Invited Session

Enhancing Key Endpoint Evaluation and Monitoring with AI/ML and Risk-Based Strategies

46th ANNUAL MEETING

May 18-21, 2025

VANCOUVER
CANADA

SCT
SOCIETY FOR CLINICAL TRIALS

Leveraging AI-assisted Central Statistical Monitoring to Elevate Clinical Trial Oversight and Data Quality

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SCT | 46TH ANNUAL MEETING

Disclosure

- Jiang Lu is an employee of BeOne Medicines USA, Inc. (formerly BeiGene USA, Inc.)

Outline

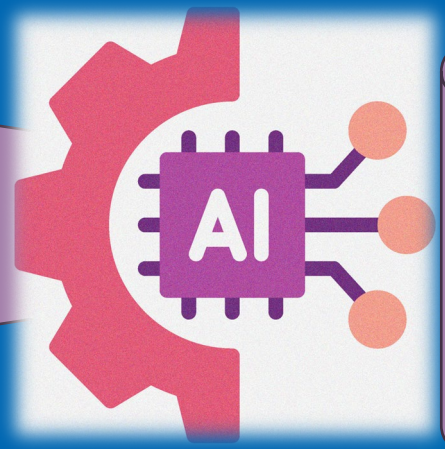
Clinical Trial Monitoring

Shift and Trend

Centralized Monitoring

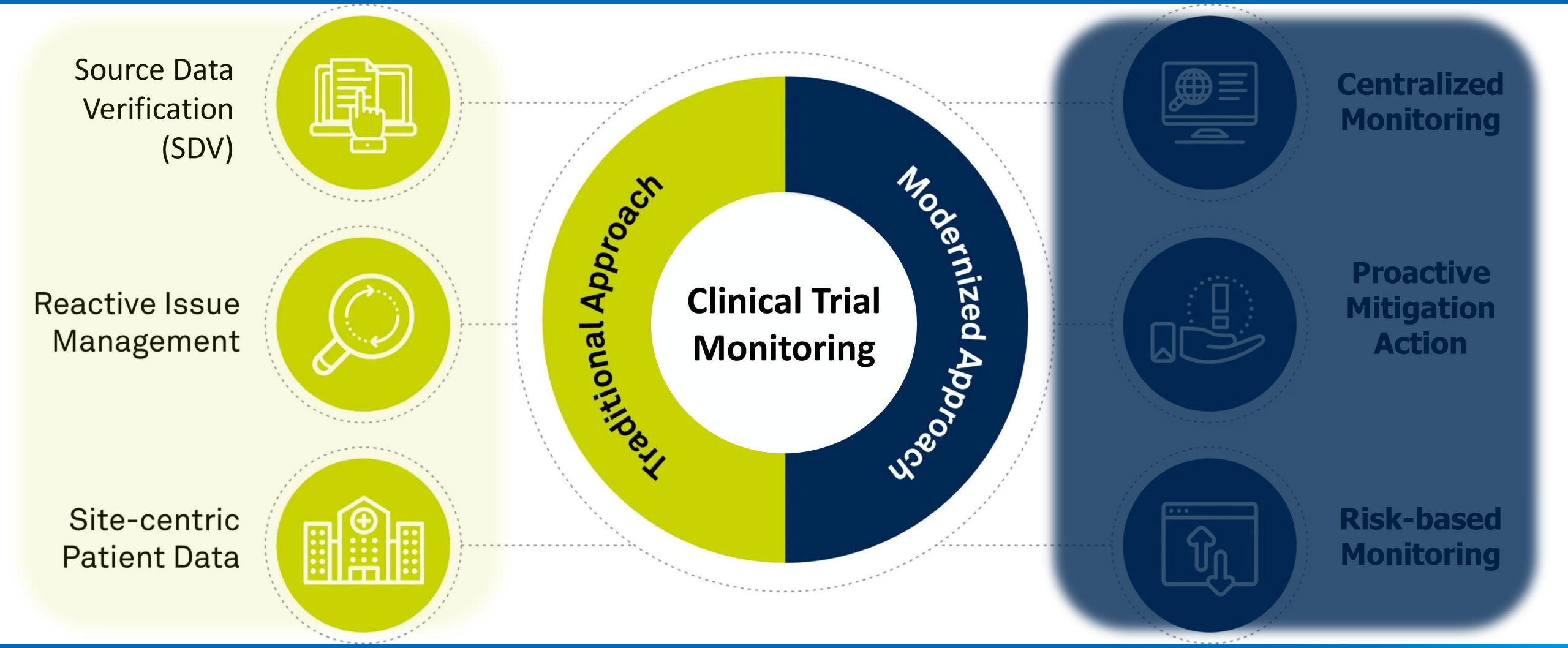
Infrastructure

Central Statistical Monitoring



AI-assisted CSM

Paradigm Shift in Clinical Trial Monitoring

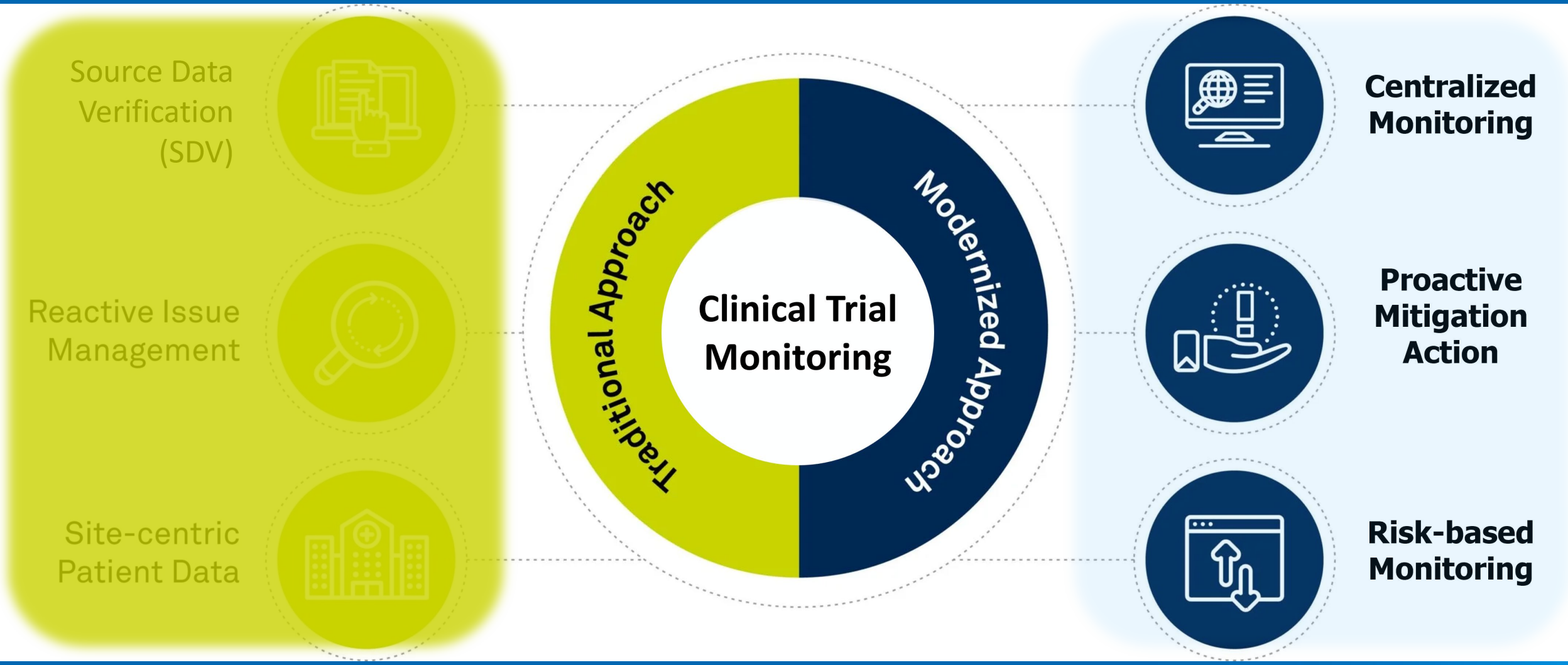


Infographic adapted from Medidata

SDV: "Spot-Difference-Visual" Game

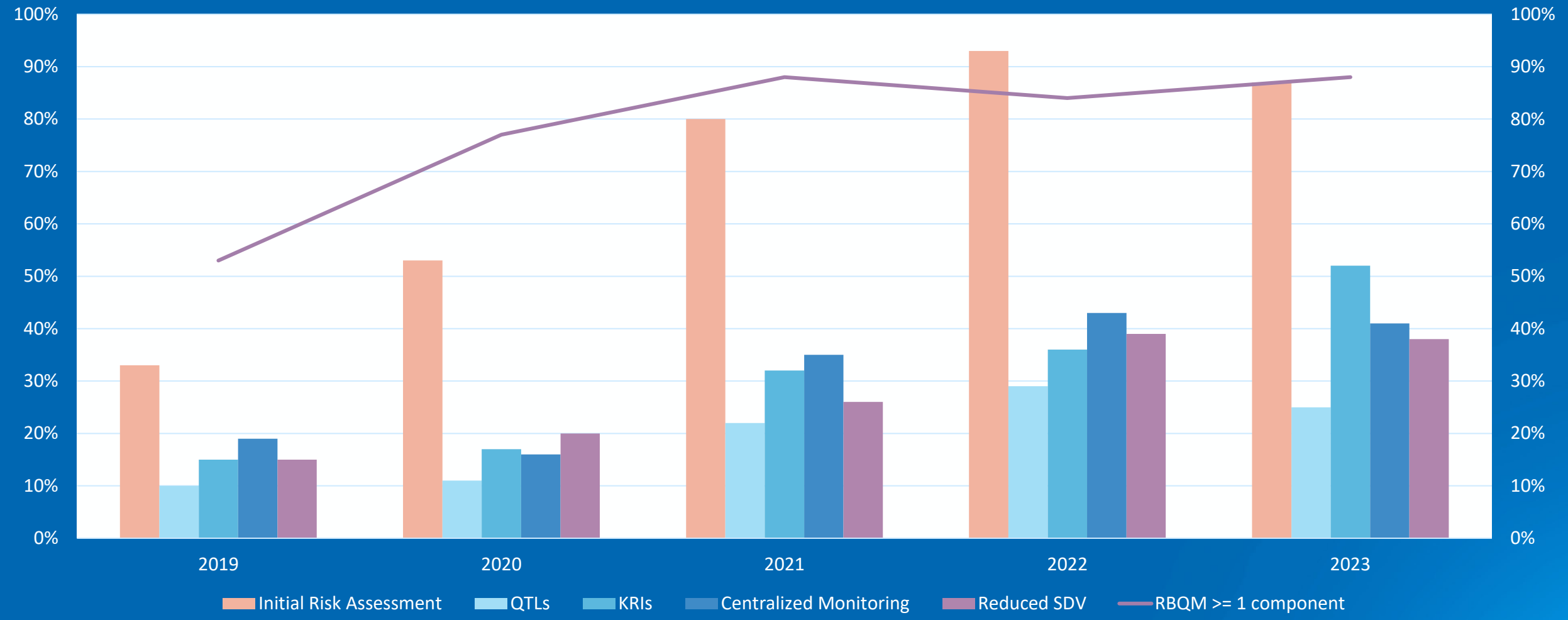
Source: Jagranjosh.com

Paradigm Shift in Clinical Trial Monitoring



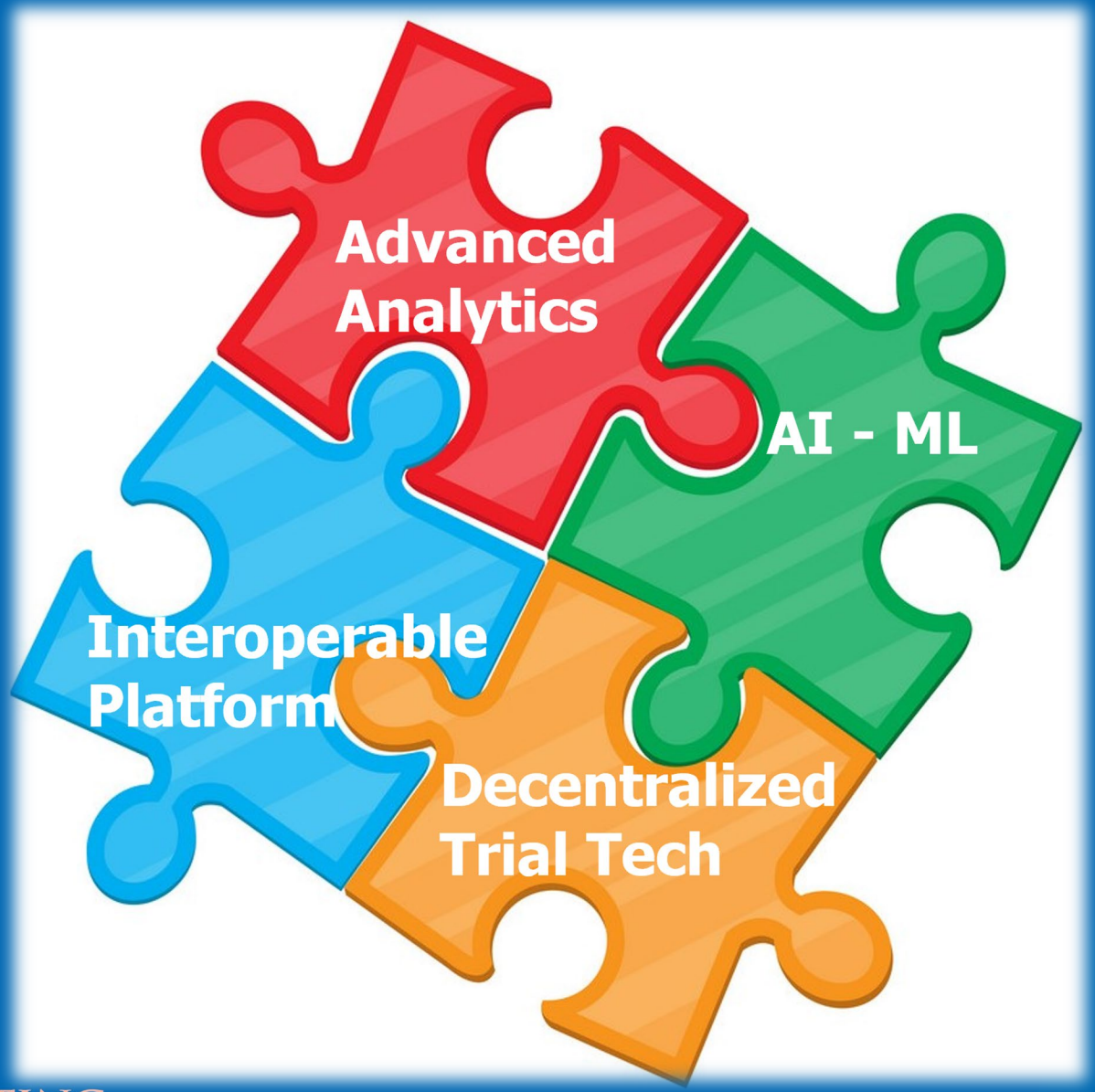
Infographic adapted from Medidata

Trend of Industry Adoption[1]



1. ACRO 2024 Survey

Cutting-edge Technology in Clinical Trials



Infrastructure for Centralized Monitoring

Source: ICH E6(R3)

