Sentinel

Insights on Harmonizing Laboratory Results Data in the Sentinel System

ISPE 2025 Symposium SW-2F:
Overcoming Challenges in CDM Harmonization from Within-Country Coordination to International Collaboration

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SCAN ME

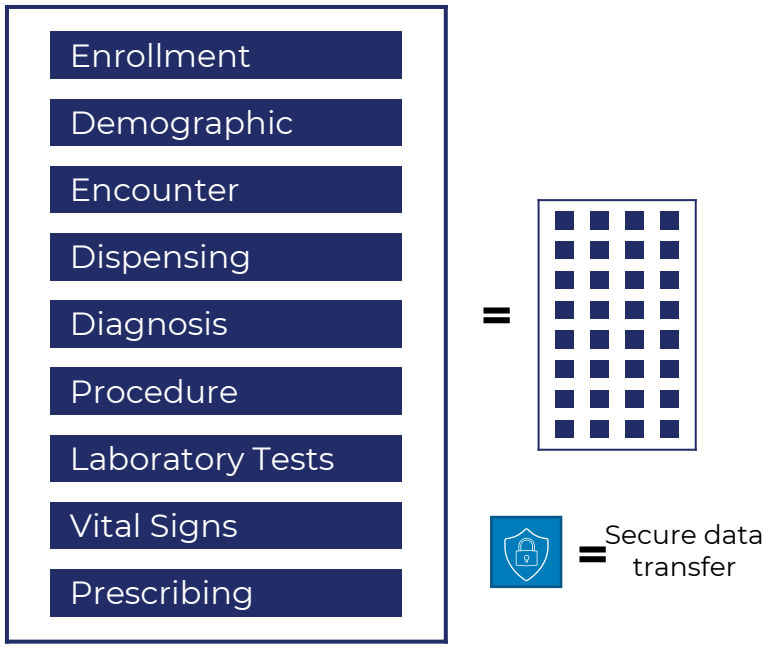
24 August 2025

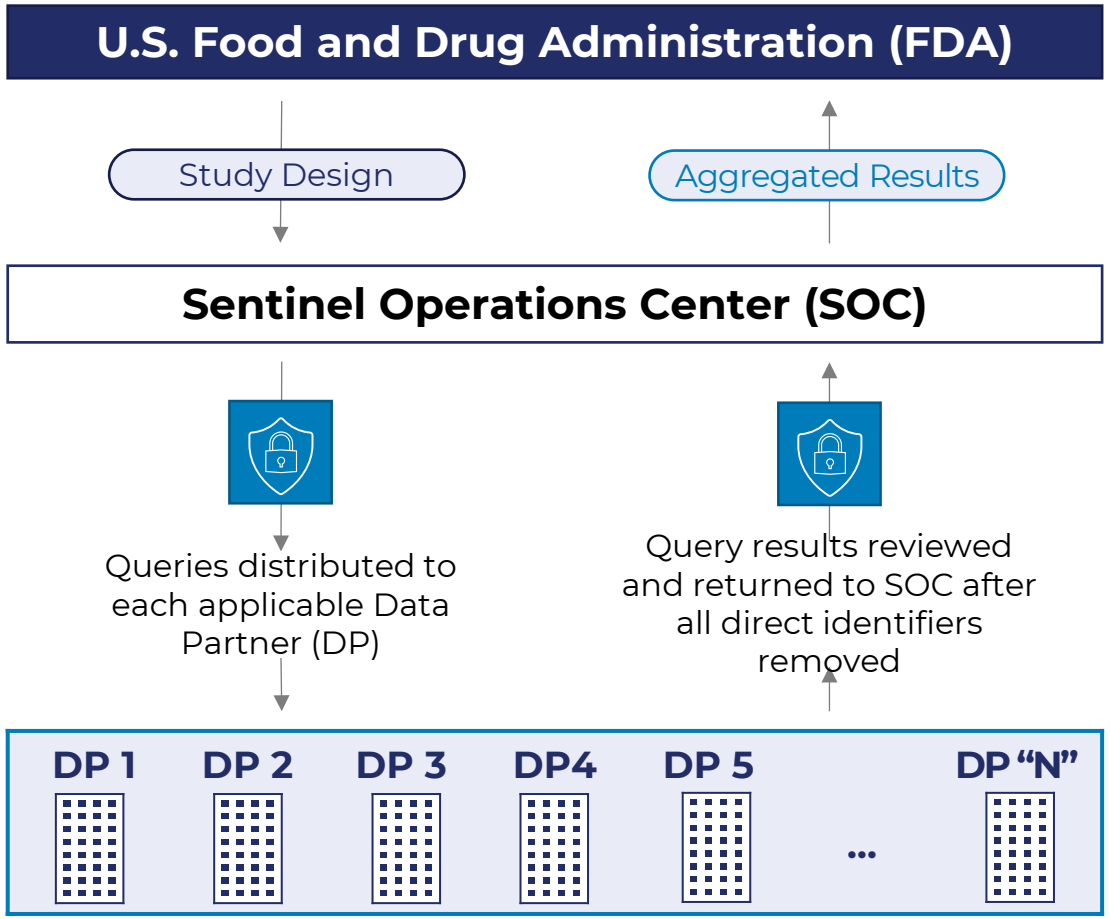
Disclaimers

- Ashley is an employee of Harvard Pilgrim Health Care Institute, a non-profit organization that conducts work for government and private organizations, including pharmaceutical companies.
- The contents are those of the authors and do not necessarily represent the official views of, nor and endorsement, by FDA/HHS, or the U.S. Government.

