

[PHUSE EU Connect 2022 – RE05]

Is Your Analytics Platform ready for handling Real World Data for regulatory grade Real World Evidence?

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Disclaimer

- This presentation reflects the opinions of the presenters and should not be construed or considered to represent regulatory authorities' views or policies.



AGENDA

01

RWE related regulatory
landscape

02

Features of a Modern
RWE Analytics Platform

03

Q & A

Real World Data (RWD) & Real World Evidence (RWE)

*RWD are data relating to patient health status and/or the **delivery of health care routinely collected** from a variety of sources. RWE is the **clinical evidence** regarding the usage and potential benefits, or risks of a medical product **derived from analysis of RWD**.*

.....Sources include real-world data (such as electronic health records, insurance claims data and data from patient registries), genomics, clinical trials, spontaneous adverse drug reaction reports, social media and wearable devices.....

The purpose of RWD Working Group is to deal with regulatory issues related to Real World Data (RWD) such as utilization of medical information databases. Medical information databases includes electronic medical records, diagnosis procedure combination (DPC) from hospital information system; Claims for medical fees and dispensing fees; and disease registry. etc.



U.S. FOOD & DRUG
ADMINISTRATION

FRAME1

**REAL-WORLD
EVIDENCE
PROGRAM**

Framework for FDA's RWE Program



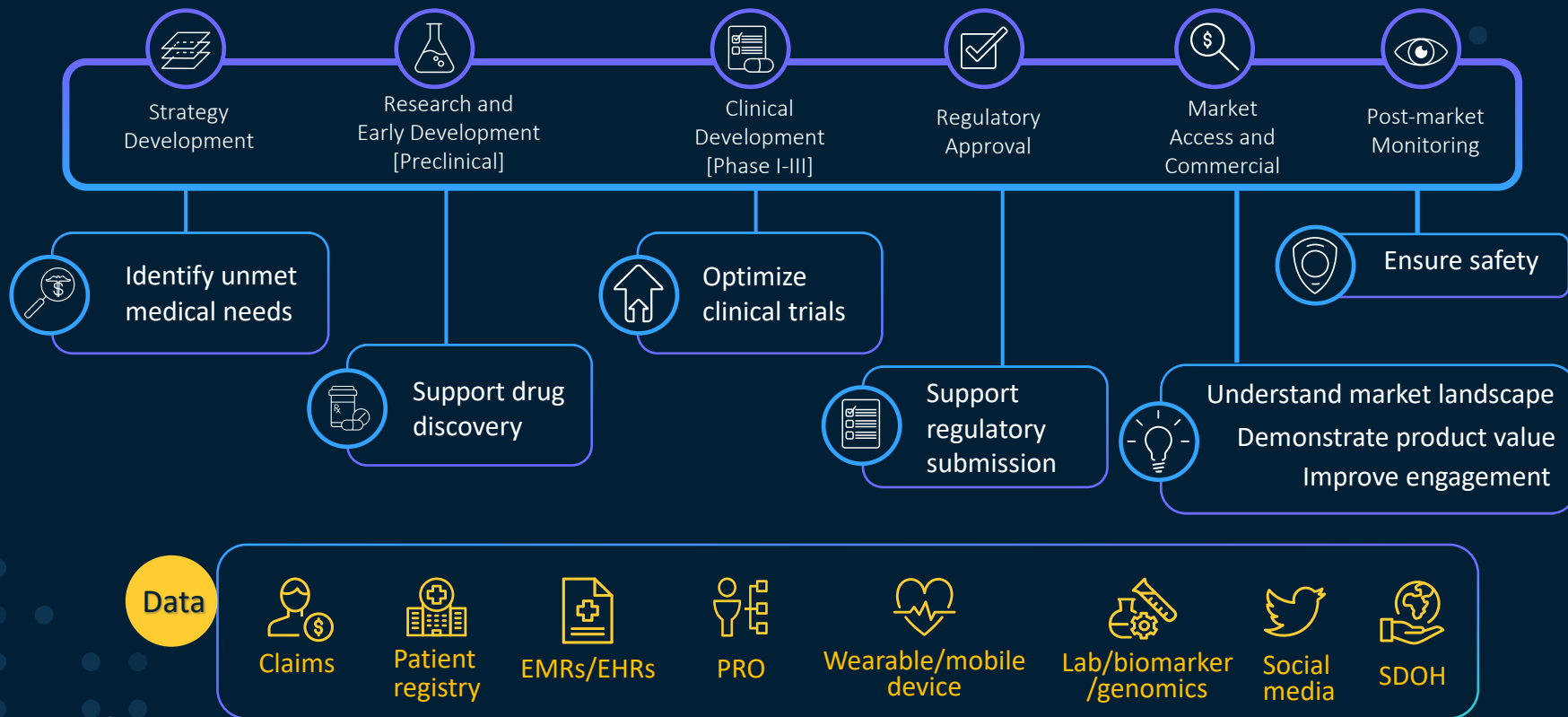
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

HMA/EMA Big Data Task Force



Japan Pharmaceuticals and Medical
Devices Agency - RWD WG

Application of RWE Across Pharmaceutical Product Life Cycle



PRO: Patient-reported outcome

SDOH: Social determinants of health

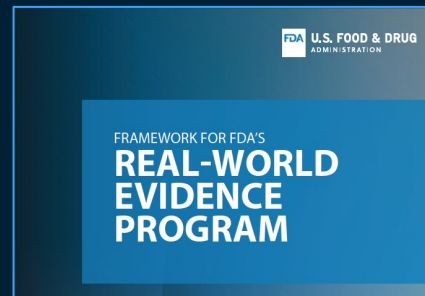
EMRs/EHRs: Electronic medical/health records