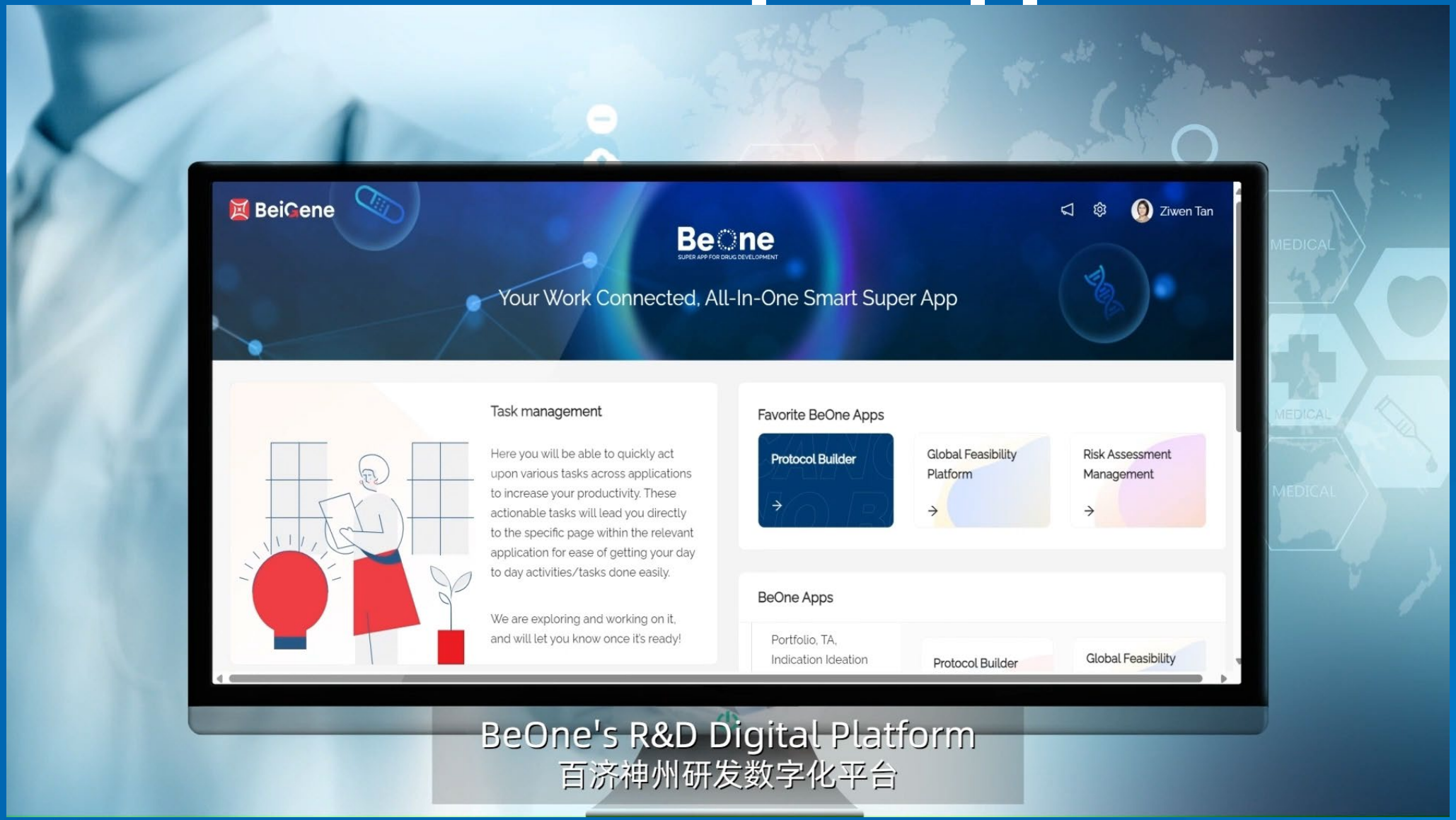
System Foundation

- Integrated **workflow**
- Interoperable **data pipeline**
- Cohesive **interface**
- Scalable **functionality**

- Novartis – **Formula One**[2]
- GSK – **Onyx**[3]
- AstraZeneca – **Evinova**[4]
- BeOne Medicines USA – **BeOne Super App - RBQMNet**
- **…**

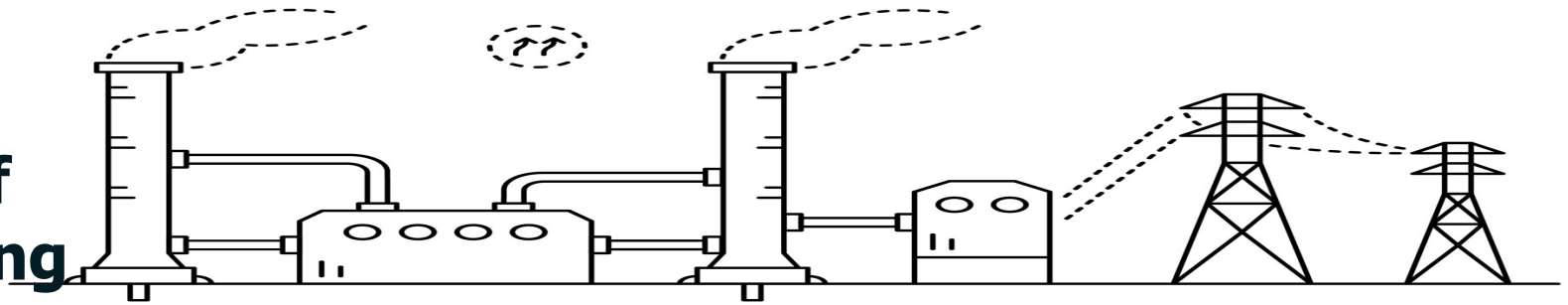
2, 3, 4. See reference slide

Showcase – BeOne Super App



RBQMNet

The Powerhouse of Centralized Monitoring



01 Risk Assessment ⟷ 02 Central Monitoring ⟷ 03 Issue Management

System Level ⟷ Study Level

- Risks across domains interact with each other:
  - process level
  - vendor level
  - program level
  - study level

Operational Level

Central Statistical Monitoring

- Define QTLs, KRIs and DQA
- Robust statistical techniques to measure QTLs, KRIs, and DQA
- Interactive visualization to show risk signals

Signal & Action Tracker

- Track signal detection
- Document investigation results
- Track mitigation actions to ensure risks are addressed before they become serious issues

Integration with Systems for review

- Support the issue management workflow and collaboration across functions
- Track issues across domains and provide data visualizations

Update risk assessment to account for new risks and mitigations

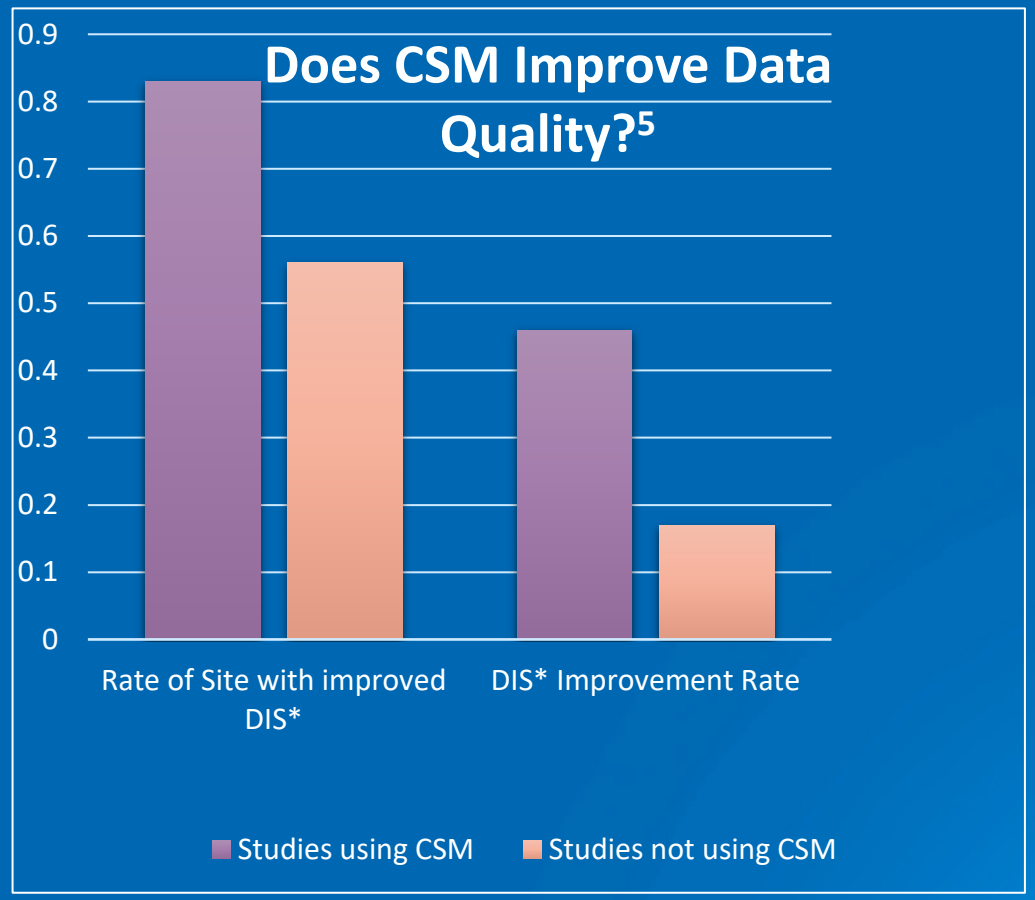
Engine 1 Risk Assessment Module

RBQMNet

Engine 2 Central Statistical Monitoring

Impact of Central Statistical Monitoring

- Enhance clinical trial oversight
  - Proactive risk management
  - Real-time monitoring
  - Regulatory compliance
- Improve data quality
  - Anomaly detection
  - CtQ-driven quality control
  - Statistics-based inference
  - Study, site, and subject hierarchic approach

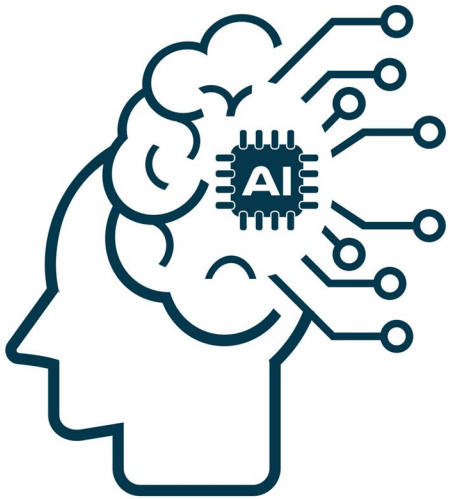


* DIS: Data Inconsistency Score

5. de Viron et al., "Does Central Statistical Monitoring Improve Data Quality?"

GenAI Reshapes Clinical Development[6]

Protocol Design



Recruitment
Retention
Dropout

Trial Feasibility

Site Selection

Central Statistical Monitoring

Data Analysis

Regulatory Submission

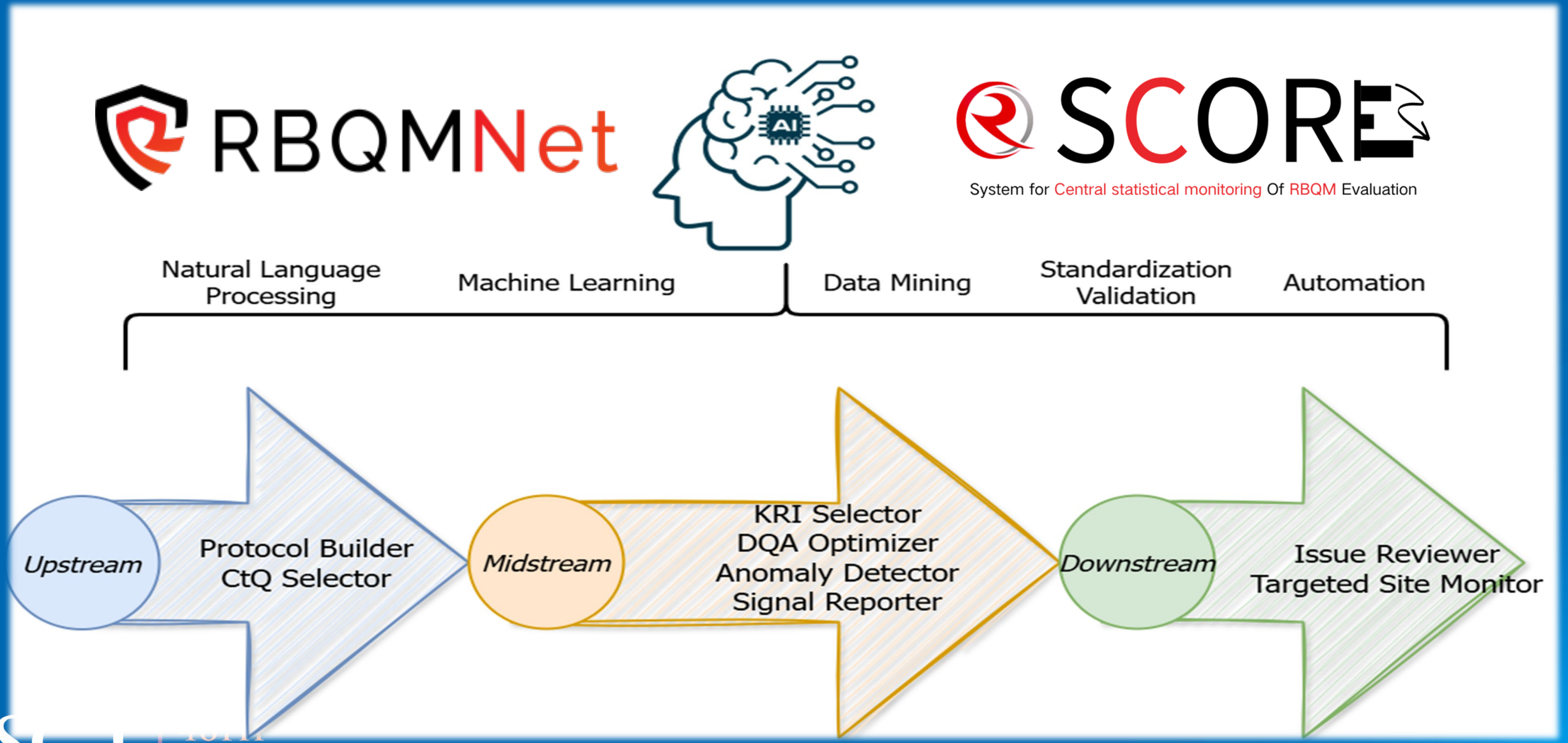
6. World Economic Forum. "Using Gen AI to Fast-Track Therapeutic Innovations."

AI Applications in RBQM System

Application	Mechanism	Impact on Quality	Example Tool
Anomaly Detection	ML algorithms detect data irregularities	Reconciliate complex data and detects anomaly	Medidata Detect (Medidata AI)[7]
Protocol Analysis	LLMs summarize protocols, identify risks	Cuts protocol amendment	AutoTrial arXiv[8]
Predictive Analytics	Forecasts risks using historical and industrial database	Predicts system risks	Cytel Solara[9]
Automated Data Review	Automates reconciliation with NLP, ML	Generates review report much faster with standardized structure	Medidata Clinical Data Studio[10]
Data Fraud Detection	GenAI detects misconduct or fraudulence	Prevents compromise of data integrity	Pfizer eDiary[11]