Sentinel Distributed Data Network

- Data Partners (DPs) hold data in the Sentinel Common Data Model format

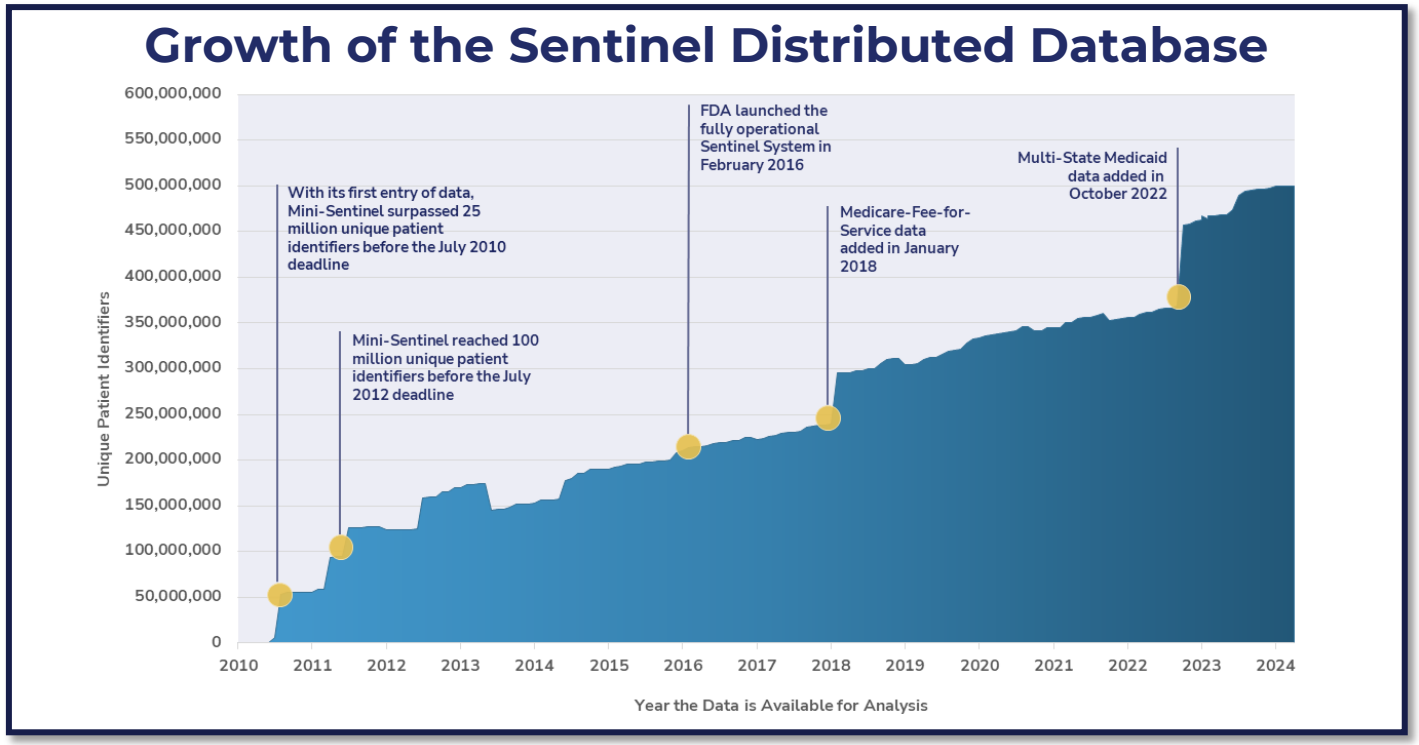




https://www.sentinelinitiative.org/about/how-sentinel-gets-its-data

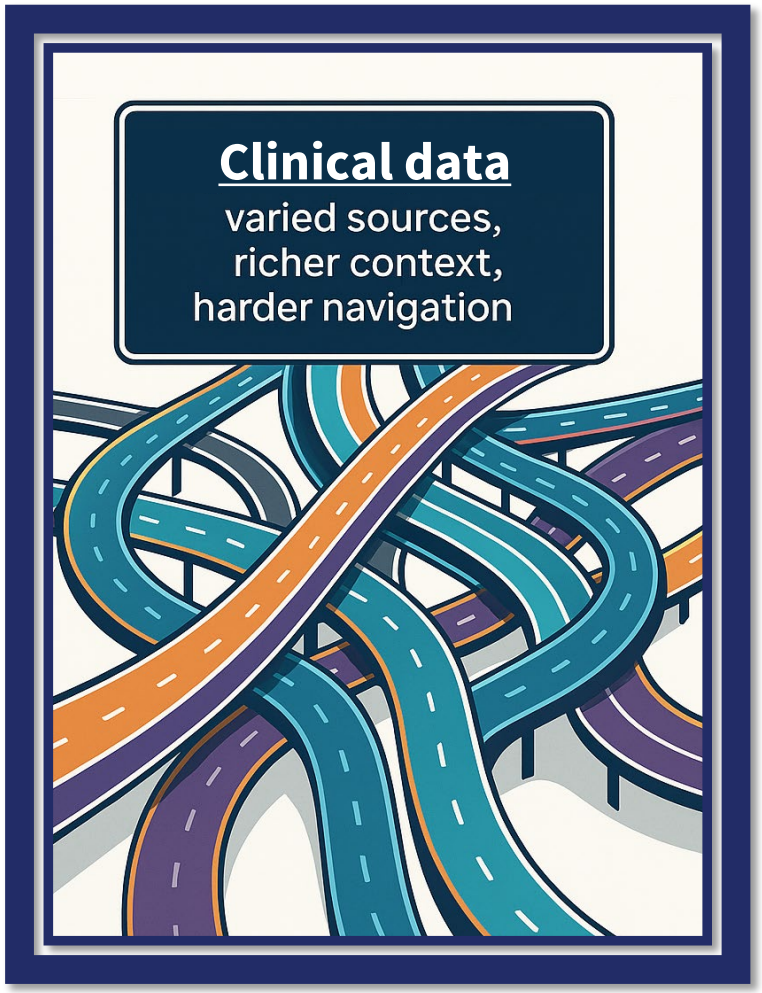
Sentinel Distributed Database Growth

- Sentinel Distributed Database came online in 2010, composed primarily of administrative claims data
- Now contains >500 million unique patient IDs from enrolled 2000 – 2024
  - ~370 million have ≥1 day of medical and drug coverage
    - *~130 million currently accruing new data*
  - ~73 million members with ≥1 laboratory result



Current as of April 2024; https://sentinelinitiative.org/about/key-database-statistics

Laboratory Results Data in the SCDM



- Sentinel's laboratory results data adds clinical detail
- They open new analytic doors and introduce new pitfalls
- Essential to understand:
  - Source of these data
  - How they relate to traditional claims data
  - How we can use them in querying

SCDM: Sentinel Common Data Model
Image: generated by author with OpenAI DALL·E, 4 Jun 2025

Laboratory Results Data Provenance

- Administrative claims data are generally sourced from a single billing or reimbursement form
- Laboratory results data have **three main sources** in the Sentinel System
  1. Directly input into Data Partner's EHR system at point-of-care
  2. Processed at a Data Partner's inpatient hospital, then entered into Data Partner's EHR system
  3. Drawn and processed at an external contracted laboratory facility and sent back to Data Partner as supplemental data for claims processing

Lesson:
Disparate data sources increase between-site variability

EHR: Electronic healthcare record

Strategy 1: Retain Source Data

Lesson:
Disparate data sources increase between-site variability in addition to the already variable within-site laboratory results

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Strategy:
Retain source data as much as possible

- SCDM tables based on administrative claims data are comprised almost entirely of standardized fields
- Laboratory Results table retains the original data at a minimum, in addition to "standardized" and "commonly used" transformations

SCDM: Sentinel Common Data Model

Raebel MA, Haynes K, Woodworth TS, et al. Electronic clinical laboratory test results data tables: lessons from Mini-Sentinel. *Pharmacoepidemiol Drug Saf.* 2014;23(6):609-618.

Source Data in the Common Data Model

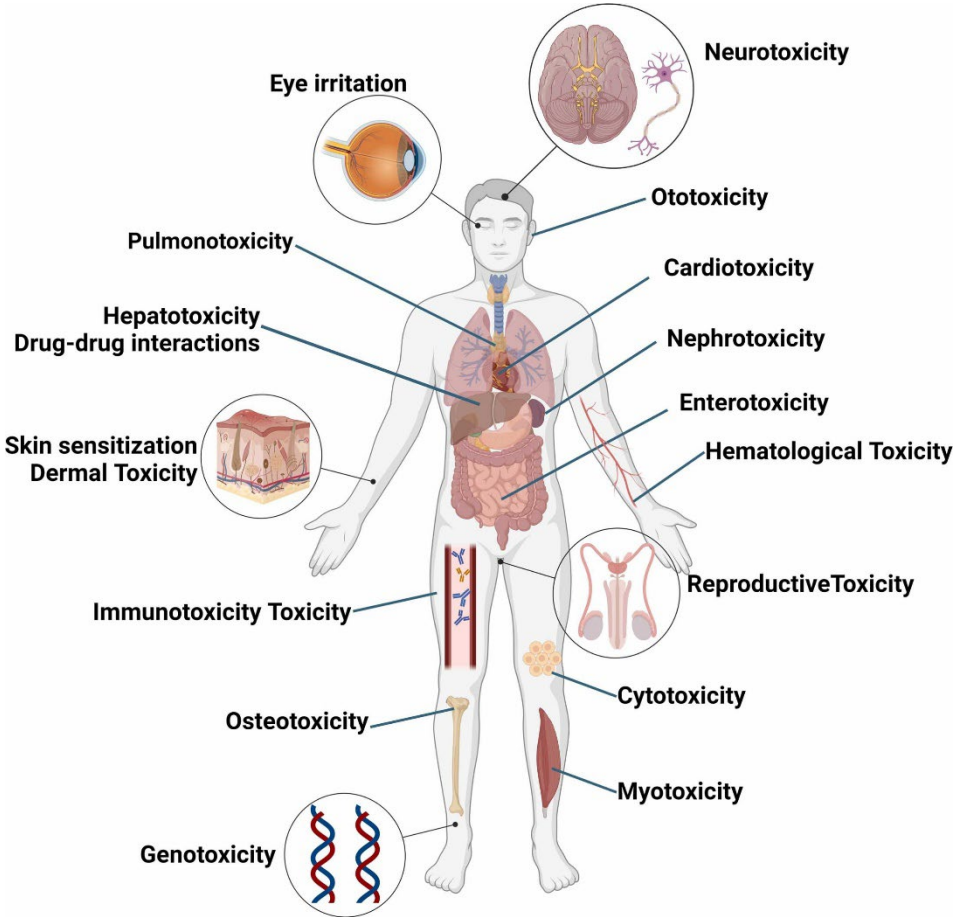
MS_Test_Name	Result_Type	MS_Test_Sub_Category	Fast_Ind	Specimen_Source	LOINC	Stat	Pt_Loc	Result_Lo	PX	PX_Code Type	Lab_dt
SARS_COV_2	C	PCR	X	UNK	94500-6	U	O	L			7/15/2021
SARS_COV_2	C	IA_RAP	X	UNK	94558-4	U	O	L	87426	C4	10/16/2020
SARS_COV_2_AB_G	C	EIA	X	SR_PLS	94563-4	U	O	L			6/7/2020
SARS_COV_2_AB_TOTAL	N	EIA	X	SR_PLS	94769-7	U	O	L			7/29/2021
UNMAPPED	U		U	UNK	31208-2	U	U	L	83655	C4	7/21/2011
UNMAPPED	U		U	UNK	787-2	U	U	L	85027	C4	7/21/2011