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US FDA Regulation and Guidance on RWE

Date Published	Title
August 2017	<u>Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices</u>
July 2018	<u>Use of Electronic Health Records in Clinical Investigations</u>
December 2018	<u>Framework for FDA's Real-World Evidence Program</u>
September 2021	<u>(DRAFT) Assessing Electronic Health Records and Medical Claims Data To Support Regulatory Decision-Making for Drug and Biological Products</u>
October 2021	<u>(DRAFT) Data Standards for Drug and Biological Product Submissions Containing Real-World Data</u>
November 2021	<u>(DRAFT) Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products</u>
December 2021	<u>(DRAFT) Considerations for the Use of Real-World Data and Real-World Evidence To Support Regulatory Decision-Making for Drug and Biological Products</u>
September 2022	<u>Submitting Documents Utilizing Real-World Data and Real-World Evidence to FDA for Drugs and Biologics</u>

<https://www.fda.gov/science-research/science-and-research-special-topics/real-world-evidence>



Evaluate the potential use of RWE to support:

- adding or modifying an indication (e.g. a change in dose, dose regimen, or route of administration)
- adding a new population;
- adding comparative effectiveness or safety information

Europe EMA Strategy and Guidance on RWE

A vision for use of real-world evidence in EU medicines regulation [← Share](#)

2021/11/24

Enabling the use of real-world evidence (RWE) and establishing its value for regulatory decision-making on the development, authorisation and supervision of medicines in Europe **by 2025...**



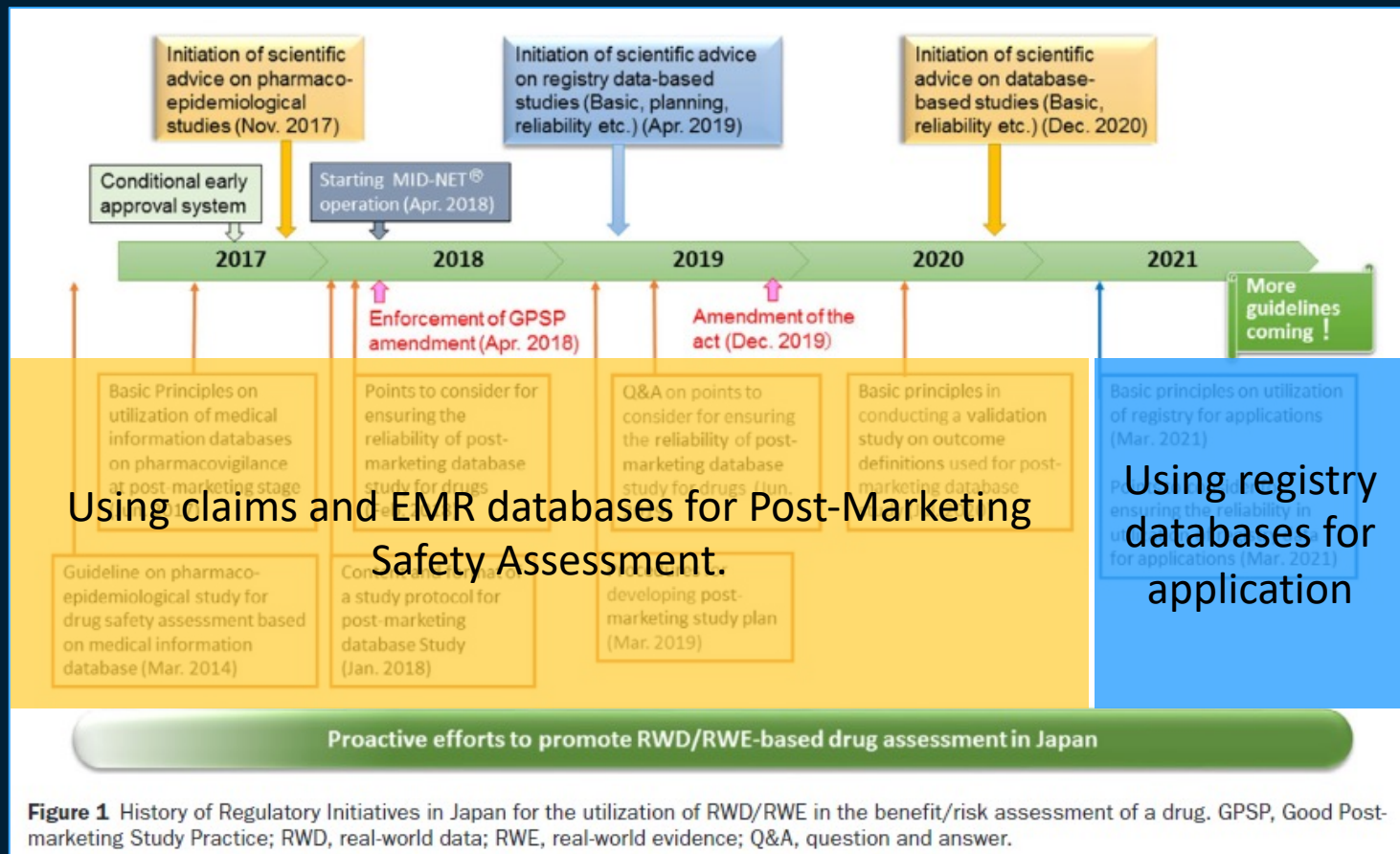
Data Analysis and Real World Interrogation Network (DARWIN EU)

