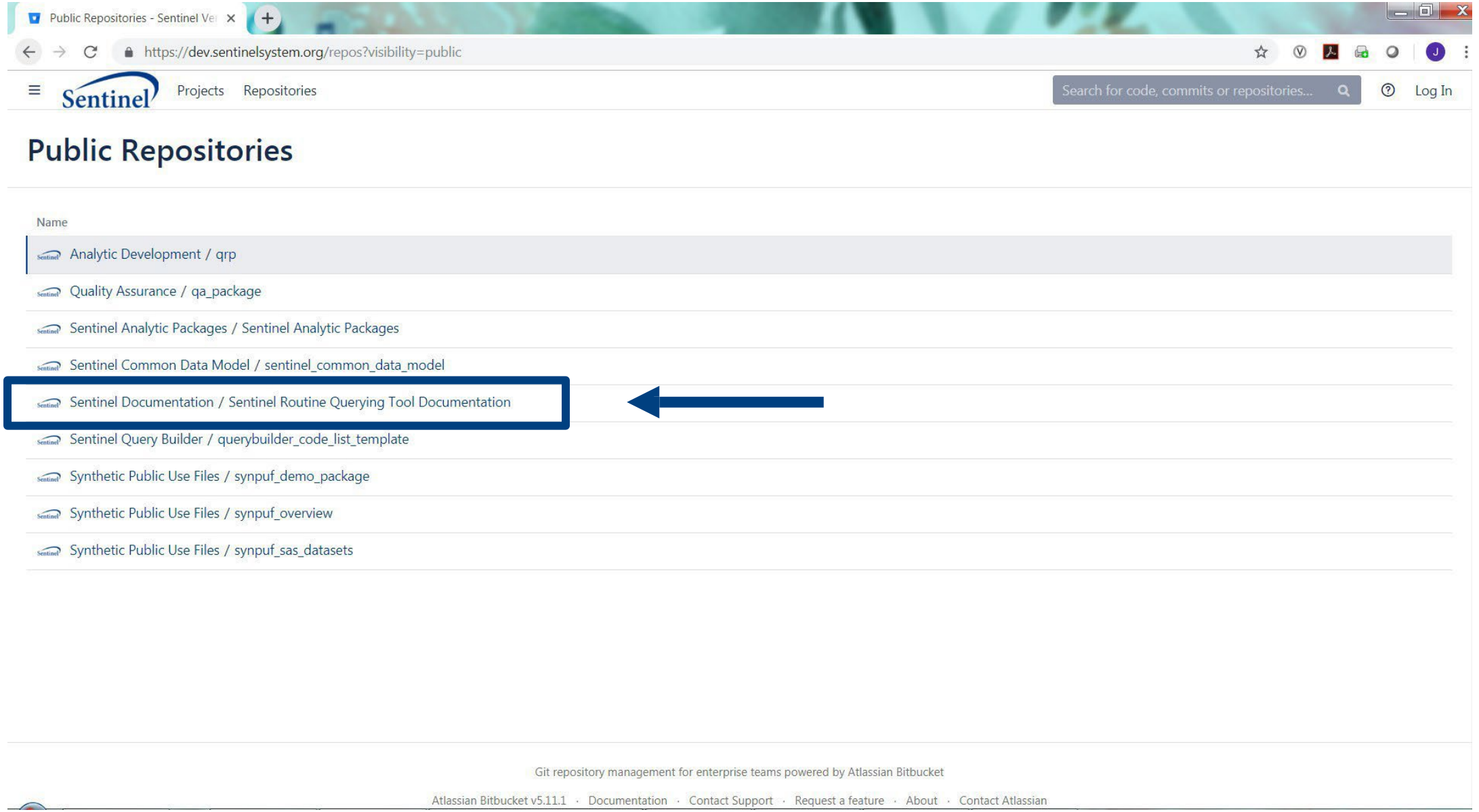
- Navigate to the “Lab” folder



Materials

- Printed:
  - Specifications
  - Answer Key
- Webpage:
  - Sentinel Routine Querying Tool Documentation
- SAS files:
  - 9 SAS programs to create input files
  - SynPUFs Test Data

CIDA Documentation (dev.sentinelsystem.org)



https://dev.sentinelsystem.org/repos?visibility=public

CIDA Type 2 Documentation

EXPOSURES AND FOLLOW-UP TIME COHORT IDENTIFICATION STRATEGY

The exposures and follow-up time cohort creation strategy defines episodes of new use of a medical product of interest and evaluates the occurrence of HOIs. There are numerous requester options, including defining new use, exposed time, and episode censoring rules.

Identifying Exposure and Creating Exposure Episodes

An exposure can be defined using any set of NDCs, procedure and/or diagnosis codes, and laboratory result values found in the SCDM. Procedure and diagnosis codes can be restricted to those observed in specific care settings (e.g., inpatient, outpatient) and diagnosis codes can be restricted by position (e.g., principal discharge diagnosis, secondary diagnosis). For example, exposure to a drug product dispensed in the outpatient setting can be defined as observation of one or more NDCs in the pharmacy dispensing table, whereas exposure to a vaccine can be defined based on observation of specific procedure codes in the procedure table.

The CIDA module queries the SDD and extracts all codes indicative of exposure during the query period. NDCs are processed and those with a part of their days supply outside enrollment episodes are truncated to constrain the supply within eligibility. Dispensing dates are modified using the stockpiling algorithm and supply is truncated again to make sure they are still in eligibility periods (stockpiling can push claims outside enrollment period).

After dispensing dates are adjusted using the stockpiling algorithm, exposure episodes are created. Exposure episodes can be defined in one of two ways: a) using outpatient pharmacy dispensing days supplied to create a sequence of continuous exposure, and b) defining a specific number of days after exposure initiation as exposed time.

Creating Exposure Episodes using Dispensing Days Supplied

An exposure episode using outpatient pharmacy dispensing days supplied is defined as a sequence of treatment that ends when interrupted by a gap in days supply greater than a requester-defined episode gap. Consider an example where five outpatient pharmacy dispensings of the exposure of interest are observed during the query period (Figure 1).

https://dev.sentinelsystem.org/projects/SENTINEL/repos/sentinel-routine-querying-tool-documentation/browse/files/file040-type02-expfollowup.md

Technical Documentation by Type

Navigate to:

- > Type 1: Calculate Background Rate
- > Type 2: Exposures and Follow-up Time
- > Type 3: Self-Controlled Risk Interval (SCRI) Design
- > Type 4: Pregnancy Episodes and Identify Medical Product Use
- > Type 5: Medical Product Utilization
- > Type 6: Manufacturer-Level Product Utilization and Switching Patterns
- > Home Page

https://dev.sentinelsystem.org/projects/SENTINEL/repos/sentinel-routine-querying-tool-documentation/browse/files/atoc-type2.md

CIDA Type 2 Functional and Technical Documentation Files

Table of Contents - Exposures and Follow-up Time (Type 2)

The documentation pages linked below provide all the information needed for building a Sentinel Routine Querying System package using the Exposures and Follow-up Time cohort identification strategy.

Note: To read the documentation in logical order, make selections from left to right.

Cohort Identification and Descriptive Analysis (CIDA) Module		
Exposures and Follow-up time Cohort Identification Strategy	Cohort Definition Options	Creation and Retention of First Valid Episodes
National Drug Code Processing and the Stockpiling Algorithm	Identifying Health Outcome of Interest (HOI)	Defining Complex Algorithms
Eligible Patients and Eligible Days	Creation of Never-exposed Cohort	Identifying Episodes of Concomitant Use
Identifying Multiple Events	Identifying and Characterizing Treatment Overlap	Covariate Assessment, Charlson/Elixhauser Combined Comorbidity Score, Medical and Drug Utilization Metrics
Incidence Rate Ratio Calculation	Prospective Surveillance with Querying Tools	Reporting Tools
Program Package and Execution	Main Program Parameters	Lookup Tables
CIDA Input Files: Required		
Cohort File	Type 2 File	Monitoring File
Cohort Codes File	User-defined Strata Levels Lookup Table	

(excerpt)

https://dev.sentinelsystem.org/projects/SENTINEL/repos/sentinel-routine-querying-tool-documentation/browse/files/atoc-type2.md

CIDA Type 2 Functional and Technical Documentation Files

Monitoring File

The Monitoring File is required for all analyses. The file enables users to specify a single monitoring period (i.e., query period) for descriptive and inferential analyses, and multiple monitoring periods for sequential analysis and sequential signal identification. Each monitoring period is denoted numerically via the parameter PERIODID. PERIODID values are then used by the run_programs.sas file, to specify what time periods included in the MONITORINGFILE the program should evaluate in a single execution of the program (specified by PERIODIDSTART and PERIODIDEND values in run_programs.sas).

The MONITORINGFILE also enables users to specify what dates bind the index date and follow-up time, via user entered dates or data driven methods. Users may specify: start of follow-up (first date patients can contribute an eligible index exposure), end of follow-up (last date patients can contribute follow-up time; may be specified via user entered date or based on database data completeness), and the last day patients can contribute an index date (either the same as end of follow-up, via a user-defined date, or data driven for fixed risk window sequential surveillance).

The program will generate output by PERIODID to support sequential monitoring activities. For Type 2 sequential analyses with a variable risk period, datasets output by PERIODID are cumulative over time. For Type 2 and Type 3 sequential analyses with a fixed risk period output by PERIODID is not cumulative over time.

For example, a user may a priori specify the following time periods for evaluation:

PERIODID=1: January 1, 2015 – March 31, 2015

PERIODID=2: January 1, 2015 – June 30, 2015

PERIODID=3: January 1, 2015 – September 30, 2015

PERIODID=4: January 1, 2015 – December 31, 2015

These four periods are included in the Monitoring File with the corresponding PERIODID values. When data are complete through March 31, 2015, SOC can distribute a program package with the above Monitoring File contents and macro parameters PERIODIDSTART=1 and PERIODIDEND=1. When data are complete through June 30, 2015, SOC can distribute the same package with macro parameters PERIODIDSTART=1 and PERIODIDEND=2 (if the user wants to execute a query starting in PERIODID 1 and ending in PERIODID 2).

The CIDA module, to support sequential monitoring activities, will generate output by PERIODID.

Table 1 contains detailed specifications for this file.

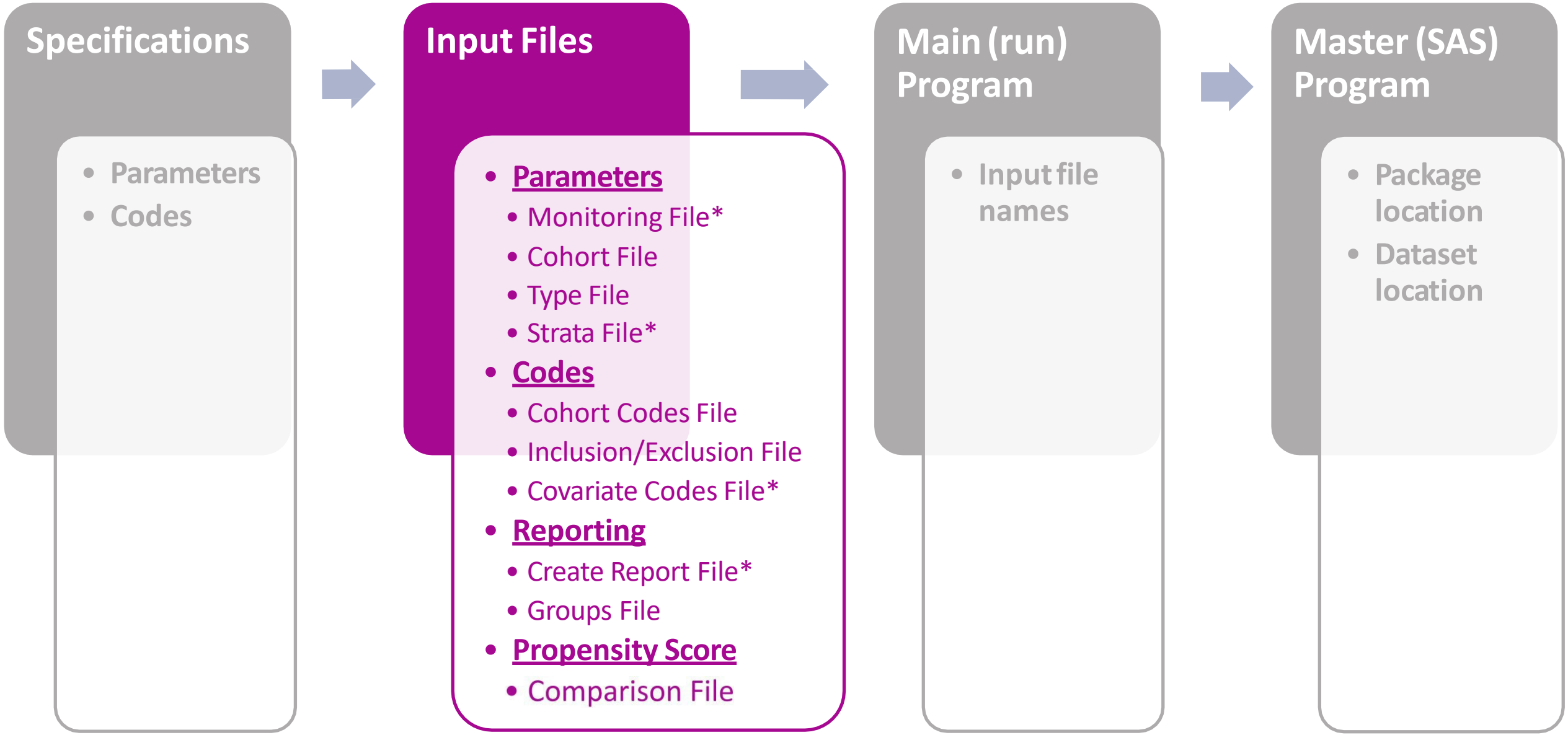
Table 1. MONITORINGFILE Specification

Parameter	Field Name	Description
Time Period Indicator	PERIODID	Identifier for each STARTDATE/FUPENDDATE combination. **Input type:** Required **Format:** Numeric **Example:** 1
Index Start Date	STARTDATE	The date on which patients may begin contributing eligible index exposures/events. Data prior to STARTDATE may be used to determine enrollment, washout, and other cohort inclusion criteria. **Input type:** Required **Format:** Numeric; Date9. **Example:** 01JAN2015
Index End Date	INDENDDATE	Last day a patient can contribute an index date to the analysis. Users have the option to explicitly set the date in this field or use INDENOPTIONS for a data driven approach to set the date.

(excerpt)

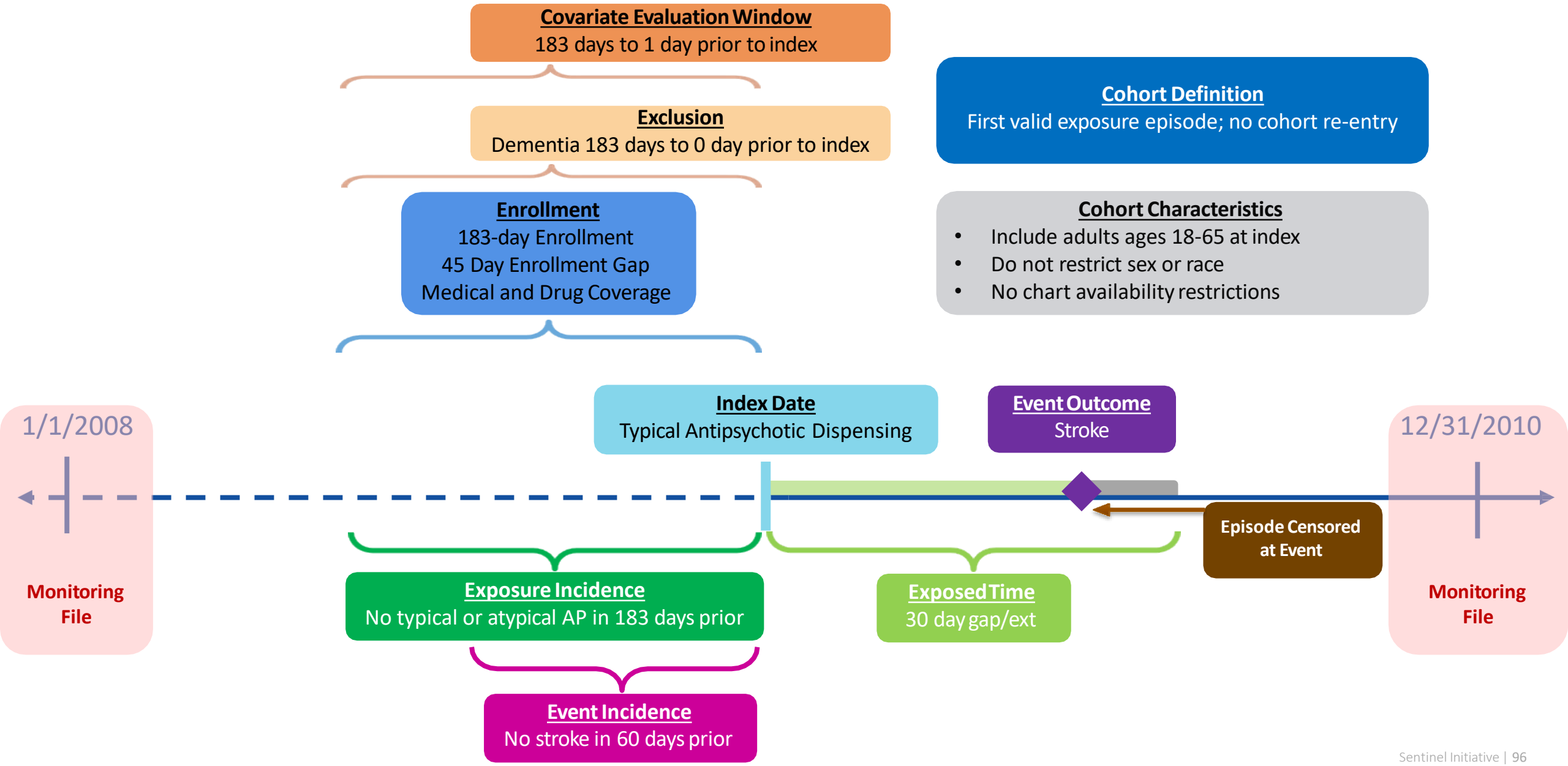
https://dev.sentinelsystem.org/projects/SENTINEL/repos/sentinel-routine-querying-tool-documentation/browse/files/file580-typeall-monitoring.md