MS_Test_Name	Orig_Result	MS_Result_C	MS_Result_N	Modifier	Orig_Result_unit	Std_Result_unit	MS_Result_unit	Norm_Range_low	Modifier_low	Norm_Range_high	Modifier_high	Abn_ind
SARS_COV_2	NEG	NEGATIVE	.	TX								UN
SARS_COV_2	NEG	NEGATIVE	.	TX								UN
SARS_COV_2_AB_G	POS	POSITIVE	.	TX	U							UN
SARS_COV_2_AB_TOTAL	1623		1623	EQ	Units per mil	U/ML	U/ML	0	GE	0	LE	UN
UNMAPPED	0		.	UN		NULL						UN
UNMAPPED	82.4		.	UN	FL	FL						UN

Excerpt using Merative™ MarketScan® Commercial data; not all Sentinel Common Data Model fields shown

Medical Product Use and Laboratory Results

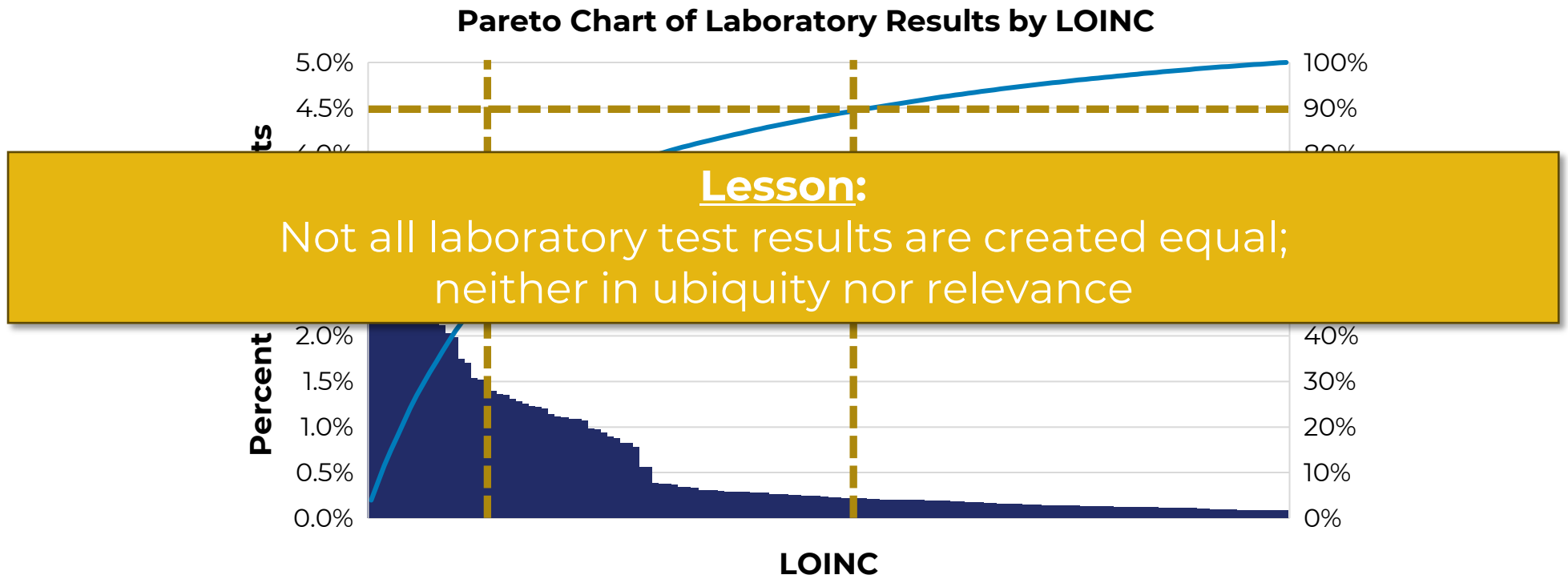
- > 50,000 LOINCs exist that identify laboratory tests, but not all are relevant to medical product use
- Key laboratory tests for the Sentinel System include those that identify adverse drug effects



LOINC: Logical Observation Identifiers Names and Codes
Figure from: doi:10.1016/j.aichem.2023.100011

The Pareto Principle Applies to Lab Results

- There are >27,000 LOINCs in the Sentinel Distributed Database
  - 0.5% of LOINCs (N=141) represent 90% of all laboratory results
  - 0.1% of LOINCs (N=23) represent 50% of all laboratory results



Statistics current as of 22 July 2025

Strategy 2: Harmonize Efficiently

Lesson:
Not all laboratory test results are created equal;
neither in ubiquity nor relevance

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Strategy:
Adapt harmonization efforts to most efficient transformations based on ubiquity and relevance

- The Sentinel Operations Center convened a workgroup to focus on a key set of common laboratory results that might also be useful for drug product safety and effectiveness studies

Efficient Laboratory Concept Harmonization

- Sentinel Data Partners "map" individual test results to one of 36 **concepts** using guidance developed by the Operations Center
  - In the SCDM, concepts are stored in the `MS_TEST_NAME` variable (e.g.: glucose, influenza, platelet count)

- **Example: Consider the following LOINCs**

MS_TEST_NAME = GLUCOSE

LOINC 41653-7
Glucose in Capillary blood by Glucometer

LOINC 1558-6
Fasting glucose in Serum or Plasma

LOINC 39480-9
Glucose in Venous blood

LOINC 2351-5
Glucose in 24-hour Urine

SCDM: Sentinel Common Data Model; LOINC: Logical Observation Identifiers Names and Codes

Impact of Laboratory Result Curation

- Of the three kinds of laboratory concepts in the SCDM:
  - **Highly curated** concepts have meaningfully interpretable results
    - May be “out of the box” ready for cohort-specific analyses
  - **Semi-curated** concepts are likely to have much heterogeneity in results
    - Cohort-specific quality assessment strongly encouraged
  - **Noncurated** concepts have mostly uninterpretable results
    - Cohort-specific quality assessment required

Laboratory Concepts in the SCDM

Highly curated

- A_1C
- ALP
- ALT
- ANC
- Bili., total
- CK, MB
- CK, MBI
- CK, total
- Creatinine
- Glucose
- Hemoglobin
- INR

Semi-curated

- Cholesterol, HDL
- Cholesterol, LDL
- Cholesterol, total
- D-Dimer
- Influenza, A nonspecific
- Influenza, A & B
- Influenza, B
- Influenza,
- Sodium
- TSH
- Triglycerides

