A framework for rapid medical product safety assessment: FDA's Sentinel toolkit

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ABSTRACT

Background: The US Food and Drug Administration's (FDA) Sentinel System uses customizable analytic tools (i.e., modular programs) to rapidly provide descriptive information across a large distributed electronic healthcare data network. These results help inform more complex analyses.

Objective: To describe Sentinel "Level 1" modular program (MPL1) querying capabilities that support medical product safety surveillance activities.

Methods: Sentinel includes **16** data partners (DPs) that together have healthcare information for over 193 million individuals contributing 351 million person-years of quality-checked data from 2000 to 2015. Each DP routinely transforms its healthcare data into the Sentinel Common Data Model (SCDM) and stores the transformed data locally, within its firewall. DPs execute standardized modular programs distributed securely by the Sentinel Operations Center (SOC) and only return de-identified, aggregated results needed for the analysis. MPL1 use customizable parameters such as inclusion/ exclusion criteria, enrollment requirements, and flexible exposure and outcome definitions based on medical product use, diagnosis and procedure codes to perform unadjusted analysis. Complementary tools to perform confounder adjustment (Level 2 and 3 analyses) are also available (not described here).

Results: Modular programs can describe: 1) background rates 2) uptake, use, and persistence of medical products 3) health outcomes following medical product exposure 4) concomitant medical product use 5) health outcomes during concomitant use 6) frequently observed diagnoses, procedures, or drug dispensing and 7) baseline distributions of potential confounders. Analyses can be stratified by age group, sex, year, month, comorbidity score, or healthcare utilization metrics. In 2015, the SOC supported 57 FDA Level 1 requests that evaluated nearly 1,500 unique sets of query parameter combinations and generated over 80 reports. Requests typically take 4 weeks to complete from the time query parameters are finalized.

Conclusion: These publicly available modular programs are the backbone of Sentinel's distributed querying system, contributing to the FDA's ability to rapidly generate information on medical product safety questions.

BACKGROUND

- None.

CONFLICT OF INTEREST

- In response to the 2007 FDA Amendments Act (FDAAA), the FDA created the Sentinel System to conduct active safety surveillance of regulated medical products.
- A distributed data approach is used, allowing data partners to maintain data security and confidentiality/patient privacy.
- Sentinel has developed customizable tools that run against a common data model for rapid assessments, returning de-identified aggregated results.

OBJECTIVE

- To describe Sentinel "Level 1" modular program querying capabilities that support medical product safety surveillance activities.

METHODS

Data Source:

- Sentinel includes:
  - 16 data partners (DPs)
  - ~193 million individuals
  - ~351 million person-years
  - Data from 2000 to 2015
- Each DP routinely transforms claims and EHR data into a common data model (CDM), which undergoes regular quality assurance.

Modular Programs:

Figure 1. Structure of Sentinel rapid querying system

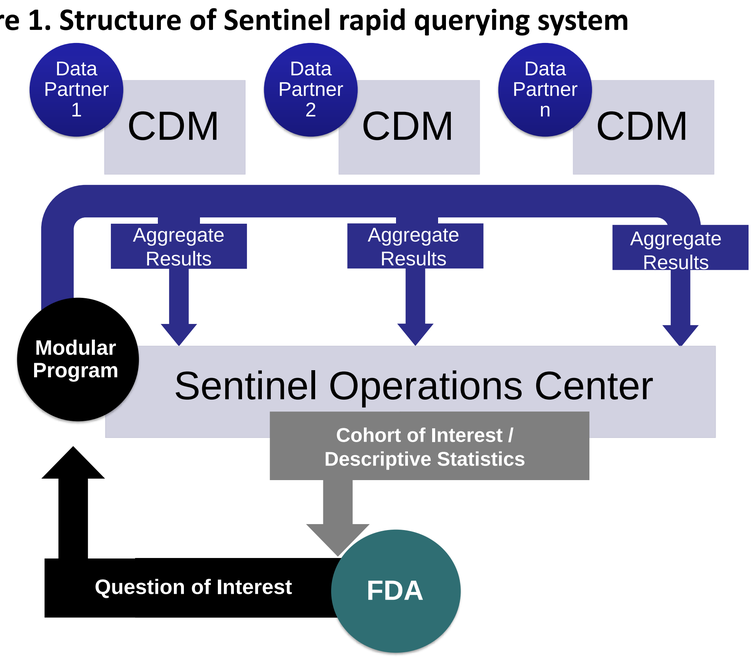


Figure 2. Customizable Level 1 MP parameters

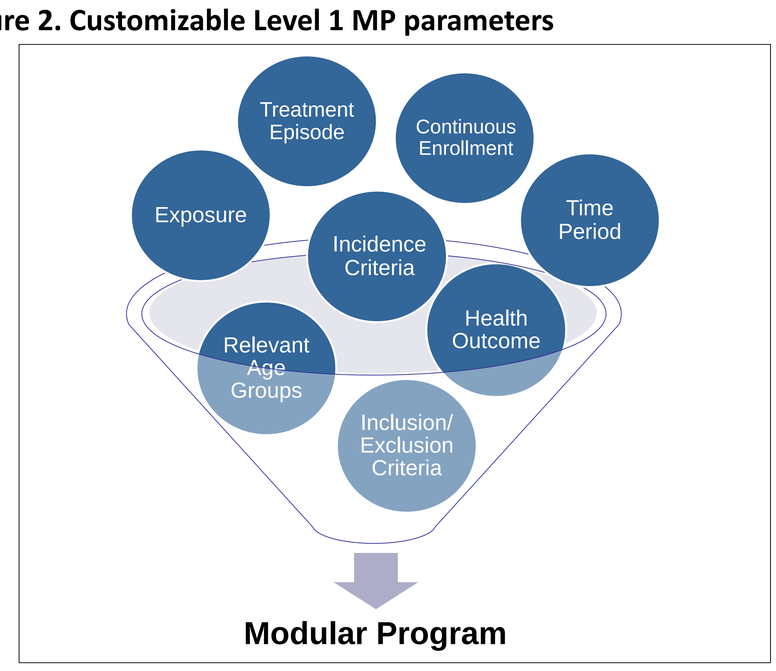
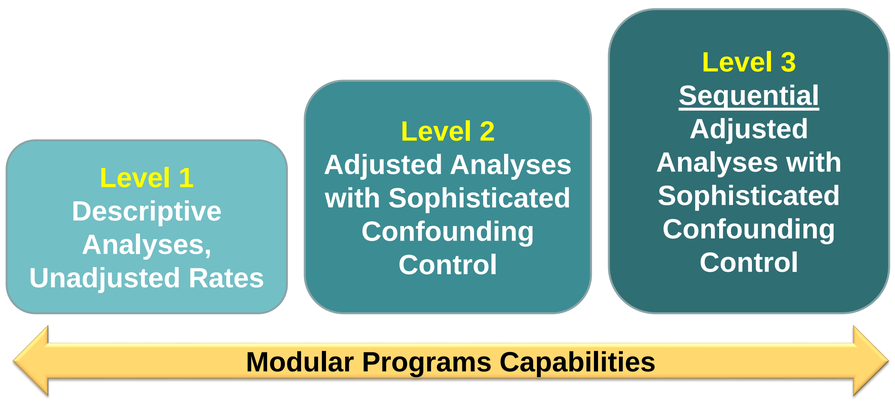


Figure 3. Comparison of Level 1, Level 2, and Level 3 MPs



- Complex analyses with confounder adjustment performed with Level 2 and 3 tools include:
  - Propensity score matching
  - Self-controlled risk interval design
  - Adjusted incidence rate ratio (IRR)

RESULTS

Table 1. Types and examples of cohort characterization and descriptive analyses performed by Level 1 MP

Type of Analysis	Example
Calculate background rates of health outcomes	Number of patients with a Type II diabetes diagnosis
Identify numbers of medical product users	Number of new metformin users per 10,000 eligible members
Describe uptake, use, and persistence of new medical products	Evaluate trends by uptake following months of approval of a newly approved SGLT2 inhibitor
Describe time exposed to medical product and evaluate the occurrence of health outcomes within relevant exposure periods (either as treated or intent-to-treat)	Identify the proportion of patients who have diabetic ketoacidosis while on a particular antidiabetic treatments
Characterize concomitant use of medical products and occurrence of health outcomes during period of concomitant use	Assess concomitant use of an oral antidiabetic medication and insulin
Characterize frequently observed diagnoses, procedures, or drug dispensing during specific time periods of interest	Ascertain the most frequently observed diagnoses before and after initiation of a new medication
Describe baseline distributions of covariates	Create a "Table 1" to compare baseline characteristics of specific comorbidities among various diabetes medications