Step 2: Input File Creation

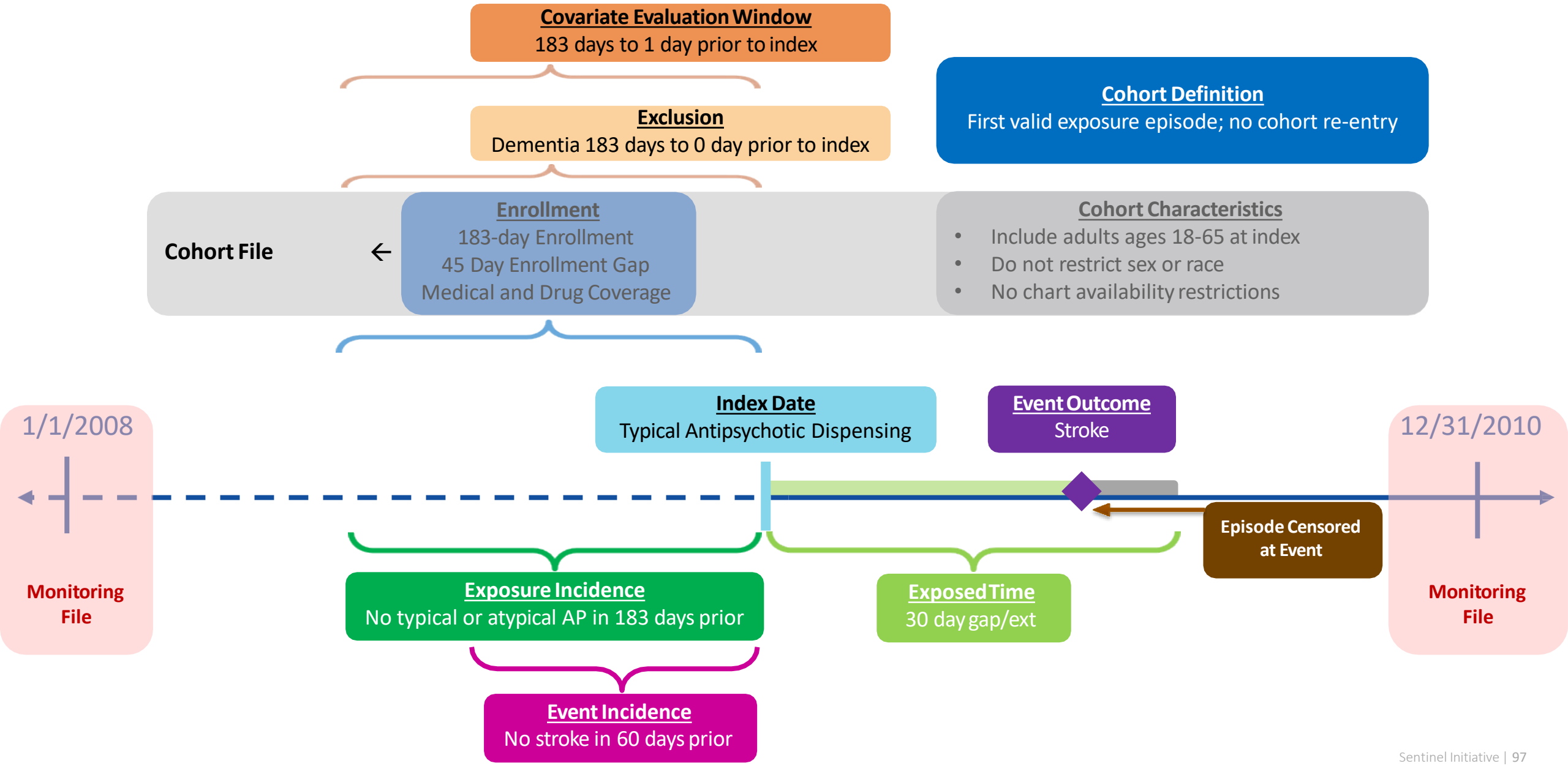


*Global Parameter Files

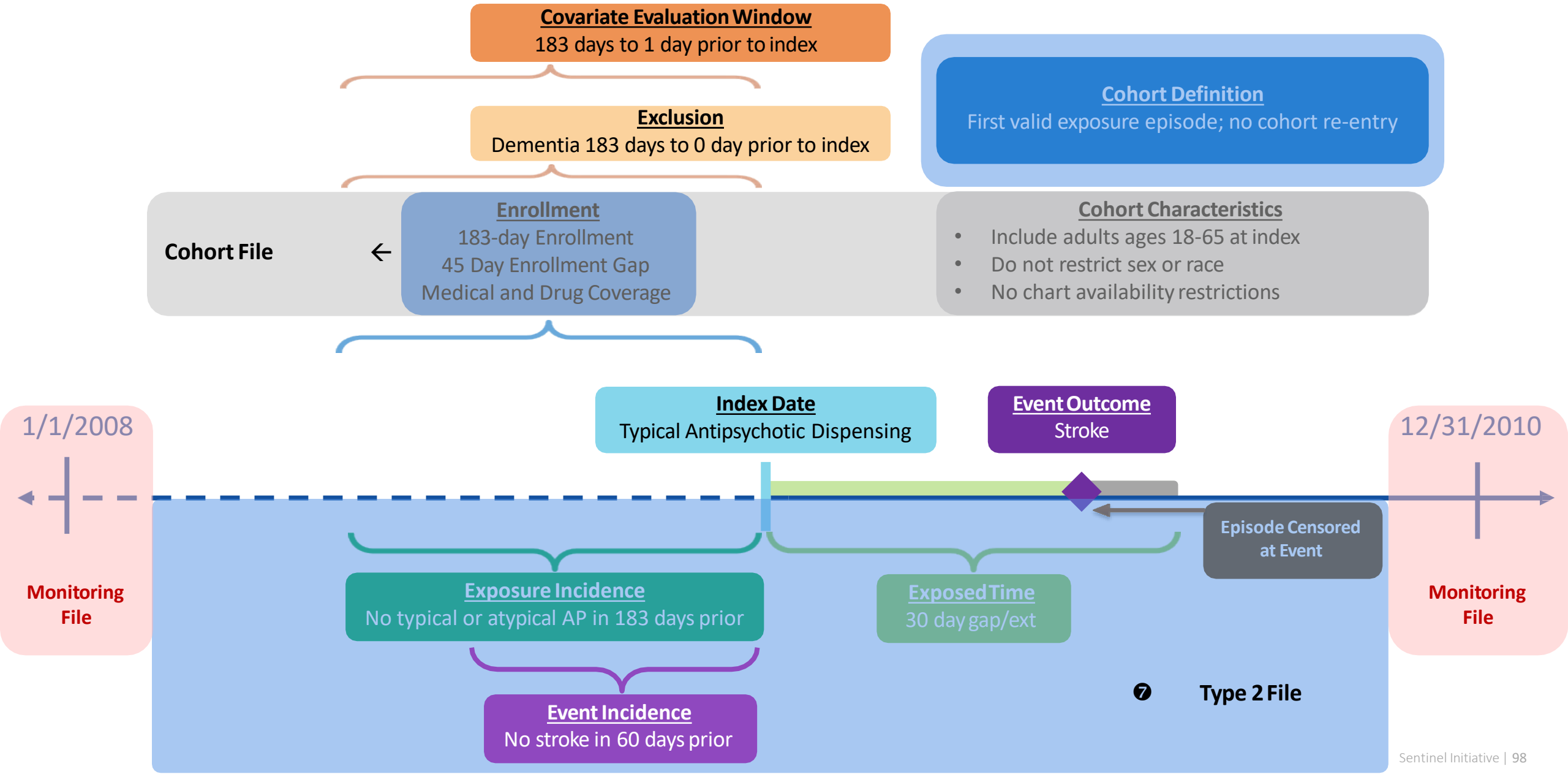
Inputs: Monitoring File



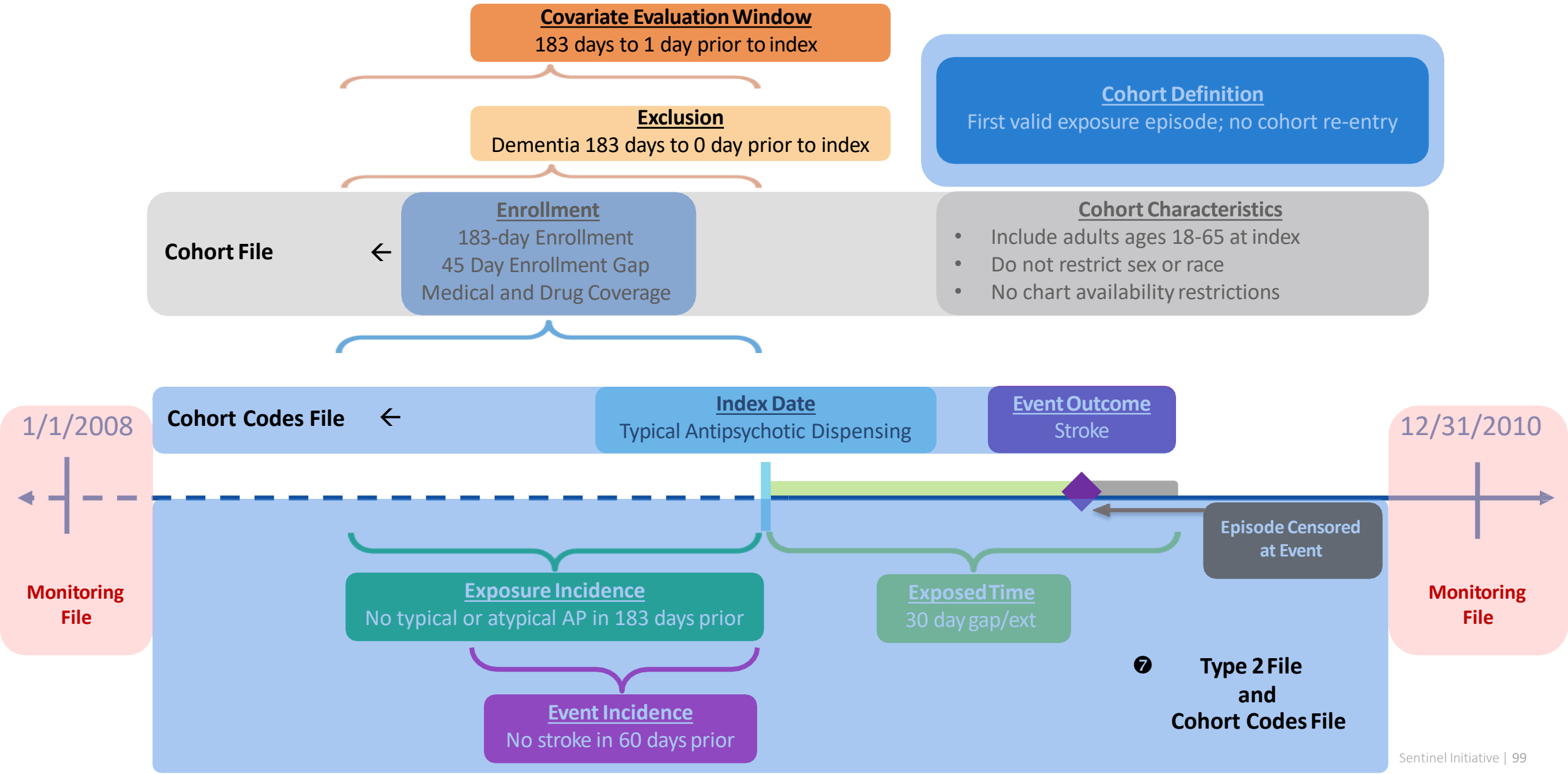
Inputs: Cohort File



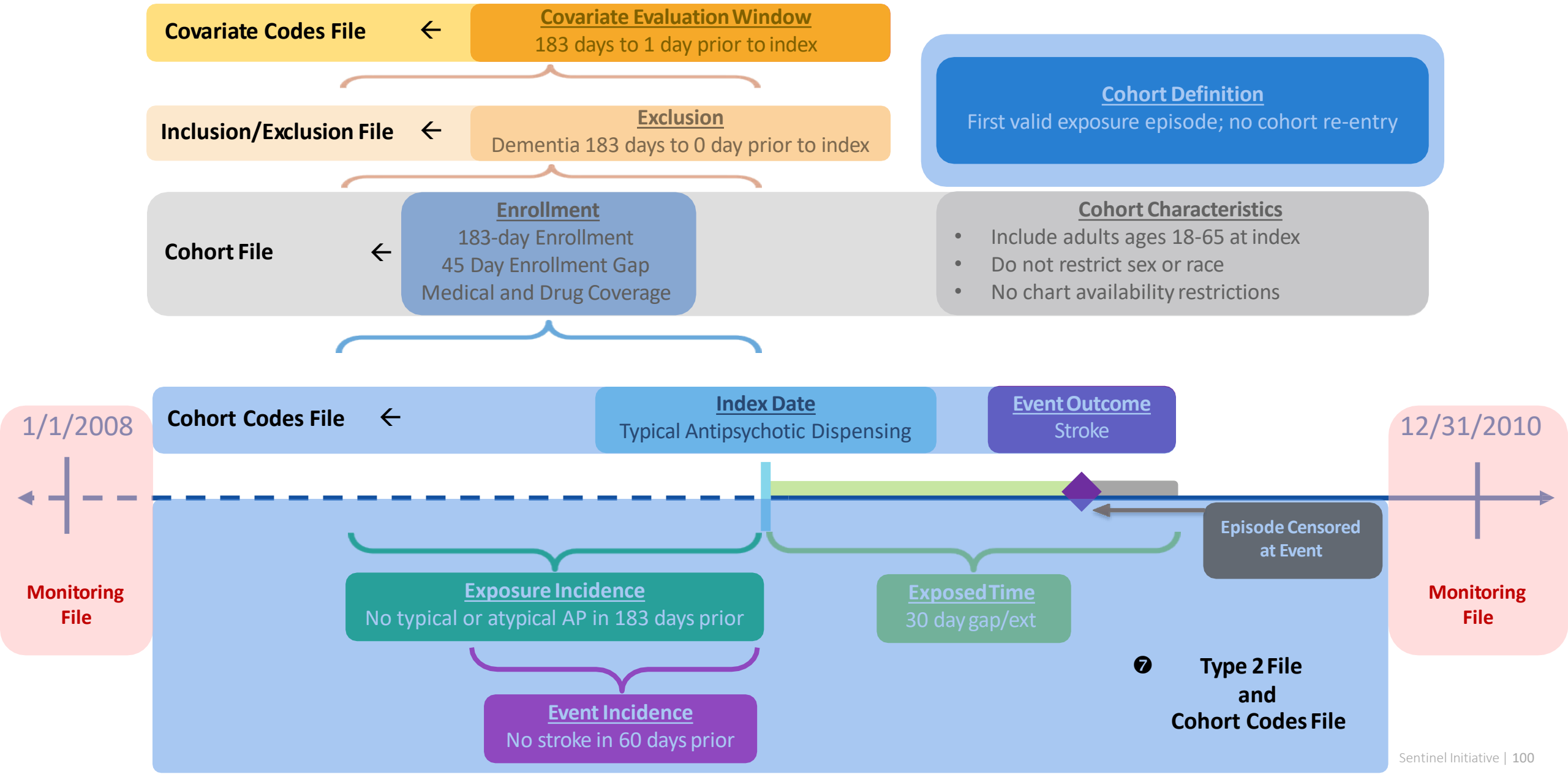
Inputs: Type 2 File



Inputs: Cohort Codes File



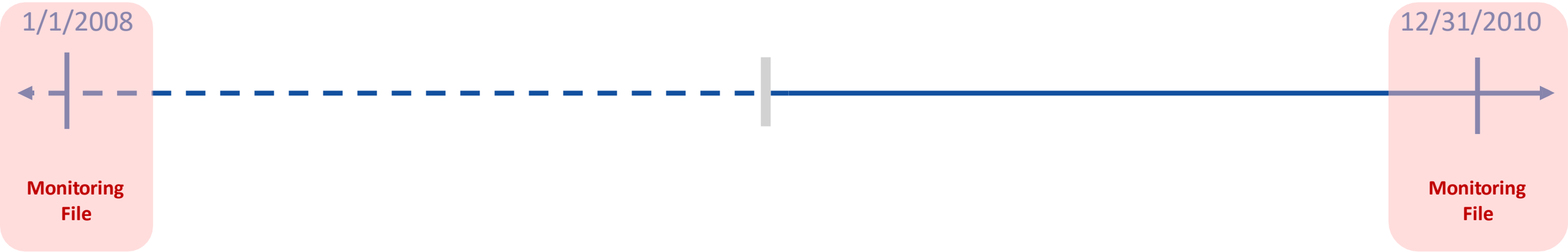
Inputs: Inclusion/Exclusion and Covariate Codes File



MONITORING FILE:

PURPOSE: To establish the time period in which index dates can occur

PARAMETERS: 6



Specifications: Defining Query Period

* **Query period:**	1/1/2008 - 12/31/2010
Coverage requirement:	Medical and Drug
Pre-index enrollment requirement:	183 days
Post-index enrollment requirement:	0
Enrollment gap:	45 days
Age groups:	18-39, 40-54, 55-65 years
* **Stratifications:**	Age group, Sex, Calendar Year
Censor output categorization:	0-364, 365-729, 730-1094, 1095+ days
* **Envelope macro:**	Reclassify encounters during inpatient stay as inpatient
Propensity score analysis:	1:1 matching
Propensity score caliper:	0.05

*** Global Parameters**

Create Monitoring File

- Open **1_monitoring.sas** program

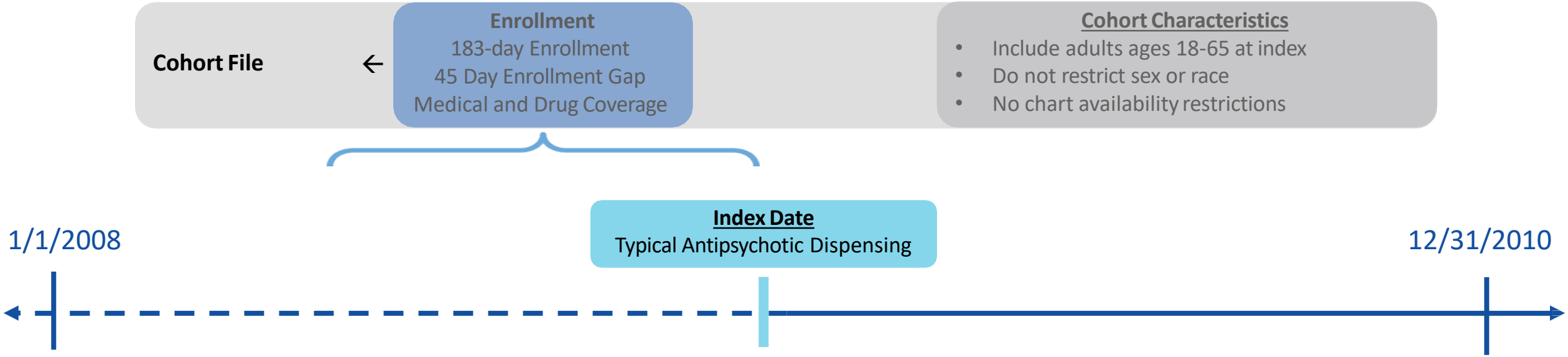
	periodid	startdate	indenddate	indendoptions	fupenddate	cdpend
1	1	01JAN2008	31DEC2010		31DEC2010	N

```
data out.&wpnum._monitoring;
    format periodid 8. startdate date9. indenddate date9. indendoptions $10. fupenddate date9. cdpend $1. ;
    periodid = 1;
    startdate = '01JAN2008'd;  /* Index Start Date; Valid values: calendar date in format "29AUG2019"d; Required */
    indenddate = '31DEC2010'd; /* Index End Date; Valid values: calendar date in format "29AUG2019"d; Required */
    indendoptions = ' ';
    fupenddate = '31DEC2010'd; /* Follow-Up End Date; Valid values: calendar date in format "29AUG2019"d; Required */
    cdpend = 'N';              /* Censor on Common Components Data Completeness Date Indicator; Valid values: 'Y' or 'N'; Required */
run;
```

COHORT FILE:

PURPOSE: To define high level parameters for exposure-outcome cohorts

PARAMETERS: 16



Specifying Scenarios

	Exposure									
Group	Index Exposure	Cohort definition	Incident exposure washout period	Incident w/ respect to:	Treatment episode gap	Exposure episode extension	Minimum exposure episode duration	Minimum days supplied	Maximum exposure episode duration	Censor treatment episode at evidence of:
1 typ_IS	Typical Antipsychotics	First valid exposure episode during query period	183 days	Typical and atypical antipsychotics	30 days	30 days	1	1	None	Death; DP end date; Query end date; Atypical antipsychotics;
2 typ_ICH	Typical Antipsychotics	First valid exposure episode during query period	183 days	Typical and atypical antipsychotics	30 days	30 days	1	1	None	Death; DP end date; Query end date; Atypical antipsychotics;
3 atyp_IS	Atypical Antipsychotics	First valid exposure episode during query period	183 days	Typical and atypical antipsychotics	30 days	30 days	1	1	None	Death; DP end date; Query end date; Typical antipsychotics;
4 atyp_ICH	Atypical Antipsychotics	First valid exposure episode during query period	183 days	Typical and atypical antipsychotics	30 days	30 days	1	1	None	Death; DP end date; Query end date; Typical antipsychotics;

Specifications: Stratifications and Demographics

* **Query period:**	1/1/2008 - 12/31/2010
Coverage requirement:	Medical and Drug
Pre-index enrollment requirement:	183 days
Post-index enrollment requirement:	0
Enrollment gap:	45 days
Age groups:	18-39, 40-54, 55-65 years
* **Stratifications:**	Age group, Sex, Calendar Year
Censor output categorization:	0-364, 365-729, 730-1094, 1095+ days
* **Envelope macro:**	Reclassify encounters during inpatient stay as inpatient
Propensity score analysis:	1:1 matching
Propensity score caliper:	0.05

*** Global Parameters**

Create Cohort File

- Open **2_cohort.sas** program

	cohortgrp	coverage	enrolgap	enrdays	enrdaysaftind	type1	type2	type3	type4	type5	type6	chartres	sex	race	hispanic	agestrat
1	typ_is	MD	45	183	.	N	Y	N	N	N	N	N				18-39 40-54 55-65
2	typ_ich	MD	45	183	.	N	Y	N	N	N	N	N				18-39 40-54 55-65
3	atyp_is	MD	45	183	.	N	Y	N	N	N	N	N				18-39 40-54 55-65
4	atyp_ich	MD	45	183	.	N	Y	N	N	N	N	N				18-39 40-54 55-65

```
data work.cht;
format cohortgrp $40. coverage $2. enrolgap 8. enrdays 8. enrdaysaftind 8. type1 $1. type2 $1. type3 $1. type4 $1. type5 $1. type6 $1.
        chartres $1. sex $3. race $1. hispanic $1. agestrat $100.;
cohortgrp = "&curr_name";
```

Create Cohort File

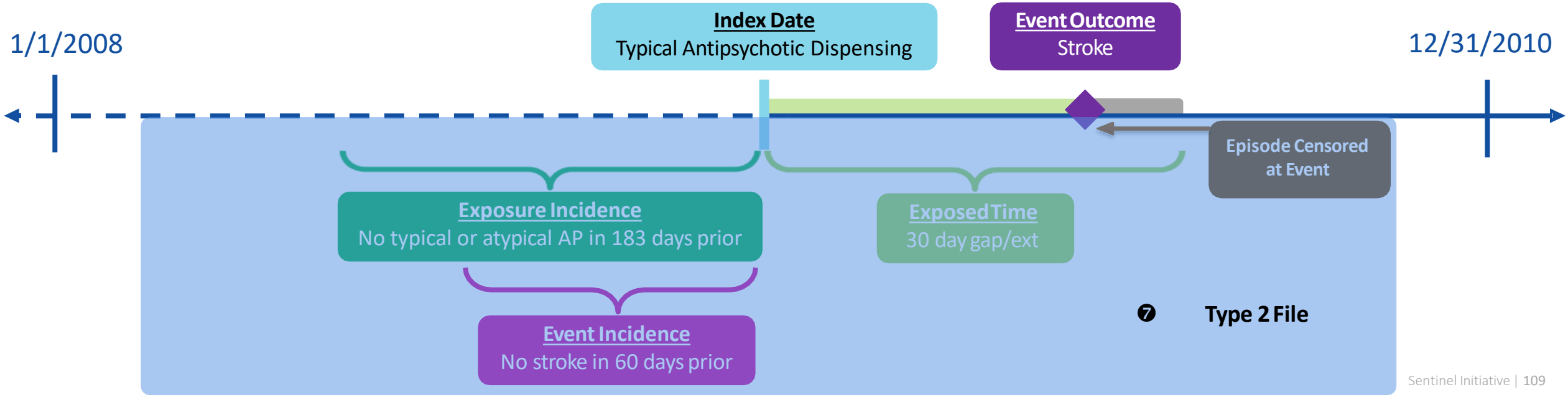
```
data work.cht;
format cohortgrp $40. coverage $2. enrolgap 8. enrdays 8. enrdaysaftind 8. type1 $1. type2 $1. type3 $1. type4 $1. type5 $1. type6 $1.
       chartres $1. sex $3. race $1. hispanic $1. agestrat $100.;
cohortgrp = "&curr_name";
coverage = 'MD'; /* Coverage Type Requirement; Valid values: 'MD' 'M' or 'D' for medical and drug, medical only, or drug only*/
enrolgap = 45 ; /* Enrollment Gap; Numerical */
enrdays = 183 ; /* Minimum Pre-Index Enrollment Days; Numerical*/
enrdaysaftind = .;
type1 = 'N'; /* Type 1 Cohort Identification Strategy Indicator; Valid values: 'Y' or 'N' */
type2 = 'Y'; /* Type 2 Cohort Identification Strategy Indicator; Valid values: 'Y' or 'N' */
type3 = 'N'; /* Type 3 Cohort Identification Strategy Indicator; Valid values: 'Y' or 'N' */
type4 = 'N'; /* Type 4 Cohort Identification Strategy Indicator; Valid values: 'Y' or 'N' */
type5 = 'N'; /* Type 5 Cohort Identification Strategy Indicator; Valid values: 'Y' or 'N' */
type6 = 'N'; /* Type 6 Cohort Identification Strategy Indicator; Valid values: 'Y' or 'N' */
sex = ''; /* Sex criteria to apply to cohort; Valid values: 'A' 'F' 'M' 'U'; Leave blank if no restrictions */
race = ''; /* Race criteria to apply to cohort; Leave blank if no restrictions */
hispanic = ''; /* Hispanic criteria to apply to cohort; Leave blank if no restrictions */
agestrat = '18-39 40-54 55-65';
chartres = 'N';
run;
```

Cohort Definition
First valid exposure episode; no cohort re-entry

TYPE 2 FILE:

PURPOSE: To define exposure and follow-up time strategies, per cohort

PARAMETERS: 18



Specifications: Groups

		Exposure								
	Group	Index Exposure	Cohort definition	Incident exposure washout period	Incident w/ respect to:	Treatment episode gap	Exposure episode extension	Minimum exposure episode duration	Minimum days supplied	Maximum exposure episode duration	Censor treatment episode at evidence of:
1	typ_IS	Typical Antipsychotics	First valid exposure episode during query period	183 days	Typical and atypical antipsychotics	30 days	30 days	1	1	None	Death; DP end date; Query end date; Atypical antipsychotics;
2	typ_ICH	Typical Antipsychotics	First valid exposure episode during query period	183 days	Typical and atypical antipsychotics	30 days	30 days	1	1	None	Death; DP end date; Query end date; Atypical antipsychotics;
3	atyp_IS	Atypical Antipsychotics	First valid exposure episode during query period	183 days	Typical and atypical antipsychotics	30 days	30 days	1	1	None	Death; DP end date; Query end date; Typical antipsychotics;
4	atyp_ICH	Atypical Antipsychotics	First valid exposure episode during query period	183 days	Typical and atypical antipsychotics	30 days	30 days	1	1	None	Death; DP end date; Query end date; Typical antipsychotics;

Specifications: Event Outcome

	Event Outcome						
Group	Event	Care setting	Principal diagnosis position	Event washout conditions	Event washout care setting	Event washout period	Blackout period
1 typ_IS	Ischemic stroke	Inpatient hospital stay	Principal	Stroke (ischemic stroke and intracranial hemorrhage)	Any care setting	60	1
2 typ_ICH	Intracranial hemorrhage	Inpatient hospital stay	Principal	Stroke (ischemic stroke and intracranial hemorrhage)	Any care setting	60	1
3 atyp_IS	Ischemic stroke	Inpatient hospital stay	Principal	Stroke (ischemic stroke and intracranial hemorrhage)	Any care setting	60	1
4 atyp_ICH	Intracranial hemorrhage	Inpatient hospital stay	Principal	Stroke (ischemic stroke and intracranial hemorrhage)	Any care setting	60	1

Create Type 2 File

- Open **3_type.sas** program

	group	t2cohortdef	t2washper	ittdays	episodegaptype	episodegap	expextper	minepisdur	maxepisdur	mindaysupp	enrdaysaftepi
1	typ_is	01	183	.	F	30	30	1	.	1	.
2	typ_ich	01	183	.	F	30	30	1	.	1	.
3	atyp_is	01	183	.	F	30	30	1	.	1	.
4	atyp_ich	01	183	.	F	30	30	1	.	1	.

t2fupwashper	blackoutper	eventcount	censor_output_cat	censor_dth	neverexposedcohort	t2atriskstart
60	1	2	0-364 365-729 730-1094 1095+	Y	N	.
60	1	2	0-364 365-729 730-1094 1095+	Y	N	.
60	1	2	0-364 365-729 730-1094 1095+	Y	N	.
60	1	2	0-364 365-729 730-1094 1095+	Y	N	.