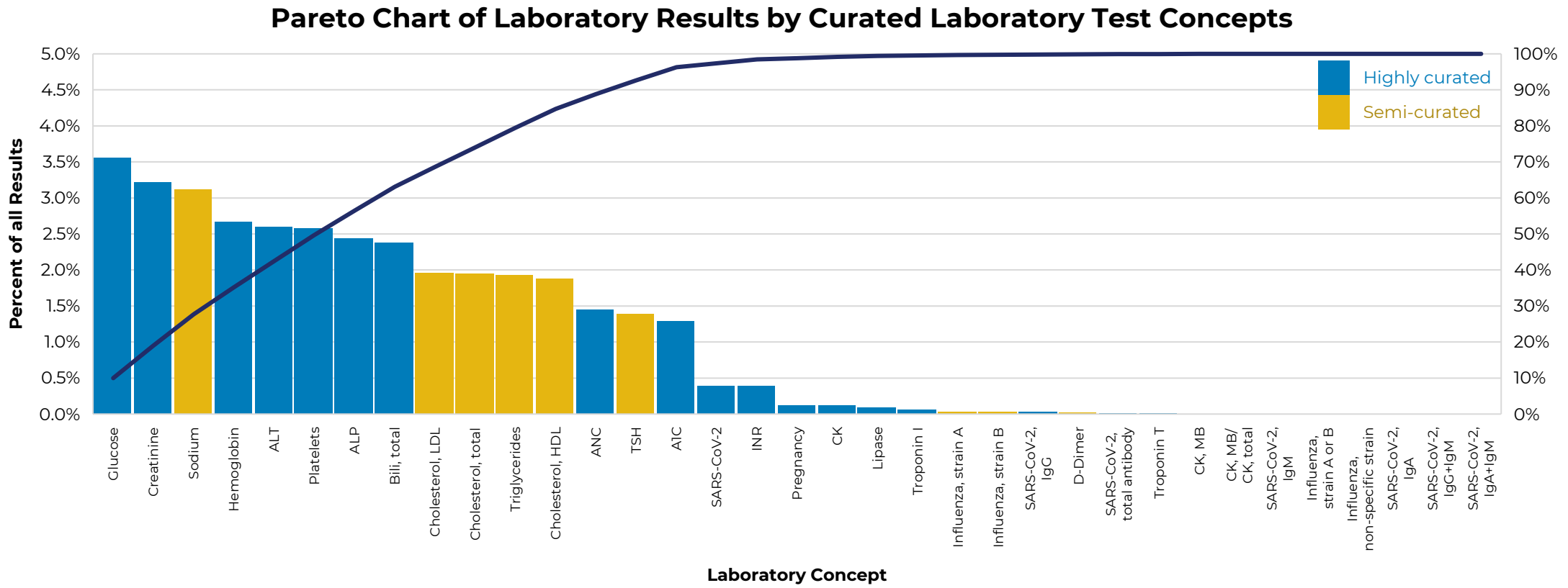
- Lipase
- Platelets
- Pregnancy test
- SARS-CoV-2, diagnostic
- SARS-CoV-2, IgA
- SARS-CoV-2, IgA & IgM
- SARS-CoV-2, IgG
- SARS-CoV-2, IgG & IgM
- SARS-CoV-2, IgM
- SARS-CoV-2, total antibody
- Troponin, I
- Troponin, T

All others (noncurated)

ALP: alkaline phosphatase; ALT: alanine aminotransferase; ANC: absolute neutrophil count; Bili: Bilirubin; CK: creatine kinase: INR: international normalized ratio; SCDM: Sentinel Common Data Model; TSH: thyroid stimulating hormone

Distribution of Laboratory Results by Concept

- 64% of all laboratory results in the Sentinel Distributed Database are for UNMAPPED concepts. The remaining 46% are dominated by 10/36 mapped concepts



ALP: alkaline phosphatase; ALT: alanine aminotransferase; ANC: absolute neutrophil count; Bili: Bilirubin; CK: creatine kinase: INR: international normalized ratio; SCDM: Sentinel Common Data Model; TSH: thyroid stimulating hormone

Exploring the Utility of Laboratory Results

- We have assessed the utility of leveraging laboratory results and other clinical data from EHRs for medical product assessment studies
  - Some studies have found certain laboratory results augment cohort identification
    - Augmenting CKD diagnosis-based cohort w/laboratory results data **doubled cohort size**, but differences in baseline characteristics remained

DOI: 10.1002/pds.4583

BRIEF REPORT

WILEY

Diagnosis-based cohort augmentation using laboratory results data: The case of chronic kidney disease

David H. Smith[1] | Susan Shetterly[2] | James Flory[3] | Kevin Haynes[4] | Christine Y. Lu[5] | Joshua J. Gagne[6] | Lisa Herrinton[7] | Carsie Nyirenda[2] | Elisabetta Patorno[6] | Azadeh Shoaibi[8] | Marsha A. Raebel[2,9]

TABLE 1 Baseline characteristics of the cohort

Characteristics[a]	Total N = 209 864	DXGroup[b] N = 107 607 (51.3% of total)	2-LabGroup N = 29 755 (14.2% of total)	1-LabGroup N = 72 502 (34.6% of total)	Standardized difference 2-LabGroup versus DXGroup	Standardized difference 1-LabGroup versus DXGroup
Age in years, mean (SD)	71.8 ± 10.8	72.6 ± 10.9	74.2 ± 9.5	69.6 ± 10.8	0.15	0.28
Age categories, y (%)						
<65	48 270 (23.0)	20 874 (19.4)	5047 (17.0)	22 349 (30.8)	Ref	Ref
65-74	67 113 (32.0)	33 733 (31.3)	8996 (30.2)	24 384 (33.6)	0.02	0.05
75-89	94 481 (45.0)	53 000 (49.3)	15 712 (52.8)	25 769 (35.5)	0.07	0.28
Female sex, N (%)	116 957 (55.7)	57 248 (53.2)	17 775 (59.7)	41 934 (57.8)	0.13	0.09
Comorbidity score, mean (SD)[d]	1.0 ± 2.1	1.4 ± 2.3	0.7 ± 1.8	0.5 ± 1.7	0.37	0.44
No encounters in prior 365 days, N (%)	2386 (1.1)	1016 (0.9)	0 (0.0)	1370 (1.9)	0.14	0.08
Number of ambulatory medical visits during baseline, mean (SD)	9.4 ± 10.1	10.1 ± 10.6	9.3 ± 8.9	8.2 ± 9.5	0.08	0.19
Emergency department visit during baseline, N (%) yes	53 978 (25.7)	32 997 (30.7)	6405 (21.5)	14 576 (20.1)	0.21	0.24
Hospitalization during baseline, N (%)	26 086 (12.4)	17 930 (16.7)	2431 (8.2)	5725 (7.9)	0.26	0.27
Institutional stay during baseline, N (%)	6192 (3.0)	4668 (4.3)	502 (1.7)	1022 (1.4)	0.16	0.18

CKD: chronic kidney disease; EHR: electronic healthcare record

Smith DH, Shetterly S, Flory J, et al. *Pharmacoepidemiol Drug Saf*. 2018;27(8):872-877.