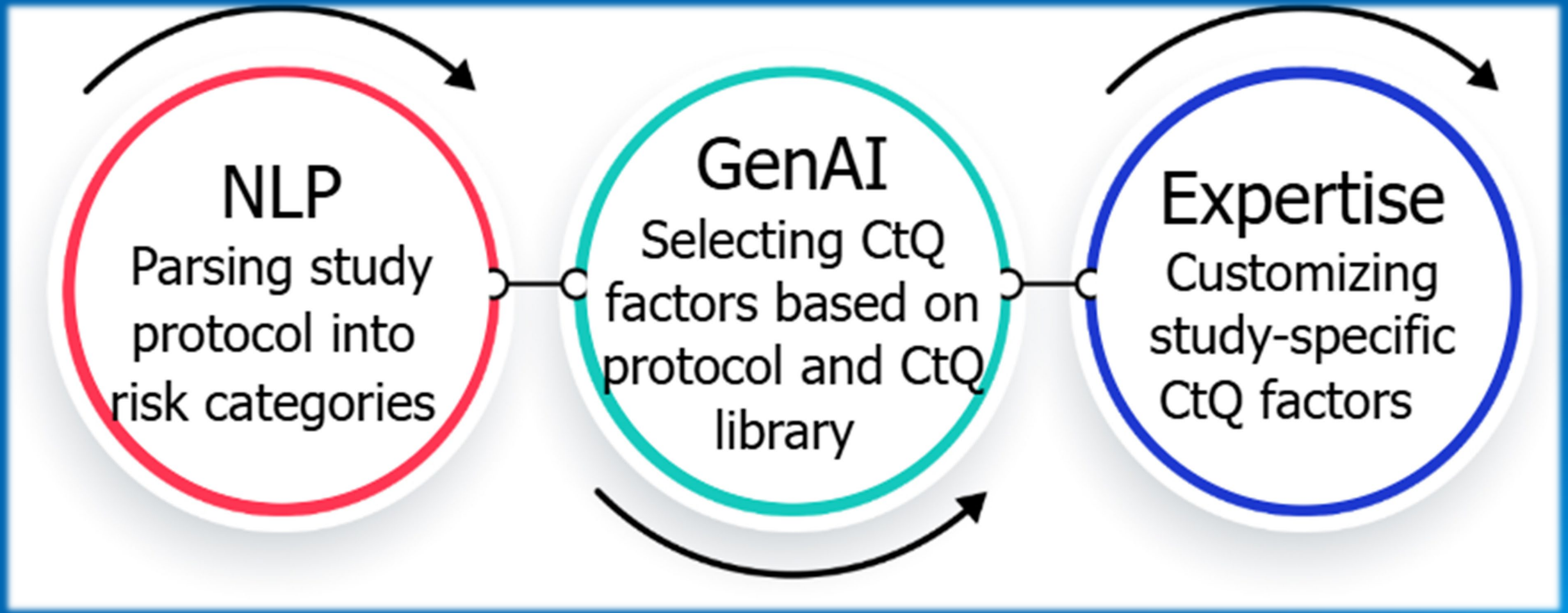
7, 8, 9, 10, 11: See reference slide

AI-assisted CSM in RBQMNet



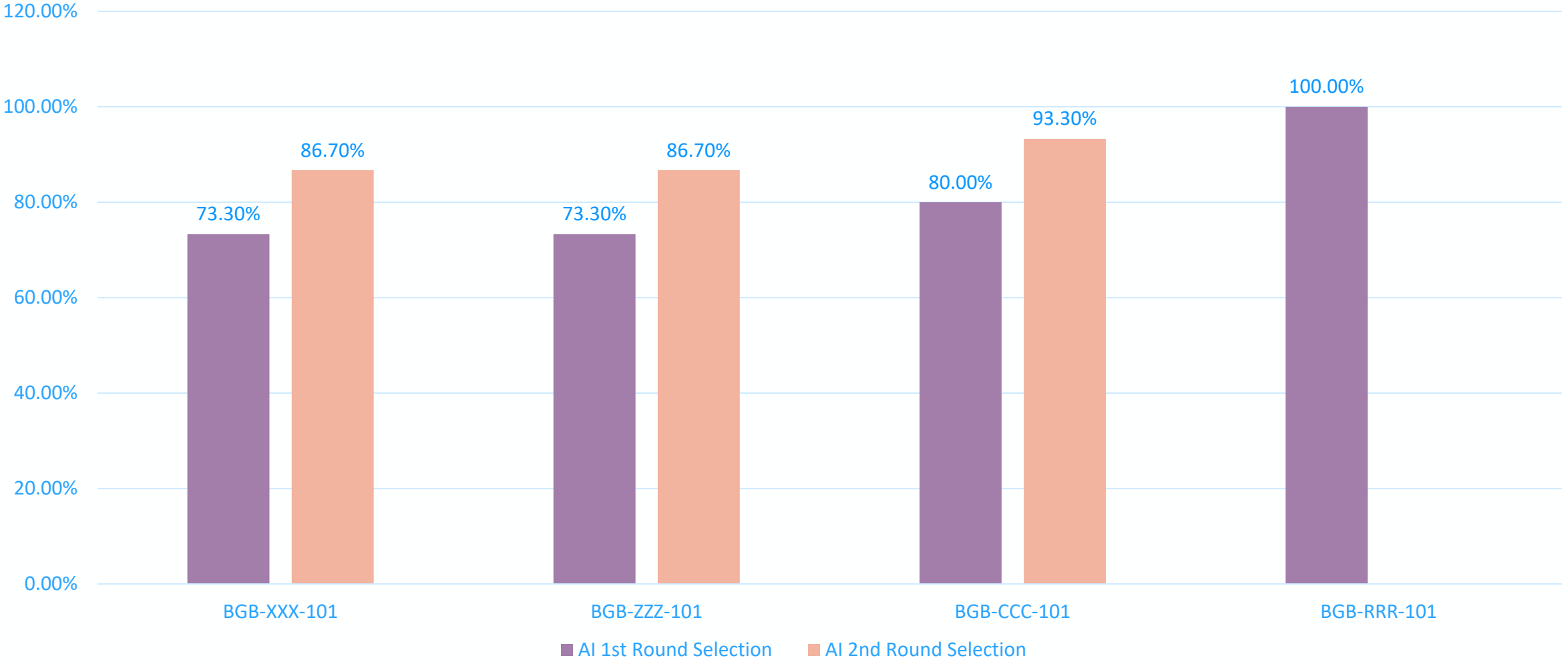
Showcase – CtQ AI Assistant

Design Elements – CtQ AI Assistant[12]



12. Talathi, Sunil "RBQMNet Critical to Quality (CtQ) Factor AI Assistant: Enhancing Risk Assessment Efficiency"

Accuracy rate by study
GenAI's first and second round of CtQ selection[12]



12. Talathi, Sunil "RBQMNet Critical to Quality (CtQ) Factor AI Assistant: Enhancing Risk Assessment Efficiency"

Expansion and Extension of AI Tools

🔍Risk Identification

AI-driven Protocol Intelligence

Key risk summary

🧠Risk Evaluation

AI-assisted Risk Evaluator

Structured and impactful risk statements of Critical to Quality (CtQ) factors

🛠️Risk Control

AI-driven recommendation Engine

Key Risk Indicators (KRIs) and Quality Tolerance Limits (QTLs)

♻️Risk Review

AI-powered Risk Library and Bot

Risk database management and potential risk signals

📈Risk Reporting

Real-time Insights and Automation

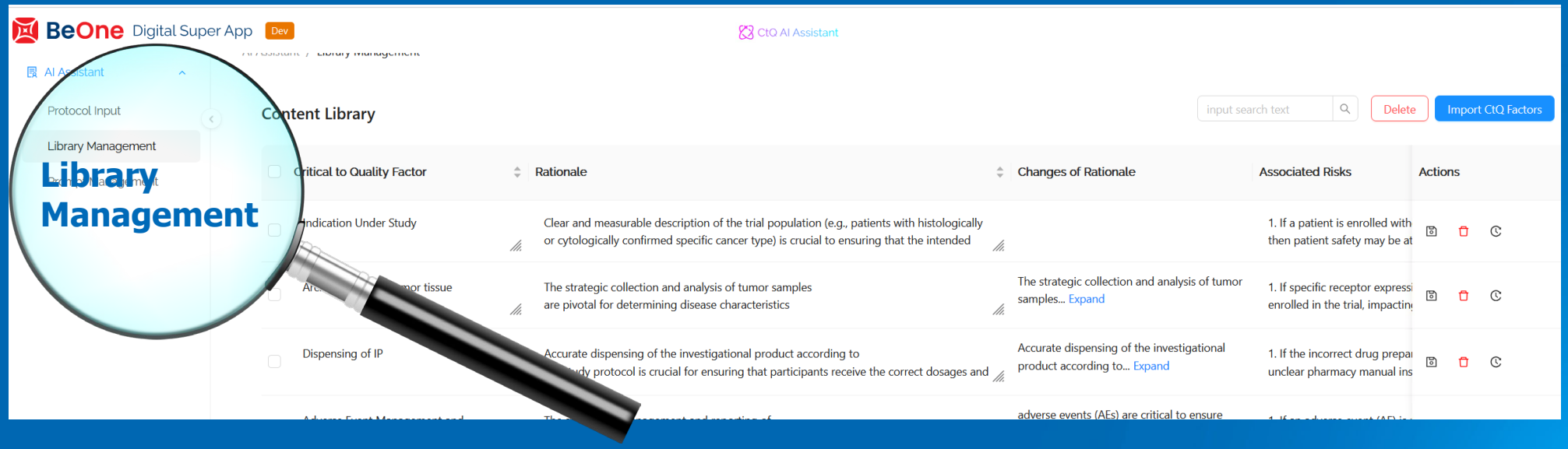
Integrated bots and automated dashboards

Lessons Learned When Working With AI …

- **Domain expertise** drives
- **Prompts** matter
- **User feedback** helps
- **Training-Validation-Testing** iterates

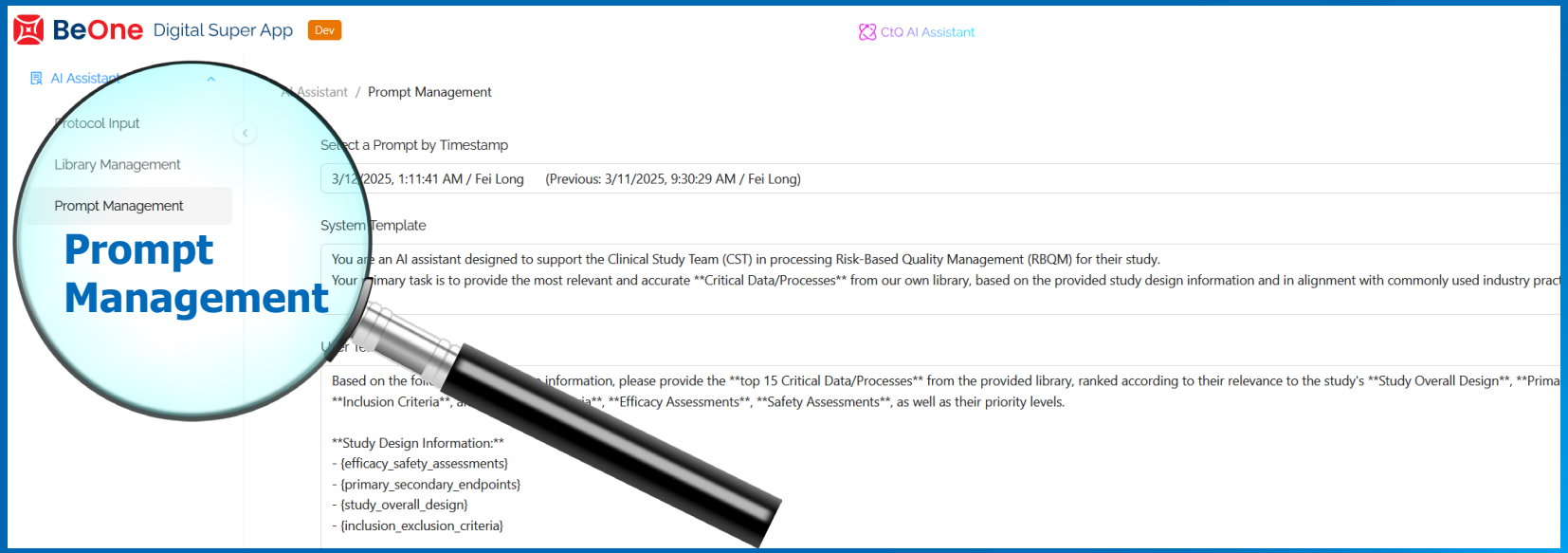
Lesson 1 - Domain Expertise

- Consult RBQM lead and experts in clinical development and operation
- Review industry practice and literature regularly
- Integrate public library with in-house library for a comprehensive collection



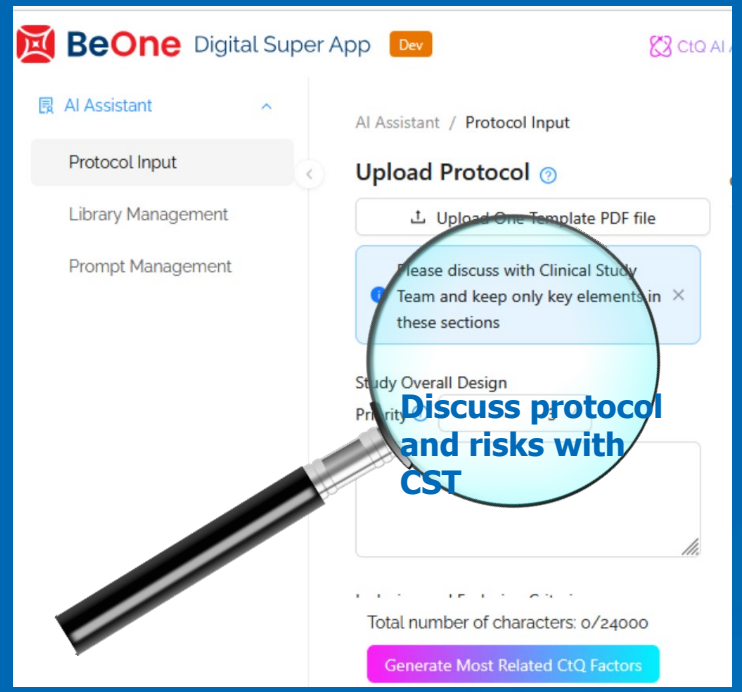
Lesson 2 - Prompt Engineering

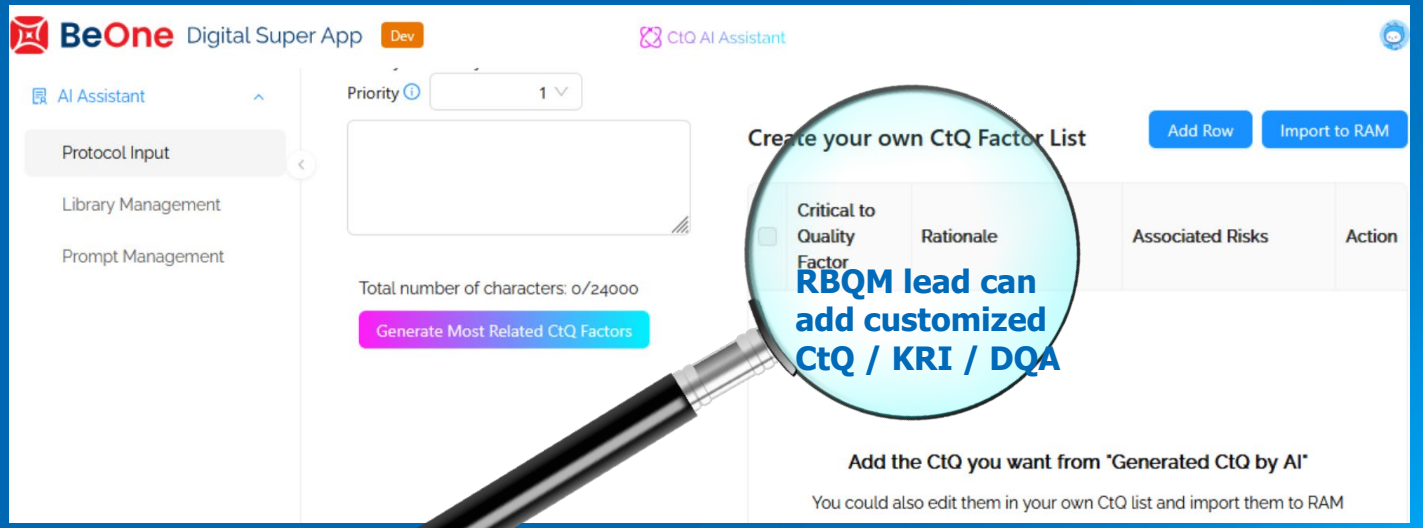
- Craft context-rich prompts
- Refine prompts incrementally
- Standardize prompt templates
- Validate outputs to ensure compliance with ICH E6 (R3)
- Automate prompt management