Create Type 2 File

```
data work.type;
format group $40. t2cohortdef $2. t2washper 8. ittdays 8. episodegaptype $1. episodegap 8. expextper 8.
       minepisdur 8. maxepisdur 8. mindaysupp 8. enrdaysaftepi 8. t2fupwashper 8. blackoutper 8. eventcount 8.
        censor_output_cat $30. censor_dth $1. neverexposedcohort $1. t2atriskstart 8.;
group = "&curr_name";
t2cohortdef = '01'; /* Allowed Number of Exposure Episodes per Individual;
                       Valid values: '01' '02' '03' for first episode only, all episodes, or all episodes until event*/
t2washper = 183 ; /* Type 2 Exposure Washout Period; Numerical; Required - enter 0 if not using */
ittdays = . ; /* Requester-defined Exposure Episode Length; Numerical; Leave blank if creating as-treated episodes */
episodegaptype= 'F'; /* Treatment Episode Gap Type; Valid values: 'F' or 'P' for fixed or percent */
episodegap = 30; /* Exposure Episode Gap; Numerical; Required - enter 0 if not using */
expextper = 30; /* Exposure Episode Extension Period; Numerical; Optional */
minepisdur = 1; /* Minimum Exposure Episode Duration; Numerical; Required - enter 0 if not using */
maxepisdur = .; /* Maximum Exposure Episode Duration; Numerical; Optional */
mindaysupp = 1; /* Minimum Days Supplied; Numerical; Required - enter 0 if not using */
t2fupwashper = 60; /* Type 2 HOI Washout Period; Numerical; Required - enter 0 if not using */
blackoutper = 1; /* HOI Blackout Period; Numerical; Required - enter 0 if not using */
censor_dth = 'Y'; /* Censor Episodes at Evidence of Death; Valid values: 'Y' or 'N'; Required*/
censor_output_cat = '0-364 365-729 730-1094 1095+';
enrdaysaftepi = .;
eventcount = 2;
neverexposedcohort= 'N';
t2atriskstart = .;
run;
```

USER-DEFINED STRATA FILE:

PURPOSE: To define both the output tables that will be returned as well as the stratifications of each output table

PARAMETERS: 3

Specifications: Stratifications

* **Query period:**	1/1/2008 - 12/31/2010
Coverage requirement:	Medical and Drug
Pre-index enrollment requirement:	183 days
Post-index enrollment requirement:	0
Enrollment gap:	45 days
Age groups:	18-39, 40-54, 55-65 years
* **Stratifications:**	Age group, Sex, Calendar Year
Censor output categorization:	0-364, 365-729, 730-1094, 1095+ days
* **Envelope macro:**	Reclassify encounters during inpatient stay as inpatient
Propensity score analysis:	1:1 matching
Propensity score caliper:	0.05

*** Global Parameters**

CIDA Type 2 Technical Documentation: Input Files

Table of Contents - Exposures and Follow-up Time (Type 2)

The documentation pages linked below provide all the information needed for building a Sentinel Routine Querying System package using the Exposures and Follow-up Time cohort identification strategy.

Note: To read the documentation in logical order, make selections from left to right.

Cohort Identification and Descriptive Analysis (CIDA) Module		
Exposures and Follow-up time Cohort Identification Strategy	Cohort Definition Options	Creation and Retention of First Valid Episodes
National Drug Code Processing and the Stockpiling Algorithm	Identifying Health Outcome of Interest (HOI)	Defining Complex Algorithms
Eligible Patients and Eligible Days	Creation of Never-exposed Cohort	Identifying Episodes of Concomitant Use
Identifying Multiple Events	Identifying and Characterizing Treatment Overlap	Covariate Assessment, Charlson/Elixhauser Combined Comorbidity Score, Medical and Drug Utilization Metrics
Incidence Rate Ratio Calculation	Prospective Surveillance with Querying Tools	Reporting Tools
Program Package and Execution	Main Program Parameters	Lookup Tables
CIDA Input Files: Required		
Cohort File	Type 2 File	Monitoring File
Cohort Codes File	User-defined Strata Levels Lookup Table	

(excerpt)

https://dev.sentinelsystem.org/projects/SENTINEL/repos/sentinel-routine-querying-tool-documentation/browse/files/atoc-type2.md

Lookup Valid Stratifications for a Type 2

Table 4. Valid Stratification Variables for a Type 2 Analysis (Exposure and Follow-up Time)

Variable Name	t2_cida	t2_censor
agegroup	X	X
cb_reg	X	
censdays_value		X
censdays_value_cat		X
covarn	X	
Event_Flag		X
hhs_reg	X	
hispanic	X	
month	X	
race	X	
sex	X	X
state	X	
year	X	X
zip_uncertain	X	
zip3	X	

*** Query period:** 1/1/2008 - 12/31/2010
Coverage requirement: Medical and Drug
Pre-index enrollment requirement: 183 days
Post-index enrollment requirement: 0
Enrollment gap: 45 days
Age groups: 18-39, 40-54, 55-65 years
*** Stratifications:** Age group, Sex, Calendar Year
Censor output categorization: 0-364, 365-729, 730-1094, 1095+ days
*** Envelope macro:** Reclassify encounters during inpatient stay as inpatient
Propensity score analysis: 1:1 matching
Propensity score caliper: 0.05

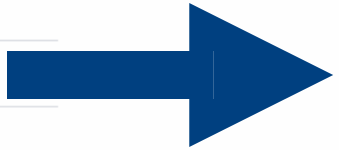
https://dev.sentinelsystem.org/projects/SENTINEL/repos/sentinel-routine-querying-tool-documentation/browse/files/file626-typeall-strata.md

Standard Strata Levels

Table 2. Standard Strata Level IDs

These stratfication levels apply for the following datasets: ([RUNID]_ prefix and sas7bdat extension removed): t1_cida, t2_cida,

LevelID	LevelVars
000	*blank*
001	year
002	sex
003	agegroup
004	sex agegroup
005	sex agegroup year
006	sex agegroup year month
007	agegroup year
008	agegroup year month
009	sex year
010	sex year month
011	year month
020	zip3
021	zip3 zip_uncertain
022	zip3 sex



	tableid	levelid	levelvars
1	t2cida	000	
2	t2cida	001	year
3	t2cida	002	sex
4	t2cida	003	agegroup
5	t2censor	701	censdays_value_cat

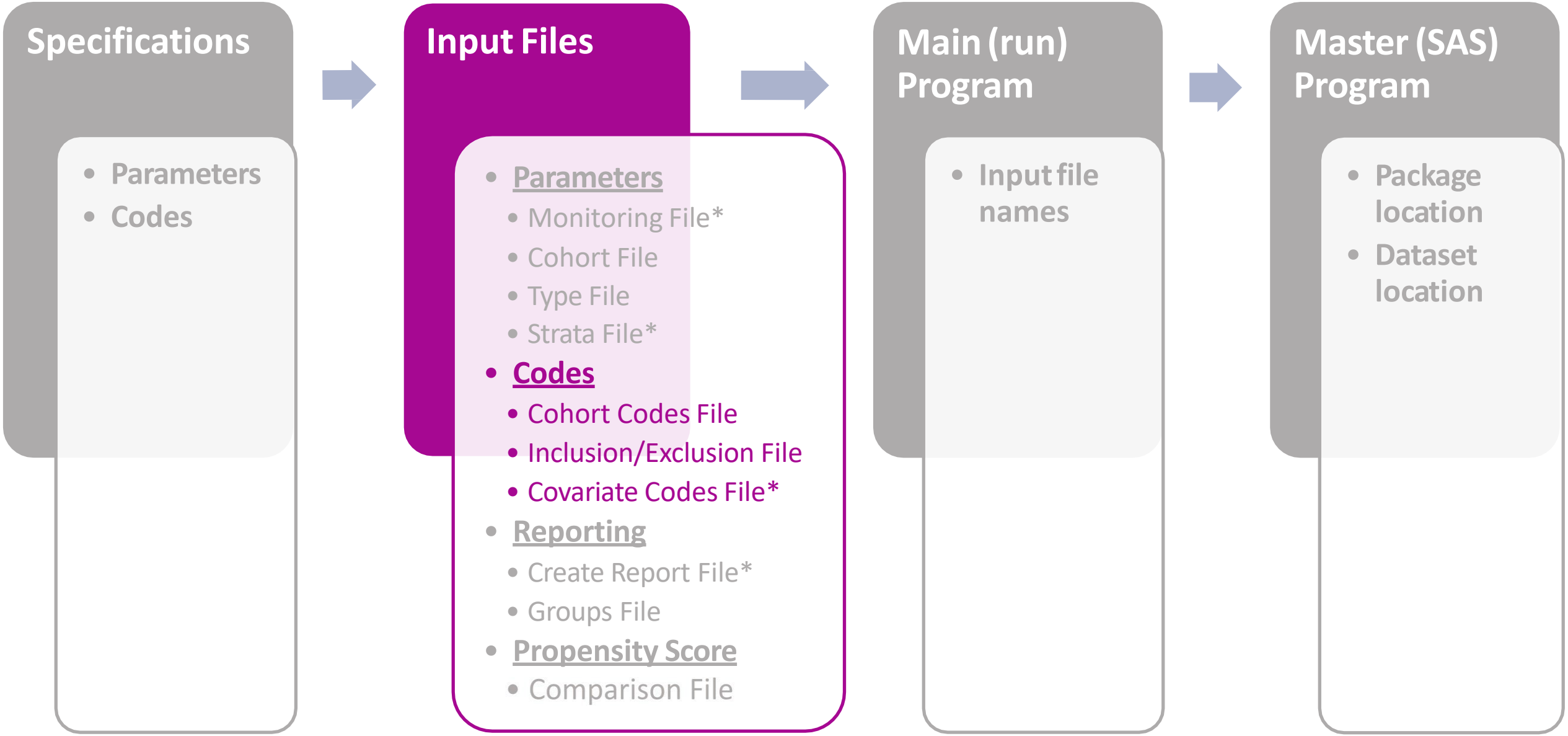
https://dev.sentinelsystem.org/projects/SENTINEL/repos/sentinel-routine-querying-tool-documentation/browse/files/file626-typeall-strata.md

User-defined Strata File Overview

- Specify which output tables should be produced and with which strata levels

```
data out.&wpnum._type2strata;
format tableid $20. levelid $3. levelvars $30.;
tableid = "t2cida";
levelid = "000";
levelvars = "";
output;

tableid = "t2cida";
levelid = "001";
levelvars = "year";
output;

tableid = "t2cida";
levelid = "002";
levelvars = "sex";
output;

tableid = "t2cida";
levelid = "003";
levelvars = "agegroup";
output;

tableid = "t2censor";
levelid = "701";
levelvars = "censdays_value_cat";
output;
run;
```

Step 2: Moving on to Code Files

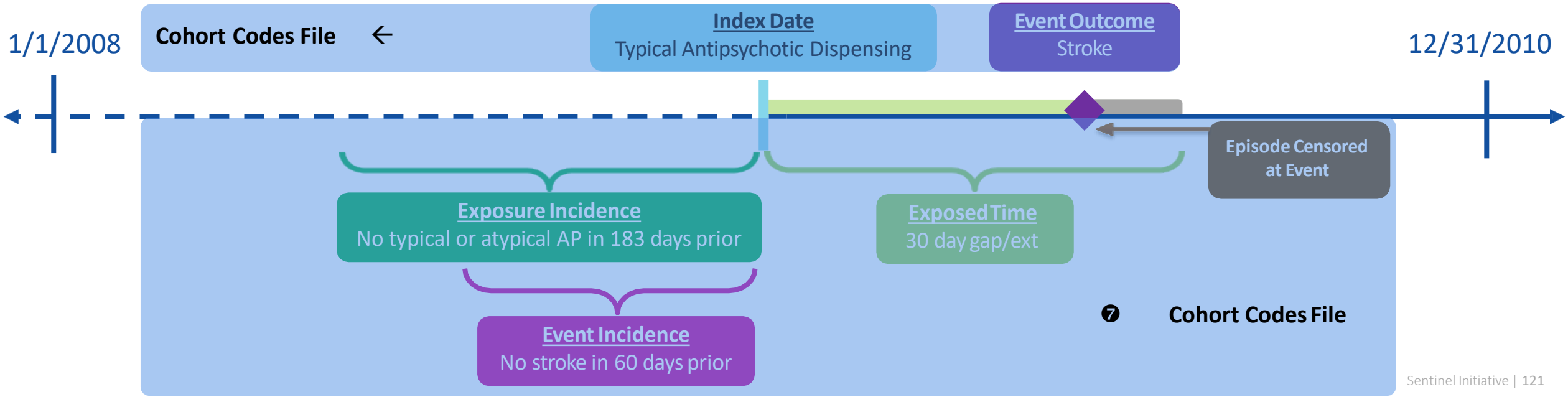


*Global Parameter Files

COHORT CODES FILE:

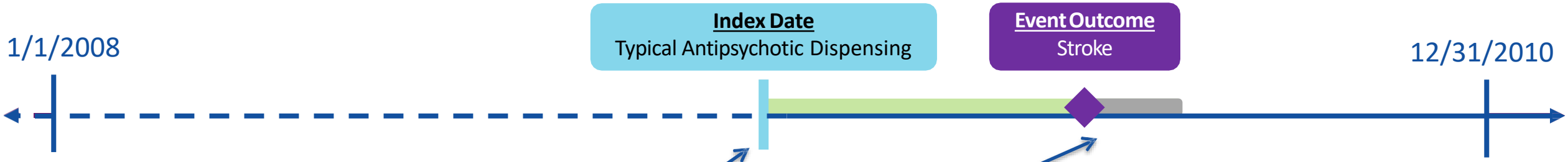
PURPOSE: Assignment of roles to relevant codes for roles in cohort identification

PARAMETERS: 23



Create Cohort Codes File

- Open **5_cohortcodes.sas** program



Focused on 2 Anchor Points

1. Index (t#_index in CIDA)
2. Outcome (t#_fup in CIDA)

Cohort Codes File: Specifications

		Exposure									
	Group	Index Exposure	Cohort definition	Incident exposure washout period	Incident w/ respect to:	Treatment episode gap	Exposure episode extension	Minimum exposure episode duration	Minimum days supplied	Maximum exposure episode duration	Censor treatment episode at evidence of:
1	typ_IS	Typical Antipsychotics	First valid exposure episode during query period	183 days	Typical and atypical antipsychotics	30 days	30 days	1	1	None	Death; DP end date; Query end date; Atypical antipsychotics;
2	typ_ICH	Antips[illegible]notics	First valid exposure episode during query period	183 days	Ty[illegible]nd antip[illegible]notics	30 days	30 days	1	1	None	Death; DP end Query en[illegible]te; Atypical a[illegible]psychotics;
3	atyp_IS	At[illegible]al	First valid exposure episode during query period	183 days	Typi[illegible] and	30 days	30 days	1	1	None	Death; DP[illegible] Qu[illegible] Ty[illegible]cs;
4	atyp_ICH	Atypical Antipsychotics	First valid exposure episode during query period	183 days	Typical and atypical antipsychotics	30 days	30 days	1	1	None	Death; DP end date; Query end date; Typical antipsychotics;

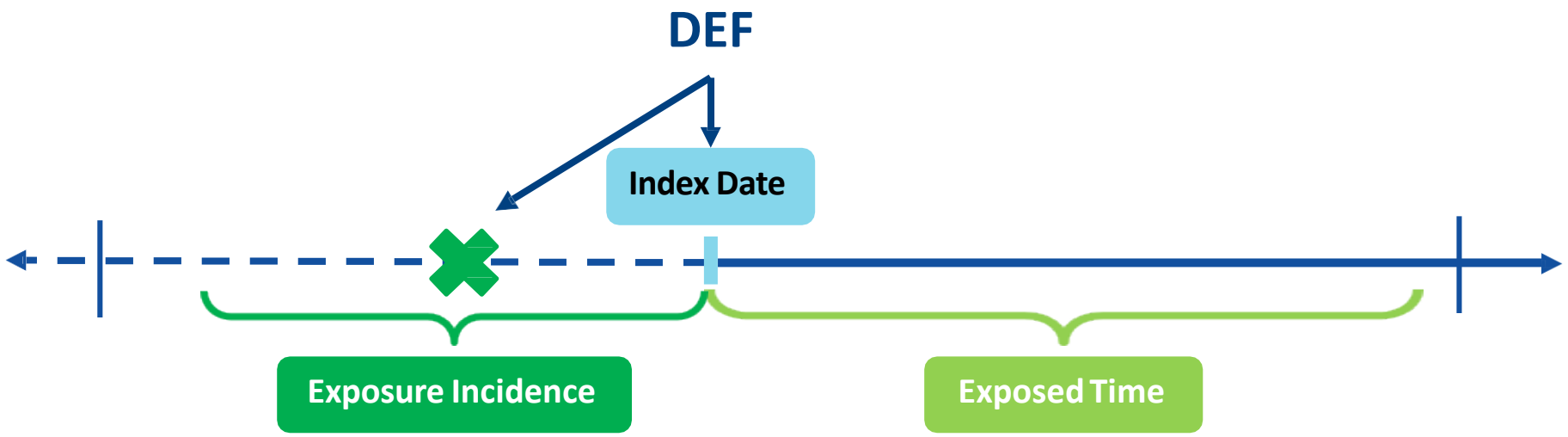
Index (DEF)

Incidence (IOT/IOD)

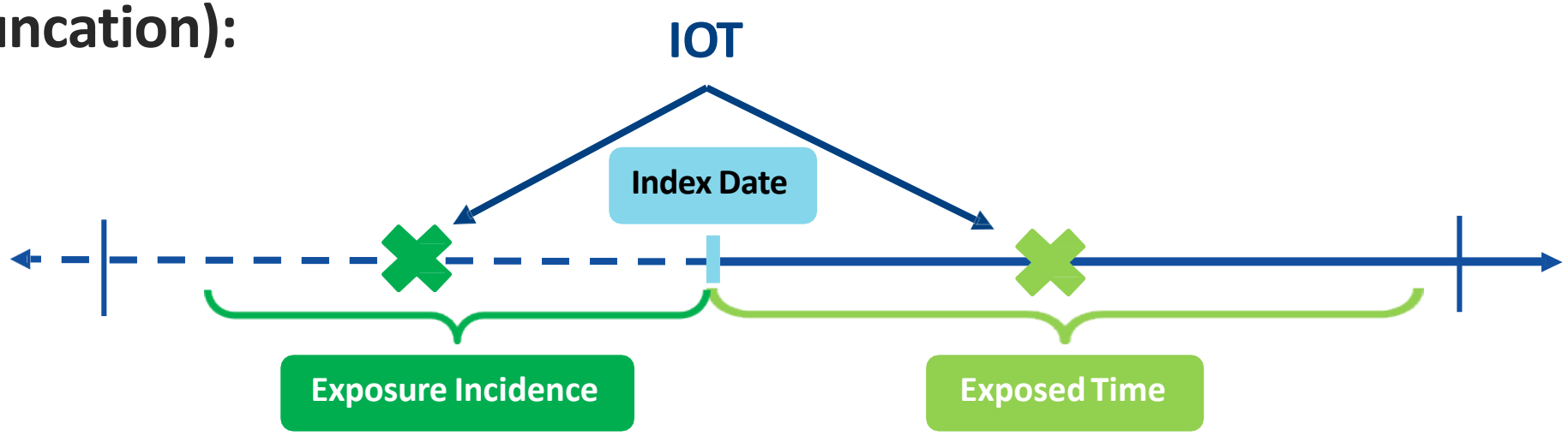
Censoring (IOT/FUT)

Cohort Codes File: Parameter T2_INDEX

DEF (Definition):
Code defines index date and incidence criteria



IOT (Incidence or Truncation):
Code defines incidence and truncation criteria



Create Cohort Codes File

Group	t2_index = DEF	t2_index = IOT
typ_is	typical_antipsychotics	
typ_ich		
atyp_is		
atyp_ich		

Code List Key	
Clinical Concept	SAS Dataset with Codes
Typical antipsychotics	typical_antipsychotics
Atypical antipsychotics	atypical_antipsychotics
Ischemic stroke	ischemic_stroke
Intracranial hemorrhage	intracranial_hemorrhage

Create Cohort Codes File

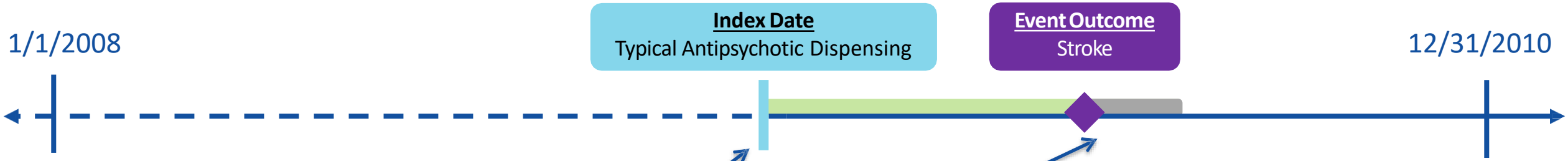
Group	t2_index = DEF	t2_index = IOT	t2_fup = DEF	t2_fup = IOC
typ_is	typical_antipsychotics	atypical_antipsychotics		
typ_ich	typical_antipsychotics	atypical_antipsychotics		
atyp_is	atypical_antipsychotics	typical_antipsychotics		
atyp_ich	atypical_antipsychotics	typical_antipsychotics		

Code List Key	
Clinical Concept	SAS Dataset with Codes
Typical antipsychotics	typical_antipsychotics
Atypical antipsychotics	atypical_antipsychotics
Ischemic stroke	ischemic_stroke
Intracranial hemorrhage	intracranial_hemorrhage

Cohort Codes File: Sample

	group	stockgroup	codecat	codetype	code	caresettingprincipal	t2_index	t2_fup
10099	typ_is	FLUPHENAZINEHCL	RX	11	68084084695		DEF	NOT
10100	typ_is	FLUPHENAZINEHCL	RX	11	68084095025		DEF	NOT
10101	typ_is	FLUPHENAZINEHCL	RX	11	68084095095		DEF	NOT
10102	typ_is	TRIFLUOPERAZINEHCL	RX	11	68115058600		DEF	NOT
10103	typ_is	MOLINDONEHCL	RX	11	68115071000		DEF	NOT
10104	typ_is	HALOPERIDOL	RX	11	68382007901		DEF	NOT
10105	typ_is	HALOPERIDOL	RX	11	68382007910		DEF	NOT
10106	typ_is	HALOPERIDOL	RX	11	68382008001		DEF	NOT
10107	typ_is	HALOPERIDOL	RX	11	68382008010		DEF	NOT
10108	typ_is	HALOPERIDOL	RX	11	68382008101		DEF	NOT
10109	typ_is	OLANZAPINEFLUOXETINEHCL	RX	11	00002323030		IOT	NOT
10110	typ_is	OLANZAPINEFLUOXETINEHCL	RX	11	00002323101		IOT	NOT
10111	typ_is	OLANZAPINEFLUOXETINEHCL	RX	11	00002323130		IOT	NOT
10112	typ_is	OLANZAPINEFLUOXETINEHCL	RX	11	00002323133		IOT	NOT
10113	typ_is	OLANZAPINEFLUOXETINEHCL	RX	11	00002323201		IOT	NOT
10114	typ_is	OLANZAPINEFLUOXETINEHCL	RX	11	00002323230		IOT	NOT
10115	typ_is	OLANZAPINEFLUOXETINEHCL	RX	11	00002323233		IOT	NOT
10116	typ_is	OLANZAPINEFLUOXETINEHCL	RX	11	00002323301		IOT	NOT
10117	typ_is	OLANZAPINEFLUOXETINEHCL	RX	11	00002323330		IOT	NOT
10118	typ_is	OLANZAPINEFLUOXETINEHCL	RX	11	00002323333		IOT	NOT