Exploring the Utility of Laboratory Results

- We have assessed the utility of leveraging laboratory results and other clinical data from EHRs for medical product assessment studies
  - Some studies have found certain laboratory results augment cohort identification
  - Others have found that laboratory results add little to cohort identification
    - Adding hemoglobin results to non-inpatient UGI diagnoses **ID'd few additional cases**

Drug Saf (2017) 40:91–100
DOI 10.1007/s40264-016-0472-3

CrossMark

ORIGINAL RESEARCH ARTICLE

The Role of Hemoglobin Laboratory Test Results for the Detection of Upper Gastrointestinal Bleeding Outcomes Resulting from the Use of Medications in Observational Studies

Elisabetta Patorno[1] · Joshua J. Gagne[1] · Christine Y. Lu[2] · Kevin Haynes[3] · Andrew T. Sterrett[4] · Jason Roy[5] · Xingmei Wang[5] · Marsha A. Raebel[4]

Table 3 Upper gastrointestinal bleeding outcomes within 30 days after non-steroidal anti-inflammatory drug initiation using varied outcomes definitions, overall and by site

Outcome		Data partner site			
		All sites	Site 1	Site 2	Site 3
	Bleeding outcomes definition[a]				
1	Inpatient diagnoses (with or without an observed HGB drop ≥3 g/dl)	1657 (21.7)	30 (11.7)	520 (14.9)	1107 (28.4)
2	Non-inpatient diagnosis with drop in HGB ≥3 g/dl	58 (0.8)	2 (0.8)	41 (1.2)	15 (0.4)
3	Observed drop in HBG ≥3 g/dl (no coded UGI bleeding diagnosis)	2619 (34.3)	148 (57.6)	2160 (61.9)	311 (8.0)
4	Non-inpatient diagnosis without observed drop in HGB	3303 (43.3)	77 (30.0)	769 (22.0)	2457 (63.2)
1–4	Total bleeding outcomes	7637	257	3490	3890
	Bleeding outcomes definition excluding outcome 3[a]				
1	Inpatient diagnoses (with or without an observed HGB drop ≥3 g/dl)	1657 (33.0)	30 (27.5)	520 (39.1)	1107 (30.9)
2	Non-inpatient diagnosis with drop in HGB ≥3 g/dl	58 (1.2)	2 (1.8)	41 (3.1)	15 (0.4)
4	Non-inpatient diagnosis without observed drop in HGB	3303 (65.8)	77 (70.6)	769 (57.8)	2457 (68.7)
1, 2, 4	Total UGI bleeding outcomes without group 3	5018	109	1330	3579

HGB hemoglobin, *UGI* upper gastrointestinal

[a] Mutually exclusive groups

EHR: electronic healthcare record; UGI: upper gastrointestinal bleeding
Patorno E, Gagne JJ, Lu CY, et al. *Drug Saf.* 2017;40(1):91-100.

Exploring the Utility of Laboratory Results

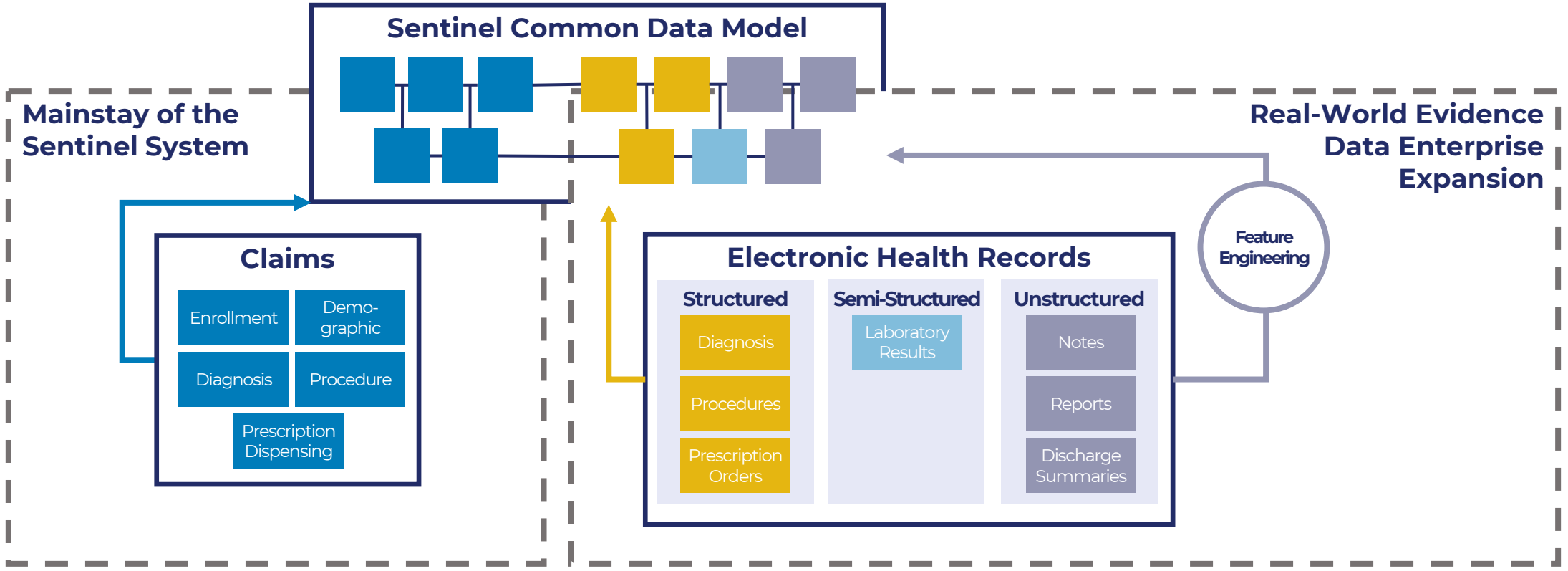
- We have assessed the utility of leveraging laboratory results and other clinical data from EHRs for medical product assessment studies
  - Some studies have found certain laboratory results augment cohort identification
  - Others have found that laboratory results add little to cohort identification
  - Adding laboratory results to other aspects of study design (including baseline characterization, confounder adjustment, and quantitative bias assessment) have also yielded variable findings

Lesson:
Regardless of whether laboratory results are highly curated, study-specific needs should always be assessed and prioritized

EHR: electronic healthcare record

Integrating EHR Data into Sentinel

- **Real-World Evidence Data Enterprise** expanded Sentinel System to include longitudinal EHRs linked with insurance claims data for at least 10 million individuals



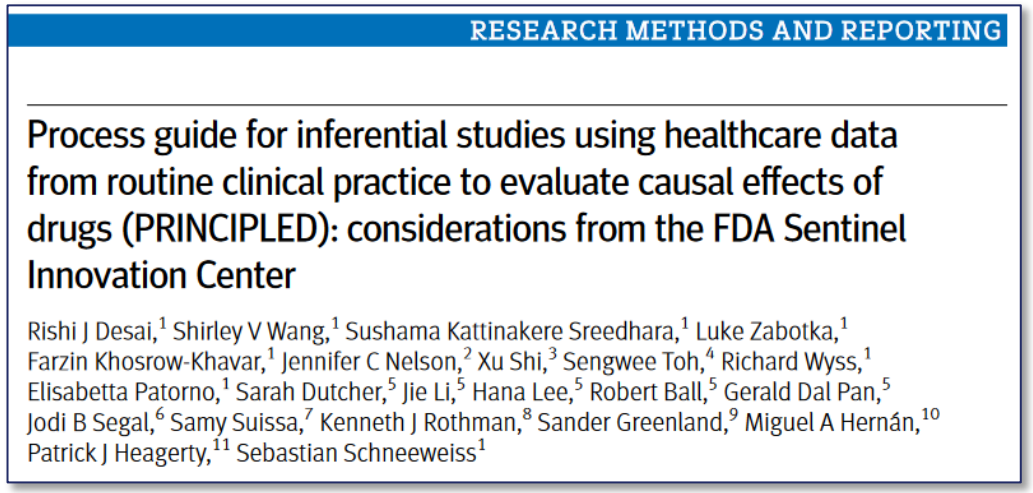
EHR: electronic healthcare record

Desai RJ, Marsolo K, Smith J, et al. The FDA Sentinel Real-World Evidence Data Enterprise (RWE-DE). *Pharmacoepidemiol Drug Saf.* 2024;33(10):e70028

Strategy 3: Ensure Data are Fit-for-Purpose

Lesson:
Regardless of whether laboratory results are highly curated, study-specific needs should always be assessed and prioritized