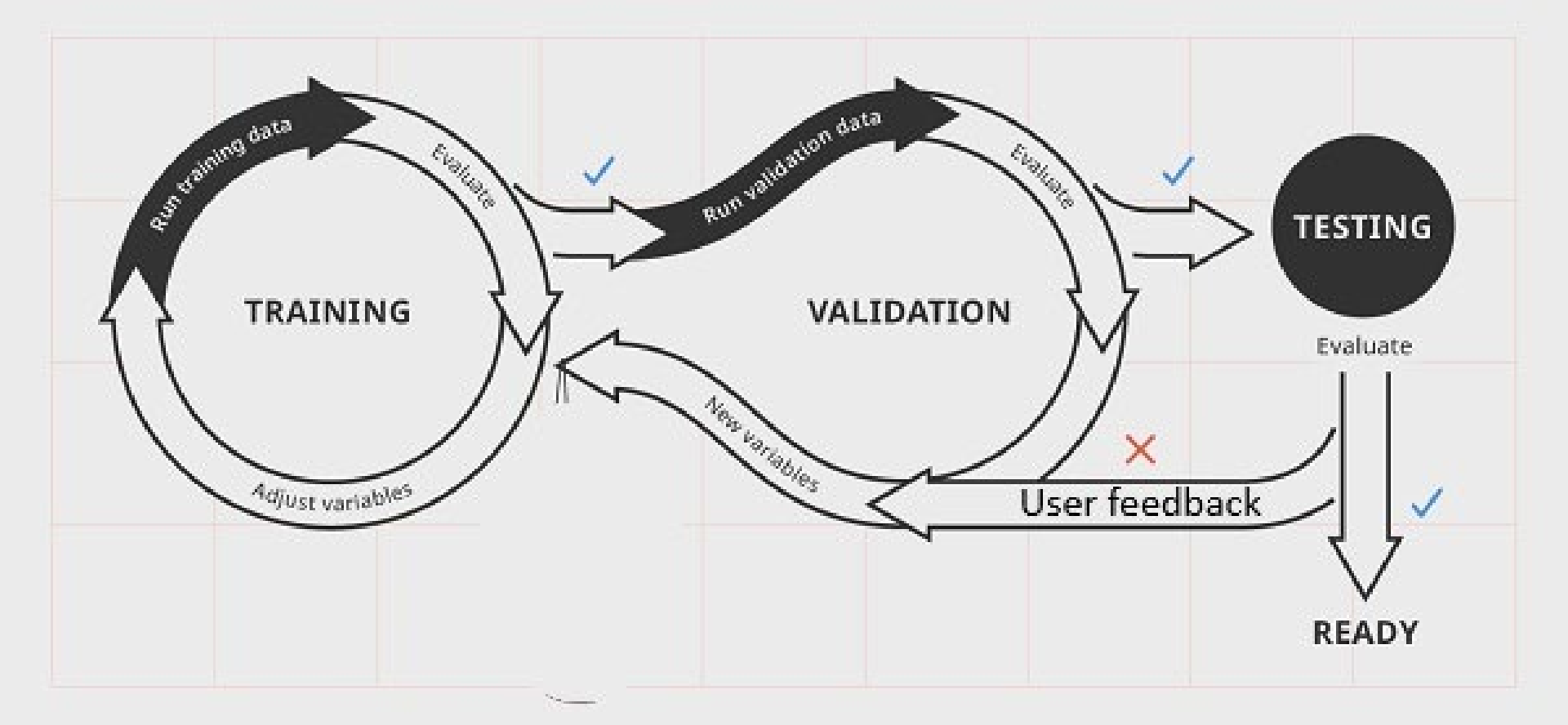
Lesson 3 - User Feedback

- Collect feedback from protocol design and amendments
- Add customized CtQs / KRIs / DQAs / QTLs
- Build structured database of user feedback
- Utilize feedback database to train and re-train AI-assistant



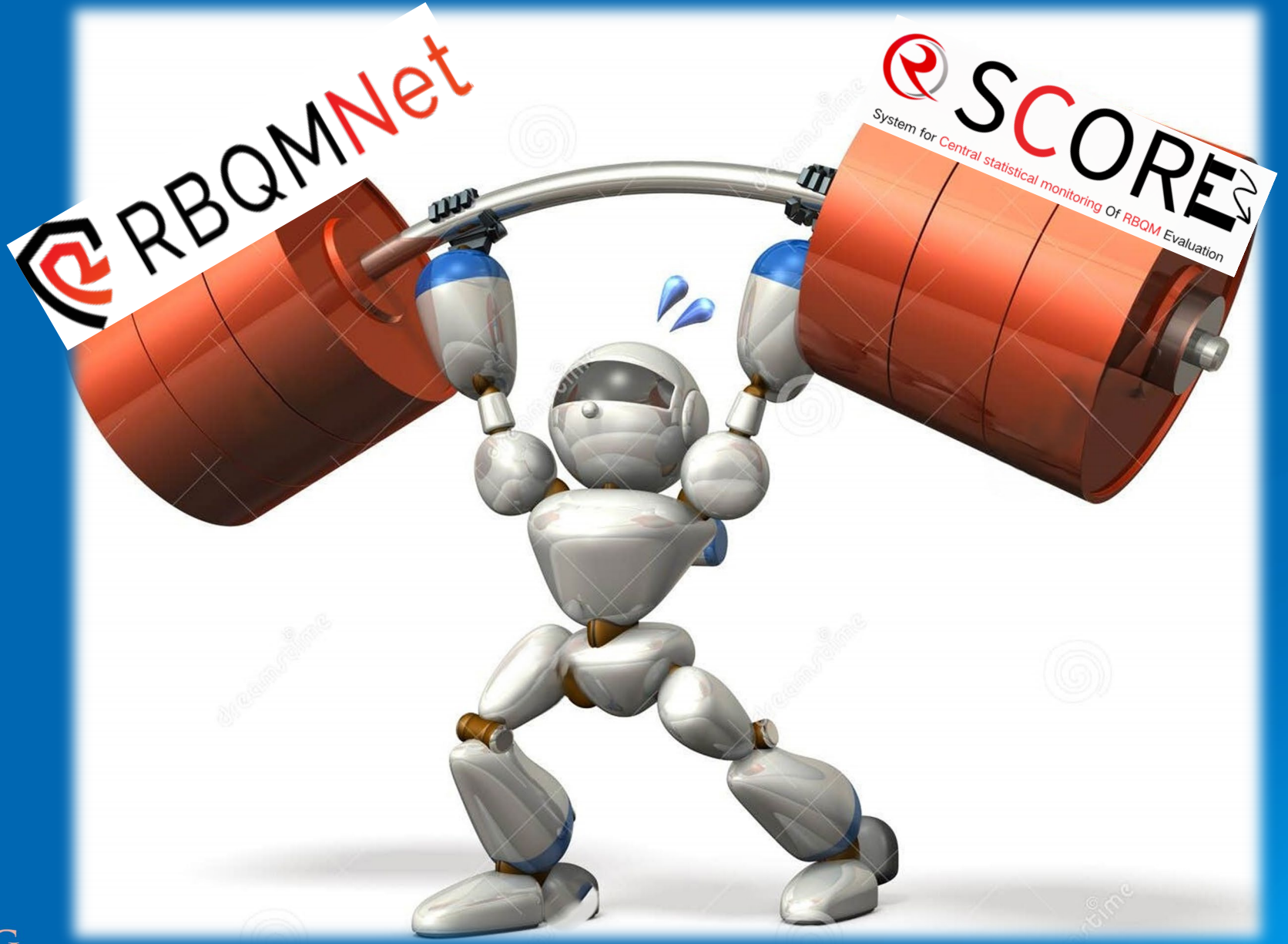


Lesson 4 - Training-Validation-Testing



Flowchart adapted from : Inside AI News Editorial Team "How Does AI Training Work?"

Conclusion


RBQMNet
SCORE
System for Central statistical monitoring Of RBQM Evaluation

Acknowledgments

Data Science and Digital Innovations

- Yasha Li
- Yilin Ye
- Yuling Zeng
- Zhijun Yao
- Fei Long
- Sunil Talathi

Global Clinical Operation

- Melissa Suprin
- Jason Salamandra
- Yiwen Sun

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11. Alsumidaie, Moe. "How Pfizer Uses AI to Transform Clinical Trial Data Oversight," March 28, 2024. https://www.clinicaltrialvanguard.com/conference-coverage/how-pfizer-uses-ai-to-transform-clinical-trial-data-oversight/
12. Talathi, Sunil "RBQMNet Critical to Quality (CtQ) Factor AI Assistant: Enhancing Risk Assessment Efficiency" Pharmaceutical Data Science Conference, April 8. 2025

Thank you!

Open-Source Risk-Based Quality Management (openRBQM) Framework for Clinical Trial Data Monitoring with AI/ML Extensions

Zhongkai (Kai) Wang, Xinlei (Ivan) Mi, George Wu, Jeremy Wildfire
Gilead Sciences Inc.

Overview

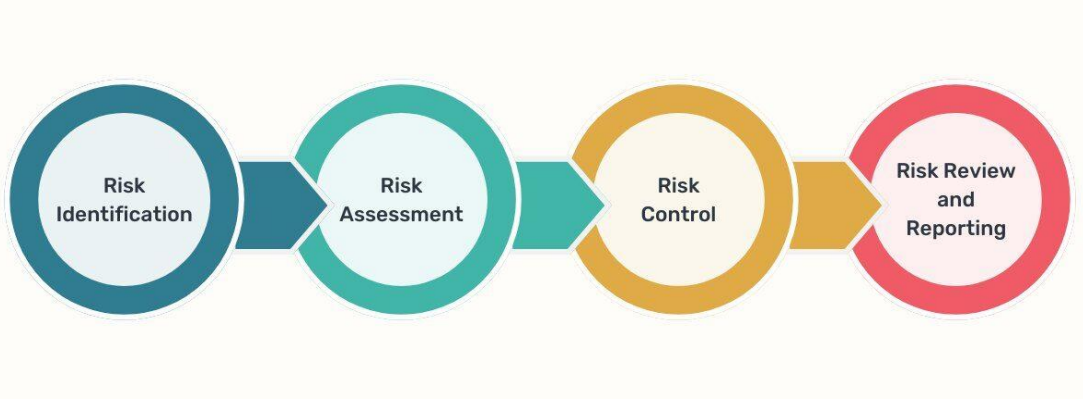
- Background
- Framework
- Extension

Centralized Monitoring (CM) and Risk-based Quality Management (RBQM)

- Centralized monitoring is a holistic view of the data to identify trends, patterns, unusual variation
- RBQM aligns with risk-based approach in ICH E6(R3), E8 (R1)
- Offers an overarching perspective that complements traditional on-site monitoring
- Helps operations teams target critical data and process risks at the study, region, country, or site level for patient safety, data integrity, and regulatory compliance

What CRAs see is extremely limited

CM/RBQM Enables a Unique, Holistic View



OpenRBQM: Pre-Competitive Collaboration on Open-Source Software for RBQM

Problem Statement

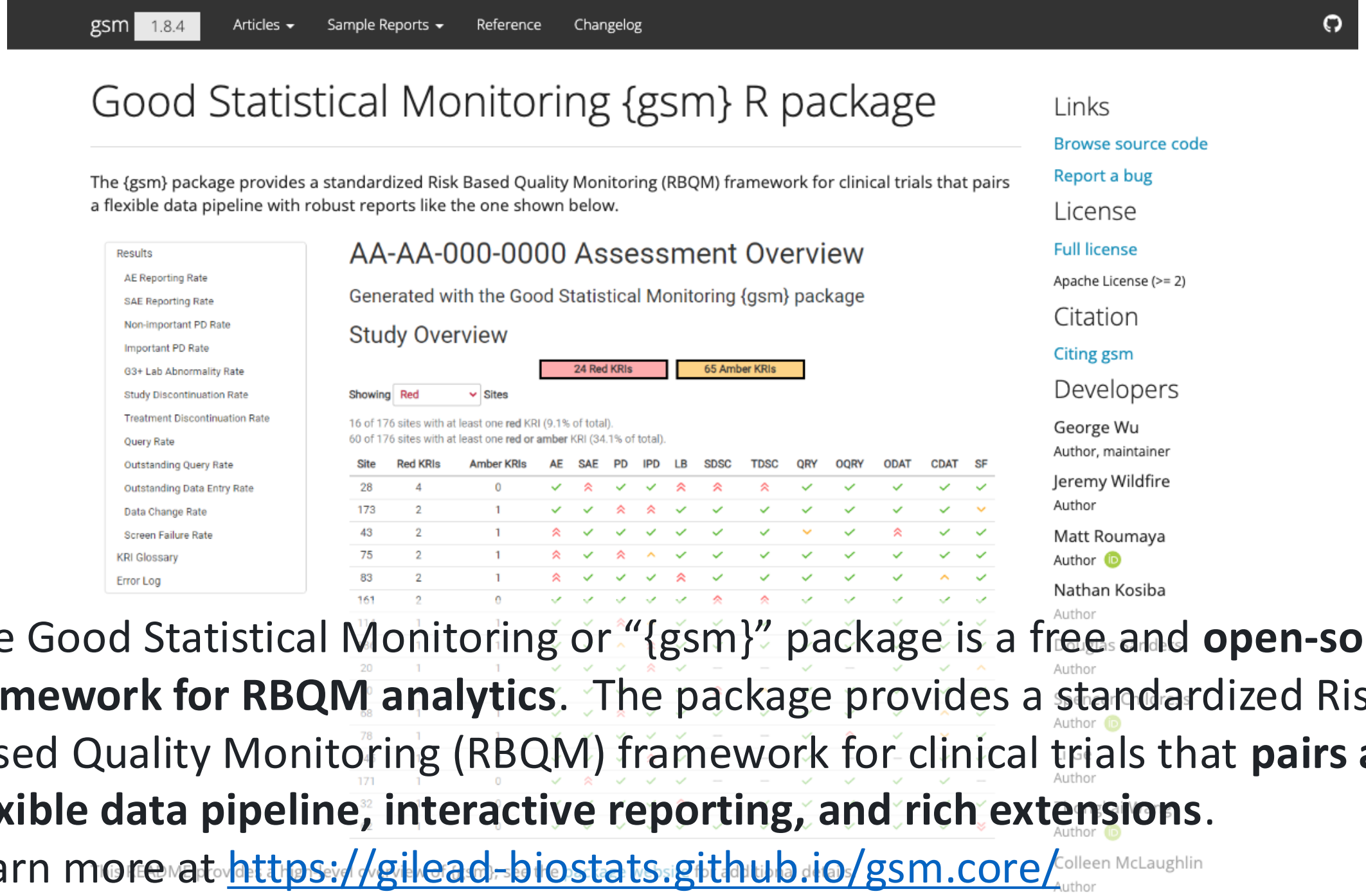
Risk-based quality management (RBQM) is a regulatory-recommended approach to detect and effectively manage risk in a clinical trial. While there is a significant body of literature describing RBQM implementation and best practices (1, 2), there are few publicly available open-source tools for RBQM available. Instead, commercial tools and custom company-specific RBQM implementations currently serve as the industry standard for RBQM implementation.

Project Scope

We propose forming an Open-Source RBQM Working Group and an associated development sub-team.

Open-Source RBQM Working Group – A Working group that will discuss open-source projects related to RBQM. This will be a cross-functional team that will consider how open-source solutions can be developed using RBQM best practices. Monthly meetings will include discussion of RBQM software best practices, design discussions for development team deliverables and demos of RBQM tools developed.

RBQM Development Team – This team will focus on pre-competitive co-development of RBQM centralised monitoring tools. The primary focus will be on R package development, though other technologies may be considered. The team will start with a focus on creating reports and interactive graphics related to centralised statistical monitoring (e.g. digit preference charts, missing data analysis, fraud detection). All development will be done using GitHub. The team will meet every other week in 2024.

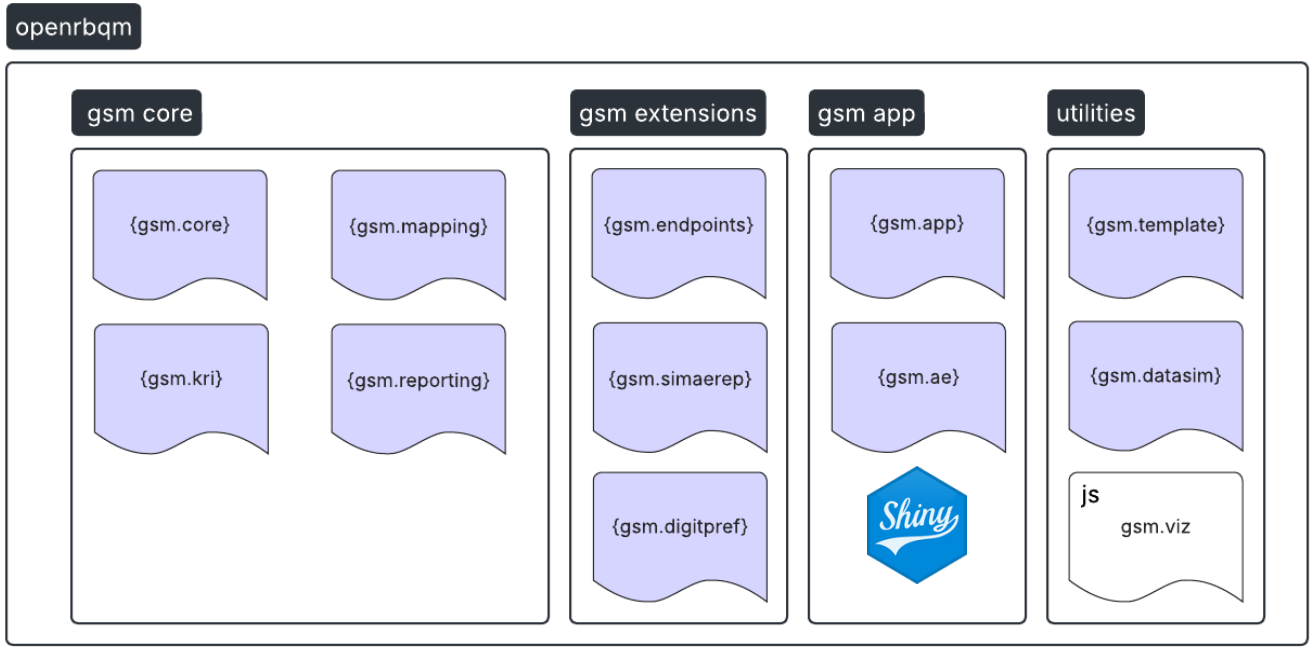


The Good Statistical Monitoring or "{gsm}" package is a free and **open-source framework for RBQM analytics**. The package provides a standardized Risk Based Quality Monitoring (RBQM) framework for clinical trials that **pairs a flexible data pipeline, interactive reporting, and rich extensions**.