- A network of data, expertise and services
- To provide timely and reliable evidence on the use, safety and effectiveness of medicines for human use, including vaccines, from real world healthcare databases across the EU

Guideline on registry-based studies

First published: 26/10/2021

Japan PMDA Regulation and Guidance on RWE



Submission including RWE

Drug	FDA approval date	Type of RWE	Regulatory action supported	Limitations of RWE identified by FDA reviewers	FDA decision
Avelumab	March 23, 2017	EHR data as historical control for efficacy	Original marketing application approval for MCC	Exploratory nature of analyses Small sample size Selection bias	Accepted
Pembrolizumab	May 23, 2017	Expanded access study data (submitted as part of a major amendment to the sBLA) to support clinical efficacy	Supplementary indication approval for microsatellite instability-high or mismatch repair deficient cancers (Original marketing application approval was for unresectable or metastatic melanoma)	No specific comments on RWE	Accepted
Lutetium Lu 177 dotatate	January 26, 2018	Expanded access study data (events captured through retrospective medical record review) to support clinical efficacy and safety	Original marketing application approval for SSTR-positive GEP-NETS	Differences in patient populations Differences in drug dose Differences in timing and criteria used for efficacy and safety assessments Exploratory nature of analyses	Accepted
Blinatumomab	March 29, 2018	Retrospective data from clinical sites as historical control for efficacy	Supplementary indication approval for MRD-positive ALL (Original marketing application approval was for Philadelphia chromosome-negative relapsed or refractory B-cell precursor ALL)	Small sample size Differences in lengths of follow-up Confounding	Accepted
Palbociclib	April 4, 2019	EHR data, claims data, and post-marketing safety reports to support clinical efficacy and safety in new patient population	Supplemental indication approval for male breast cancer (Original marketing application approval was for post-menopausal women with hormone receptor-positive, human epidermal growth factor receptor 2-negative advanced or metastatic breast cancer)	Small sample size Differences in patient populations	Accepted

Therapy (year of approval)	FDA-recommended indication	FDA designations	RWE source	RWE purpose	Study population matched to trial	Primary endpoint	RWE used in decision	FDA comment
Capmatinib (2020)	Treatment of adult patients with metastatic NSCLC whose tumors have a <i>metastatic NSCLC</i>	Orphan Drug Breakthrough Therapy Priority Review Accelerated Approval	Chart review	Contextualization	No	ORR	Yes	The FDA cannot independently verify results based on the incomplete data submitted. FDA agreed that the RWE study provided an estimate of disease natural history. RWE findings are clinically significant and fill an unmet medical need in the context of the limited treatment options available for this difficult-to-treat population.
Tafasitamab (2020)			Chart review	Contextualization		ORR, CR	Yes	The FDA "generally agrees" with the real-world study design but notes that choice of covariates to include in the matching may not be fully sufficient and covariates in the matched cohorts are not well-balanced. The FDA did not consider endpoints that were different between the clinical trial setting and clinical practice on they were measured. The FDA also claims that the potential for outcome misclassification exists due to lack of IRC-assessed response

Extract

U):27-35.

Extracted from [Feinberg et al. Value Health. 2020 Oct;23\(10\):1358-1365.](#)

FDA approves new use of transplant drug based on real-world evidence

Liver, kidney, heart transplants → + Lung transplants

*FDA approved a new use for Prograf (tacrolimus) **based on a non-interventional (observational) study providing real-world evidence (RWE) of effectiveness.** FDA approved Prograf for use in combination with other immunosuppressant drugs to prevent organ rejection in adult and pediatric patients receiving lung transplantation*

<https://www.fda.gov/drugs/news-events-human-drugs/fda-approves-new-use-transplant-drug-based-real-world-evidence>



Pfizer Uses EHR Data to Support Expanded Indication for Male Breast Cancer

Female breast cancer → + Male breast cancer

*“**The approval is based on RWD** from electronic health records and post-marketing reports of Ibrance™ (Palbociclib) in male patients sourced from three databases: IQVIA Insurance database, Flatiron Health Breast Cancer database and the Pfizer global safety database”*

<https://www.raps.org/news-and-articles/news-articles/2019/4/pfizer-uses-ehr-data-to-support-expanded-indication>



Key Considerations for the Use of RWE in Submission

Data

Whether the RWD are
fit for use

Framework for FDA's RWE Program

Methods

Whether the trial or study
design used to generate
RWE can provide adequate
scientific evidence to answer
or help answer the
regulatory question