Strategy:
Include robustness assessments and sensitivity analyses in study planning to ensure laboratory results data are fit-for-purpose



RESEARCH METHODS AND REPORTING

Process guide for inferential studies using healthcare data from routine clinical practice to evaluate causal effects of drugs (PRINCIPLED): considerations from the FDA Sentinel Innovation Center

Rishi J Desai,[1] Shirley V Wang,[1] Sushama Kattinakere Sreedhara,[1] Luke Zabotka,[1] Farzin Khosrow-Khavar,[1] Jennifer C Nelson,[2] Xu Shi,[3] Sengwee Toh,[4] Richard Wyss,[1] Elisabetta Patorno,[1] Sarah Dutcher,[5] Jie Li,[5] Hana Lee,[5] Robert Ball,[5] Gerald Dal Pan,[5] Jodi B Segal,[6] Samy Suissa,[7] Kenneth J Rothman,[8] Sander Greenland,[9] Miguel A Hernán,[10] Patrick J Heagerty,[11] Sebastian Schneeweiss[1]

Desai RJ, Wang SV, Sreedhara SK, et al. Process guide for inferential studies using healthcare data from routine clinical practice to evaluate causal effects of drugs (PRINCIPLED): considerations from the FDA Sentinel Innovation Center. *BMJ*. 2024;384:e076460. doi:10.1136/bmj-2023-076460

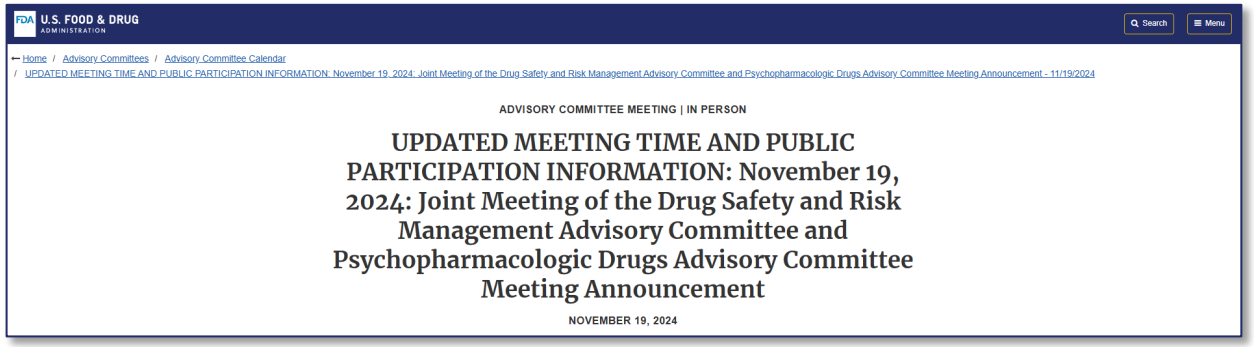
Integrating Quality Assessments into Study Design

- FDA leveraged both the SDD and RWE-DE to support the reevaluation of the clozapine REMS program
  - Clozapine REMS required frequent ANC monitoring to prevent a potential severe neutropenia adverse effect
  - Study planning included **extensive ANC laboratory result characterization**, which led to key study design decisions, including the choice to restrict assessments to clozapine users with complete ANC laboratory results data streams

Table 19. Select Demographic, Clinical, and Health Care Utilization and Medication Characteristics Among Clozapine Incident Users With a 30-Day Washout Period Among 13 Data Partners and the Subset Population With Complete Concordance

Characteristics	13-Data Partners	8 Data Partners With Linked ANC Test Data	Standardized Mean Difference (SMD)
Total episodes	164,10,473	10,473	
Age, mean (SD)	45.6 (14.8)	46.3 (16.5)	0.045
Female sex, %	41.1	44.6	0.072
Comorbidities, percentage			
Schizophrenia	85.2	77.9	0.188
Bipolar disorder	36.3	38.4	0.043
Depressive disorder	33.6	35.3	0.035
Rheumatoid arthritis	4.1	5.2	0.052
Health care utilization, mean (SD)			
Ambulatory	19.3 (23.3)	13.8 (13.9)	0.287
Inpatient	0.6 (1.2)	0.7 (2.1)	0.058
Prescriptions	31.1 (27.3)	25.2 (21.8)	0.239
Unique drugs	9.0 (6.1)	8.5 (5.9)	0.083

Source: Generated from study results.
Abbreviations: ANC, absolute neutrophil count; SD, standard deviation; SMD, standardized mean difference



ANC: absolute neutrophil count; REMS: Risk Evaluation and Mitigation Strategies; RWE-DE: Real-World Evidence Data Enterprise; SDD: Sentinel Distributed Database

REMS for Clozapine Products: Joint Meeting of the Drug Safety and Risk Management Advisory Committee and the Psychopharmacologic Drugs Advisory Committee.; FDA Briefing Document; 2024:43-47

Conclusion

- Laboratory results data is a key piece of clinical data that has the potential to greatly improve real-world evidence generation
- Strategies used in the Sentinel System to optimize the utility of laboratory results include:
  - Retain source data as much as possible
  - Adapt harmonization efforts based on ubiquity and relevance
  - Include robustness assessments and sensitivity analyses in study planning
- With careful planning and implementation, laboratory results data can be cleaned, harmonized, and assessed for the quality required for regulatory decision making

Thank You

Questions?

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or

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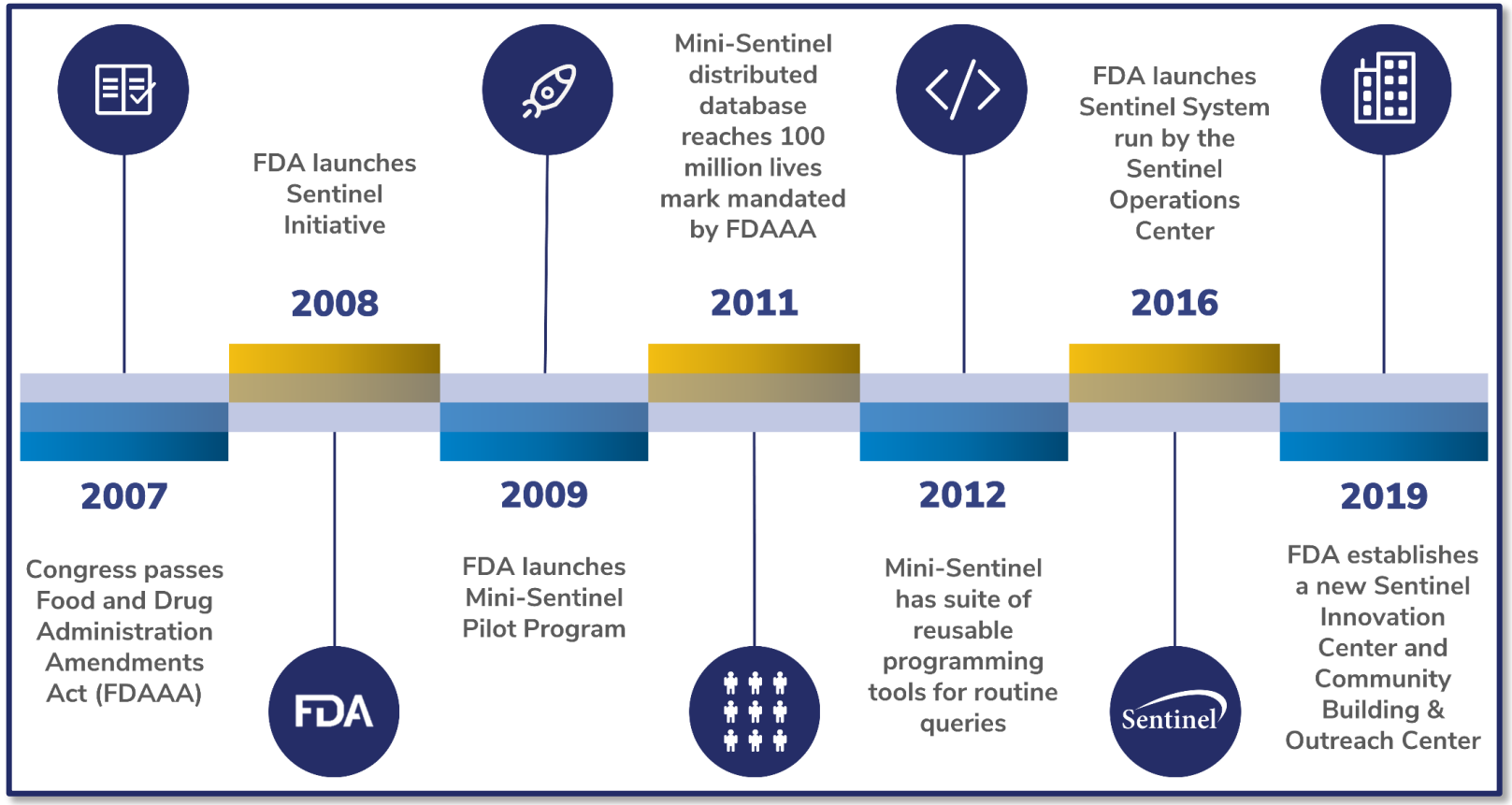
Supplementary Slides