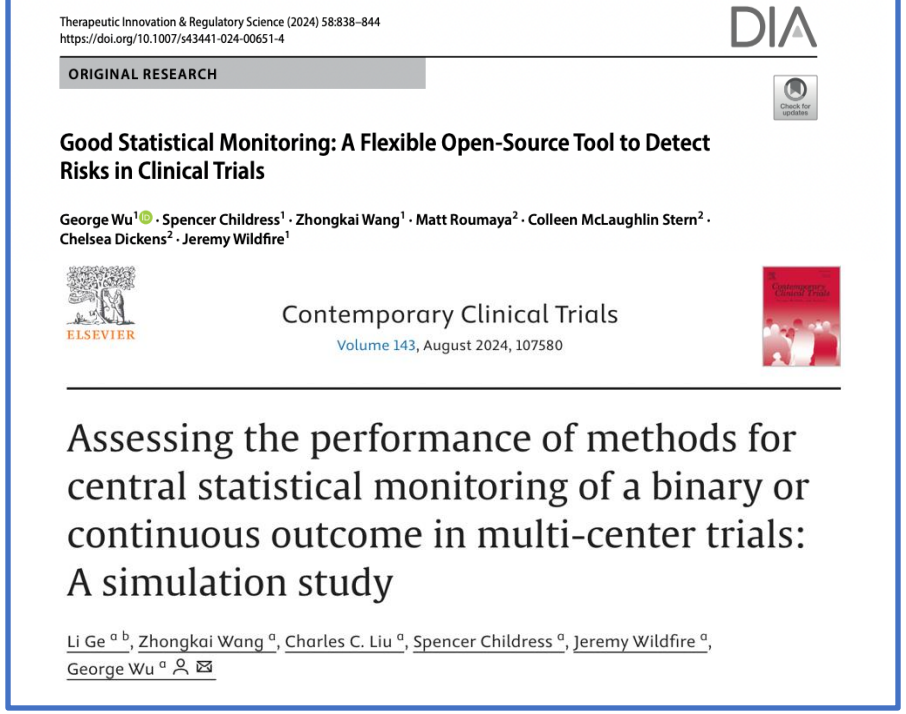
Learn more at https://gilead-biostats.github.io/gsm.core/

Accomplishments

12 Packages Released



2 Papers Published



Therapeutic Innovation & Regulatory Science (2024) 58:838–844
https://doi.org/10.1007/s43441-024-00651-4

DIA

ORIGINAL RESEARCH

Good Statistical Monitoring: A Flexible Open-Source Tool to Detect Risks in Clinical Trials

George Wu[1] · Spencer Childress[1] · Zhongkai Wang[1] · Matt Roumaya[2] · Colleen McLaughlin Stern[2] · Chelsea Dickens[2] · Jeremy Wildfire[1]

ELSEVIER

Contemporary Clinical Trials
Volume 143, August 2024, 107580

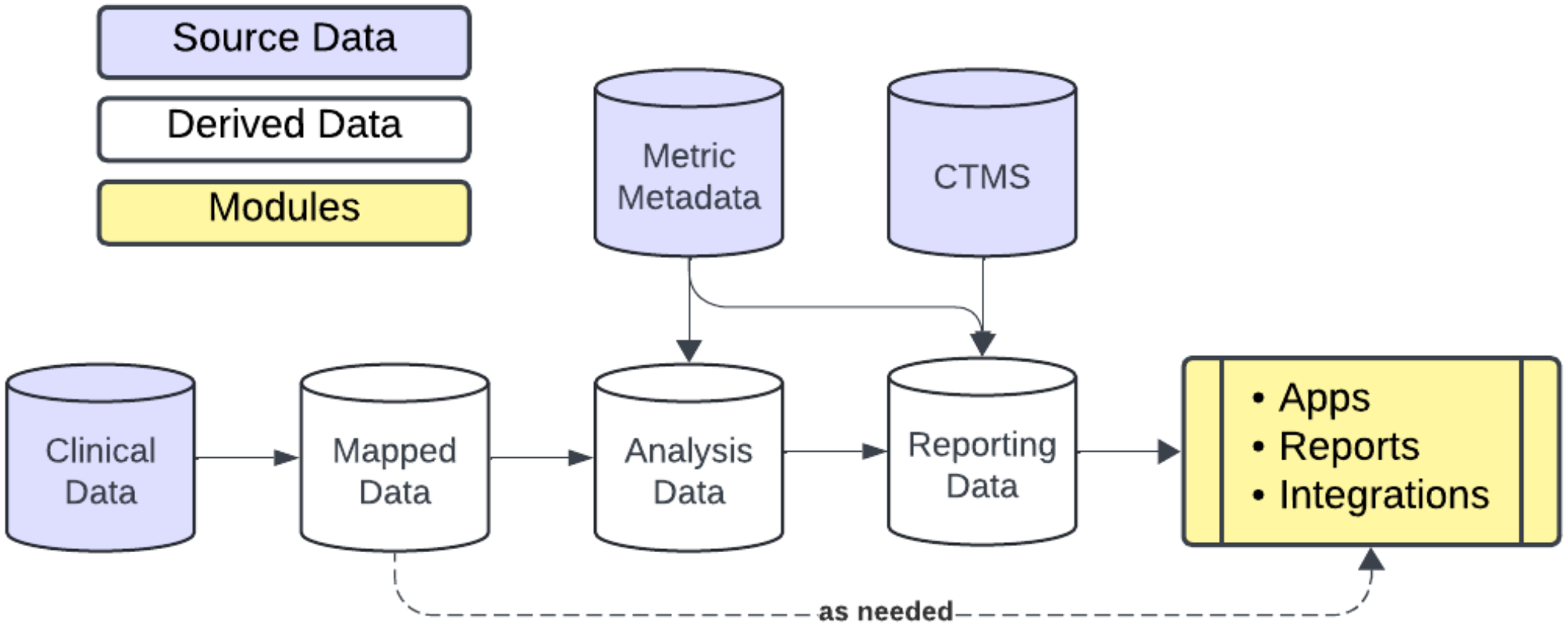
Assessing the performance of methods for central statistical monitoring of a binary or continuous outcome in multi-center trials: A simulation study

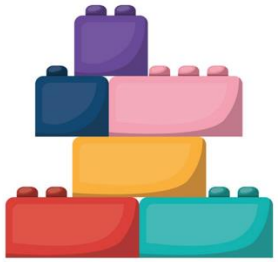
Li Ge [a b], Zhongkai Wang [a], Charles C. Liu [a], Spencer Childress [a], Jeremy Wildfire [a], George Wu [a]

- More extensions such as {gsm.qtl} and proof-of-concept AI/ML application/extension

- 1 manuscript under review on Quality Tolerance Limit (QTL) statistical methodology - joint Special Working Group of Statisticians in the Pharmaceutical Industry (PSI), European Federation of Statisticians in the Pharmaceutical Industry (EFSPI), American Statistical Association (ASA) Biopharmaceutical section

OpenRBQM Analysis Data Pipeline





OpenRBQM Analysis Workflow

Raw+ (1gb)
Standardized Study Data

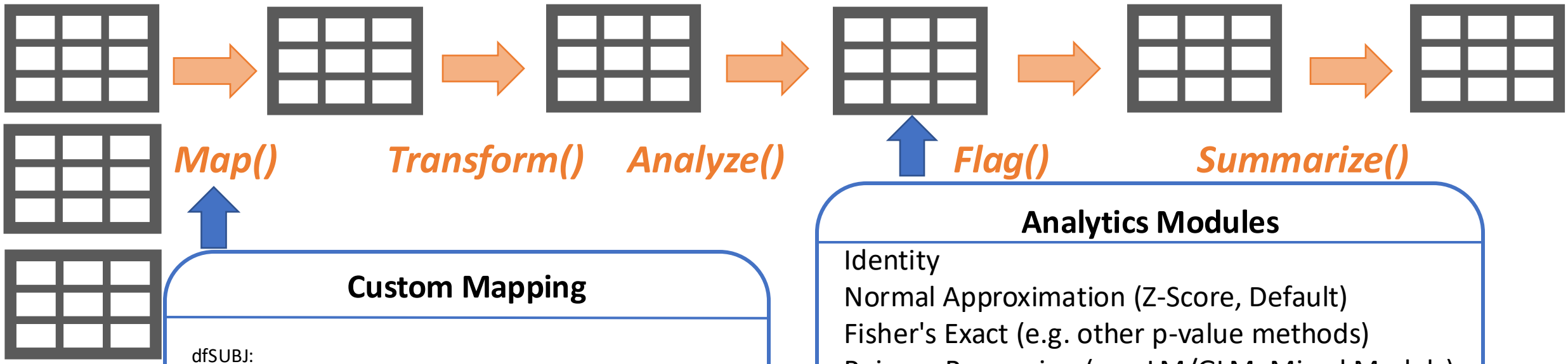
Input (100kb)
Cross-domain Participant-level data

Transformed
Site-level derived data

Analyzed
Site-level analysis results

Flagged
Site-level with flags

Summary
Site-level aggregated



Map() *Transform()* *Analyze()* *Flag()* *Summarize()*

Custom Mapping

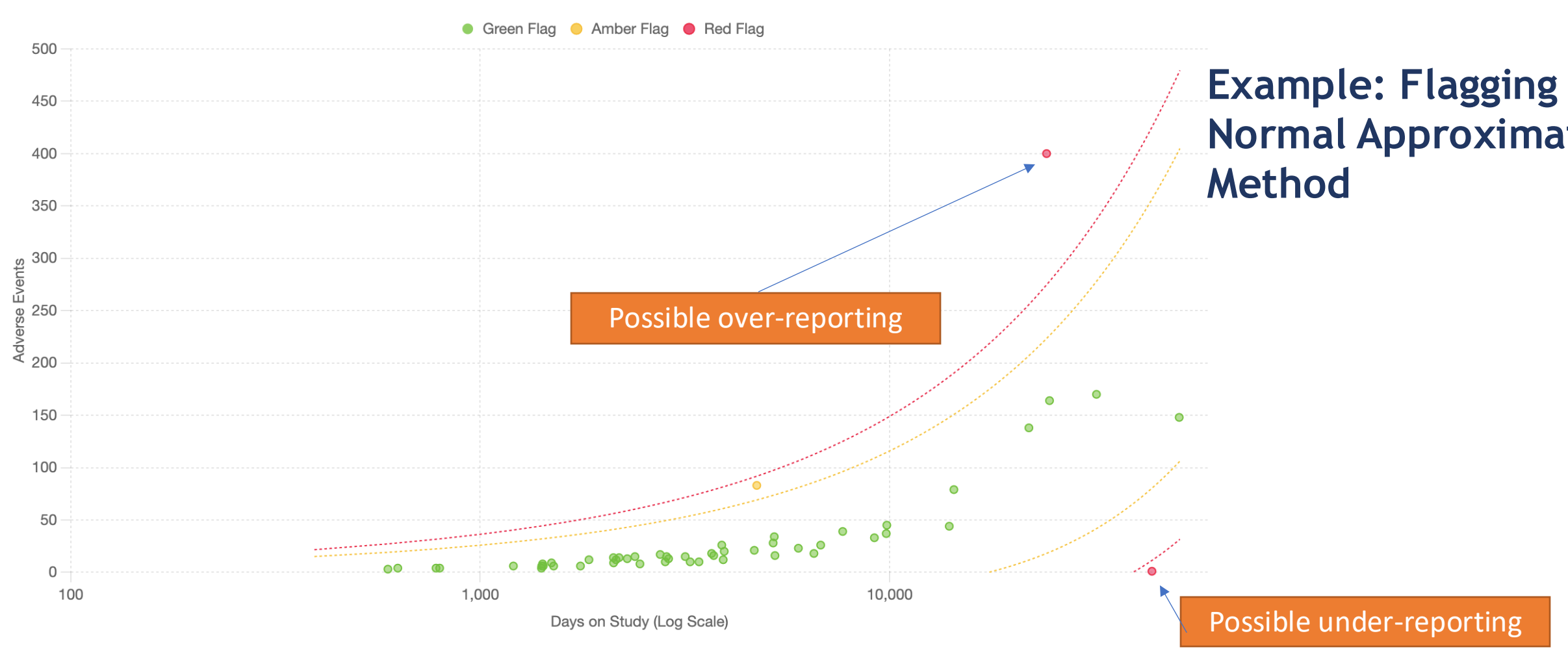
```
dfSUBJ:
  strStudyCol: studyid
  strSiteCol: siteid
  strIDCol: subjid
  strStudyStartDateCol: firstparticipantdate
  strStudyEndDateCol: lastparticipantdate
  strTimeOnStudyCol: timeonstudy
```

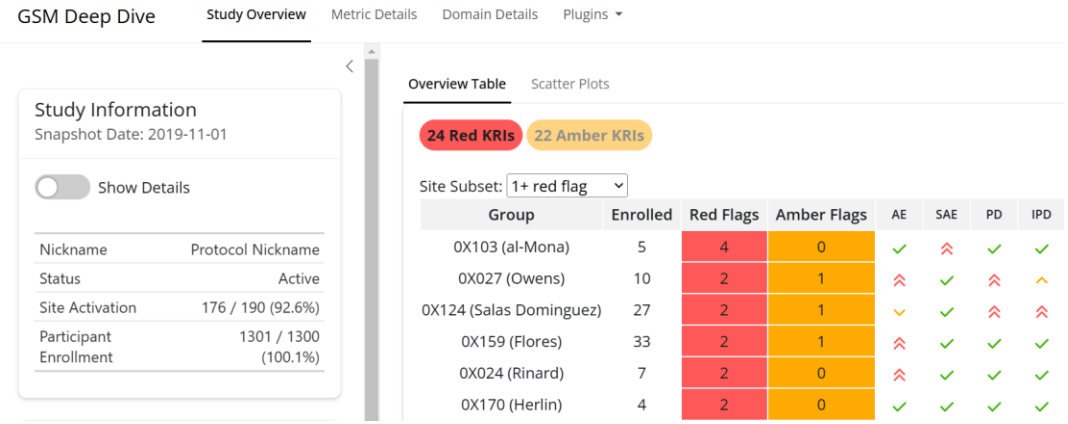
Analytics Modules

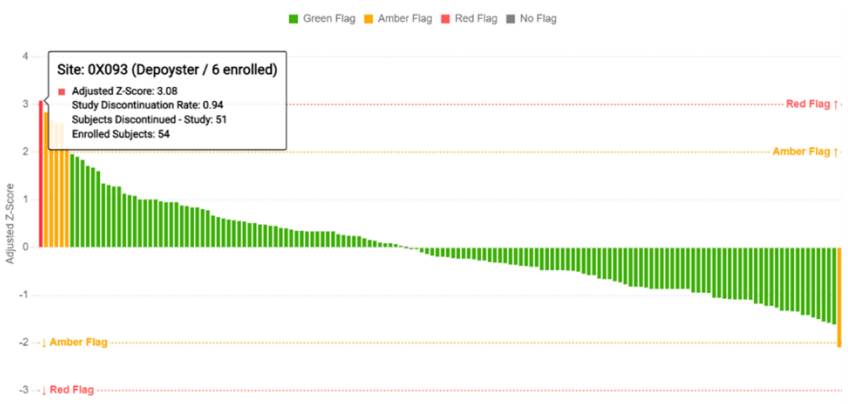
Identity
Normal Approximation (Z-Score, Default)
Fisher's Exact (e.g. other p-value methods)
Poisson Regression (e.g. LM/GLM, Mixed Models)
Bayesian Approach (e.g. BHM)
AI/ML