Process

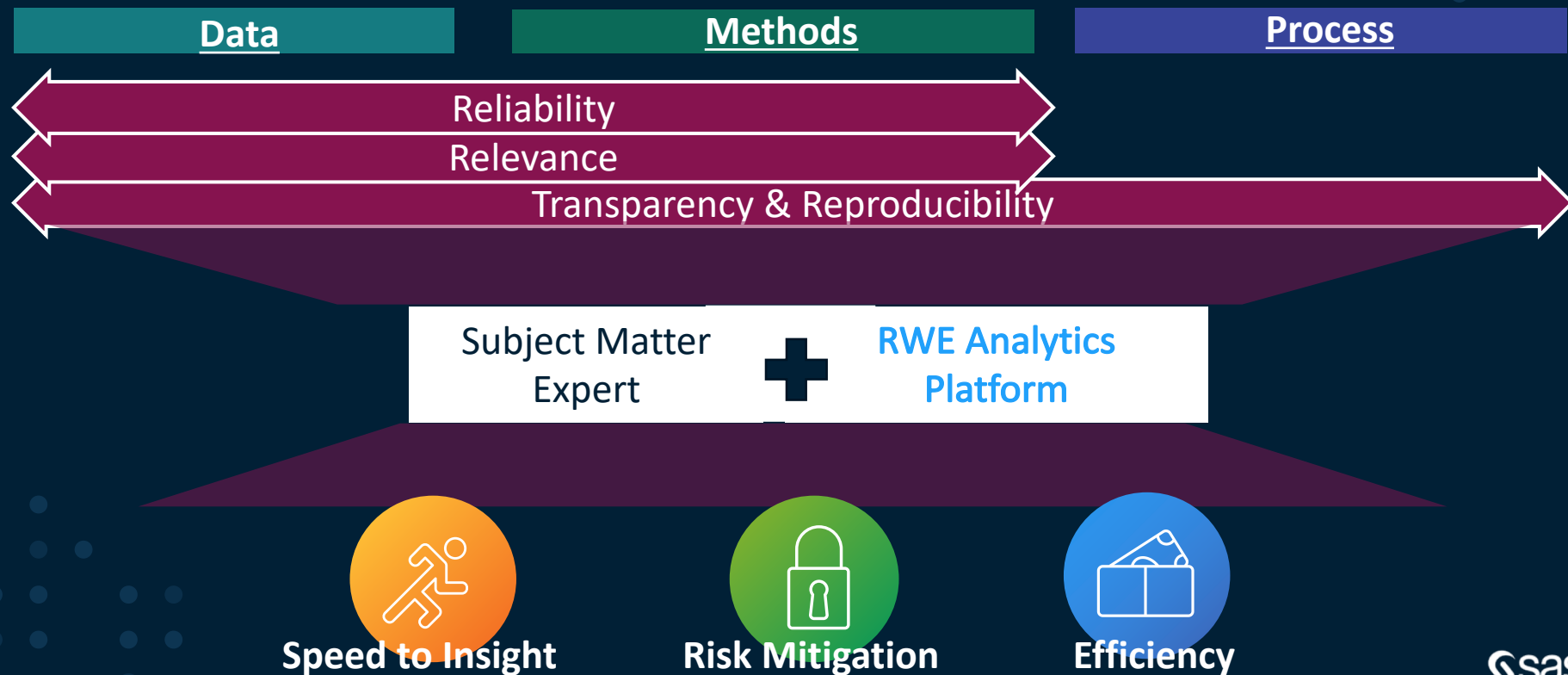
Whether the study
conduct meets FDA
regulatory requirements

Reliability

Relevance

Transparency & Reproducibility

A Modern RWE Analytics Platform can help...



Features of A Modern RWE Analytics Platform

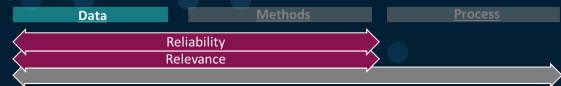
Data – Reliability & Relevance

Quickly profile large volumes of data via data visualization and automated profiling

Systematic approach to control data quality, secure data provenance and automate repetitive tasks for data preparation

Common data model and common representation (terminologies, vocabularies, coding)

Consume multiple types of data from a wide variety of environments



Features of A Modern RWE Analytics Platform

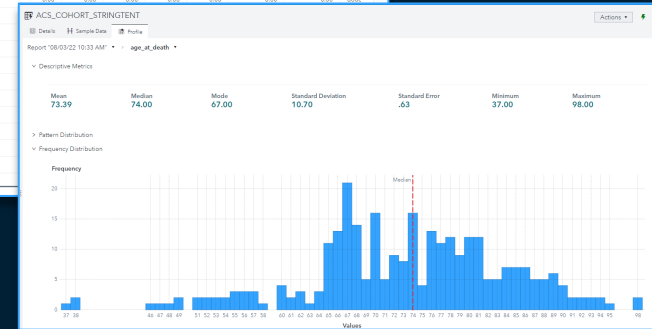
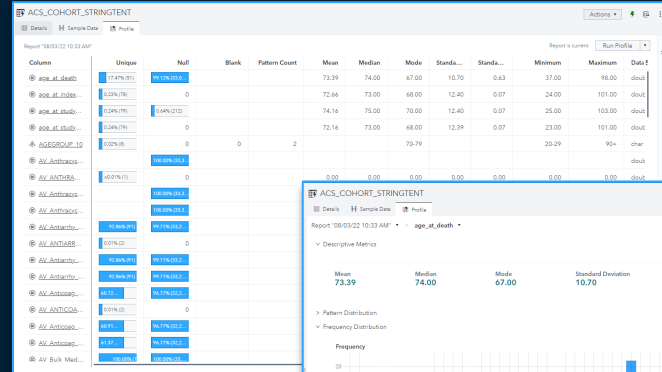
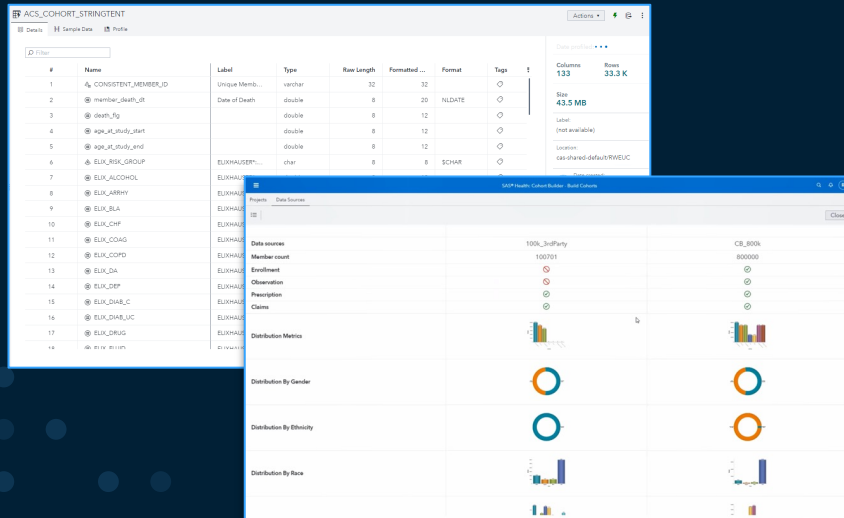
Data – Reliability & Relevance