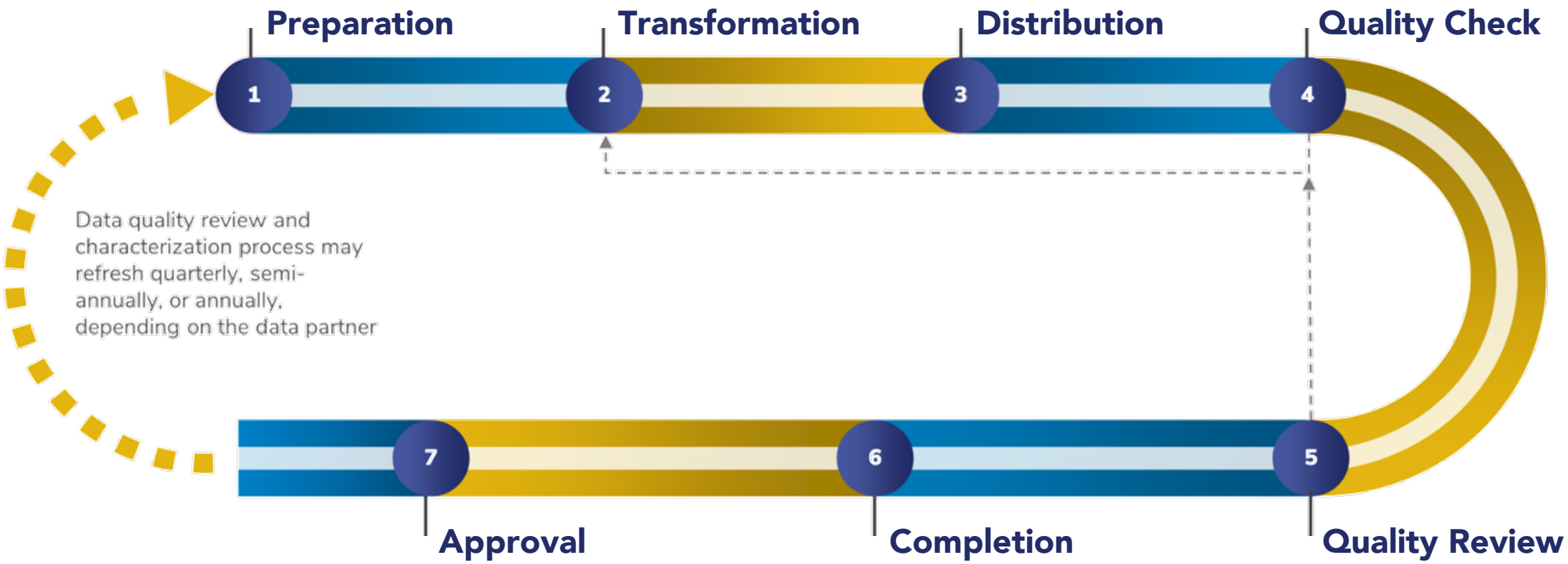
The U.S. FDA's Sentinel System

- Sentinel is the FDA's national electronic system for monitoring the safety of FDA-regulated medical products