Link: GSM Data Pipeline Vignette

Example: Flagging with Normal Approximation Method







Standard GSM Metrics – 12 KRIs

KRI	Metric	Numerator	Denominator
0001	AE Reporting Rate	# of AEs	Days in Study
0002	SAE Reporting Rate	# of SAEs	Days in Study
0003	Non-important Protocol Deviation Rate	Non-Important PDs	Days in Study
0004	Important Protocol Deviation Rate	Important PDs	Days in Study
0005	G3 or higher Lab Abnormality Rate	G3+ Abnormal Labs Samples	Total Lab Samples
0006	Subject Discontinuation	Subjects Discontinued	Total Subjects
0007	Subject Treatment Discontinuation	Subjects with Treatment Discontinued	Total Subjects
0008	Query Rate	Total # of Queries	Total Data Points
0009	Query Age	Queries Open > 30 days	Total Queries
0010	Visit Entry Lag (visit date to entry date)	Form Entered > 10 days	Total Forms
0011	Data Change Rate	Fields with 1+ Change	Total Fields
0012	Screen Failure	Screen Failures	Total Screened

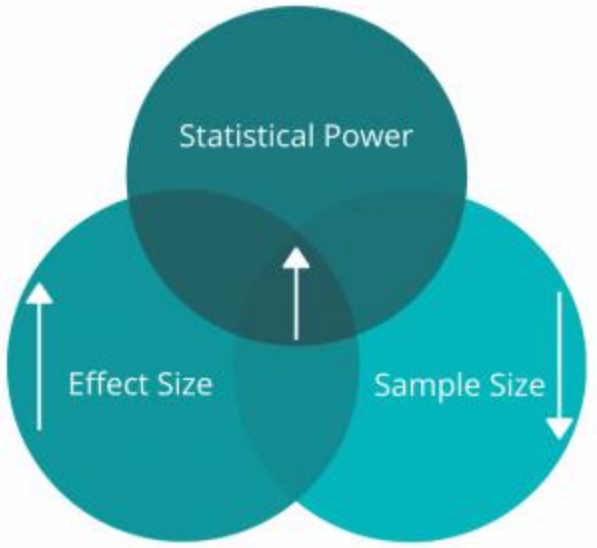
Example KRI0001: AE Reporting Rate

Data Sources: Rawplus (AE, DM)
Analysis Set: Enrolled
Num: All adverse events
Denom: Enroll to d/c date

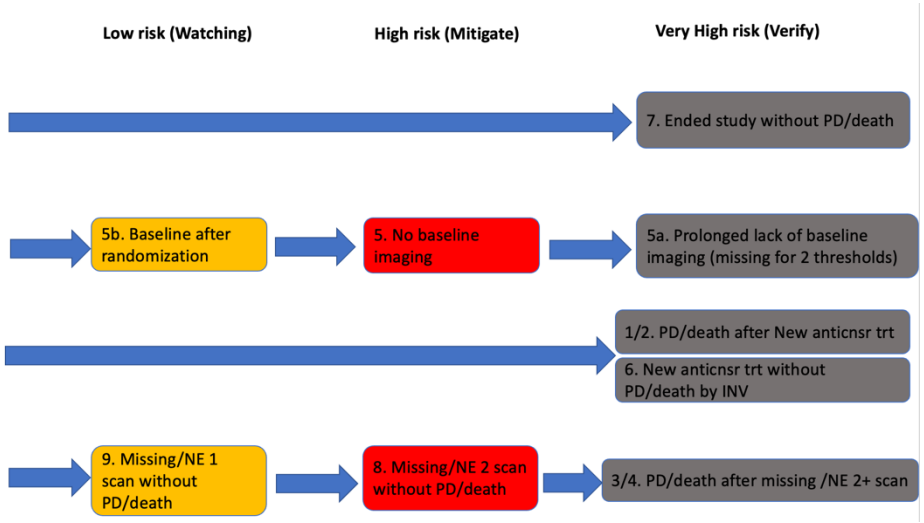
Example of new working KRIs: PK Sample Compliance, Eligibility,

GSM Extensibility: Endpoint Monitoring {gsm.endpoints}

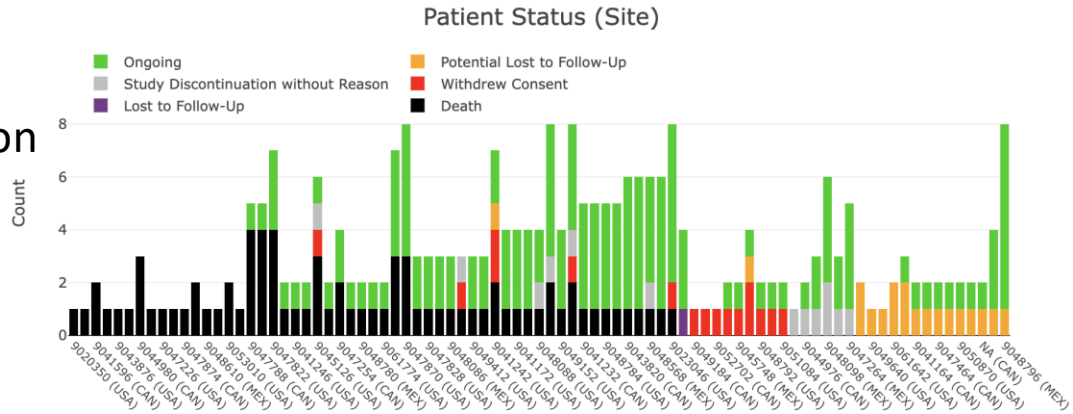
- {gsm.endpoints} extension for endpoint data monitoring
- Evaluates risks to premature censoring of key endpoint data
- Enables early detection of data quality trends
- Complex data derivation in *map()* layer of GSM
- Study-specific, but high benefit for critical risk identification



PFS Monitoring



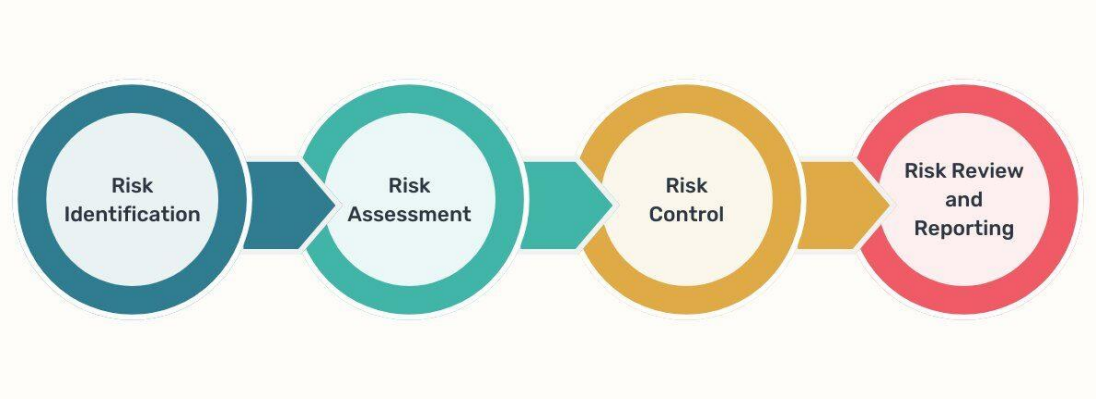
OS/Retention Monitoring



GSM Extensibility: AI/ML Applications and Extensions

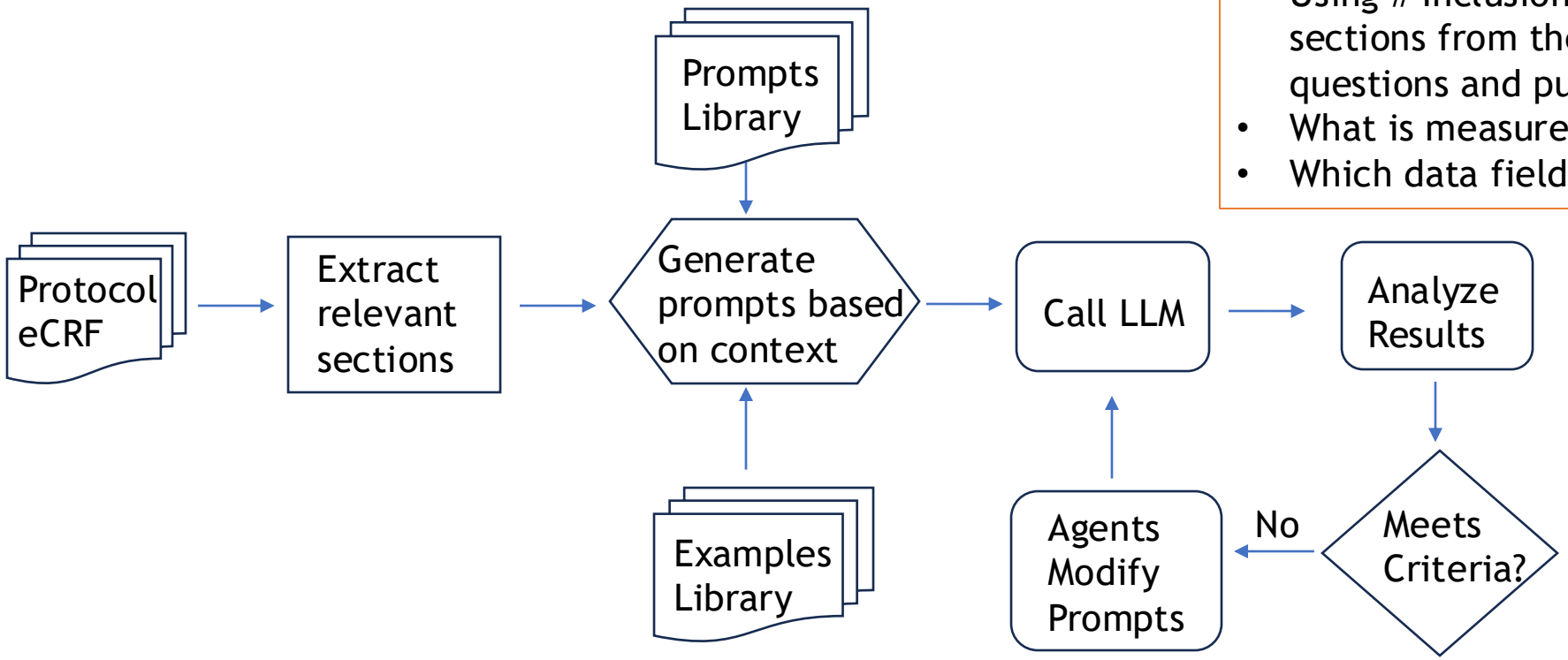
1. **Identification:** Generate Risk Management Plan (RMP) based on protocol, database, etc.
2. **Assessment:** Automate risk signal and abnormality detection from clinical data
3. **Mitigation & Reporting:** Summarize historical risk signals trends with AI-generated recommended actions

More ……



1. Identify Study Risks and Generate Plans

Prompt example (*multiple pages*):
<Example Text> ……
<Instructions>
- Using # Inclusion Criteria #, # Exclusion Criteria # sections from the protocol, answer the following questions and put them in a table …
- What is measured in Inclusion Criteria 1…
- Which data field from CRF correspond…



Python: 3.10
Model ID: anthropic.claude-3-opus
Anthropic Version: bedrock-2023-05-31
Max Tokens: 4096
Temperature: 0 (no randomness of the model's outputs)

Example Output:

Study Metadata
- Test drug
- Population
- Therapeutic Area
- …

Protocol Specifics, Study Design Details
- Design type
- Treatment
- Objective
- Endpoint
- …

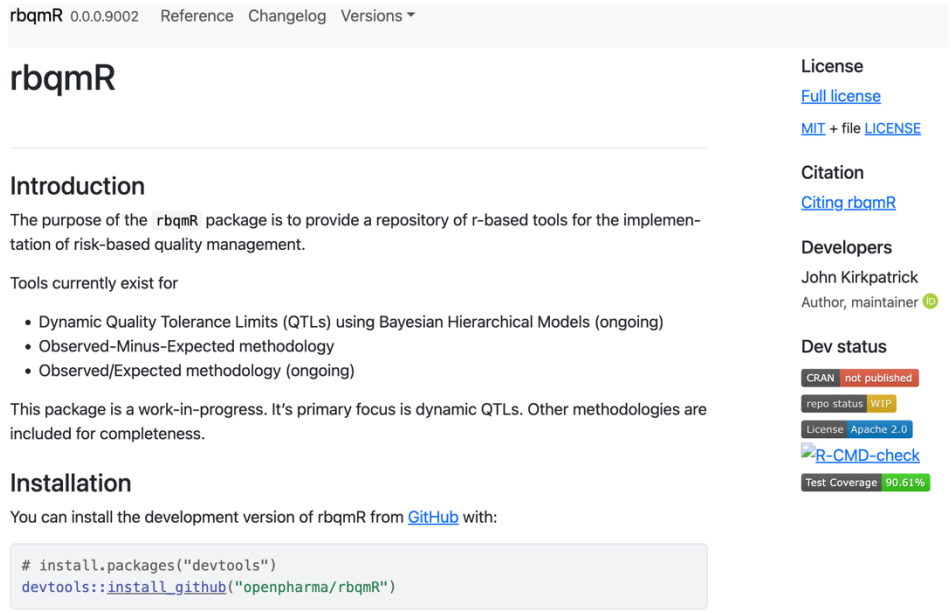
Critical Data and Critical Processes
- Eligibility Criteria
- Endpoint Data
- Safety
- Operational

2. AI/ML Assessment and Detection of Risk Signals

- We piloted the implementation existing ML algorithms for RBQM analyses from the industry and literatures

Kirkpatrick (rbqmR) - Bayesian Hierarchical Model (BHM) for Flagging

- BHM uses the quantiles of the posterior distribution of the probability of the event to define the metric of interest
- The classification rule for BHM is based on the median $\hat{m}$, that is compared with pre-defined limits $l_U(p)$. If $\hat{m} > \mathrm{l_u(p)}$ then the metric is defined as breach



rbqmR 0.0.0.9002 Reference Changelog Versions

rbqmR

Introduction

The purpose of the `rbqmR` package is to provide a repository of r-based tools for the implementation of risk-based quality management.

Tools currently exist for

- Dynamic Quality Tolerance Limits (QTLs) using Bayesian Hierarchical Models (ongoing)
- Observed-Minus-Expected methodology
- Observed/Expected methodology (ongoing)

This package is a work-in-progress. It's primary focus is dynamic QTLs. Other methodologies are included for completeness.