WHAT?

Quickly profile large volumes of data via data visualization and automated profiling

WHY?

Understand key data elements, size of population and data issues



Data Methods Process

Reliability
Relevance

Features of A Modern RWE Analytics Platform

Data – Reliability & Relevance

WHAT?

Systematic approach to control data quality, secure data provenance and automate repetitive tasks for data preparation

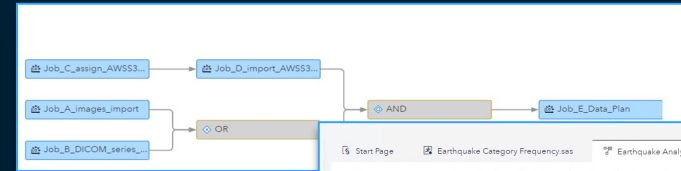
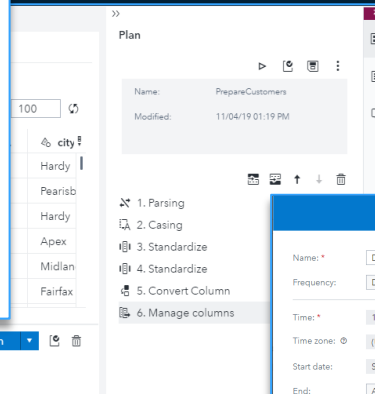
WHY?

Increase confidence in the resultant data during data curation and data transformation

Data Source: 800K_CLINICAL Tuesday, March 8, 2022 12:51:03 PM

Overall Data Quality for the CASLIB 800K_CLINICAL: **PASSED**

Table	Records	Status
RWE_ENROLL	1378340	PASSED
RWE_MEMBER	711479	PASSED
RWE_OBSN	4092534	PASSED
RWE_PROVIDER	1141691	PASSED
RWE_RX	34265671	PASSED
RWE_SERVICES	34502214	PASSED
RWE_SERVICE_CODES	186338479	PASSED



New Trigger

Name: Daily trigger

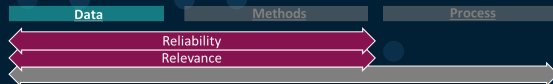
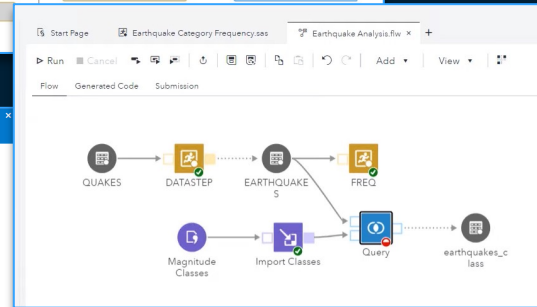
Frequency: Daily Interval: 1 days

Time: 12:01

Time zone: (UTC-05:00) New York

Start date: Sep 23, 2020

End: After number of times 1 times



Features of A Modern RWE Analytics Platform

Data – Reliability & Relevance

WHAT?

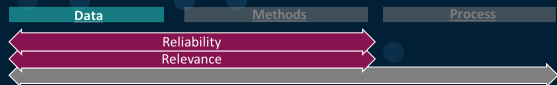
WHY?

Common data model and common representation (terminologies, vocabularies)

Gain insights from various RWD assets efficiently and ensure data quality

The collage displays several key features of the SAS Viya RWE Analytics Platform:

- Data Sources:** Two bar charts showing data distribution for '100K_3rdParty' (Date modified: Jan 29, 2021) and '800K_ICD10' (Date modified: Dec 18, 2020). Both are marked as 'Registered'.
- Expressions:** A panel for defining data queries using variables and filters.
- Code Search:** A search interface for finding specific codes, showing results for 'Diabetes mellitus' and related conditions.
- View Menu:** A dropdown menu showing various data categories: Demographics, Diagnoses (CCS, ICD-10CM, ICD-9CM, MEDDRA), Diagnosis Related Groups, EPIC, Prescriptions (CVX, FDB, MULTUM, NDC, NDDF, RXNORM, UNII), Procedures (CDT, CPT, HCPCS, ICD-10PCS, ICD-9PCS, PENFS), Revenue Codes, and Snomed (SNOMED CT).