Create Cohort Codes File



Focused on 2 Anchor Points

1. Index (t#_index in CIDA)
2. Outcome (t#_fup in CIDA)

Specifications: Cohort Codes

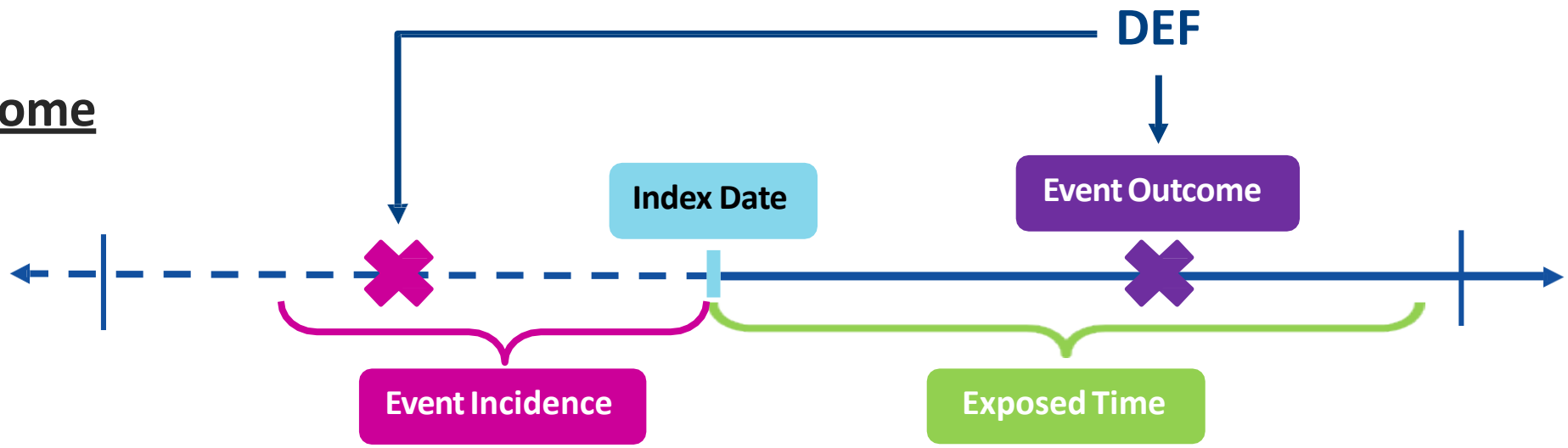
		Event Outcome						
	Group	Event	Care setting	Principal diagnosis position	Event washout conditions	Event washout care setting	Event washout period	Blackout period
1	typ_IS	Ischemic stroke	Inpatient hospital stay	Principal	Stroke (ischemic stroke and intracranial hemorrhage)	Any care setting	60	1
2	typ_ICH	Intracranial hemorrhage	Inpat hosp	Principal	Stroke (ischemic stroke a intracranial hemorr	Any care setting	60	1
3	atyp_IS	Ischemic stroke	Inpat t hospita ay	Principal	Stroke (ischemic stroke an intracra	Any care setting	60	1
4	atyp_ICH	Intracranial hemorrhage		Principal	(ische intracranial hemorrhage)	setting	60	1

Outcome

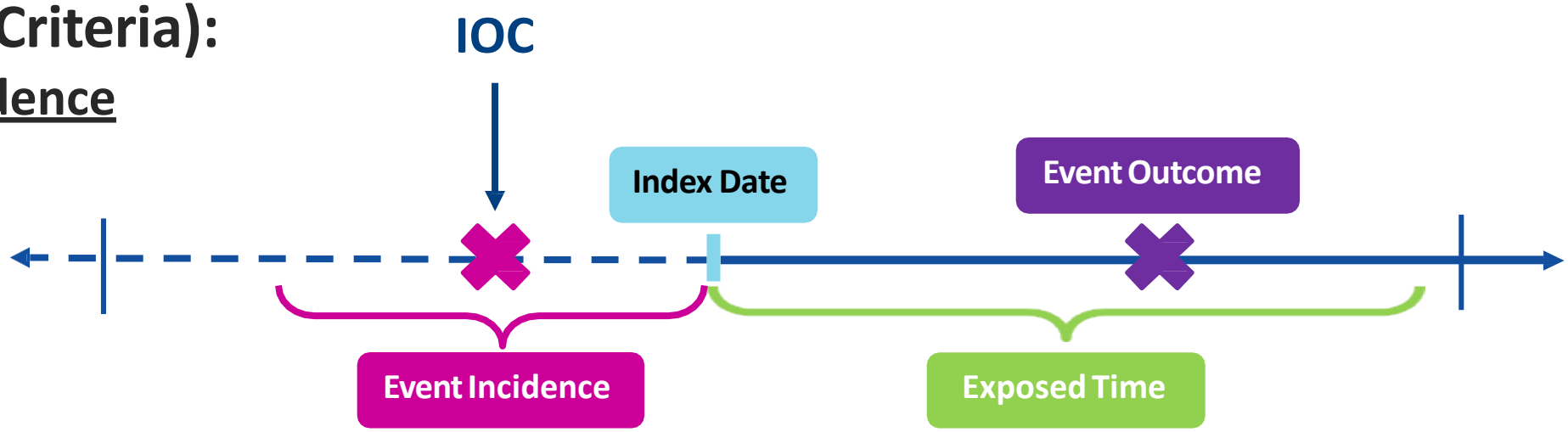
Outcome Incidence (IOC)

Cohort Codes File: Parameter T2_FUP

DEF (Definition):
Code defines event outcome and incidence criteria



IOC (Incidence Only Criteria):
Code defines event incidence criteria



Create Cohort Codes File

Group	t2_index = DEF	t2_index = IOT	t2_fup = DEF	t2_fup = IOC
typ_is	typical_antipsychotics	atypical_antipsychotics	ischemic_stroke	
typ_ich	typical_antipsychotics	atypical_antipsychotics		
atyp_is	atypical_antipsychotics	typical_antipsychotics		
atyp_ich	atypical_antipsychotics	typical_antipsychotics		

Code List Key	
Clinical Concept	SAS Dataset with Codes
Typical antipsychotics	typical_antipsychotics
Atypical antipsychotics	atypical_antipsychotics
Ischemic stroke	ischemic_stroke
Intracranial hemorrhage	intracranial_hemorrhage

Create Cohort Codes File

Group	t2_index = DEF	t2_index = IOT	t2_fup = DEF	t2_fup = IOC
typ_is	typical_antipsychotics	atypical_antipsychotics	ischemic_stroke	intracranial_hemorrhage
typ_ich	typical_antipsychotics	atypical_antipsychotics	intracranial_hemorrhage	ischemic_stroke
atyp_is	atypical_antipsychotics	typical_antipsychotics	ischemic_stroke	intracranial_hemorrhage
atyp_ich	atypical_antipsychotics	typical_antipsychotics	intracranial_hemorrhage	ischemic_stroke

Code List Key	
Clinical Concept	SAS Dataset with Codes
Typical antipsychotics	typical_antipsychotics
Atypical antipsychotics	atypical_antipsychotics
Ischemic stroke	ischemic_stroke
Intracranial hemorrhage	intracranial_hemorrhage

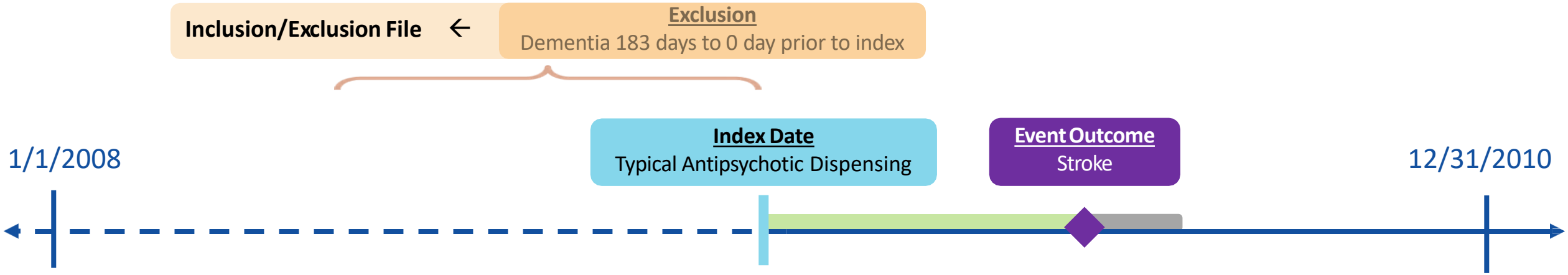
Cohort Codes File: Sample

	group	stockgroup	codecat	codetype	code	caresettingprincipal	t2_index	t2_fup
12105	typ_is	Ischemicstroke	DX	09	43301	'IPP'	NOT	DEF
12106	typ_is	Ischemicstroke	DX	09	43311	'IPP'	NOT	DEF
12107	typ_is	Ischemicstroke	DX	09	43321	'IPP'	NOT	DEF
12108	typ_is	Ischemicstroke	DX	09	43331	'IPP'	NOT	DEF
12109	typ_is	Ischemicstroke	DX	09	43381	'IPP'	NOT	DEF
12110	typ_is	Ischemicstroke	DX	09	43391	'IPP'	NOT	DEF
12111	typ_is	Ischemicstroke	DX	09	43401	'IPP'	NOT	DEF
12112	typ_is	Ischemicstroke	DX	09	43411	'IPP'	NOT	DEF
12113	typ_is	Ischemicstroke	DX	09	43491	'IPP'	NOT	DEF
12114	typ_is	Ischemicstroke	DX	09	436	'IPP'	NOT	DEF
12115	typ_is	Intracranialhemorrhage	DX	09	430		NOT	IOC
12116	typ_is	Intracranialhemorrhage	DX	09	431		NOT	IOC

INCLUSION/EXCLUSION CODES FILE

PURPOSE: Assignment of roles to relevant codes for restriction of cohort due to inclusion/exclusion criteria

PARAMETERS: 19



Specifications: Inclusion/Exclusion Codes

		Inclusion/Exclusion Criteria						
	Group	Inclusion/ exclusion group	Criteria	Care setting	Principal diagnosis position	Evaluation period start	Evaluation period end	Number of instances the criteria should be found in evaluation period
1	typ_IS	Dementia	Exclude	Any care setting	Any position	-183	0	1
2	typ_ICH	Dementia	Exclude	Any care setting	Any position	-183	0	1
3	atyp_IS	Dementia	Exclude	Any care setting	Any position	-183	0	1
4	atyp_ICH	Dementia	Exclude	Any care setting	Any position	-183	0	1

Create Inclusion/Exclusion Codes File

- Open **6_exclusion.sas** program

```
data work.excl;
format group $40. stockgroup $30. caresettingprincipal $30. code $11. codecat $2. codetype $3.
       condinclusion 8. subcondinclusion 8. condlevel $30. subcondlevel $30.
       condfrom 8. condto 8. codedays 8. codesupply 8. excludesupply $1.
       codepop $2. indexdate $30. rawlabdatetype $3. rawlabresult $30. ;

set in.dementia;
group = "&curr_name";
stockgroup = compress (descrip, ", .//_-<>=;&[]'(){}%");
caresettingprincipal = " ";
code = compress (code1, ' .//_-()%');
codecat = codecat1;
codetype = codetype1;

condinclusion = 0; /* Condition Exclusion Indicator; Numerical; Valid values: 0 or 1 to exclude or include if evidence of condition; Required */
condlevel = "dementia"; /* Name of inclusion/exclusion condition; Required*/
condfrom = -183; /* Evaluation Period Start; Numerical; Required */
condto = 0; /* Evaluation Period End; Numerical; Required */
codedays = 1; /* Indicates number of instances the criteria should be found in evaluation period; Numerical; Required */

subcondinclusion = 1;
subcondlevel = "dementia";
codesupply= .;
excludesupply= "N";
codepop="";
indexdate="";
rawlabdatetype = "";
rawlabresult = "";
drop code1 codecat1 codetype1 descrip ;
run;
```

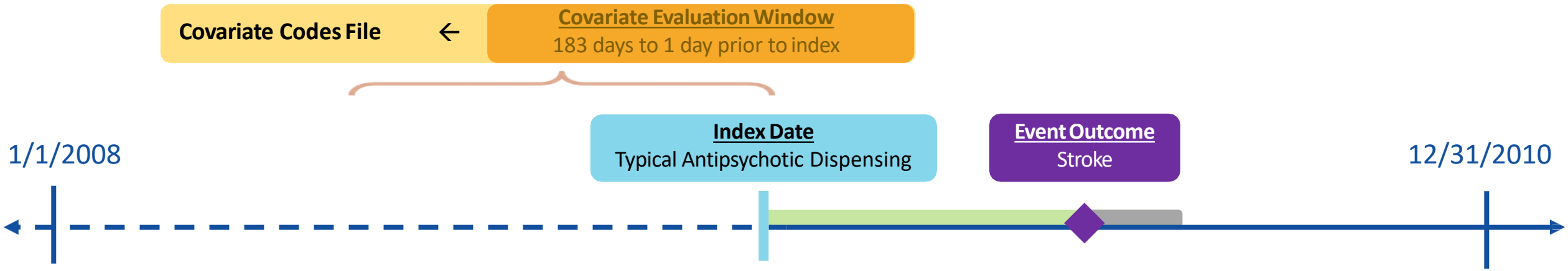
Finished Inclusion/Exclusion Codes File Sample

	group	stockgroup	caresettingprincipal	code	codecat	codetype	condinclusion	subcondinclusion	condlevel	subcondlevel	condfrom	condto	codedays
1	typ_is	Dementia		2900	DX	09	0	1	dementia	dementia	-183	0	1
2	typ_is	Dementia		29010	DX	09	0	1	dementia	dementia	-183	0	1
3	typ_is	Dementia		29011	DX	09	0	1	dementia	dementia	-183	0	1
4	typ_is	Dementia		29012	DX	09	0	1	dementia	dementia	-183	0	1
5	typ_is	Dementia		29013	DX	09	0	1	dementia	dementia	-183	0	1
6	typ_is	Dementia		29020	DX	09	0	1	dementia	dementia	-183	0	1
7	typ_is	Dementia		29021	DX	09	0	1	dementia	dementia	-183	0	1
8	typ_is	Dementia		2903	DX	09	0	1	dementia	dementia	-183	0	1
9	typ_is	Dementia		29040	DX	09	0	1	dementia	dementia	-183	0	1
10	typ_is	Dementia		29041	DX	09	0	1	dementia	dementia	-183	0	1
11	typ_is	Dementia		29042	DX	09	0	1	dementia	dementia	-183	0	1
12	typ_is	Dementia		29043	DX	09	0	1	dementia	dementia	-183	0	1
13	typ_is	Dementia		2940	DX	09	0	1	dementia	dementia	-183	0	1
14	typ_is	Dementia		29410	DX	09	0	1	dementia	dementia	-183	0	1
15	typ_is	Dementia		29411	DX	09	0	1	dementia	dementia	-183	0	1
16	typ_is	Dementia		29420	DX	09	0	1	dementia	dementia	-183	0	1
17	typ_is	Dementia		29421	DX	09	0	1	dementia	dementia	-183	0	1
18	typ_is	Dementia		2948	DX	09	0	1	dementia	dementia	-183	0	1
19	typ_is	Dementia		3310	DX	09	0	1	dementia	dementia	-183	0	1
20	typ_is	Dementia		33111	DX	09	0	1	dementia	dementia	-183	0	1
21	typ_is	Dementia		33119	DX	09	0	1	dementia	dementia	-183	0	1
22	typ_is	Dementia		3312	DX	09	0	1	dementia	dementia	-183	0	1
23	typ_is	Dementia		3317	DX	09	0	1	dementia	dementia	-183	0	1
24	typ_is	Dementia		797	DX	09	0	1	dementia	dementia	-183	0	1

COVARIATE CODES FILE:

PURPOSE: Assignment of codes for evaluation of covariates, relative to the exposure index

PARAMETERS: 13



Specifications: Covariates

Covariates					
Covariate	Care setting	Principal diagnosis position	Evaluation period start	Evaluation period end	Number of instances the covariate should be found in evaluation period
Acute myocardial infarction	Any	Any	-183	-1	1
Diabetes	Any	Any	-183	-1	1
Heart failure	Any	Any	-183	-1	1
Hypercholesterolemia	Any	Any	-183	-1	1
Hypertension	Any	Any	-183	-1	1
Kidney failure	Any	Any	-183	-1	1
Transient ischemic attack	Any	Any	-183	-1	1
Depression	Any	Any	-183	-1	1
Anxiety	Any	Any	-183	-1	1
Bipolar	Any	Any	-183	-1	1
Schizophrenia/psychotic disorder	Any	Any	-183	-1	1
Substance abuse	Any	Any	-183	-1	1

Finished Covariate Codes File Sample

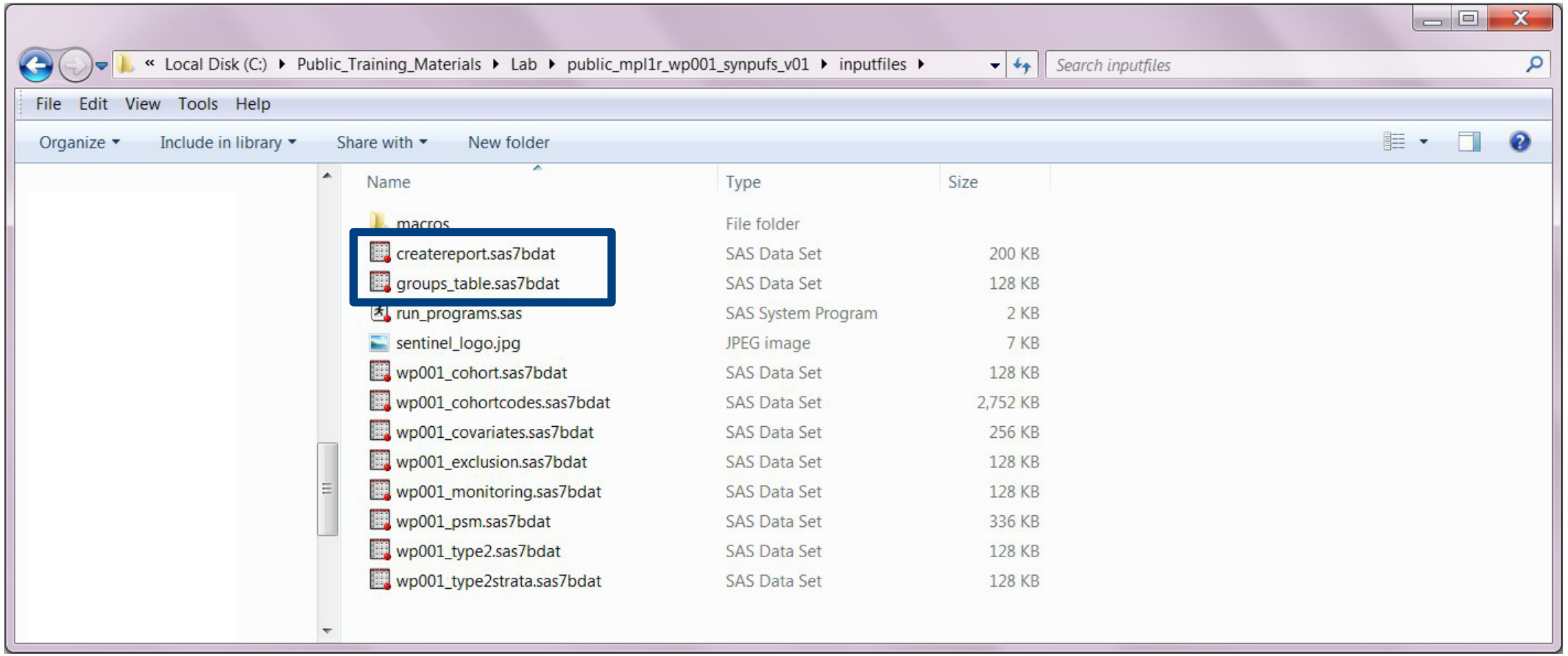
	studyname	covarnum	code	stockgroup	codecat	codetype	caresettingprincipal	covfrom	covto	keep	codedays	codesupply	excludesupply
1	AMI	1	4100	AMI	DX	09		-183	-1	0	1	.	
2	AMI	1	410	AMI	DX	09		-183	-1	0	1	.	
3	AMI	1	41000	AMI	DX	09		-183	-1	0	1	.	
4	AMI	1	41001	AMI	DX	09		-183	-1	0	1	.	
5	AMI	1	41002	AMI	DX	09		-183	-1	0	1	.	
6	AMI	1	4101	AMI	DX	09		-183	-1	0	1	.	
7	AMI	1	41010	AMI	DX	09		-183	-1	0	1	.	
8	AMI	1	41011	AMI	DX	09		-183	-1	0	1	.	
9	AMI	1	41012	AMI	DX	09		-183	-1	0	1	.	
10	AMI	1	4102	AMI	DX	09		-183	-1	0	1	.	
11	AMI	1	41020	AMI	DX	09		-183	-1	0	1	.	
12	AMI	1	41021	AMI	DX	09		-183	-1	0	1	.	
13	AMI	1	41022	AMI	DX	09		-183	-1	0	1	.	
14	AMI	1	41030	AMI	DX	09		-183	-1	0	1	.	
15	AMI	1	4103	AMI	DX	09		-183	-1	0	1	.	
16	AMI	1	41031	AMI	DX	09		-183	-1	0	1	.	
17	AMI	1	41032	AMI	DX	09		-183	-1	0	1	.	
18	AMI	1	41040	AMI	DX	09		-183	-1	0	1	.	
19	AMI	1	4104	AMI	DX	09		-183	-1	0	1	.	
20	AMI	1	41041	AMI	DX	09		-183	-1	0	1	.	
21	AMI	1	41042	AMI	DX	09		-183	-1	0	1	.	
22	AMI	1	4105	AMI	DX	09		-183	-1	0	1	.	
23	AMI	1	41050	AMI	DX	09		-183	-1	0	1	.	
24	AMI	1	41051	AMI	DX	09		-183	-1	0	1	.	

LOCAL REPORT FILES:

PURPOSE: Specify what to include in the automated report

Local Report Files

- The local report input files have been created for you
  - createreport.sas7bdat and groups_table.sas7bdat



Create Report File (Excerpt)

	requestid	groups_table	columns_table	type	alltypefiles	monitoringfile	cohortfile	userstrata	covariatecodes
1	public_mpl1r_wp001	groups_table		2	wp001_type2	wp001_monitoring	wp001_cohort	wp001_type2strata	wp001_covariates

customtitle	exclude	stratify_by_level	zipfile	agegroupfmt	logo	output_baselinetable	look_start	look_end	output_cdf_km
Typical and Atypical Antipsychotics and Stroke	8	000 001 002 003			sentinel_logo.jpg	Y	1	1	N

...