Installation

You can install the development version of rbqmR from GitHub with:

```
# install.packages("devtools")
devtools::install_github("openpharma/rbqmR")
```

License

Full license

MIT + file LICENSE

Citation

Citing rbqmR

Developers

John Kirkpatrick

Author, maintainer

Dev status

CRAN not published

repo status WIP

License Apache 2.0

R-CMD-check

Test Coverage 90.61%

Yan et al. (2025) - ML Algorithm for QTL

Therapeutic Innovation & Regulatory Science (2025) 59:566–578
https://doi.org/10.1007/s43441-025-00754-6

DIA

RESEARCH

Check for updates

Optimizing Quality Tolerance Limits Monitoring in Clinical Trials Through Machine Learning Methods

Lei Yan[1] · Ziji Yu[2] · Liwen Wu[2] · Rachael Liu[2] · Jianchang Lin[2]

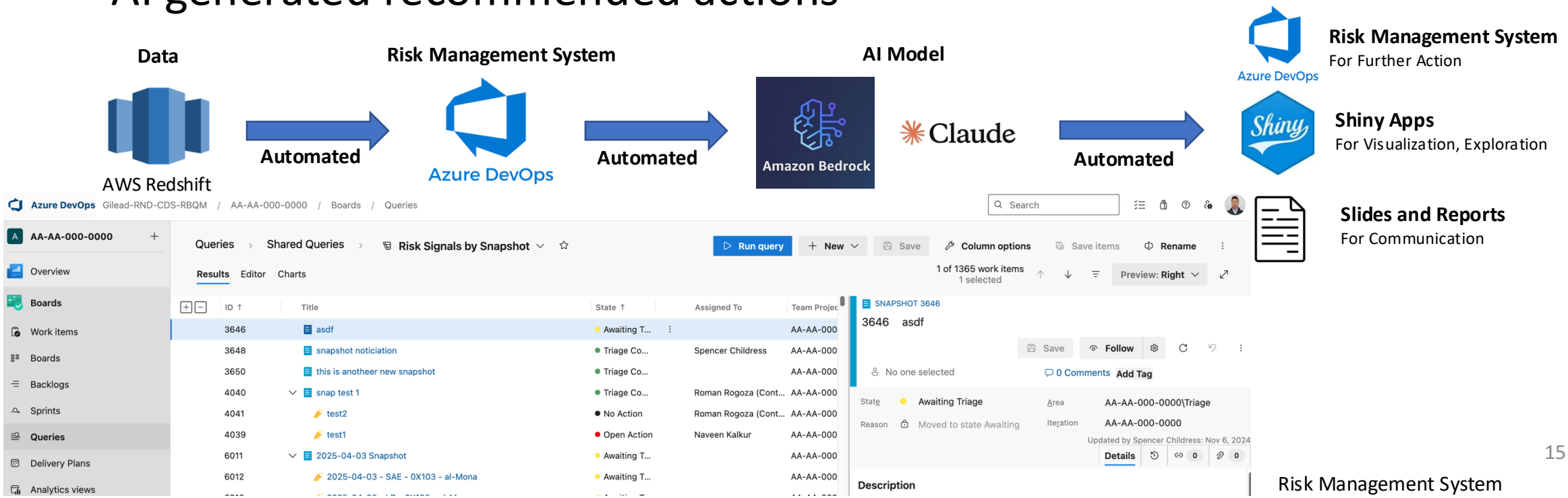
Input: Data $\mathrm{x} = \{\mathrm{x}_i\}_{i=1}^{N_1}, \mathrm{y} = \{y_i\}_{i=1}^{N_1}$, function forms f, mappings $\{h_j\}_{j=1}^{N_2}, \{g_j\}_{j=1}^{N_2}$ and $\{\tilde{h}_k\}_{k=1}^{N_3}$, $\{\tilde{g}_k\}_{k=1}^{N_3}$, threshold α.

Output: Top level indices $\mathcal{I} \in \{1, 2, \ldots, N_3\}$ that trigger QTL breach.

1. Initialize $\mathcal{I} = \{\}$;
2. Apply machine learning algorithms to obtain $f(\hat{\theta}_i)$ with data x and y;
3. Divide $\mathrm{y} = \{y_i\}_{i=1}^{N_1}$ and $\hat{\mathrm{F}} = \{f(\hat{\theta}_i)\}_{i=1}^{N_1}$ into N_2 sets $\{\mathrm{y}_j\}_{j=1}^{N_2}, \{\hat{\mathrm{F}}_j\}_{j=1}^{N_2}$;
4. **for** $j = 1,2, \ldots, N_2$ **do**:
5. Apply mappings $h_j: \mathbb{R}^{n_j} \mapsto \mathbb{R}, h_j(\mathrm{y}_j) = \tilde{y}_j$ and $g_j: D^{n_j} \mapsto D, g_j(\hat{\mathrm{F}}_j) = \tilde{f}(\hat{\tilde{\theta}}_j)$;
6. **end for**
7. Divide $\tilde{\mathrm{y}} = \{\tilde{y}_j\}_{j=1}^{N_2}$ and $\hat{\tilde{\mathrm{F}}} = \left\{\tilde{f}\left(\hat{\tilde{\theta}}_j\right)\right\}_{j=1}^{N_2}$ into N_3 sets $\{\tilde{y}_k\}_{k=1}^{N_3}, \{\hat{\tilde{\mathrm{F}}}_k\}_{k=1}^{N_3}$;
8. **for** $k = 1,2, \ldots, N_3$ **do**:
9. Apply mappings $\tilde{h}_k: \mathbb{R}^{\tilde{n}_k} \mapsto \mathbb{R}, \tilde{h}_k(\tilde{\mathrm{y}}_k) = \breve{y}_k$ and $\tilde{g}_k: D^{\tilde{n}_k} \mapsto D, \tilde{g}_k\left(\hat{\tilde{\mathrm{F}}}_k\right) = \breve{f}\left(\hat{\tilde{\theta}}_k\right)$;
10. **end for**
11. **for** $k = 1,2, \ldots, N_3$ **do**:
12. Compute $S(\breve{y}_k) = P(\breve{Y}_k < \breve{y}_k)$ or $S(\breve{y}_k) = P(\breve{Y}_k > \breve{y}_k)$, where P is the CDF associated with $\breve{f}\left(\hat{\tilde{\theta}}_k\right)$;
13. **if** $S(\breve{y}_k) < \alpha$ **then**
14. Add k to the set $\mathcal{I}$;
15. **end if**
16. **end for**

3. Manage Risk Signal Trends & Generate Recommended Actions

- Risk signal management with historical issues at varies levels and trend
- AI generated recommended actions



Summary & Future Directions

- **Extensible, workflow-driven framework enables new tools**
- **Future new openRBQM extensions:**
  - Domain-specific modules: {gsm.simaerep} (AE simulation), {gsm.ae} (AE deep-dive), {gsm.query} (operational metrics)
  - New therapeutic area metrics: {gsm.endpoints} (+multiple TAs)
  - Data quality evaluation: {gsm.digitpref} (digit preference, fraud detection)
- **Future goals:**
  - Expand “qualityverse” to new data domains & therapeutic areas
  - More comprehensive risk understanding
  - Expand AI/ML capability

Thank you.

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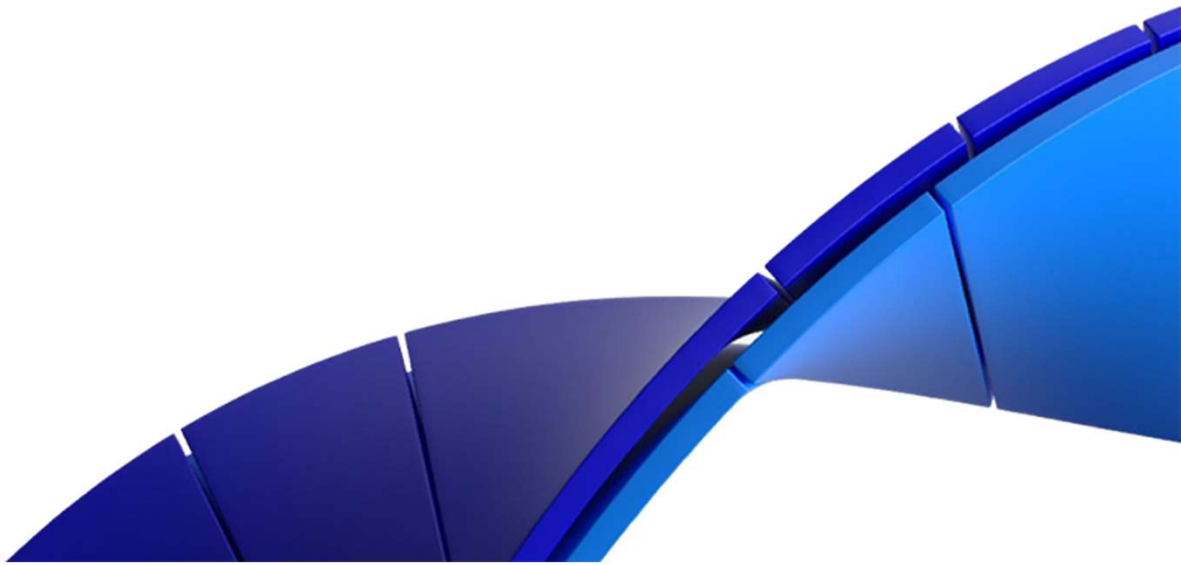
Xinlei (Ivan) Mi (Ivan.mi@gilead.com)

k-step ahead Multiple Endpoint Anomaly Detection through Bayesian Latent Class Modeling

Yuxi Zhao, Margaret Gamalo

Pfizer
Research & Development



k-step ahead Multiple Endpoint Anomaly Detection through Bayesian Latent Class Modeling

- Motivation
- Methology
- Simulation
- Data Application
- Discussion

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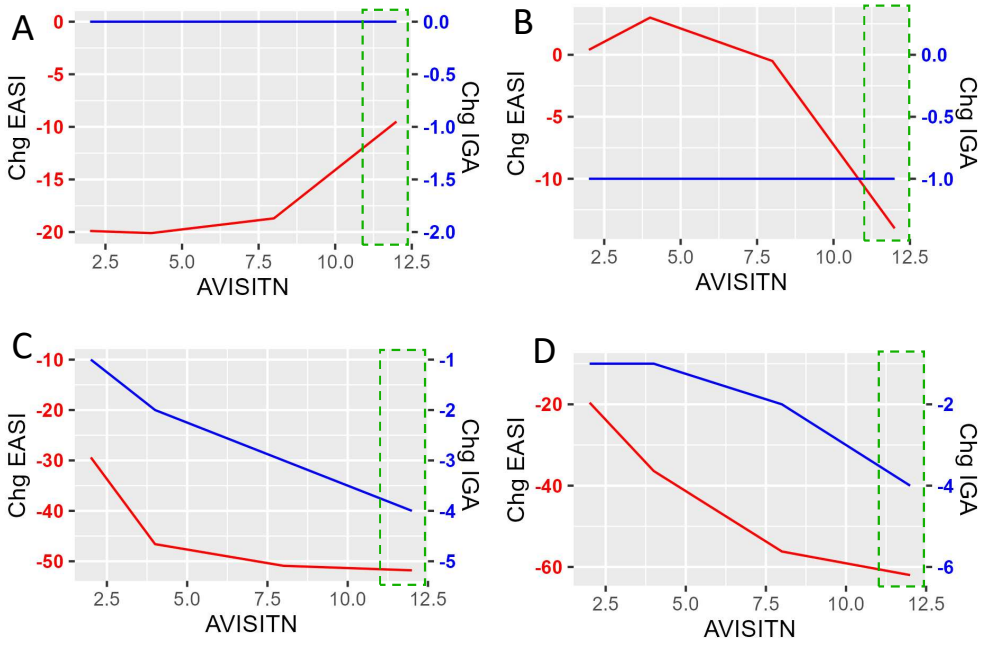
Motivation

- Validity and quality of data is paramount for clinical trials, which necessitates data monitoring
- Inconsistencies between multiple endpoints
- Example: Atopic Dermititis (AD)
  - EASI Score
  - IGA Score



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Motivation

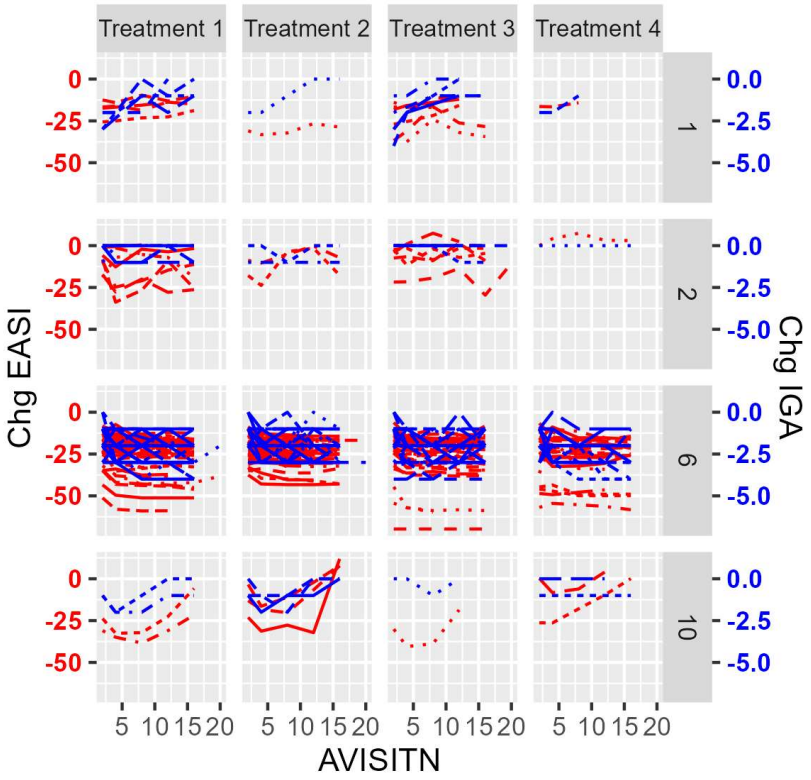
- Review of Data monitoring Strategies:
  - Extensive: 100% source data verification
  - Reduced: random sampling
  - Targeted: risk-based monitoring (RBM), statistical monitoring (StM)

- Review of Tools:
  - RBM: data entry errors and alterations, e.g. Target e*CRF (Mitchel et al., 2011)
  - StM: descriptive statistical techniques, e.g., Bauer and Johnson (2000), JM et al. (2001), Carstensen et al. (2024)

- Objective: automatic queries for anomalous data adjusted for risk factors

Methology: Latent Class Approach

- A statistical method used to identify subgroups or “classes” within a population based on patterns of responses or characteristics
- By analyzing similarities and differences among individuals without prior knowledge of group membership (unsupervised clustering)
- Advantage of identifying smaller sized subgroups



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Methology: Model Setup

- Endpoints: $\boldsymbol{x_i} = \{x_{ij}, j = 1, \cdots, n_i^x\}$, $\boldsymbol{y_i} = \{y_{ij}, j = 1, \cdots, n_i^y\}$
- Timepoints: $t_i^x = \{t_{ij}^x, j = 1, \cdots, n_i^x\}$, $t_i^y = \{t_{ij}^y, j = 1, \cdots, n_i^y\}$
- Risk factors (e.g. sites): $\boldsymbol{s_i} = \{s_{i1}, \cdots, s_{iM}\}$
- Latent class membership: $z_i = \{z_{i1}, \cdots, z_{iC}\}$, C: maximum #classes (finite mixture)
- Model:

$$x_{ij}, y_{ij} \mid s_i, z_{ic}, \eta \sim \boldsymbol{f}(x_{ij} \mid z_{ic}, \eta_c)\boldsymbol{f}(y_{ij} \mid z_{ic}, \eta_c)$$

$$s_i \mid z_{ic} \sim f(s_i \mid z_{ic}, p_c)$$

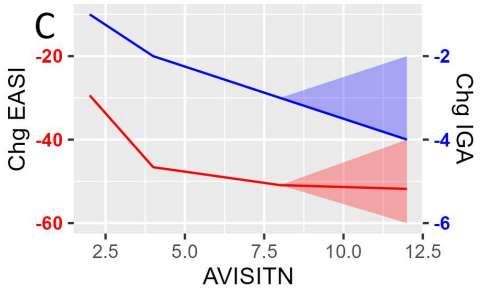
$$(\eta_c, p_c) \sim G$$

$$G \sim DP$$

- $\boldsymbol{f}$ ~ Norm. with class-specific quadratic curve and site RE, and subject RE
- Software: JAGS

Methology: Poterior prediction k-step ahead

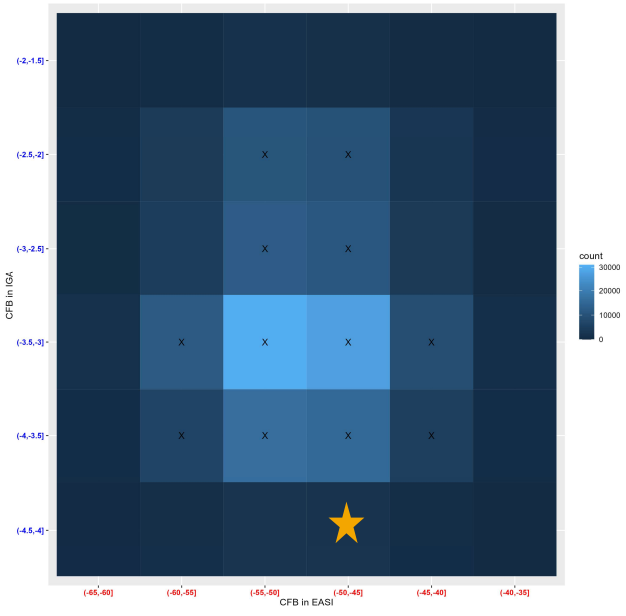
- Given posterior sampler from trained data
- Newly observed data $[x_{ij}^*]$, $[y_{ij}^*]$ for a new subject