Features of A Modern RWE Analytics Platform

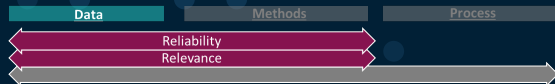
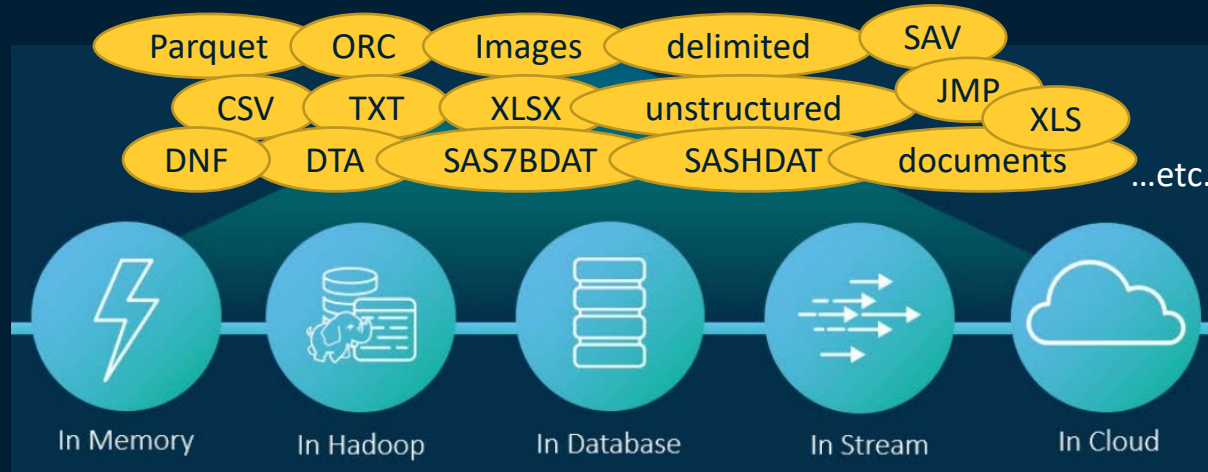
Data – Reliability & Relevance

WHAT?

Consume multiple types of data from a wide variety of environments

WHY?

Leverage more diverse RWD in large volume to gain deeper insights



Features of A Modern RWE Analytics Platform

Methods – Reliability & Relevance

Manage repetitive feasibility evaluations and quickly identify the patient cohort with customized criteria

Efficiently manage analytical assets generated from multiple projects and develop standard templates

Process – Transparency & Reproducibility

Ensure a clear governance on data and analyses on a central environment



Features of A Modern RWE Analytics Platform

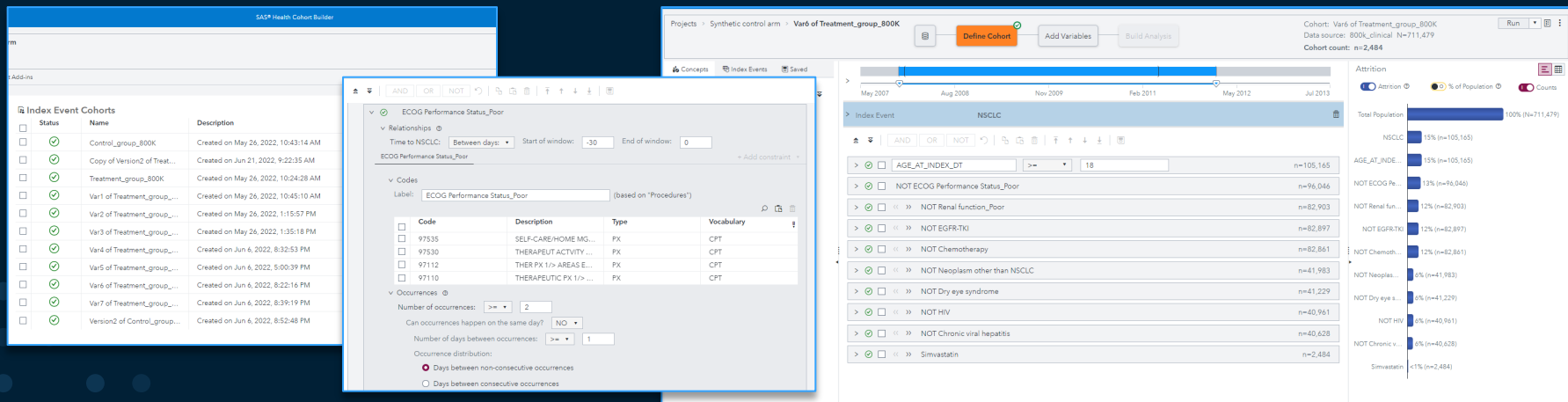
Methods – Reliability & Relevance

WHAT?

Manage repetitive feasibility evaluations and quickly identify the patient cohort with customized criteria

WHY?