Create Report File

```
data out.createreport;
format type 1. requestid $23. groups_table $30. columns_table $30. alltypefiles $50.
monitoringfile $30. cohortfile $30. userstrata $30. covariatecodes $30.
customtitle $50. exclude $50. stratify_by_level $50.
zipfile $15. agegroupfmt $100. logo $30. output_baselinetable $1. look_start 1. look_end 1.
output_cdf_km $1. cdf_title1 $50. km_title1 $50. km_title2 $50. cdf_footnote1 $50. cdf_footnote2 $50.
km_footnote1 $50. km_footnote2 $50. cdf_xmin 8. cdf_xmax 8. cdf_xtick 8. km_xmin 8. km_xmax 8. km_xtick 8.
cdf_ymin 8. cdf_ymax 8. cdf_ytick 8. km_ymin 8. km_ymax 8. km_ytick 8. km_ep_xmin 8. km_ep_xmax 8. km_ep_xtick 8.
km_ep_ymin 8. km_ep_ymax 8. km_ep_ytick 8. censoring_display $40. cens_elig $20. cens_dth $20. cens_dpend $20. cens_qryend $20.
cens_episend $20. cens_spec $20. cens_event $20. displayn $1. line_spacing 8.;

type=2;
requestid= 'public_mpl1r_wp001';
groups_table= 'groups_table';
columns_table= '';
alltypefiles='wp001_type2';
monitoringfile= 'wp001_monitoring';
cohortfile= 'wp001_cohort';
userstrata= 'wp001_type2strata';
covariatecodes = 'wp001_covariates';
customtitle= 'Typical and Atypical Antipsychotics and Stroke';
exclude= '8';
stratify_by_level= '000 001 002 003';
zipfile= '';
agegroupfmt= '';
logo= 'sentinel_logo.jpg';
output_baselinetable= 'Y';
look_start= 1;
look_end= 1;
output_cdf_km= 'N';
...
```

Groups File

```
%macro groups (title,group,grouplabel,header);
data groups_table&title.;
    format header $60. group1 $30. runid1 $10. group2 $30. runid2 $10. grouplabel $100.
           combinedgroupname $50. order 8. Historyofuse $50. Recordedhistory $50.
           Utilizationintensity $50. highlight_vars $60. alphabetical_covarsort $1. Baselinelabel $50.;
    header = "&header.";
    group1 = "&group.";
    runid1= 'r01';
    group2 = "";
    runid2 = "";
    grouplabel= "&grouplabel.";
    combinedgroupname= "";
    order = &title.;
    Historyofuse = "";
    Recordedhistory = "";
    Utilizationintensity = "";
    highlight_vars = "";
    alphabetical_covarsort = 'N';
    Baselinelabel = "";
    run;
%mend;
```

```
%groups (1,typ_is, Typical Antipsychotics, Ischemic Stroke);
%groups (2,typ_ich, Typical Antipsychotics, Intracranial Hemorrhage);
%groups (3,atyp_is, Atypical Antipsychotics, Ischemic Stroke);
%groups (4,atyp_ich, Atypical Antipsychotics, Intracranial Hemorrhage);
```

Groups File

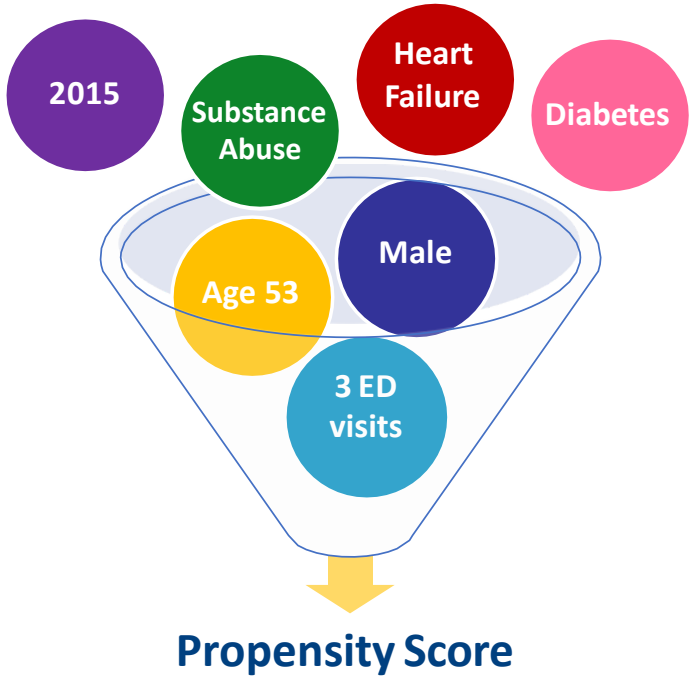
	header	group1	runid1	group2	runid2	grouplabel	combinedgroupname
1	Ischemic Stroke	typ_is	r01			Typical Antipsychotics	
2	Intracranial Hemorrhage	typ_ich	r01			Typical Antipsychotics	
3	Ischemic Stroke	atyp_is	r01			Atypical Antipsychotics	
4	Intracranial Hemorrhage	atyp_ich	r01			Atypical Antipsychotics	

order	Historyofuse	Recordedhistory	Utilizationintensity	highlight_vars	alphabetical_covars	Baselinelabel
1					N	
2					N	
3					N	
4					N	

PROPENSITY SCORE COMPARISON FILE:

PURPOSE: Specify all exposure/comparator pairs that should be evaluated in the propensity score analysis

PARAMETERS: 12



Specifications: Propensity Score

* **Query period:**	1/1/2008 - 12/31/2010
Coverage requirement:	Medical and Drug
Pre-index enrollment requirement:	183 days
Post-index enrollment requirement:	0
Enrollment gap:	45 days
Age groups:	18-39, 40-54, 55-65 years
* **Stratifications:**	Age group, Sex, Calendar Year
Censor output categorization:	0-364, 365-729, 730-1094, 1095+ days
* **Envelope macro:**	Reclassify encounters during inpatient stay as inpatient
Propensity score analysis:	1:1 matching
Propensity score caliper:	0.05

*** Global Parameters**

Create Propensity Score Comparison File

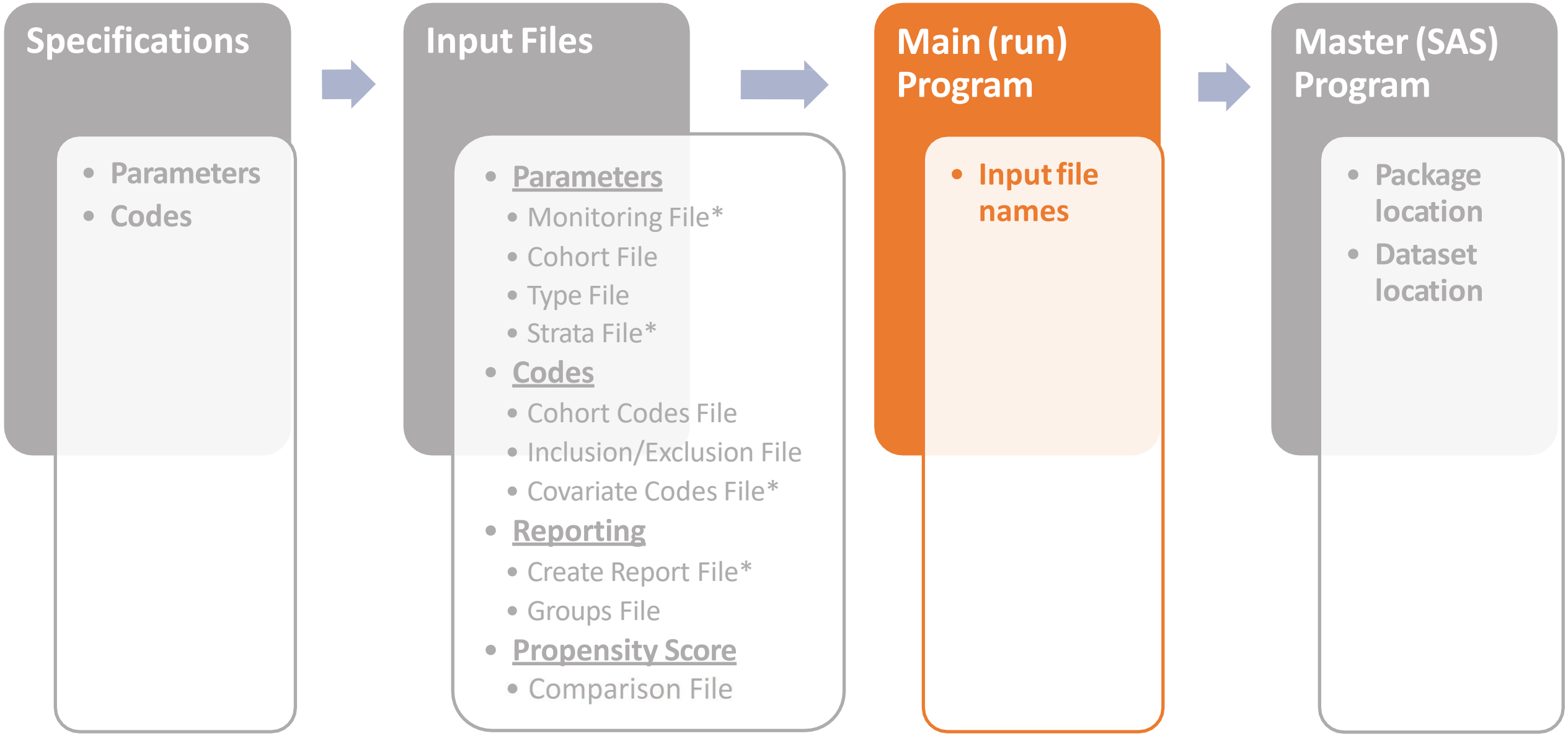
- Open **9_propensityscore.sas** program

	analysisgrp	matchanalysis	eoi	ref	caliper	ratio	class	noclass	hdps	hdpswinfrom	hdpswinto	matchvars
1	ischemic_stroke	PS	typ_is	atyp_is	0.05	1	Sex Covar1 Covar2 Covar3 Covar4 Covar5 Covar6 Covar7 Covar8 Covar9 Covar10 Covar11 Covar12	Age	N	.	.	
2	intracranial_hemorrhage	PS	typ_ich	atyp_ich	0.05	1	Sex Covar1 Covar2 Covar3 Covar4 Covar5 Covar6 Covar7 Covar8 Covar9 Covar10 Covar11 Covar12	Age	N	.	.	

```
%macro psm (title,analysis,eoi,ref);
    data psm&title.;
    format analysisgrp $40. matchanalysis $40. eoi $40. ref $40. caliper best12. ratio 8. class $999. noclass $999.
           hdps $1. hdpswinfrom 8. hdpswinto 8. matchvars $40.;
    analysisgrp = "&analysis.";
    matchanalysis = 'PS';
    eoi = "&eoi."; /* Exposure of Interest; Valid values: typ_is typ_ich atyp_is atyp_ich; Required */
    ref = "&ref."; /* Reference Group; Valid values: typ_is typ_ich atyp_is atyp_ich; Required */
    caliper=0.05; /* Matching Caliper; Numerical; Valid values: Any value between 0-1; Required */
    ratio = 1 ; /* Matching Ratio; Numerical; Valid values: For 1:1 fixed matching, enter 1.
                   For 1:n variable matching, enter numerical value for n; Required */
    class='Sex Covar1 Covar2 Covar3 Covar4 Covar5 Covar6 Covar7 Covar8 Covar9 Covar10 Covar11 Covar12';
    noclass='Age';
    hdps='N';
    hdpswinfrom=.;
    hdpswinto=.;
    matchvars='';
    run;
%mend;
```

```
%psm (1,ischemic_stroke,typ_is,atyp_is);  /* Fill in label for analysis, group 1 name (exposure of interest), and group 3 name (reference group) */
%psm (2,intracranial_hemorrhage,typ_ich,atyp_ich); /* Fill in label for analysis, group 2 name (exposure of interest), and group 4 name (reference group)
```

Step 3: Name and Locate Input Files



*Global Parameter Files

RUN_PROGRAMS:

PURPOSE: Reference names of all input files and specify run level parameters

Run_Programs

```
/*** Macro Parameters ***/
/*** Do not include file extensions for any dataset names ***/
%let RUNID=r01;
%let PERIODIDSTART=1;
%let PERIODIDEND=1;
%let ANALYSIS=;
%let MONITORINGFILE=wp001_monitoring;
%let USERSTRATA=wp001_type2strata;
%let COMBOFILE=;
%let COHORTFILE=wp001_cohort;
%let COHORTCODES=wp001_cohortcodes;
%let INCLUSIONCODES=wp001_exclusion;
%let STOCKPILINGFILE=;
%let RUN_ENVELOPE =0;
%let FREEZEDATA=N;
%let ZIPFILE=;
%let LABSCODEMAP=; /*must be specified if lab data are used*/
%let DISTINDEX =;

*Type files;
%let TYPE1FILE=;
%let TYPE2FILE=wp001_type2;
%let TYPE3FILE=;
%let TYPE4FILE=;
%let PREGDUR=;
%let TYPE5FILE=;
%let TYPE6FILE=;

** Sequential Analysis parameters **;
%let METADATAFILE=;
%let SURVEILLANCEMODE=;

*Baseline Table files;
%let COVARIATECODES=wp001_covariates;
%let UTILFILE=;
%let COMORBFILE=;
%let DRUGCLASSFILE=;
%let PROFILE = ;
%let MFUFILE = ;
```

Run ID

Input Files

Additional Options

Input Files

Run_Programs

```
*Additional analyses files: multiple events, overlap,
 adherence, ITS, switching, concomittant episodes;
%let MULTEVENTFILE=;
%let MULTEVENTFILE_ADHERE=;
%let OVERLAPFILE=;
%let OVERLAPFILE_ADHERE=;
%let ITSFILE = ;
%let CONCFILE=;
%let TREATMENTPATHWAYS=;

*Mother-Infant Cohort file;
%let MICOHORTFILE=;

** Treescan parameters **;
%let TREEFILE = ;
%let TREELOOKUP=;
%let ICD10ICD9MAP=;

** Propensity Score and Multi-Factor Matching parameters ** ;
%let COMPARISON = wp001_psm;
%let COVARIATES_CONSIDERED= ;
%let COVARIATES_SELECTED= ;
%let RANKING= ;
%let ZERO_CELL_CORR= ;
%let PERCENTILES=10;
%let DIAGNOSTICS=Y;
%let INDLEVEL=N;
%let UNCONDITIONAL=Y;
%let ANALYTICSUBGROUPS=;

** Macro Call RUN 1 ** ;

%include "&sasmacr.runqrp.sas";

/** Report Macro Parameters **/
%let CREATEREPORT_TYPE = 2;
%let CREATEREPORT_T1T2_FILE = createreport;
%let CREATEREPORT_T5_FILE = ;

%include "&reportmacr.runreport.sas";
```

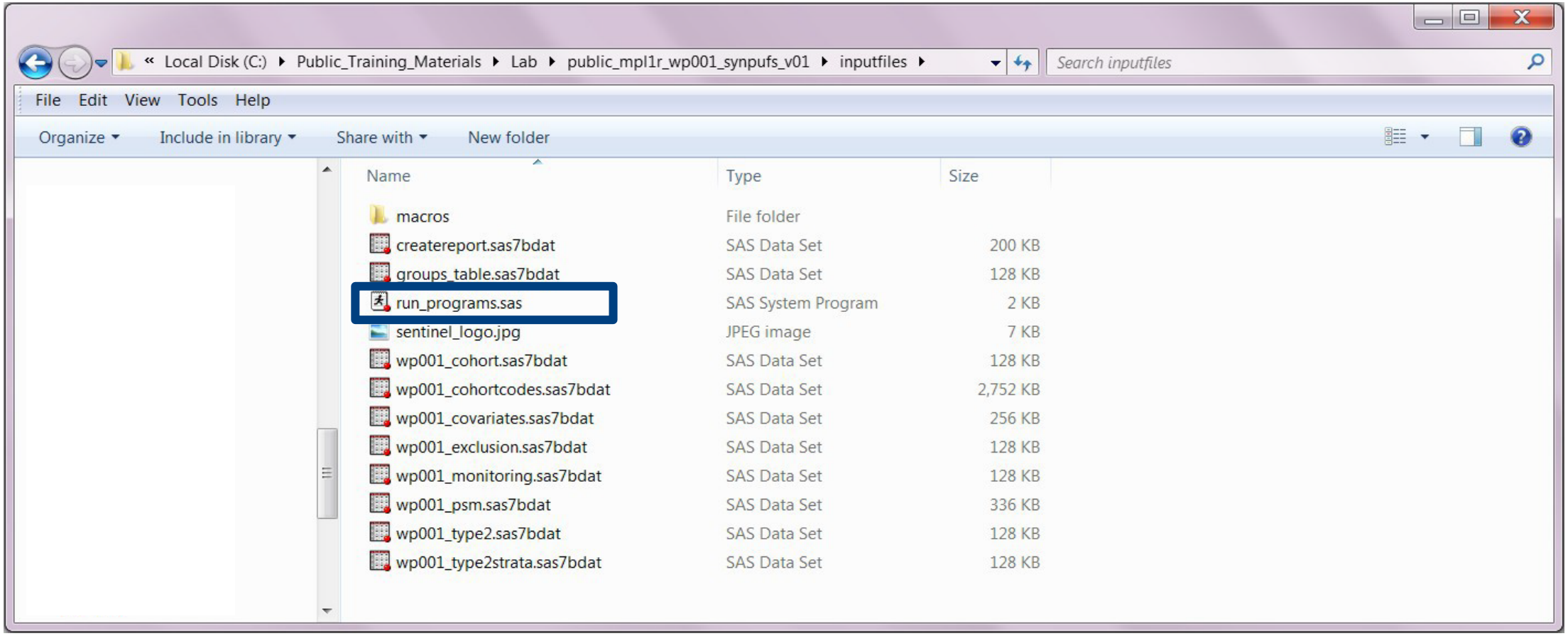
Type Specific Optional Parameters

Inferential L2 Related Parameters

Reporting Files

RUN_PROGRAMS.SAS

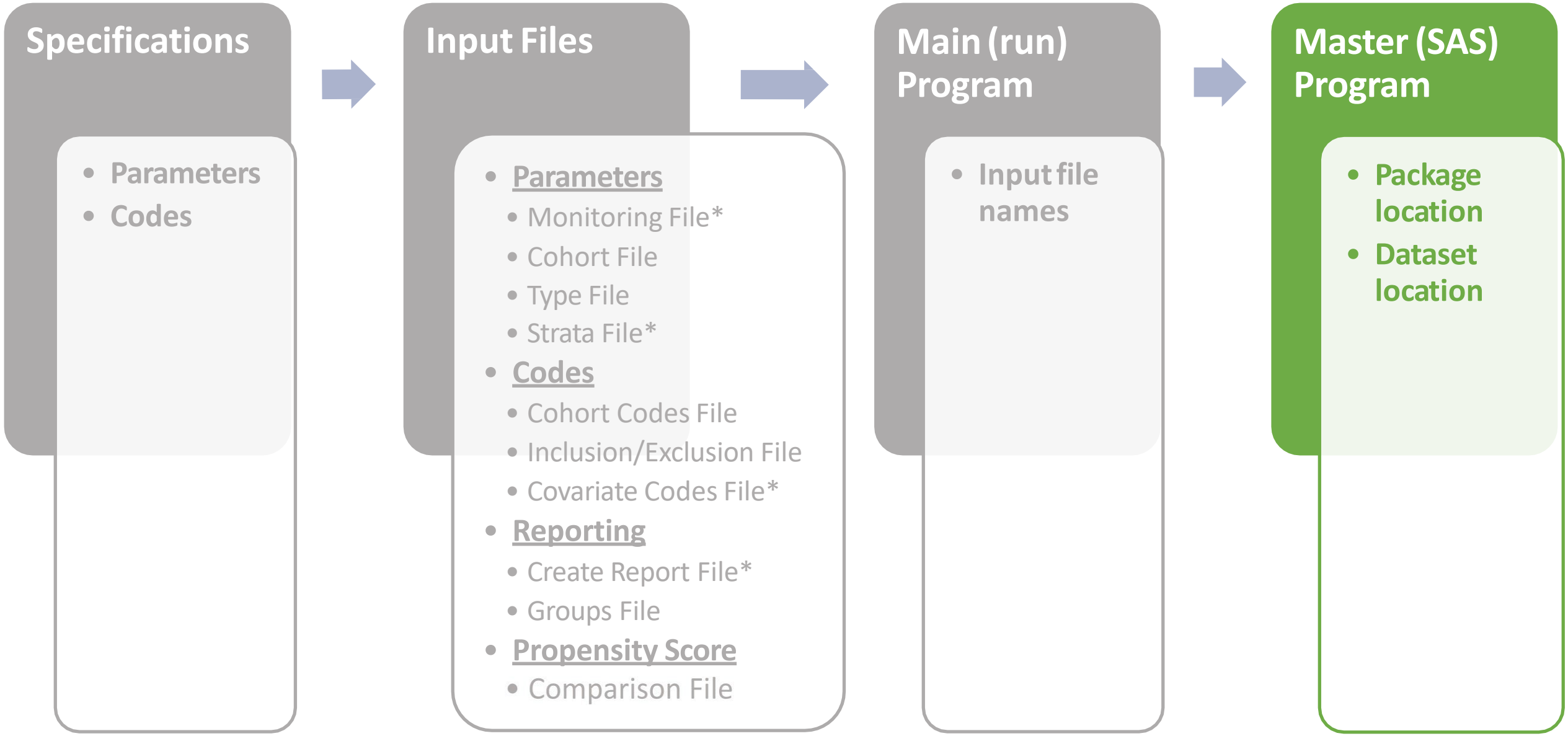
- Referred to as **“main program”** in CIDA documentation
- Review the completed run_programs.sas file in your inputfiles folder



SASPROGRAMS:

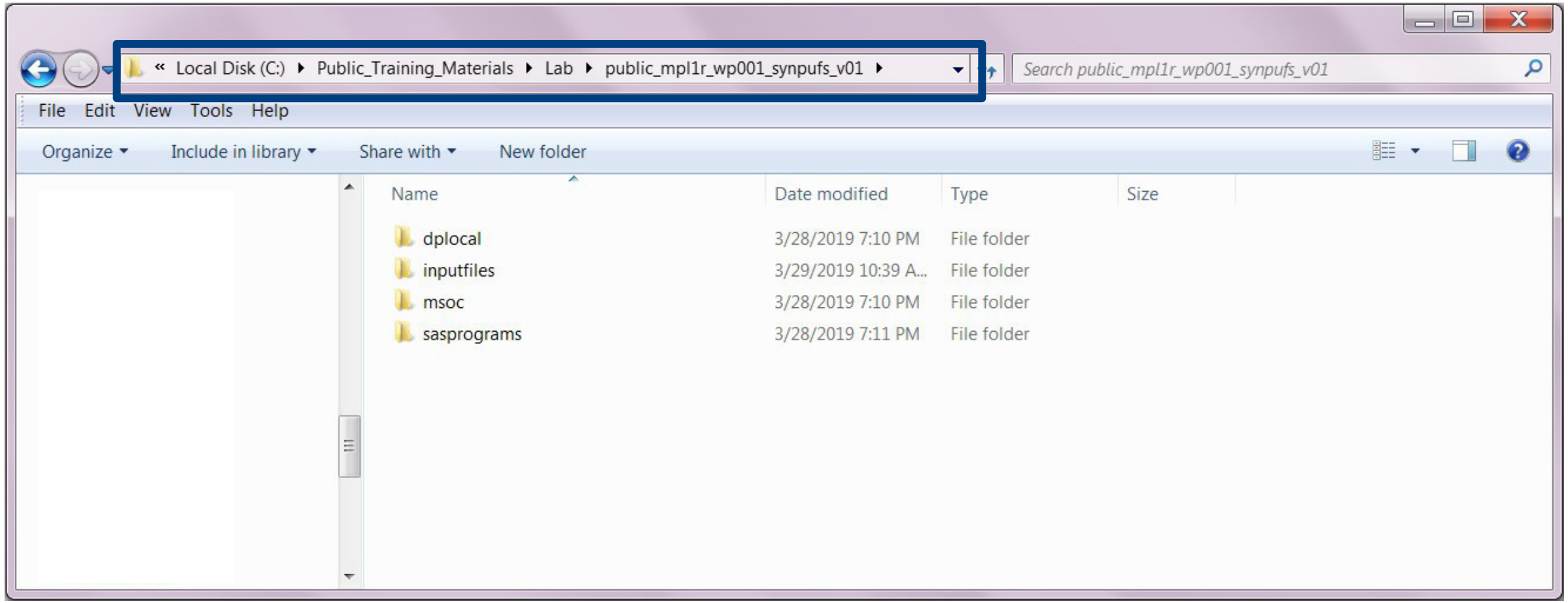
PURPOSE: Establish test data location and execute package on test data