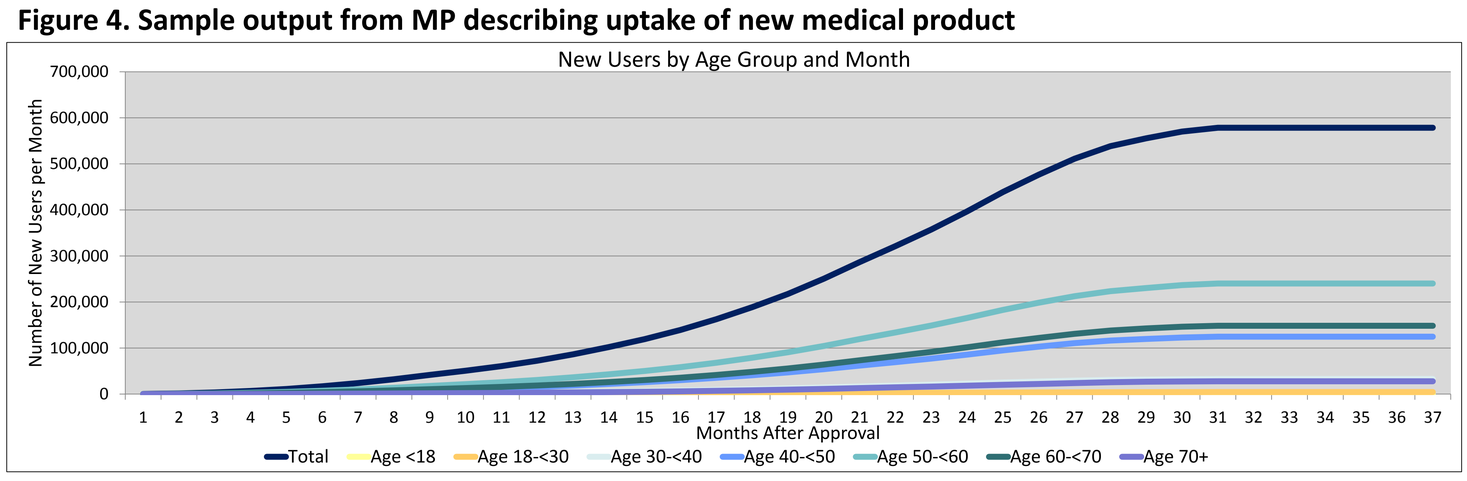
Level 1 Modular Program Output:

- Summary-level counts are produced (e.g., number of new users, total amount of person-time at risk).
- Output can be stratified by various parameters, including:
  - Age group
  - Sex
  - Year
  - Month
  - Comorbidity score
  - Healthcare utilization metrics

Table 2. Sample output from baseline covariate MP

	Exposure A		Exposure B	
Characteristic				
	N	**%/Std Dev**	**N**	**%/Std Dev**
Exposed patients	200,000	100.0%	100,000	100.0%
Events during follow-up	1,000	0.5%	800	0.6%
Mean person-days at risk	150	200.0	200	250.0
Patient Characteristics				
Gender (F)	120,000	60.0%	40,000	40.0%
Mean age (std dev)	45	10.0	60	12.5
Recorded History of:				
Hypertension	10,000	5.0%	8,000	8.0%
Myocardial Infarction	5,000	2.5%	6,000	6.0%
Metformin use	20,000	10.0%	15,000	15.0%
Combined Comorbidity Score	2.0	2.1	2.5	2.1

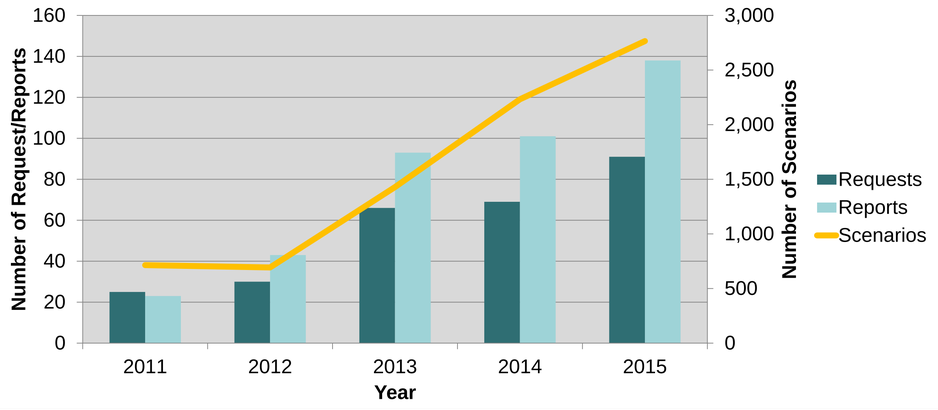
Figure 4. Sample output from MP describing uptake of new medical product



Modular Program Utilization:

- Sentinel began utilizing modular programs in 2011. Use has increased steadily over time.
- By the end of 2015, Sentinel had run total of **281** modular program requests, evaluating nearly 8,000 separate scenarios, and generated nearly 400 reports.
- Once a query has been finalized, it takes about 4 weeks to provide results to FDA.

Figure 5. Utilization of Modular Programs by Year



CONCLUSION

- Modular programs are the backbone of Sentinel's querying system, contributing to the FDA's ability to rapidly generate information on medical product safety questions.
- These publicly available tools have value beyond Sentinel and have been used by the National Institutes of Health, medical product sponsors, and others to support additional needs.

FUNDING SOURCE

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DISCLAIMER

- The views expressed in this poster are those of the authors and are not intended to convey official US FDA policy or guidance.