Reduce turnaround time of evaluation and clearly document evaluation process to show appropriateness of the study design



Features of A Modern RWE Analytics Platform

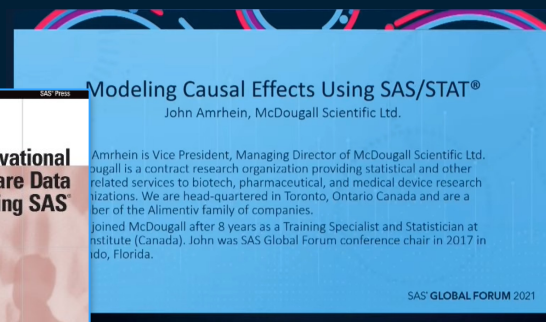
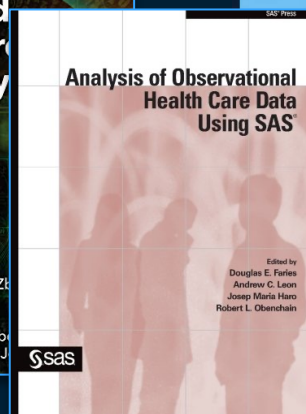
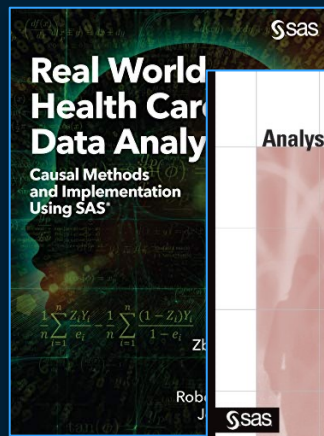
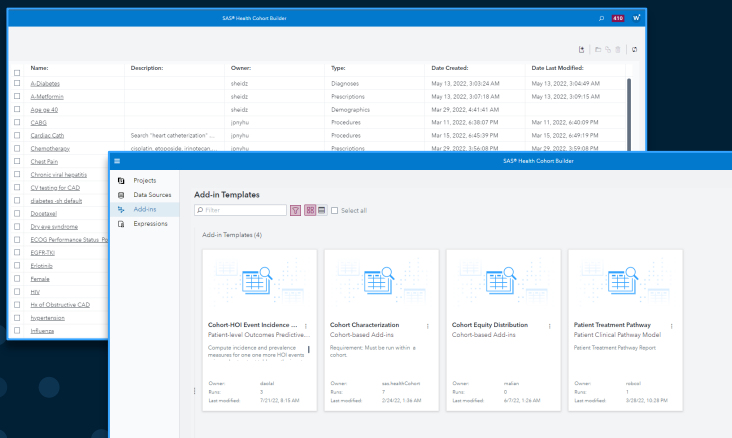
Methods – Reliability & Relevance

WHAT?

WHY?

Efficiently manage analytical assets generated from multiple projects and develop standard templates

Leverage validated analytic assets to produce reliable results and establish best practices for studies (e.g., routine, simple, complex)



Features of A Modern RWE Analytics Platform

Process – Transparency & Reproducibility

WHAT?

WHY?

Ensure a clear governance on data and analyses on a central environment

Increase transparency, reproducibility and traceability of the analyses

The image displays four overlapping screenshots of the SAS Linqage Viewer interface, illustrating different stages of job execution and data lineage exploration.

- Top Left: Job Configuration** - Shows the 'Afib Cohort Characterization' job setup. It includes a 'Name' field, a 'Description' field, and a list of users (Sherrine Eid) who have created or modified the job.
- Top Right: Job Execution** - Shows the 'Cohort Characterization' job execution page. It displays a log of messages and warnings, including a warning about the number of nodes (1999+).
- Bottom Left: Job Execution** - Shows the 'PrepareCustomers' job execution page. It displays a log of messages and warnings, including a warning about the number of nodes (1999+).
- Bottom Right: Data Lineage** - Shows the 'SAS Linqage Viewer - Explore Lineage' page. It displays a diagram of data lineage, showing the flow of data from source tables (e.g., CUSTOMERS, CUSTOMERS_NEW) through various jobs (e.g., PrepareCustomers, CUSTOMERS_NEW) to target tables (e.g., CUSTOMERS_NEW).



Features of A Modern RWE Analytics Platform

Other considerations to streamline the RWE generation process

Cloud-native

- Necessary computing power and storage
- Scalability and Flexibility
- In-database and in-memory parallel processing
- Hosting environment (GxP-qualified) to reduce the burden of IT
- Access everywhere for smooth collaboration

Collaboration

- For cross-functional and various skills
- Low-code/no-code UIs and programming interfaces
- Shared access to breakdown silos

Classical Statistics + Advanced Analytics

- AI/Machine Learning
- Computer vision
- Natural language processing
- Transparency in advanced analytics