Step 4: Name and Locate Formatted Data

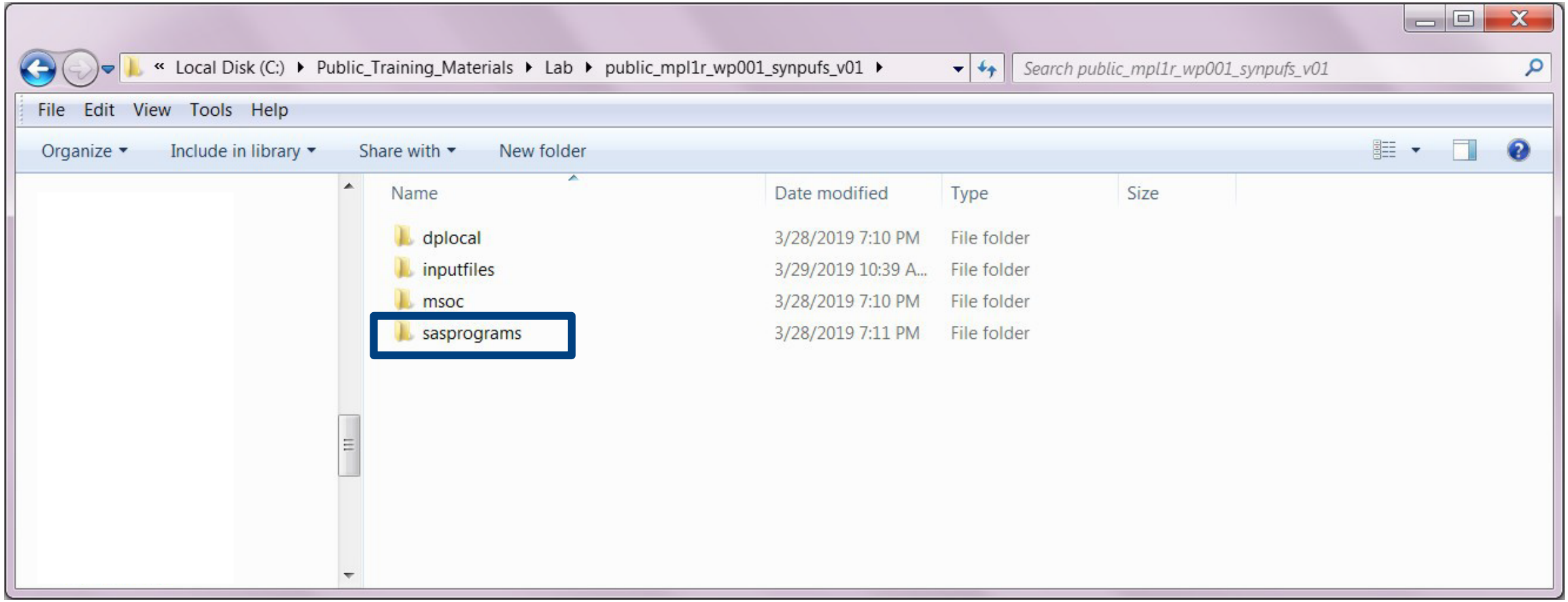


*Global Parameter Files

Prepare Request Package

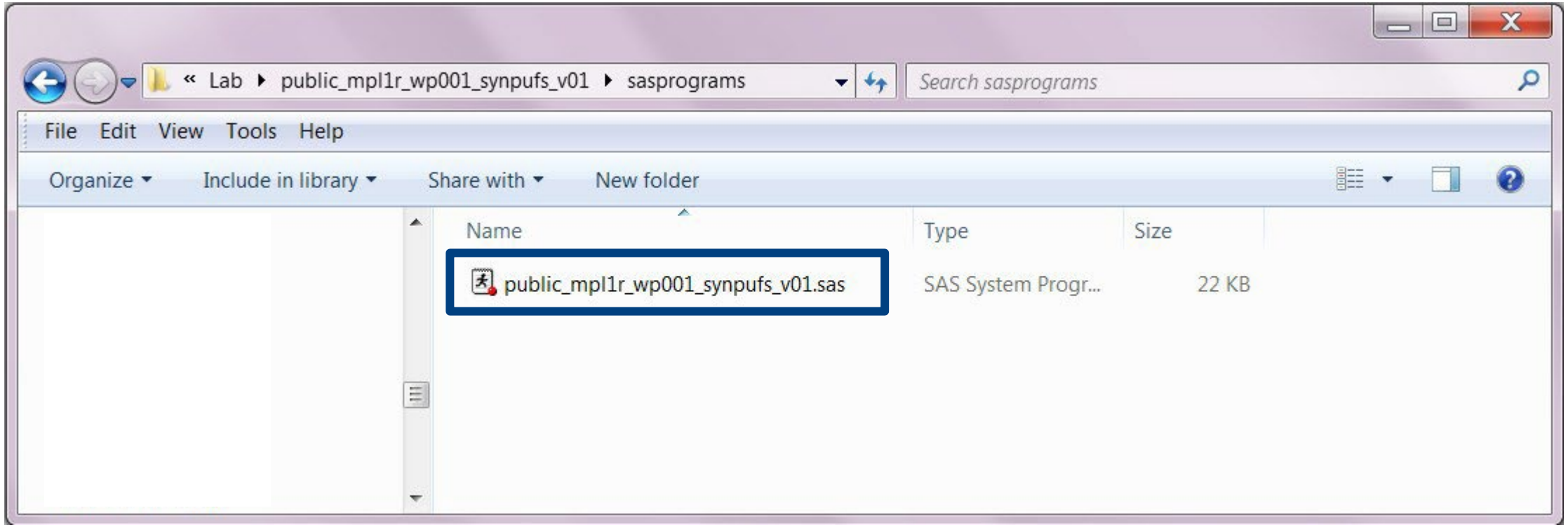


Name and Locate Formatted Data



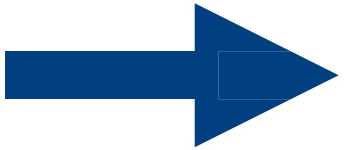
Name and Locate Formatted Data

- Referred to as **“master program”** in CIDA documentation
- Identifies claims database for analysis
- Specifies package location using multiple identifiers



Update Master (SAS) Program

- Update file paths under %let _packageroot and %let prod_scdm



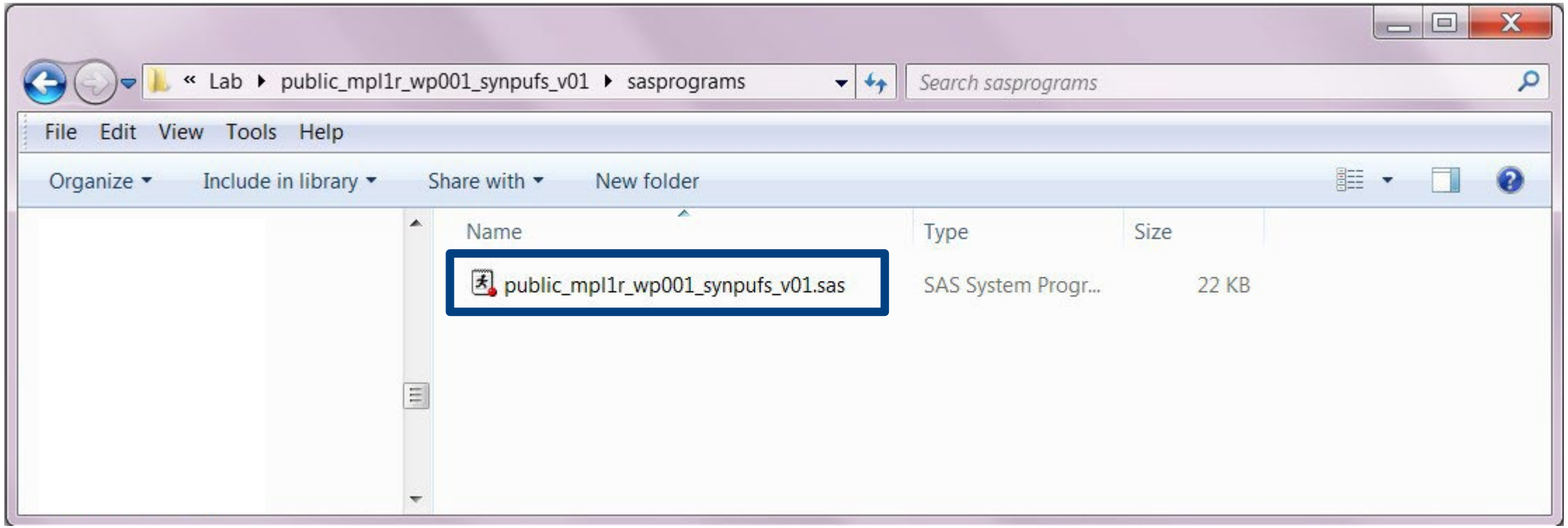
```
/*************************************************************************************/
/* 1c. OPTIONAL: Organizations WITHOUT Common Components define parameters in this
      section, leaving STEP 1a. above blank.                                          */

   /* _DP is a descriptive identifier for your organization. Specify a 3-6 UPPERCASE
      character abbreviation for _DP. Example: %let DP=ABCDE ;                        */
      %let _DP= synpuf;

   /* Specify the location of this request package, containing the 4 subfolders:
      dplocal, msoc, inputfiles, and sasprograms */
   /* Example: %let packageroot = A:/sentinel/qa_mil_package/                         */
      %let _packageroot = C:\Public_Training_Materials\Lab\public_mpl1r_wp001_synpufs_v01;

   /* Specify the file path to the location of your Phase A Sentinel Common Data Model
     (SCDM) datasets.  Example: %let prod_scdm=A:/sentinel/etl1/phaseA/scdm/ ;       */
      %let prod_scdm= C:\Public_Training_Materials\Lab\test_data;

   /* The following metadata describe characteristics of your SCDM. If known, modify the
      following parameters:
   /* DP_MinDate: Specify the overall SCDM minimum date in the format "DDMMMYYYY"d
                  Default value is "01Jan2000"d                                       */
      %let _DP_MinDate="01Jan2008"d ;

   /* DP_MaxDate: Specify the overall SCDM maximum date in the format "DDMMMYYYY"d
                   Default value is today's date (e.g. "&sysdate."d)                  */
      %let _DP_MaxDate = "01Dec2010"d ;
```

Update Master (SAS) Program

```
/*-----------------------------------------------------------------------------------*/
/* SECTION 2: SOC Programmer/Analyst preparing the Request sets each parameter prior
              to distributing to DP
/*-----------------------------------------------------------------------------------*/
 /* Specific request IDs are made up of the following 5 tokens:
    project-ID, workplan-type, workplan-ID, unique-DPID, version-ID */
 /*-----------------------------------------------------------------------------*/
  *  If this is your request   . . . . . . . then set parameter values as follows
  *  ---------------------------------       ---------------------------------------
  *   [Project-ID: CDER]                      %let ProjID= cder ;
  *   [Workplan-Type: ad hoc request]         %let WPType = ahr ;
  *   [Workplan-ID: 5]                        %let WPID =   wp005 ;
  *   [Unique-DPID: non-specific DP]          %let DPID =   nsdp ;
  *   [Version-ID: beta 3]                    %let VerID =  b03 ;
  *   [use underscores as delimiter]          %let dlm = _ ;
  *
  *   The example values above would produce Request-ID --> cder_ahr_wp005_nsdp_b03 ;
 /*-----------------------------------------------------------------------------------*/
 /* Specify project-ID, workplan-type, workplan-ID, workplan-type, dpid, version-ID    */
   %let ProjID = public ;
   %let WPType = mpl1r ;
   %let WPID =   wp001 ;
   %let DPID =   synpufs ;
   %let VerID =  v01 ;

  /* Create request-id delimiter - Default is underscore (_)                          */
   %let dlm = _ ;  /* Do not edit */
```

Execute Request Package

- Right click on master program and batch submit the program



CIDA Output and Report Interpretation

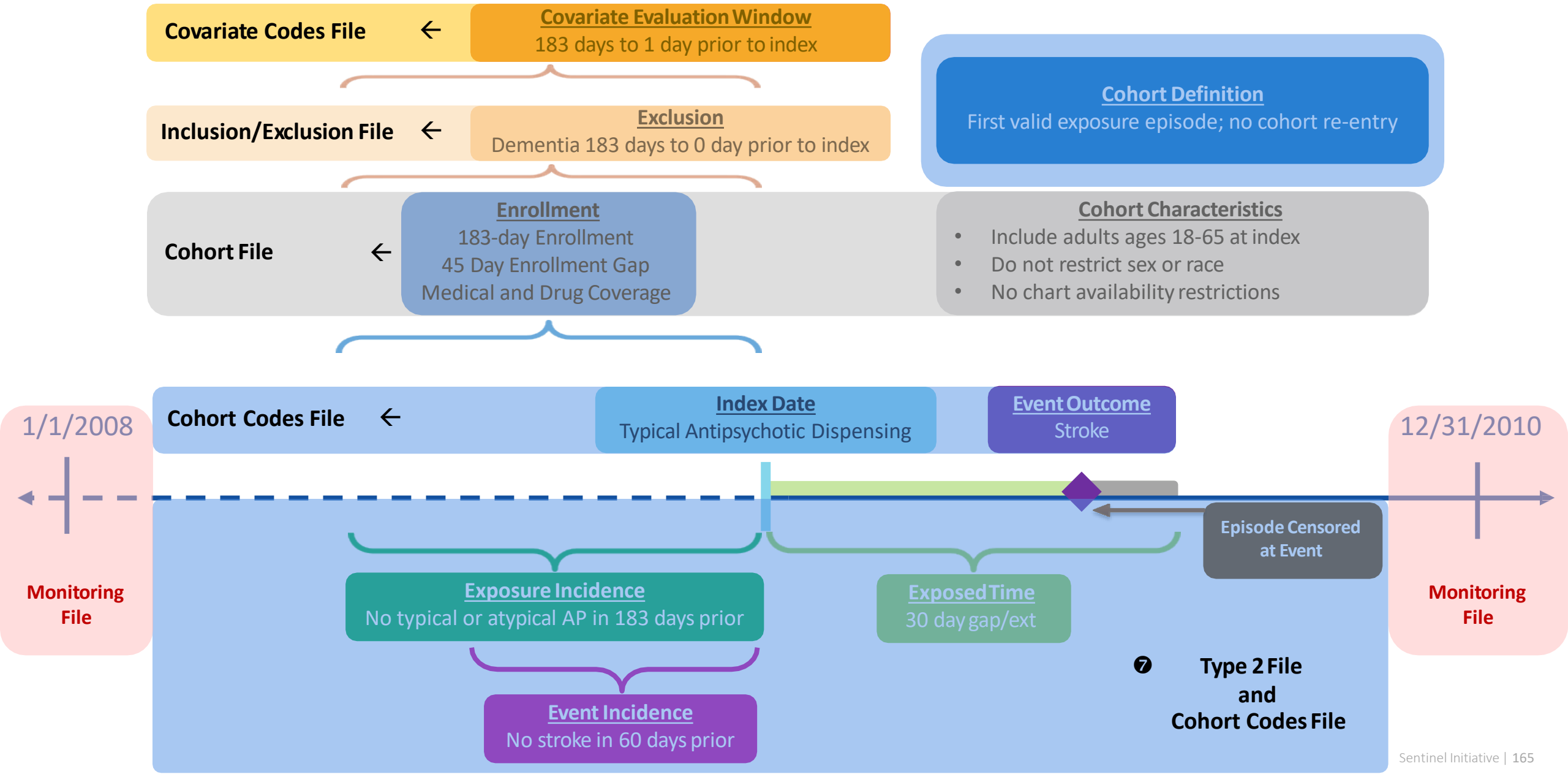
Agenda

- Review of Query Design
- By Topic
  - SAS Output
  - Interpretation of Report Contents

Topics

- Signature file
- Baseline characteristics
- Type 2 Report
- Attrition
- Censor
- Propensity Score Analysis

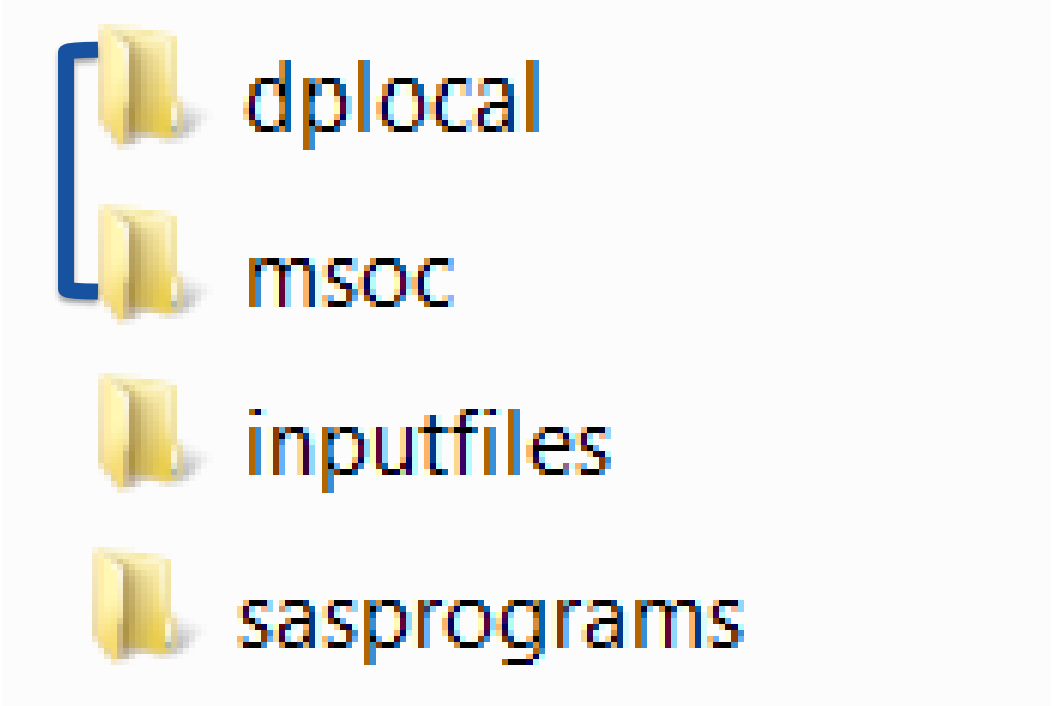
Incidence Rates Design Diagram and File Map



SAS Output from a CIDA Type 2 Analysis: Overview

- Data gets output to *msoc* and *dplocal* folders

OUTPUT



For Sentinel queries, the Sentinel Operations Center does not have access to datasets in *dplocal*

SAS Output from a CIDA Type 2 Analysis

- Signature
- Baseline
- T2_CIDA
- Attrition
- Censor_CIDA

SAS Output from a CIDA Type 2 Analysis

msoc

- Signature
- Baseline
- T2_CIDA
- Attrition
- Censor_CIDA

Signature Output

- Provides metadata associated with the request
  - Request identifiers
    - Workplan number
    - CIDA QRP Version
    - Scenario count
    - Input files referenced
  - Database characteristics
    - Data Partner max and min dates
    - If ‘Patients to Exclude’ macro was utilized
    - If data was frozen
  - Run time metrics
    - Execution time
    - Start and stop time stamps

Signature Output File: Example

Request identifiers

QRP version

Run time and database information

	NAME OF FORMER VARIABLE	VALUE
1	ReqID	public_mpl1r_wp001_synpufs_v02
2	ProjID	public
3	WPType	mpl1r
4	WPID	wp001
5	DPID	synpufs
6	VerID	v02
7	RunID	r01
8	MPVer	8.0.2
9	CustomCodeVersion	
10	StartTime	18JUL2019:09:26:46.40
11	StopTime	18JUL2019:09:35:50.50
12	Seconds	544 s
13	ExecutionTime	0 h 9 m 4 s
14	DP	synpuf
15	DPMINDATE	01JAN2008
16	DPMAXDATE	01DEC2010
17	PATIDEXCL	No
18	ETLNUMBER	1
19	BYPASSCC	Y
20	RUNTYPE	BACK
21	SASVERSION	9.4
22	SASVERSIONLONG	9.04.01M4P110916
23	OSABBR	LIN X64
24	OSNAME	Linux
25	NCPU	4

	NAME OF FORMER VARIABLE	VALUE
26	ScenarioCnt	4
27	PERIODIDSTART	1
28	PERIODIDEND	1
29	ANALYSIS	
30	MONITORINGFILE	wp001_monitoring
31	USERSTRATA	wp001_type2strata
32	COMBOFILE	
33	COHORTFILE	wp001_cohort
34	COHORTCODES	wp001_cohortcodes
35	INCLUSIONCODES	wp001_exclusion
36	STOCKPILINGFILE	
37	RUN_ENVELOPE	0
38	FREEZEDATA	n
39	ZIPFILE	
40	LABSCODEMAP	
41	DISTINDEX	
42	TYPE1FILE	
43	TYPE2FILE	wp001_type2
44	TYPE3FILE	
45	TYPE4FILE	
46	PREGDUR	
47	TYPE5FILE	
48	TYPE6FILE	
49	METADATAFILE	
50	SURVEILLANCEMODE	

• • •

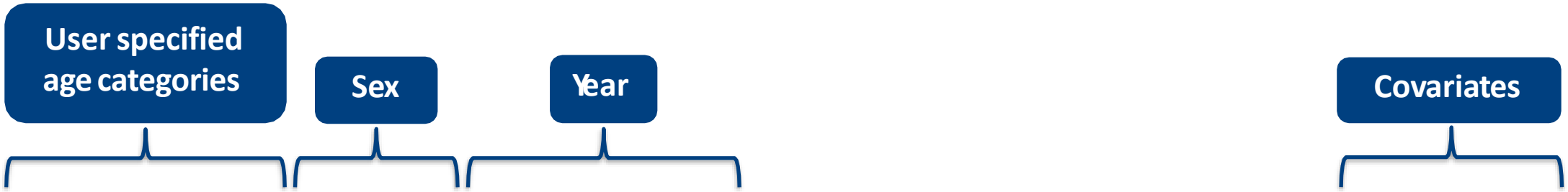
Input files

SAS Output from a CIDA Type 2 Analysis

msoc

- Signature
- Baseline
- T2_CIDA
- Attrition
- Censor_CIDA

Baseline Output



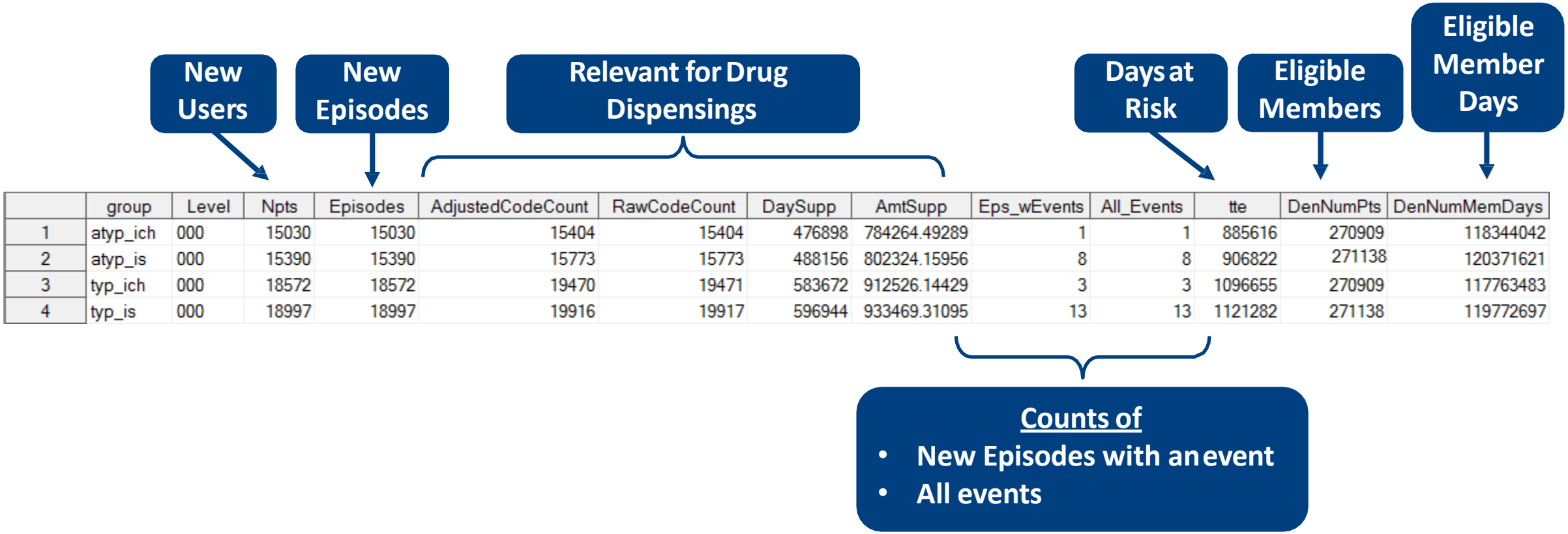
	Group	patient	AGE40_54	AGE55_65	AGE18_39	Sex_M	Sex_F	Year_2008	Year_2009	Year_2010	Race_5	Race_0	Race_3	Hispanic_N	Hispanic_Y	Hispanic_U	AMI	Anxiety	Bipolar
1	atyp_ich	15030	5665	6910	2455	7014	8016	4106	6938	3986	10967	1179	2884	10967	588	3475	1620	1918	3119
2	atyp_is	15390	5799	7078	2513	7186	8204	4223	7107	4060	11219	1203	2968	11219	597	3574	1711	1982	3221
3	typ_ich	18572	7195	8199	3178	8768	9804	5377	8562	4633	13706	1352	3514	13706	644	4222	2092	2585	4514
4	typ_is	18997	7359	8395	3243	8956	10041	5499	8782	4716	14024	1378	3595	14024	657	4316	2183	2679	4645