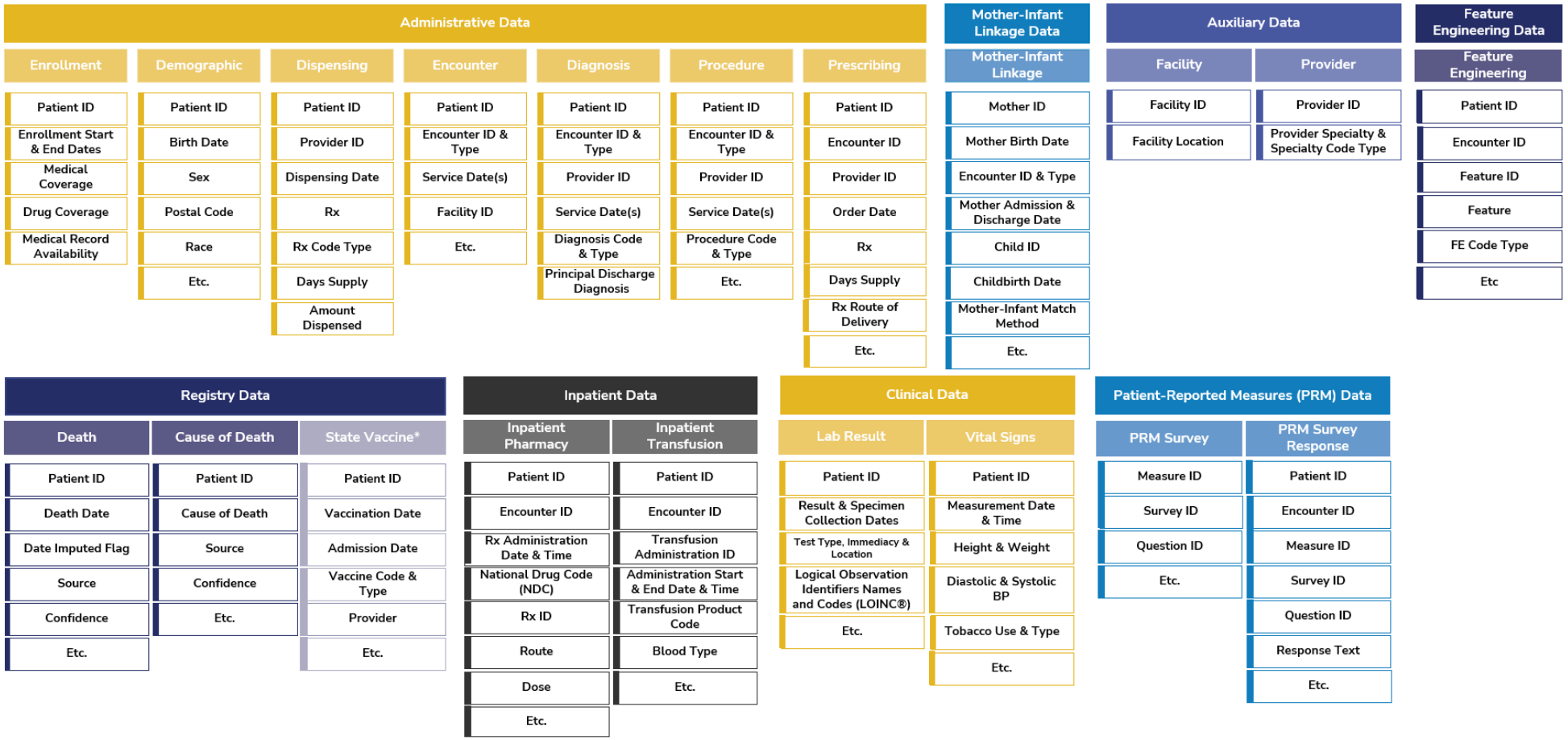
https://sentinelinitiative.org/about

Data Quality Review and Characterization



https://sentinelinitiative.org/about/how-sentinel-gets-its-data

Sentinel Common Data Model



**The State Vaccine table has not been in use since SCDM v6.0.*

Key Variables in the Laboratory Results Table

Field	Notes
Laboratory test concept (MS_TEST_NAME)	
Test result quantitative or qualitative (RESULT_TYPE)	N = numeric; C= character
Test concept sub-category (MS_TEST_SUB_CATEGORY)	Only applicable to certain concepts
Indicator for patient fasting status (FAST_IND)	
Test specimen source (SPECIMEN_SOURCE)	Characterized concepts have guidance, but strict observance is uncommon
LOINC	Optional. Guidance for characterized concepts includes lists of exemplar and unacceptable codes.
Test immediacy (STAT)	
Patient location at the time of lab (PT_LOC)	
Order, lab, or result date ([ORDER/LAB/RESULT]_DT)	Not all DPs populate all dates
Test result after curation (MS_RESULT_[C/N])	If raw data in a different unit than recommended for characterized concepts, this is a converted value.
Result modifier, e.g. “greater than” (MODIFIER)	Not always reliable
Test result unit after curation (MS_RESULT_UNIT)	Only applicable for quantitative results. For characterized concepts, must be in the recommended list.
Indicator for if result is abnormal (ABN_IND)	

Types of Data Quality Checks

Single-table checks	✓ **Completeness** *Ex: Admission date is not missing value* ✓ **Validity** *Ex: Admission date is in the "date" format*
Cross-table checks	✓ **Accuracy** *Ex: Admission date in diagnosis table occurs before patient's discharge in encounter table* ✓ **Integrity** *Ex: Admission date occurs within the patient's active enrollment period*
Cross-time checks	✓ **Trend Consistency** *Ex: No sizable percent change in admission date record counts*

https://sentinelinitiative.org/about/how-sentinel-gets-its-data

Single-Table Checks in the Laboratory Results Table

- The majority of Laboratory Results Table single-table checks will “fail” the Quality Assurance module if triggered
  - Data Partners are notified if a curated results field contains an invalid non-missing value

Single-table checks	✓ **Completeness** *Ex: Admission date is not missing value* ✓ **Validity** *Ex: Admission date is in the “date” format*

Enforcement	Check Purpose	Number of Checks
Fail	**Completeness**	34
Fail	**Conformance (value)**	94
Fail	**Conformance (relation)**	3
Warn	**Conformance (value)**	5
		136

https://www.sentinelinitiative.org/methods-data-tools/sentinel-common-data-model/data-quality-review-and-characterization-programs

Cross-Table Checks in the Laboratory Results Table

- The majority of Laboratory Results Table cross-table checks ensure that fields agree with each other

Cross-table checks

✓ **Accuracy**
Ex: Admission date in diagnosis table occurs before patient's discharge in encounter table

✓ **Integrity**
Ex: Admission date occurs within the patient's active enrollment period

Enforcement	Check Purpose	Number of Checks
Fail	**Conformance (value)**	183
Fail	**Conformance (relation)**	4
Fail	**Plausibility (atemporal)**	17
Warn	**Conformance (value)**	42
Warn	**Conformance (relation)**	4
Warn	**Plausibility (atemporal)**	17
Warn	**Plausibility (temporal)**	3
		270

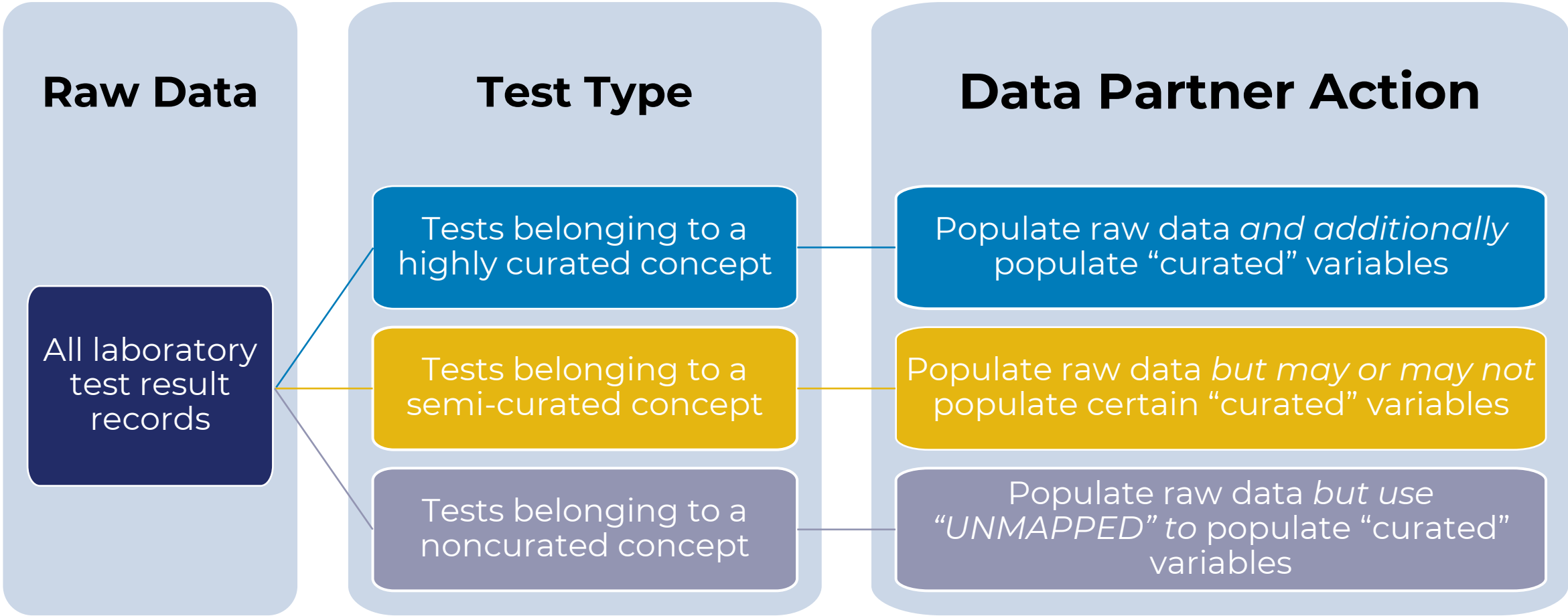
https://www.sentinelinitiative.org/methods-data-tools/sentinel-common-data-model/data-quality-review-and-characterization-programs

Cross-Time Checks in the Laboratory Results Table

- Cross-time checks rely on project-specific quality assurance because temporal trends may differ for different laboratory tests

Cross-time checks	✓ **Trend Consistency** *Ex: No sizable percent change in admission date record counts*

Selectively Curating Laboratory Results



Addressing Data Completeness for ANC

- Missing ANC laboratory results may be result of non-adherence to REMS guidelines or incomplete clinical data streams
- Metric used to assess data completeness: "ANC Lab Result: Monitoring Order Correspondence"

$$Correspondence = \frac{Number\ of\ ANC\ Monitoring\ Orders\ in\ First\ Six\ Months\ of\ Clozapine\ Treatment}{Number\ of\ ANC\ Laboratory\ Results\ in\ First\ Six\ Months\ of\ Clozapine\ Treatment}$$

  - Query team chose to assess neutropenia only among patients with 100% Correspondence

ANC: Absolute neutrophil count; DP: Data Partner; EHR: Electronic Medical Record; IDS: Integrated Delivery System