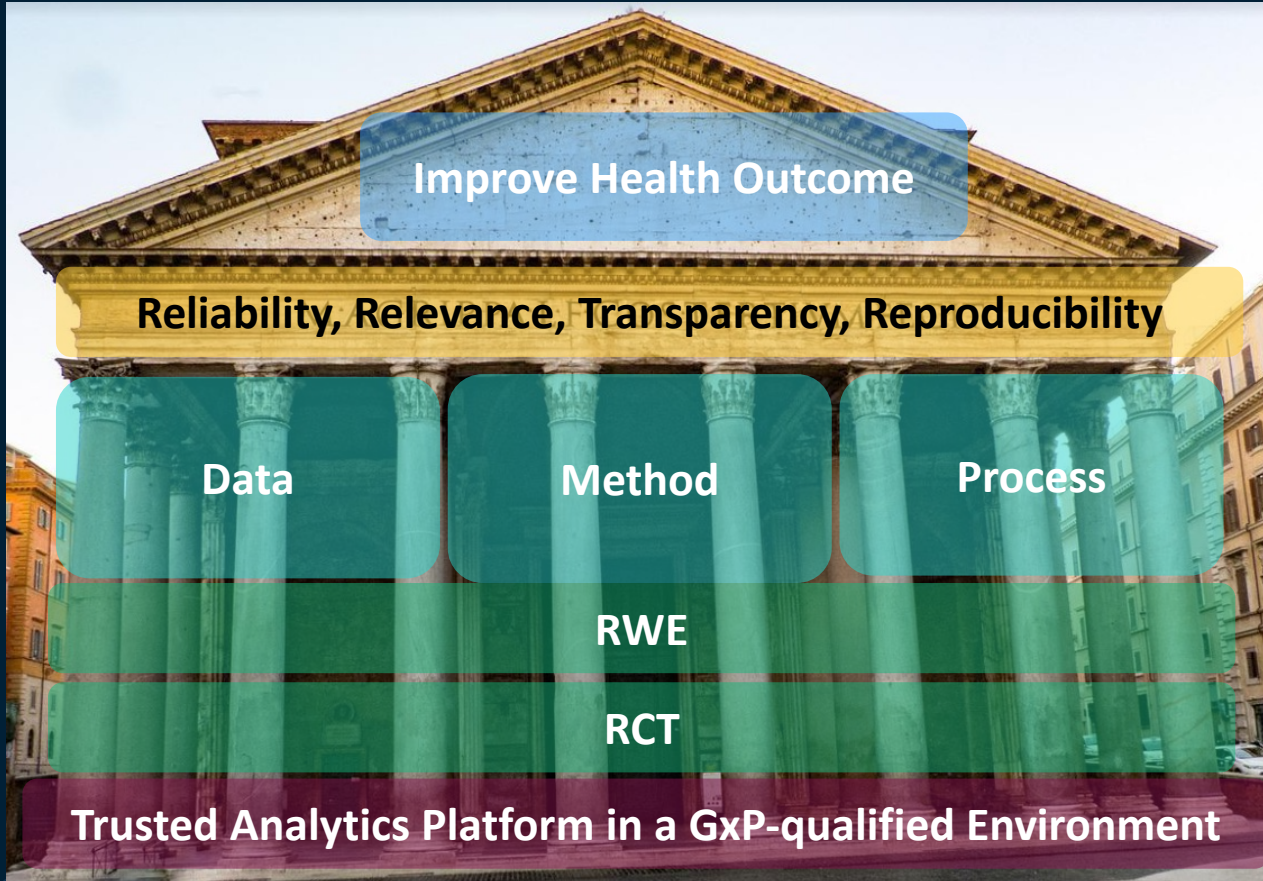
Openness

- Multiple programming languages
- 3rd party applications integration with Open APIs

Single, End-to-End

- Cover analytics lifecycle
- Improve governance and efficiency

Conclusion

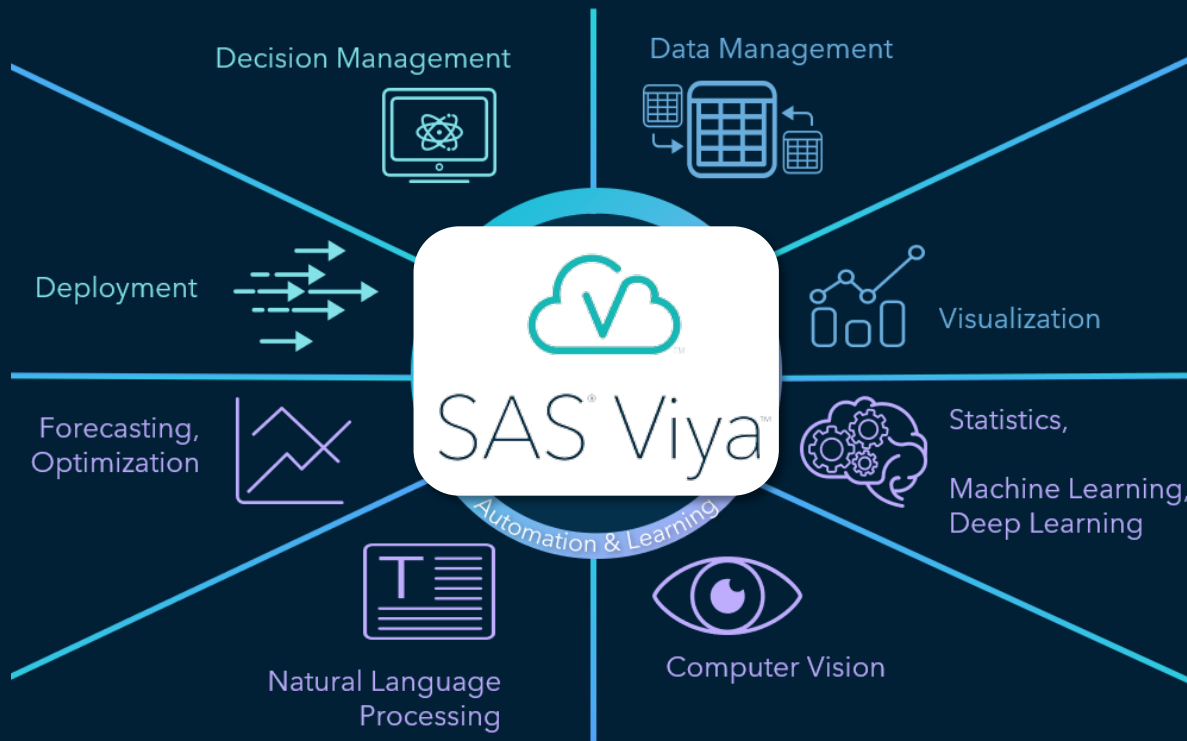


References

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Thank you!
Any Question?

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Confident decisions at every moment.