SAS Output from a CIDA Type 2 Analysis

msoc

- Signature
- Baseline
- T2_CIDA
- Attrition
- Censor_CIDA

T2_CIDA Output



	group	Level	Npts	Episodes	AdjustedCodeCount	RawCodeCount	DaySupp	AmtSupp	Eps_wEvents	All_Events	tte	DenNumPts	DenNumMemDays
1	atyp_ich	000	15030	15030	15404	15404	476898	784264.49289	1	1	885616	270909	118344042
2	atyp_is	000	15390	15390	15773	15773	488156	802324.15956	8	8	906822	271138	120371621
3	typ_ich	000	18572	18572	19470	19471	583672	912526.14429	3	3	1096655	270909	117763483
4	typ_is	000	18997	18997	19916	19917	596944	933469.31095	13	13	1121282	271138	119772697

T2_CIDA Output

	group	Level	agegroup	agegroupnum	cb_reg	hhs_reg	hispanic	month	race	sex	state	year	zip3	zip_uncertain	Npts	Episodes
1	atyp_ich	000		.				.				.			15030	15030
2	atyp_ich	001		.				.				2008			4106	4106
3	atyp_ich	001		.				.				2009			6938	6938
4	atyp_ich	001		.				.				2010			3986	3986
5	atyp_ich	002		.				.		F		.			8016	8016
6	atyp_ich	002		.				.		M		.			7014	7014
7	atyp_ich	002		.				.		O		.			0	0
8	atyp_ich	003	18-39	1				.				.			2455	2455
9	atyp_ich	003	40-54	2				.				.			5665	5665
10	atyp_ich	003	55-65	3				.				.			6910	6910

- Data reported overall and stratified by age group, sex, and year
- Stratifications are user-defined

SAS Output from a CIDA Type 2 Analysis

msoc

- Signature
- Baseline
- T2_CIDA
- Attrition
- Censor_CIDA

Attrition Output (Patient Level)

- Includes the number of individuals excluded and remaining after each cohort criterion is applied during the CIDA tool execution
  - Attrition repeats by GROUP (i.e., scenario) and is irrespective to other GROUPs
  - Type and detailed description of criterion, eg ‘Exclusion - Members must satisfy the age range condition within the query period’

Attrition: First Losses are Enrollment-based

	group	level	descr	remaining	Excluded
1	typ_is	1	Initial Member Count - Members with a non-missing birth date/sex at any enrollment episode overlapping the query period	2,224,739	.
2	typ_is	2	Exclusion – Members must be excluded if they only have enrollment episodes with DrugCov=N and MedCov=Y during the query period	2,049,969	174770
3	typ_is	3	Exclusion – Members must be excluded if they only have enrollment episodes with DrugCov=Y and MedCov=N during the query period	1,654,330	395639
4	typ_is	4	Exclusion – Members must be excluded if they only have enrollment episodes with DrugCov=Y and MedCov=N and DrugCov=N and MedCov=Y during the query period	1,554,312	100018
5	typ_is	5	Exclusion - Members must satisfy the age range condition within the query period	379,164	1175148
6	typ_is	6	Exclusion - Members must meet chart availability criterion within the query period	379,164	0
7	typ_is	7	Exclusion - Members must satisfy the demographic (sex, race and hispanic) condition	379,164	0
8	typ_is	8	Exclusion - Members must have at least one claim with cohort-identifying codes within the query period	39,569	339595
9	typ_is	9	Exclusion - Members must have at least one cohort episode beginning within the age range condition	34,664	4905
10	typ_is	10		34,664	0
11	typ_is	11	Exclusion - Members must have at least one episode defining index claim during the query period	34,524	140
12	typ_is	12	Exclusion - Members must have at least one cohort episode incident with respect to other criteria	32,101	2423
13	typ_is	13		32,101	0
14	typ_is	14	Exclusion - Members must have at least one cohort episode satisfying the pre-index enrollment criterion	24,700	7401
15	typ_is	15	Exclusion - Members must have at least one cohort episode satisfying the HOI-defined enrollment criterion	24,700	0
16	typ_is	16	Exclusion - Members must have at least one cohort episode that meets HOI incidence criterion	24,637	63
17	typ_is	17	Exclusion - Members must have at least one cohort episode satisfying the exclusion enrollment requirement	24,637	0
18	typ_is	18	Exclusion - Members must have at least one cohort episode satisfying the exclusion conditions	19,018	5619
19	typ_is	19	Exclusion - Members must have at least one cohort episode satisfying the inclusion enrollment requirement	19,018	0
20	typ_is	20	Exclusion - Members must have at least one cohort episode satisfying the inclusion conditions	19,018	0
21	typ_is	21	Exclusion - Members must have at least one cohort episode satisfying the post-index enrollment criterion	19,018	0
22	typ_is	22	Exclusion - Members must have at least one cohort episode with at least minimum days supplied	19,018	0
23	typ_is	23	Exclusion - Members must have at least one cohort episode with at least minimum days duration	19,018	0
24	typ_is	24	Exclusion - Members must have at least one cohort episode with longer than blackout days duration	18,999	19
25	typ_is	25	Exclusion - Members must have at least one cohort episode that meets HOI blackout criterion	18,999	0
26	typ_is	26		18,999	0
27	typ_is	27	Information - Members with at least one cohort claim with supply and/or amount outside specified ranges	.	0
28	typ_is	28	Information - Members with at least one HOI claim with supply and/or amount outside specified ranges	.	0
29	typ_is	29	Information - Members with at least one INCL/EXCL claim with supply and/or amount outside specified ranges	.	0
30	typ_is	30	Information - Members lost to follow-up up to end of monitoring period (Type 2, surveillance mode only)	.	0
31	typ_is	31	Information - Members still at risk at the end of monitoring period (Type 2, surveillance mode only)	18,997	.

Attrition: Next Losses are Demographic

	group	level	descr	remaining	Excluded
1	typ_is	1	Initial Member Count - Members with a non-missing birth date/sex at any enrollment episode overlapping the query period	2,224,739	.
2	typ_is	2	Exclusion – Members must be excluded if they only have enrollment episodes with DrugCov=N and MedCov=Y during the query period	2,049,969	174770
3	typ_is	3	Exclusion – Members must be excluded if they only have enrollment episodes with DrugCov=Y and MedCov=N during the query period	1,654,330	395639
4	typ_is	4	Exclusion – Members must be excluded if they only have enrollment episodes with DrugCov=Y and MedCov=N and DrugCov=N and MedCov=Y during the query period	1,554,312	100018
5	typ_is	5	Exclusion - Members must satisfy the age range condition within the query period	379,164	1175148
6	typ_is	6	Exclusion - Members must meet chart availability criterion within the query period	379,164	0
7	typ_is	7	Exclusion - Members must satisfy the demographic (sex, race and hispanic) condition	379,164	0
8	typ_is	8	Exclusion - Members must have at least one claim with cohort-identifying codes within the query period	39,569	339595
9	typ_is	9	Exclusion - Members must have at least one cohort episode beginning within the age range condition	34,664	4905
10	typ_is	10		34,664	0
11	typ_is	11	Exclusion - Members must have at least one episode defining index claim during the query period	34,524	140
12	typ_is	12	Exclusion - Members must have at least one cohort episode incident with respect to other criteria	32,101	2423
13	typ_is	13		32,101	0
14	typ_is	14	Exclusion - Members must have at least one cohort episode satisfying the pre-index enrollment criterion	24,700	7401
15	typ_is	15	Exclusion - Members must have at least one cohort episode satisfying the HOI-defined enrollment criterion	24,700	0
16	typ_is	16	Exclusion - Members must have at least one cohort episode that meets HOI incidence criterion	24,637	63
17	typ_is	17	Exclusion - Members must have at least one cohort episode satisfying the exclusion enrollment requirement	24,637	0
18	typ_is	18	Exclusion - Members must have at least one cohort episode satisfying the exclusion conditions	19,018	5619
19	typ_is	19	Exclusion - Members must have at least one cohort episode satisfying the inclusion enrollment requirement	19,018	0
20	typ_is	20	Exclusion - Members must have at least one cohort episode satisfying the inclusion conditions	19,018	0
21	typ_is	21	Exclusion - Members must have at least one cohort episode satisfying the post-index enrollment criterion	19,018	0
22	typ_is	22	Exclusion - Members must have at least one cohort episode with at least minimum days supplied	19,018	0
23	typ_is	23	Exclusion - Members must have at least one cohort episode with at least minimum days duration	19,018	0
24	typ_is	24	Exclusion - Members must have at least one cohort episode with longer than blackout days duration	18,999	19
25	typ_is	25	Exclusion - Members must have at least one cohort episode that meets HOI blackout criterion	18,999	0
26	typ_is	26		18,999	0
27	typ_is	27	Information - Members with at least one cohort claim with supply and/or amount outside specified ranges	.	0
28	typ_is	28	Information - Members with at least one HOI claim with supply and/or amount outside specified ranges	.	0
29	typ_is	29	Information - Members with at least one INCL/EXCL claim with supply and/or amount outside specified ranges	.	0
30	typ_is	30	Information - Members lost to follow-up up to end of monitoring period (Type 2, surveillance mode only)	.	0
31	typ_is	31	Information - Members still at risk at the end of monitoring period (Type 2, surveillance mode only)	18,997	.

Attrition: Next Losses are Index-related

	group	level	descr	remaining	Excluded
1	typ_is	1	Initial Member Count - Members with a non-missing birth date/sex at any enrollment episode overlapping the query period	2,224,739	.
2	typ_is	2	Exclusion – Members must be excluded if they only have enrollment episodes with DrugCov=N and MedCov=Y during the query period	2,049,969	174770
3	typ_is	3	Exclusion – Members must be excluded if they only have enrollment episodes with DrugCov=Y and MedCov=N during the query period	1,654,330	395639
4	typ_is	4	Exclusion – Members must be excluded if they only have enrollment episodes with DrugCov=Y and MedCov=N and DrugCov=N and MedCov=Y during the query period	1,554,312	100018
5	typ_is	5	Exclusion - Members must satisfy the age range condition within the query period	379,164	1175148
6	typ_is	6	Exclusion - Members must meet chart availability criterion within the query period	379,164	0
7	typ_is	7	Exclusion - Members must satisfy the demographic (sex, race and hispanic) condition	379,164	0
8	typ_is	8	Exclusion - Members must have at least one claim with cohort-identifying codes within the query period	39,569	339595
9	typ_is	9	Exclusion - Members must have at least one cohort episode beginning within the age range condition	34,664	4905
10	typ_is	10		34,664	0
11	typ_is	11	Exclusion - Members must have at least one episode defining index claim during the query period	34,524	140
12	typ_is	12	Exclusion - Members must have at least one cohort episode incident with respect to other criteria	32,101	2423
13	typ_is	13		32,101	0
14	typ_is	14	Exclusion - Members must have at least one cohort episode satisfying the pre-index enrollment criterion	24,700	7401
15	typ_is	15	Exclusion - Members must have at least one cohort episode satisfying the HOI-defined enrollment criterion	24,700	0
16	typ_is	16	Exclusion - Members must have at least one cohort episode that meets HOI incidence criterion	24,637	63
17	typ_is	17	Exclusion - Members must have at least one cohort episode satisfying the exclusion enrollment requirement	24,637	0
18	typ_is	18	Exclusion - Members must have at least one cohort episode satisfying the exclusion conditions	19,018	5619
19	typ_is	19	Exclusion - Members must have at least one cohort episode satisfying the inclusion enrollment requirement	19,018	0
20	typ_is	20	Exclusion - Members must have at least one cohort episode satisfying the inclusion conditions	19,018	0
21	typ_is	21	Exclusion - Members must have at least one cohort episode satisfying the post-index enrollment criterion	19,018	0
22	typ_is	22	Exclusion - Members must have at least one cohort episode with at least minimum days supplied	19,018	0
23	typ_is	23	Exclusion - Members must have at least one cohort episode with at least minimum days duration	19,018	0
24	typ_is	24	Exclusion - Members must have at least one cohort episode with longer than blackout days duration	18,999	19
25	typ_is	25	Exclusion - Members must have at least one cohort episode that meets HOI blackout criterion	18,999	0
26	typ_is	26		18,999	0
27	typ_is	27	Information - Members with at least one cohort claim with supply and/or amount outside specified ranges	.	0
28	typ_is	28	Information - Members with at least one HOI claim with supply and/or amount outside specified ranges	.	0
29	typ_is	29	Information - Members with at least one INCL/EXCL claim with supply and/or amount outside specified ranges	.	0
30	typ_is	30	Information - Members lost to follow-up up to end of monitoring period (Type 2, surveillance mode only)	.	0
31	typ_is	31	Information - Members still at risk at the end of monitoring period (Type 2, surveillance mode only)	18,997	.

Attrition: Last Losses are Query-Specific

	group	level	descr	remaining	Excluded
1	typ_is	1	Initial Member Count - Members with a non-missing birth date/sex at any enrollment episode overlapping the query period	2,224,739	.
2	typ_is	2	Exclusion – Members must be excluded if they only have enrollment episodes with DrugCov=N and MedCov=Y during the query period	2,049,969	174770
3	typ_is	3	Exclusion – Members must be excluded if they only have enrollment episodes with DrugCov=Y and MedCov=N during the query period	1,654,330	395639
4	typ_is	4	Exclusion – Members must be excluded if they only have enrollment episodes with DrugCov=Y and MedCov=N and DrugCov=N and MedCov=Y during the query period	1,554,312	100018
5	typ_is	5	Exclusion - Members must satisfy the age range condition within the query period	379,164	1175148
6	typ_is	6	Exclusion - Members must meet chart availability criterion within the query period	379,164	0
7	typ_is	7	Exclusion - Members must satisfy the demographic (sex, race and hispanic) condition	379,164	0
8	typ_is	8	Exclusion - Members must have at least one claim with cohort-identifying codes within the query period	39,569	339595
9	typ_is	9	Exclusion - Members must have at least one cohort episode beginning within the age range condition	34,664	4905
10	typ_is	10		34,664	0
11	typ_is	11	Exclusion - Members must have at least one episode defining index claim during the query period	34,524	140
12	typ_is	12	Exclusion - Members must have at least one cohort episode incident with respect to other criteria	32,101	2423
13	typ_is	13		32,101	0
14	typ_is	14	Exclusion - Members must have at least one cohort episode satisfying the pre-index enrollment criterion	24,700	7401
15	typ_is	15	Exclusion - Members must have at least one cohort episode satisfying the HOI-defined enrollment criterion	24,700	0
16	typ_is	16	Exclusion - Members must have at least one cohort episode that meets HOI incidence criterion	24,637	63
17	typ_is	17	Exclusion - Members must have at least one cohort episode satisfying the exclusion enrollment requirement	24,637	0
18	typ_is	18	Exclusion - Members must have at least one cohort episode satisfying the exclusion conditions	19,018	5619
19	typ_is	19	Exclusion - Members must have at least one cohort episode satisfying the inclusion enrollment requirement	19,018	0
20	typ_is	20	Exclusion - Members must have at least one cohort episode satisfying the inclusion conditions	19,018	0
21	typ_is	21	Exclusion - Members must have at least one cohort episode satisfying the post-index enrollment criterion	19,018	0
22	typ_is	22	Exclusion - Members must have at least one cohort episode with at least minimum days supplied	19,018	0
23	typ_is	23	Exclusion - Members must have at least one cohort episode with at least minimum days duration	19,018	0
24	typ_is	24	Exclusion - Members must have at least one cohort episode with longer than blackout days duration	18,999	19
25	typ_is	25	Exclusion - Members must have at least one cohort episode that meets HOI blackout criterion	18,999	0
26	typ_is	26		18,999	0
27	typ_is	27	Information - Members with at least one cohort claim with supply and/or amount outside specified ranges	.	0
28	typ_is	28	Information - Members with at least one HOI claim with supply and/or amount outside specified ranges	.	0
29	typ_is	29	Information - Members with at least one INCL/EXCL claim with supply and/or amount outside specified ranges	.	0
30	typ_is	30	Information - Members lost to follow-up up to end of monitoring period (Type 2, surveillance mode only)	.	0
31	typ_is	31	Information - Members still at risk at the end of monitoring period (Type 2, surveillance mode only)	18,997	.

SAS Output from a CIDA Type 2 Analysis

msoc

- Signature
- Baseline
- T2_CIDA
- Attrition
- Censor_CIDA

Censor_CIDA Output

	group	level	censorcat_sort	censdays_value_cat	episodes	cens_elig	cens_dth	cens_dpend	cens_qryend	cens_episend	cens_spec	cens_event
1	atyp_ich	701	1	0-364	15030	238	29	406	0	13824	579	1
2	atyp_ich	701	2	365-729	0	0	0	0	0	0	0	0
3	atyp_ich	701	3	730-1094	0	0	0	0	0	0	0	0
4	atyp_ich	701	4	1095+	0	0	0	0	0	0	0	0
5	atyp_is	701	1	0-364	15390	244	30	408	0	14156	592	8
6	atyp_is	701	2	365-729	0	0	0	0	0	0	0	0
7	atyp_is	701	3	730-1094	0	0	0	0	0	0	0	0
8	atyp_is	701	4	1095+	0	0	0	0	0	0	0	0
9	typ_ich	701	1	0-364	18572	259	30	420	0	17416	492	3
10	typ_ich	701	2	365-729	0	0	0	0	0	0	0	0
11	typ_ich	701	3	730-1094	0	0	0	0	0	0	0	0
12	typ_ich	701	4	1095+	0	0	0	0	0	0	0	0
13	typ_is	701	1	0-364	18997	268	31	421	0	17811	500	13
14	typ_is	701	2	365-729	0	0	0	0	0	0	0	0
15	typ_is	701	3	730-1094	0	0	0	0	0	0	0	0
16	typ_is	701	4	1095+	0	0	0	0	0	0	0	0

DPLocal Files

- The DPLocal folder contains output generated by the request that remains with the Data Partner and may be used to facilitate follow-up queries
- Includes patient level information about the exposure or health outcome of interest (episode start/end dates, enrollment start/end dates, patid, etc)
- Denomcounts: source dataset for eligible members and member-days metrics for the T1_CIDA and T2_CIDA tables
- Numcounts: source dataset for cohort metrics for the T#_CIDA table
- MSTR:
  - Generated for every type of cohort identification strategy (every Type in CIDA)
  - Contains one record per individual per index date for every cohort specified
  - Useful for investigating odd/outlier results

MSTR Output (Excerpt)

	Group	IndexDt	EpisodeEndDt	ENR_START	ENR_END	PatID	DeathDt	IndexDtLookEndDt	IndexLook	NumEvents	FEventDt	tte	Year	Type	EpisodeType	cens_elig	cens_dth	cens_dpend
1	atyp_ich	30JUL2009	07SEP2009	01JAN2008	01DEC2010	000954C72AF82508	01DEC2010	31DEC2010	1	.	.	39	2009	2	EPI	0	0	0
2	atyp_ich	27JAN2009	31JAN2009	01JAN2008	31JAN2009	000D5CA946B7C4C9	.	31DEC2010	1	.	.	4	2009	2	EPI	1	0	0
3	atyp_ich	20OCT2009	08DEC2009	01JAN2008	31DEC2010	000DAAA45900EE70	.	31DEC2010	1	.	.	49	2009	2	EPI	0	0	0
4	atyp_ich	11JUL2010	08SEP2010	01JAN2008	01NOV2010	000FDF324E1A7584	01NOV2010	31DEC2010	1	.	.	59	2010	2	EPI	0	0	0
5	atyp_ich	19JAN2009	19MAR2009	01FEB2008	31DEC2010	00127D219AD78492	.	31DEC2010	1	.	.	59	2009	2	EPI	0	0	0
6	atyp_ich	15JUL2008	12SEP2008	01JAN2008	31DEC2010	0017AC6D4A5BC1C2	.	31DEC2010	1	.	.	59	2008	2	EPI	0	0	0
7	atyp_ich	01SEP2009	30OCT2009	01JAN2009	31DEC2010	00187DB5DFDE4D18	.	31DEC2010	1	.	.	59	2009	2	EPI	0	0	0
8	atyp_ich	22JAN2010	22MAR2010	01JAN2008	31DEC2010	00230FE94CA7979C	.	31DEC2010	1	.	.	59	2010	2	EPI	0	0	0
9	atyp_ich	27NOV2008	25JAN2009	01JAN2008	31DEC2009	0025D5E4468E0B75	.	31DEC2010	1	.	.	59	2008	2	EPI	0	0	0
10	atyp_ich	07AUG2008	05OCT2008	01JAN2008	30SEP2010	00265D0E7B3CE85A	.	31DEC2010	1	.	.	59	2008	2	EPI	0	0	0
11	atyp_ich	24MAY2009	20SEP2009	01JAN2008	31DEC2010	002C64B90C47B523	.	31DEC2010	1	.	.	119	2009	2	EPI	0	0	0
12	atyp_ich	25OCT2008	23DEC2008	01JAN2008	31DEC2010	003006CE8F76EFBC	.	31DEC2010	1	.	.	59	2008	2	EPI	0	0	0
13	atyp_ich	30DEC2008	08FEB2009	01JAN2008	31DEC2010	00303F166AE70F9B	.	31DEC2010	1	.	.	40	2008	2	EPI	0	0	0
14	atyp_ich	02MAY2010	20JUN2010	01JAN2008	31DEC2010	0034CE1366E893BA	.	31DEC2010	1	.	.	49	2010	2	EPI	0	0	0
15	atyp_ich	24SEP2009	02NOV2009	01JAN2008	31DEC2010	003D3B2902CC59C1	.	31DEC2010	1	.	.	39	2009	2	EPI	0	0	0
16	atyp_ich	23JUL2009	20SEP2009	01JAN2008	31DEC2010	00408B995D249B7F	.	31DEC2010	1	.	.	59	2009	2	EPI	0	0	0
17	atyp_ich	19NOV2009	17JAN2010	01AUG2008	31DEC2010	00411F49FDB1454E	.	31DEC2010	1	.	.		2009	2	EPI	0	0	0
18	atyp_ich	05OCT2009	03DEC2009	01JAN2008	31DEC2010	0042D807940A55B0	.	31DEC2010	1	.	.	59	2009	2	EPI	0	0	0
19	atyp_ich	08SEP2009	06NOV2009	01JAN2008	31DEC2010	004404C039676932	.	31DEC2010	1	.	.	59	2009	2	EPI	0	0	0
20	atyp_ich	23AUG2008	21OCT2008	01JAN2008	31DEC2010	0044503881BEE445	.	31DEC2010	1	.	.	59	2008	2	EPI	0	0	0

Questions?

info@sentinelsystem.org

Parting Thoughts

- All materials to complete and run your package have been provided
- The documentation and public git are a resource

BACKUP

Propensity Score Analysis Report

Propensity Score Analysis

- By assigning an exposure of interest and comparator, the type 2 output can be leveraged in an inferential analysis to:
  - Assign members a **propensity score, based on user-defined criteria**
  - Calculate adjusted risk estimates using **matching or stratification**

- For each comparison, a **Cox proportional hazards regression model** is used to estimate hazard ratios and corresponding 95% confidence intervals
  - There is an option for risk-set level return, and patient-level return

- Propensity score analysis has a pre-processing step
  - Each patient is ONLY allowed to be in either the treatment or comparator cohort

Propensity Score Match Design Diagram

Propensity Score
- 1:1 Matching
- Caliper: 0.05
- Age, Sex
- Recorded History Parameters