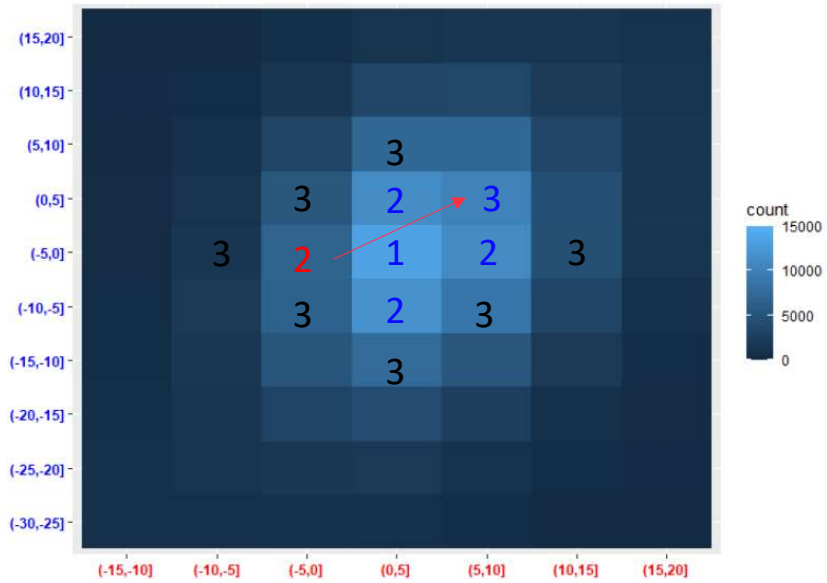
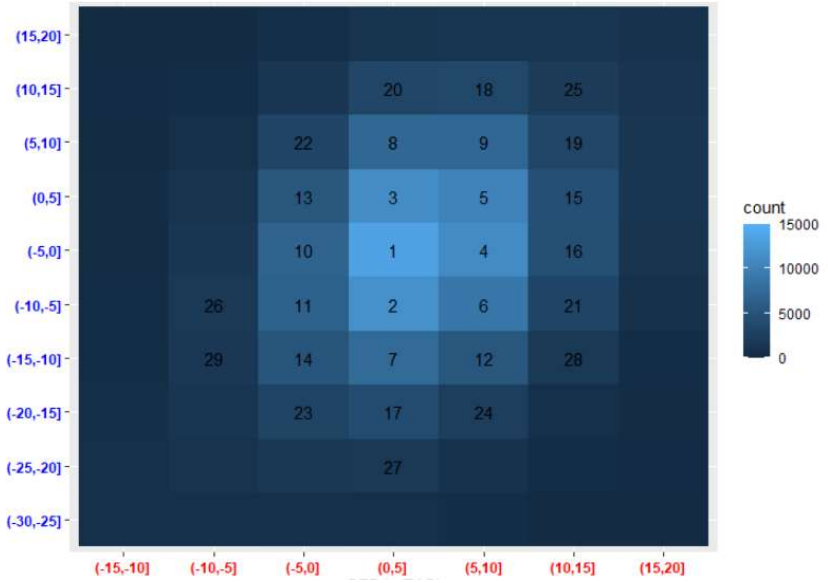
- Build a grid of $x_{ij+1}^* \cdots x_{ij+k}^*, y_{ij+1}^* \cdots y_{ij+k}^*$
- Predict $x_{ij+1}^* \cdots x_{ij+k}^*, y_{ij+1}^* \cdots y_{ij+k}^*$:

$$\mathrm{P}\left(x_{ij+1}^* \cdots x_{ij+k}^*, y_{ij+1}^* \cdots y_{ij+k}^*, \middle| [x_{ij}^*], [y_{ij}^*], \text{Data} \right)$$

$$= \frac{1}{M} \sum_m \frac{\sum_c f\left(x_{ij+1}^* \cdots x_{ij+k}^*, [x_{ij}^*] \middle| \theta_c^{(m)} \right) f\left(y_{ij+1}^* \cdots x_{ij+k}^*, [y_{ij}^*] \middle| \theta_c^{(m)} \right) \pi_c^{(m)}}{\sum_c f\left([x_{ij}^*] \middle| \theta_c^{(m)} \right) f\left([y_{ij}^*] \middle| \theta_c^{(m)} \right) \pi_c^{(m)}}$$

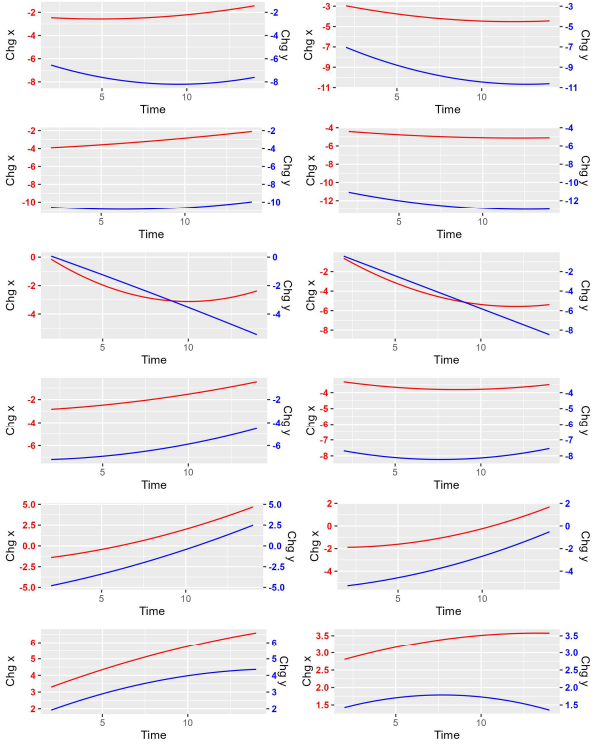


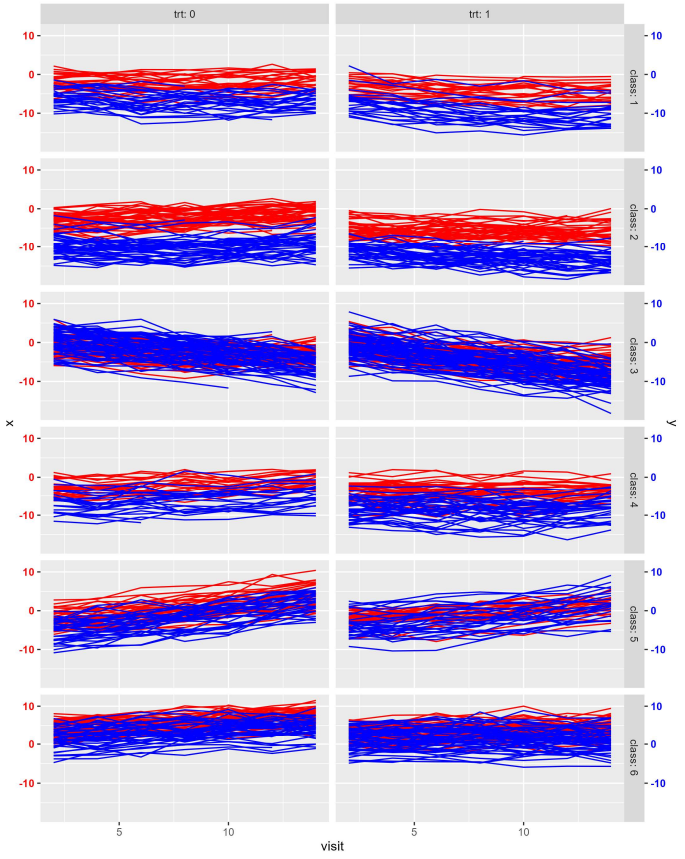
Methology: credible region

Branching out	Highest Density Region (HDR)
	

Simulation

- N=700
- 50 sites
- 6 classes
  - (1/8, 1/8, 1/4, 1/4, 1/8, 1/8)
- 100 replicates
- 70% training, 30% testing
- Credible level: 80%





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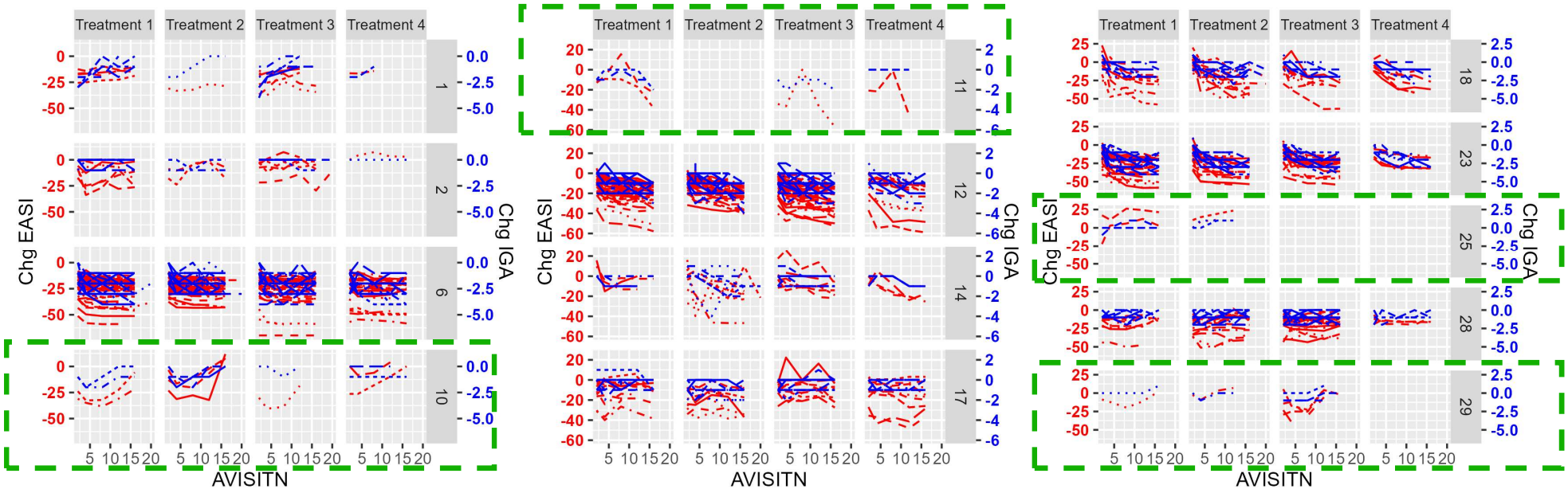
Simulation: Prediction of 4th obs. given the first three obs. - results from 100 replicates

	Branching out	HDR
Proportion of being in the regions: Mean (SD)	85.74% (3.25%)	85.66% (3.25%)
Bias: Mean (SD)	1.78% (0.200%)	1.81% (0.200%)
Sqrt. MSE: Mean (SD)	2.27% (0.216%)	2.28% (0.214%)

Credible region was set to be 80% for showcase.

Data Application : EASI and IGA
- 70% Training: C = 30



Individual Trajectory by classification (number of subjects) of 570 subjects from best configuration (Dahl, 2006): 1(12), 2(15), 6(157), 10(8), 11(4), 12(146), 14(19), 17(38), 18(39), 23(77), 25(4), 28(45), 29(6).

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Data Application : EASI and IGA
- 30% Testing

	Algorithm	Proportion of being in the regions	Bias of credible level (nomial =80%)	Sqrt. MSE of credible level (nomial =80%)
Scenario 1: - Predict Week 2 cond. on baseline	Branching out	**95.4%**	0.14%	0.17%
	HDR	**97.1%**	0.24%	0.28%
Scenario 2: - Predict 4th timepoint cond. on previous obs.	Branching out	**77.2%**	0.88%	1.06%
	HDR	**78.5%**	0.93%	1.10%

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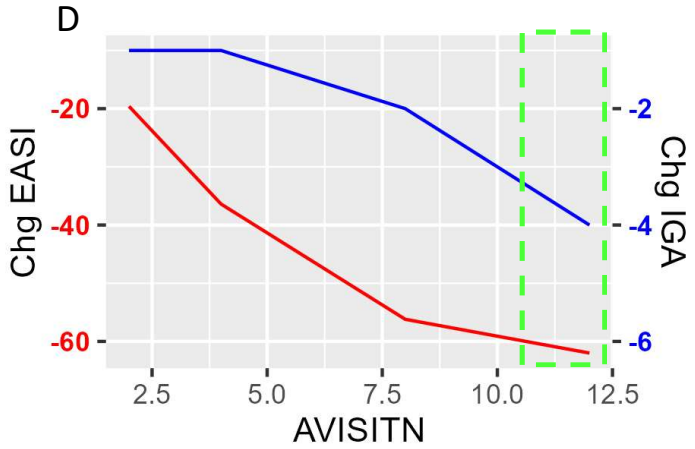
Data Application : EASI and IGA
- Testing: Selected Example from Scenario 2



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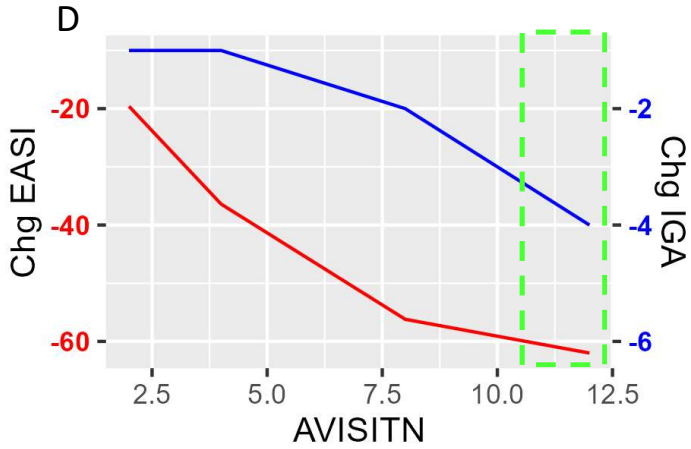
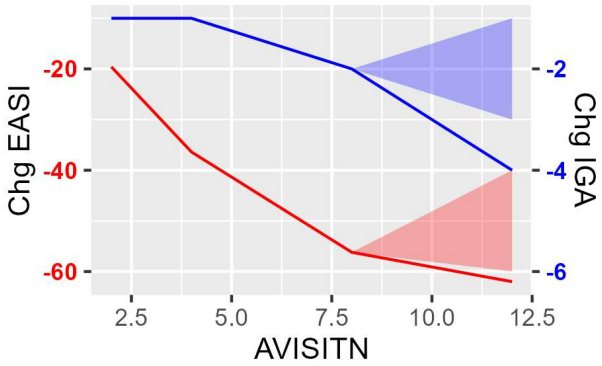
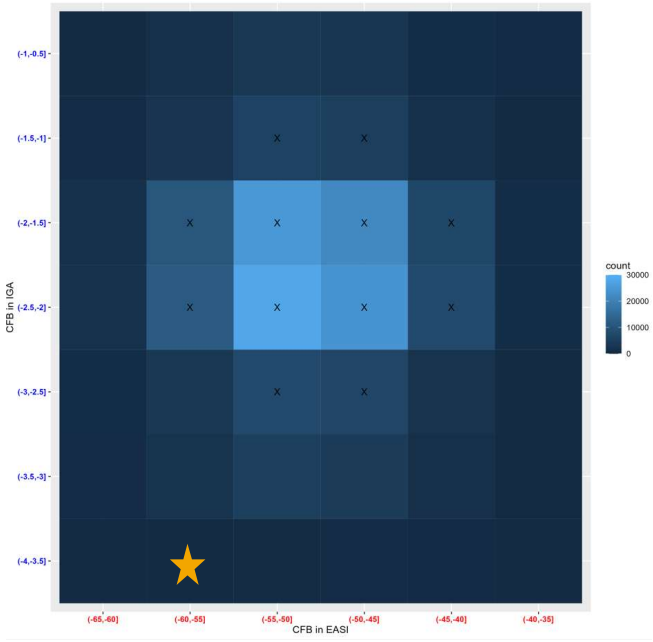
Data Application : EASI and IGA
- Testing: Selected Example from Scenario 2







Discussion

- Advantage:
  - Automatic query built on individualized predictions
  - Flexilbe framework for extensions
- Drawback:
  - Computational costly

- Future work:
  - Extensions to fractional polynomials; generalized linear mixed model
  - Unclear for how to quantify the risk in current setup

Thank you!


рахмат
danke
謝謝
ngiyabonga
شكراً جزيلاً
Баярлалаа
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Reference

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