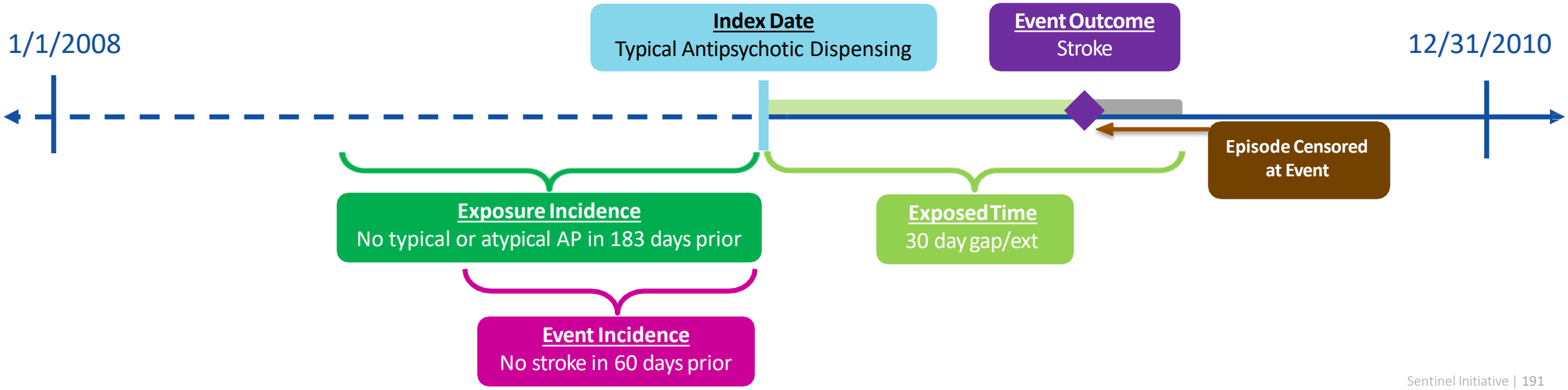
Covariate Evaluation Window
183 days to 1 day prior to index

Exclusion
Dementia 183 days to 0 day prior to index

Enrollment
183-day Enrollment
45 Day Enrollment Gap
Medical and Drug Coverage

Cohort Definition
First valid exposure episode; no cohort re-entry

Cohort Characteristics
- Include adults ages 18-65 at index
- Do not restrict sex or race
- No chart availability restrictions



Propensity Score Adjustment Output

https://dev.sentinelsystem.org/projects/SENTINEL/repos/sentinel-routine-querying-tool-documentation/browse/files/atoc-type2.md

Unmatched Baseline Characteristics

Table 1a. Cohort of New Initiators of Typical Antipsychotics and Atypical Antipsychotics, Ischemic Stroke (Unmatched, Aggregated), Ratio: 1:1, Caliper: 0.05						
	Medical Product				Covariate Balance	
Characteristic[2]	Typical Antipsychotics		Atypical Antipsychotics			
	N/Mean	%/Std Dev[1]	N/Mean	%/Std Dev[1]	Absolute Difference	Standardized Difference
Patients (N)	18,094	100.0%	14,370	100.0%	-	-
Demographics						
Mean age	51.6	10.6	52.0	10.6	-0.438	-0.041
Age: 18-39	3,075	17.0%	2,319	16.1%	0.857	0.023
Age: 40-54	6,984	38.6%	5,365	37.3%	1.264	0.026
Age: 55-65	8,035	44.4%	6,686	46.5%	-2.121	-0.043
Gender (Female)	9,560	52.8%	7,667	53.4%	-0.519	-0.010
Gender (Male)	8,534	47.2%	6,703	46.6%	0.519	0.010
Race (Black or African American)	3,425	18.9%	2,749	19.1%	-0.201	-0.005
Race (Unknown)	1,316	7.3%	1,126	7.8%	-0.563	-0.021
Race (White)	13,353	73.8%	10,495	73.0%	0.764	0.017
Hispanic Origin	625	3.5%	558	3.9%	-0.429	-0.023
Year (2008)	5,499	30.4%	4,223	29.4%	1.004	0.022
Year (2009)	8,420	46.5%	6,702	46.6%	-0.104	-0.002
Year (2010)	4,175	23.1%	3,445	24.0%	-0.900	-0.021
Recorded History of:						
AMI	2,090	11.6%	1,614	11.2%	0.319	0.010
Anxiety	2,555	14.1%	1,826	12.7%	1.414	0.041
Bipolar	4,388	24.3%	2,914	20.3%	3.973	0.096
Depression	4,696	26.0%	3,186	22.2%	3.782	0.089
Diabetes	9,635	53.2%	7,524	52.4%	0.891	0.018
Heart failure	4,360	24.1%	3,404	23.7%	0.408	0.010
Hypercholesterolemia	9,142	50.5%	7,157	49.8%	0.720	0.014
Hypertension	11,665	64.5%	9,064	63.1%	1.393	0.029
Kidney failure	4,664	25.8%	3,559	24.8%	1.010	0.023
Schizophrenia/psychotic	3,844	21.2%	2,452	17.1%	4.181	0.106
Substance abuse	1,511	8.4%	1,029	7.2%	1.190	0.045
Transient ischemic attack	577	3.2%	444	3.1%	0.099	0.006

Matched Baseline Characteristics

Table 1b. Cohort of New Initiators of Typical Antipsychotics and Atypical Antipsychotics, Ischemic Stroke (Matched, Aggregated), Ratio: 1:1, Caliper: 0.05						
	Medical Product				Covariate Balance	
Characteristic[2]	Typical Antipsychotics		Atypical Antipsychotics			
	N/Mean	%/Std Dev[1]	N/Mean	%/Std Dev[1]	Absolute Difference	Standardized Difference
Patients (N)	14,370	79.4%	14,370	100.0%	-	-
Demographics						
Mean age	52.1	10.5	52.0	10.6	0.107	0.010
Age: 18-39	2,269	15.8%	2,319	16.1%	-0.348	-0.009
Age: 40-54	5,386	37.5%	5,365	37.3%	0.146	0.003
Age: 55-65	6,715	46.7%	6,686	46.5%	0.202	0.004
Gender (Female)	7,680	53.4%	7,667	53.4%	0.090	0.002
Gender (Male)	6,690	46.6%	6,703	46.6%	-0.090	-0.002
Race (Black or African American)	2,723	18.9%	2,749	19.1%	-0.181	-0.005
Race (Unknown)	1,051	7.3%	1,126	7.8%	-0.522	-0.020
Race (White)	10,596	73.7%	10,495	73.0%	0.703	0.016
Hispanic Origin	501	3.5%	558	3.9%	-0.397	-0.021
Year (2008)	4,344	30.2%	4,223	29.4%	0.842	0.018
Year (2009)	6,654	46.3%	6,702	46.6%	-0.334	-0.007
Year (2010)	3,372	23.5%	3,445	24.0%	-0.508	-0.012
Recorded History of:						
AMI	1,612	11.2%	1,614	11.2%	-0.014	-0.000
Anxiety	1,825	12.7%	1,826	12.7%	-0.007	-0.000
Bipolar	2,876	20.0%	2,914	20.3%	-0.264	-0.007
Depression	3,137	21.8%	3,186	22.2%	-0.341	-0.008
Diabetes	7,470	52.0%	7,524	52.4%	-0.376	-0.008
Heart failure	3,373	23.5%	3,404	23.7%	-0.216	-0.005
Hypercholesterolemia	7,094	49.4%	7,157	49.8%	-0.438	-0.009
Hypertension	8,974	62.4%	9,064	63.1%	-0.626	-0.013
Kidney failure	3,524	24.5%	3,559	24.8%	-0.244	-0.006
Schizophrenia/psychotic	2,510	17.5%	2,452	17.1%	0.404	0.011
Substance abuse	1,044	7.3%	1,029	7.2%	0.104	0.004
Transient ischemic attack	432	3.0%	444	3.1%	-0.084	-0.005

Risk Estimates

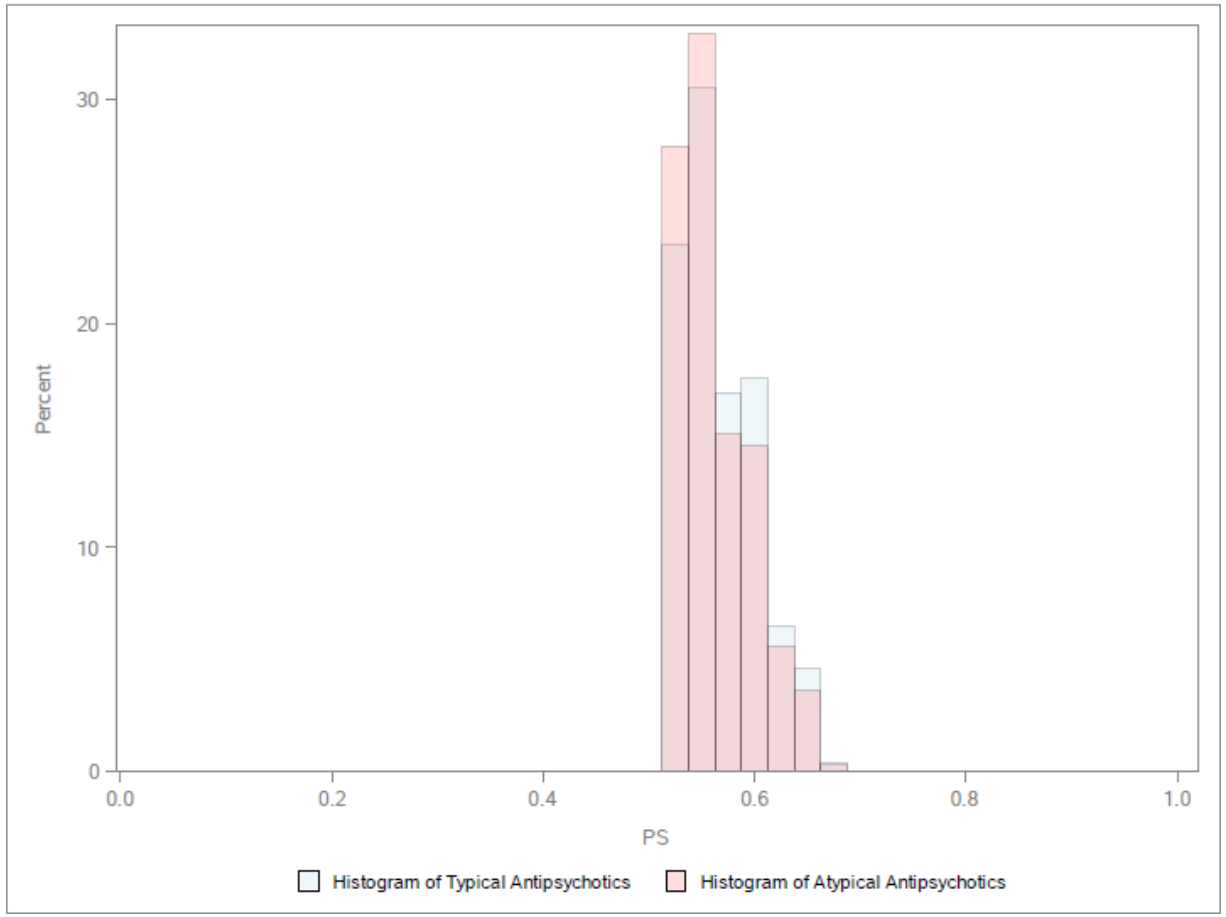
Table 2: Effect Estimates for Ischemic Stroke by Analysis Type

Medical Product	Number of New Users	Person Years at Risk	Average Person Days at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1,000 Person Years	Risk per 1,000 New Users	Incidence Rate Difference per 1,000 Person Years	Difference in Risk per 1,000 New Users	Hazard Ratio (95% CI)	Wald P-Value
Unmatched Analysis (Site-adjusted only)											
Typical Antipsychotics	18,094	2,925.80	59.06	0.16	13	4.44	0.72	1.00	0.16	1.33 (0.55, 3.23)	0.529
Atypical Antipsychotics	14,370	2,324.53	59.08	0.16	8	3.44	0.56				
1:1 Matched Conditional Analysis; Caliper= 0.05[1]											
Typical Antipsychotics	14,370	2,067.32	52.55	0.14	10	4.84	0.70	2.42	0.35	2.00 (0.68, 5.85)	0.206
Atypical Antipsychotics	14,370	2,067.32	52.55	0.14	5	2.42	0.35				
1:1 Matched Unconditional Analysis; Caliper= 0.05											
Typical Antipsychotics	14,370	2,320.71	58.99	0.16	10	4.31	0.70	0.87	0.14	1.30 (0.51, 3.32)	0.583
Atypical Antipsychotics	14,370	2,324.53	59.08	0.16	8	3.44	0.56				

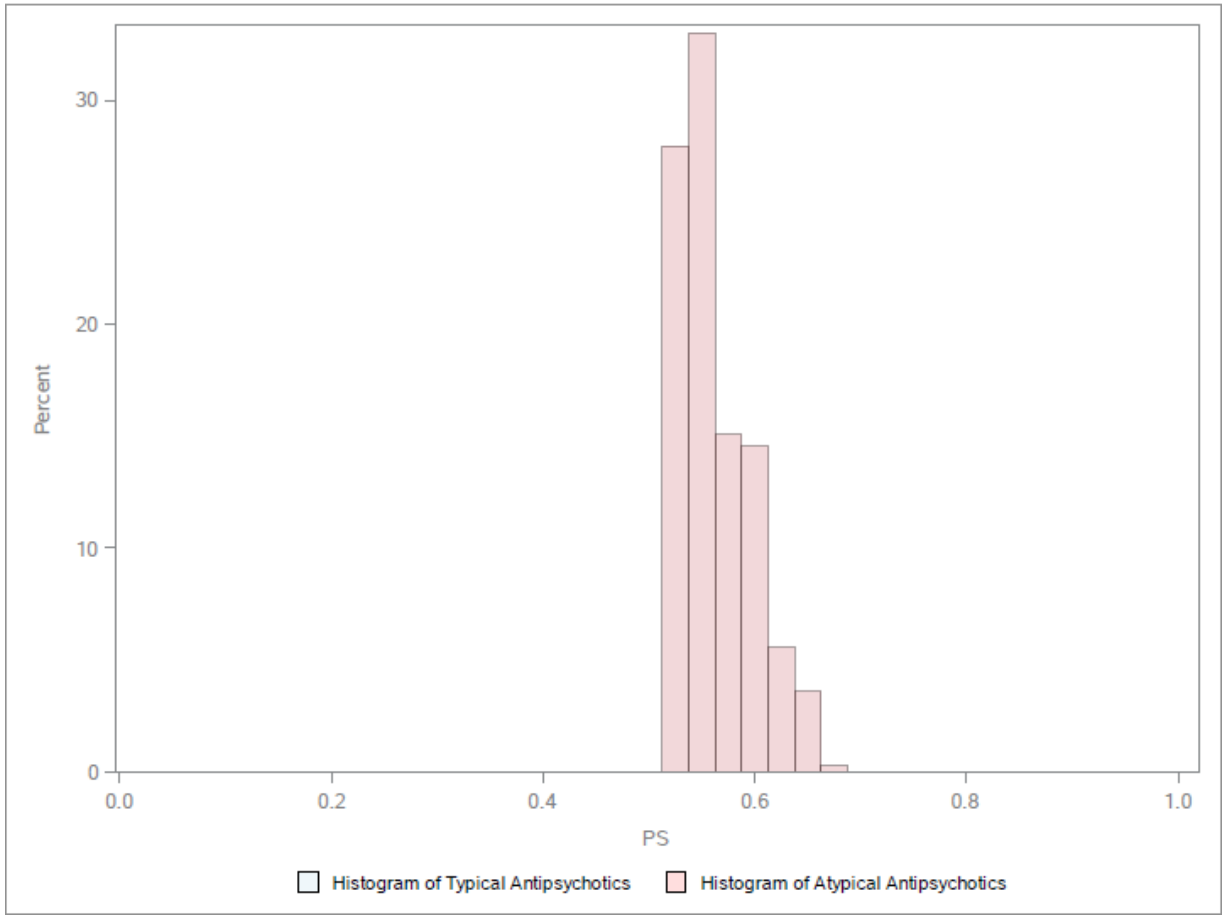
[1]Conditional analysis includes informative events and person-time.

Propensity Score Distribution

Histograms of Propensity Score Distribution Aggregated

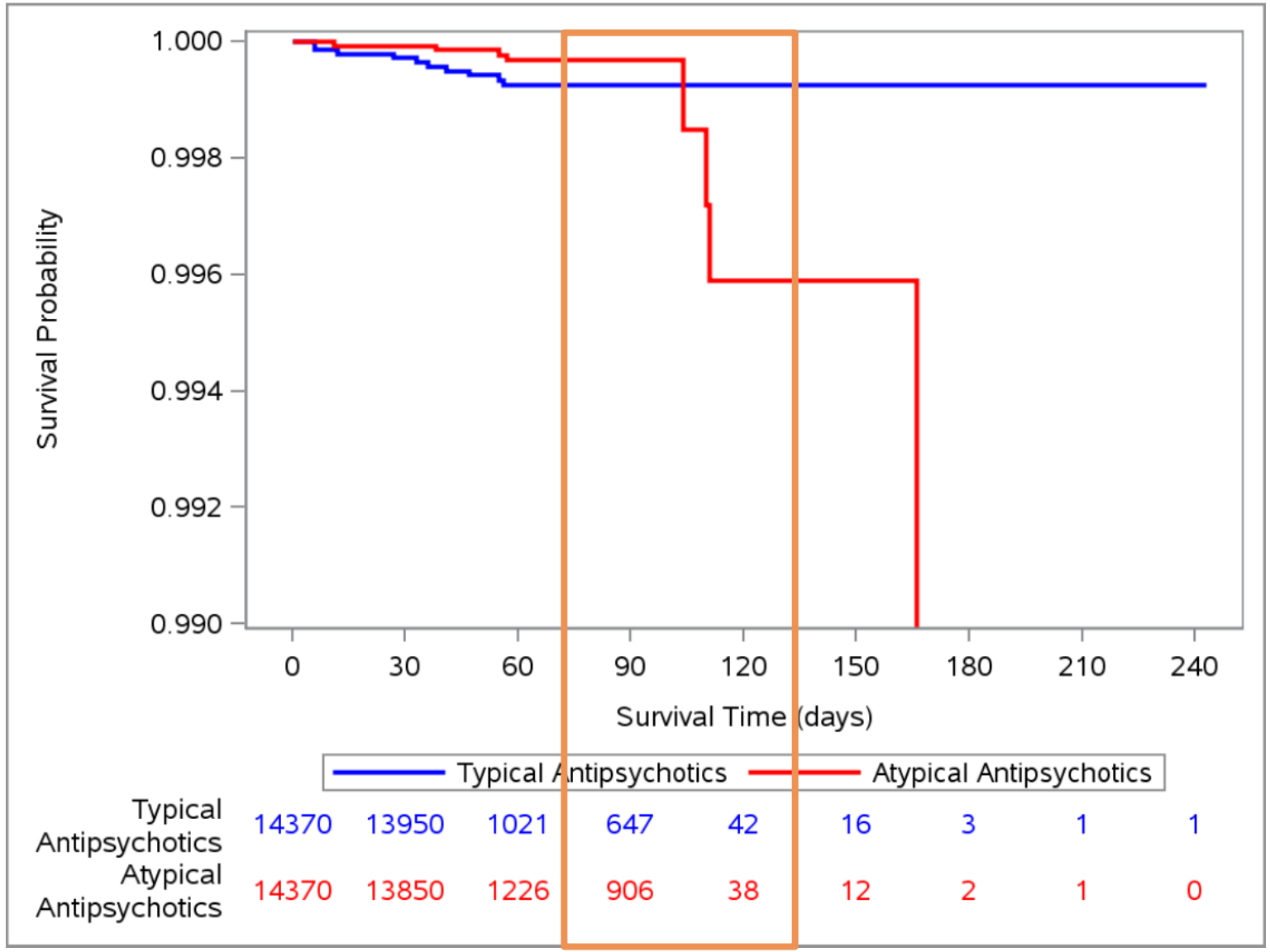


Propensity score 1:1 Aggregated Matched Cohort, Matched Caliper = 0.05



Kaplan Meier Survival Curve

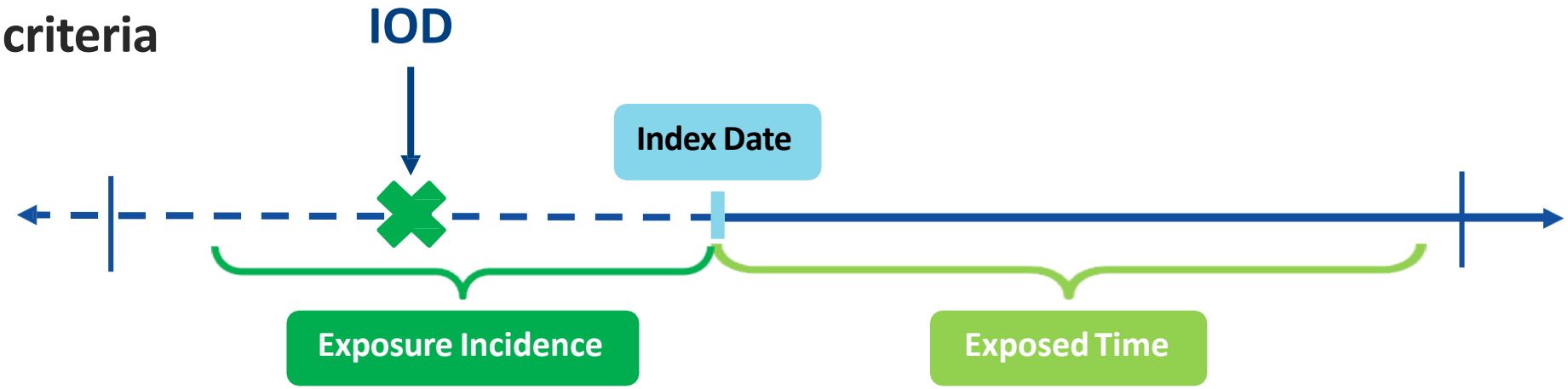
Kaplan Meier Survival Curves of Events and Followup Time for Ischemic Stroke, Unconditional Matched Cohort.

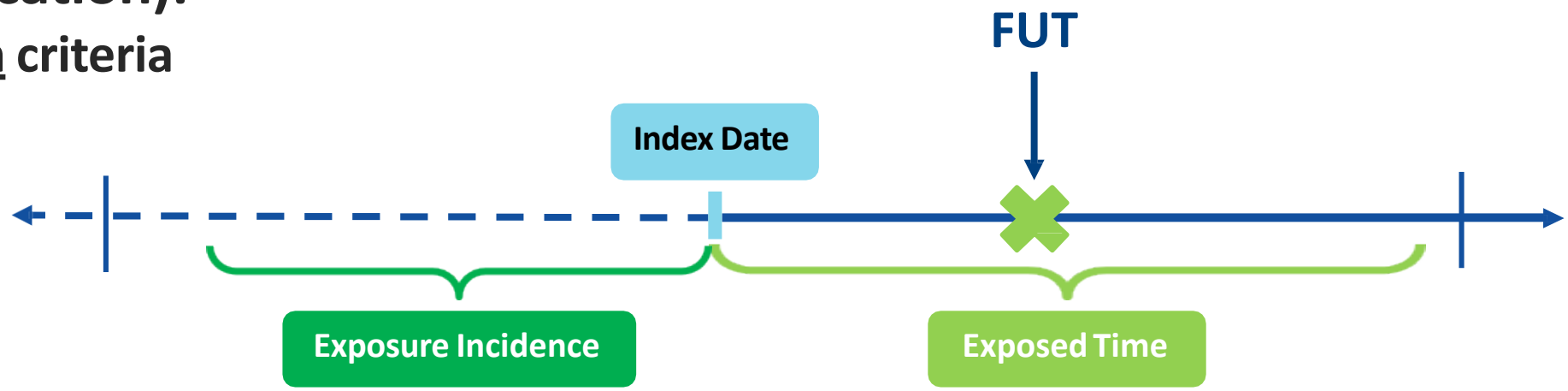


Cohort Codes File: Parameter T2_INDEX

IOD (Incidence Only Duration):

Code defines <u>incidence</u> criteria



FUT (Follow-up Truncation):

Code defines <u>truncation</u> criteria