



Introducing

GSM: Open-Source RBQM with R



Sign up for updates



Good Statistical Monitoring

<https://github.com/Gilead-BioStats/gsm>





Good Statistical Monitoring {gsm} R package

Links

[Browse source code](#)

[Report a bug](#)

License

The {gsm} package provides a standardized Risk Based Quality Monitoring (RBQM) framework for clinical trials that pairs a flexible data pipeline with robust reports like the one shown below.

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 with interactive reporting**.

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

186	1	1	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
20	1	1	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
60	1	1	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
68	1	1	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
78	1	1	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
145	1	0	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
171	1	0	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
32	1	0	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
62	1	0	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

Douglas Sanders

Author

Spencer Childress

Author

Li Ge

Author

Zhongkai Wang

Author

Colleen McLaughlin

Author

This README provides a high-level overview of {gsm}; see the [package website](#) for additional details.



Standard GSM Metrics - 12 KRIs

KRI	Metric	Metric Numerator	Metric 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	
0005	G3 or higher Lab Abnormality Rate	G3+ Abnormal Labs Sample	
0006	Subject Discontinuation	Subjects Discontinued	
0007	Subject Treatment Discontinuation	Subjects with Treatment Discont	
0008	Query Rate	Total # of Queries	
0009	Query Age	Queries Open > 30 days	
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

KRI0001: AE Reporting Rate

Data Sources: Rawplus (AE, DM)

Analysis Set: Enrolled

Num: All adverse events

Denom: Enroll to d/c date

KRI Example - Adverse Events

Are any sites potentially under- or over- reporting safety events?



Statistical Method Overview

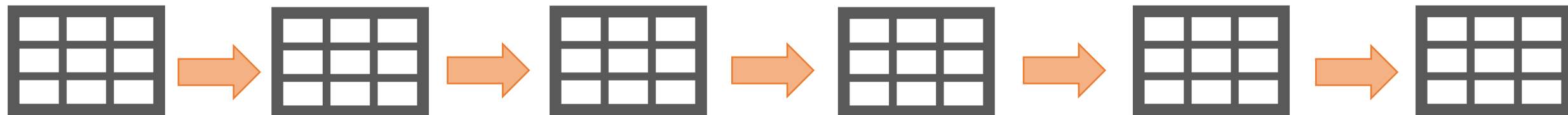
KRIs are calculated by defining a numerator and a denominator for each metric. Then by default, **GSM calculates z-scores using a normal approximation with adjustment for over-dispersion to assign risk levels.**

For KRIs that are percentages (binary outcome), the numerator is the # of events and the denominator is the # of total participants, and we then apply the normal approximation of the binomial distribution to determine a risk level.

For KRIs that are rates (count outcome), the numerator is the # of events and the denominator is the total participant exposure or study duration, and we then apply the normal approximation of the Poisson distribution to determine a risk level.

Red/Amber/Green Flags

Icon	Rule	Thresholds (Z-score)
	= Score exceeds top upper threshold value	Score > 3
	= Score lies between upper and top upper threshold values	$2 > \text{Score} > 3$
	= Score is in between upper and lower threshold values	$-2 > \text{Score} > 2$
	= Score lies between lower and bottom lower threshold values	$-3 > \text{Score} > 2$
	= Score falls below bottom lower threshold value	Score > -3
	= Score/Flag value is null/NA	Insufficient Data to Calculate Score

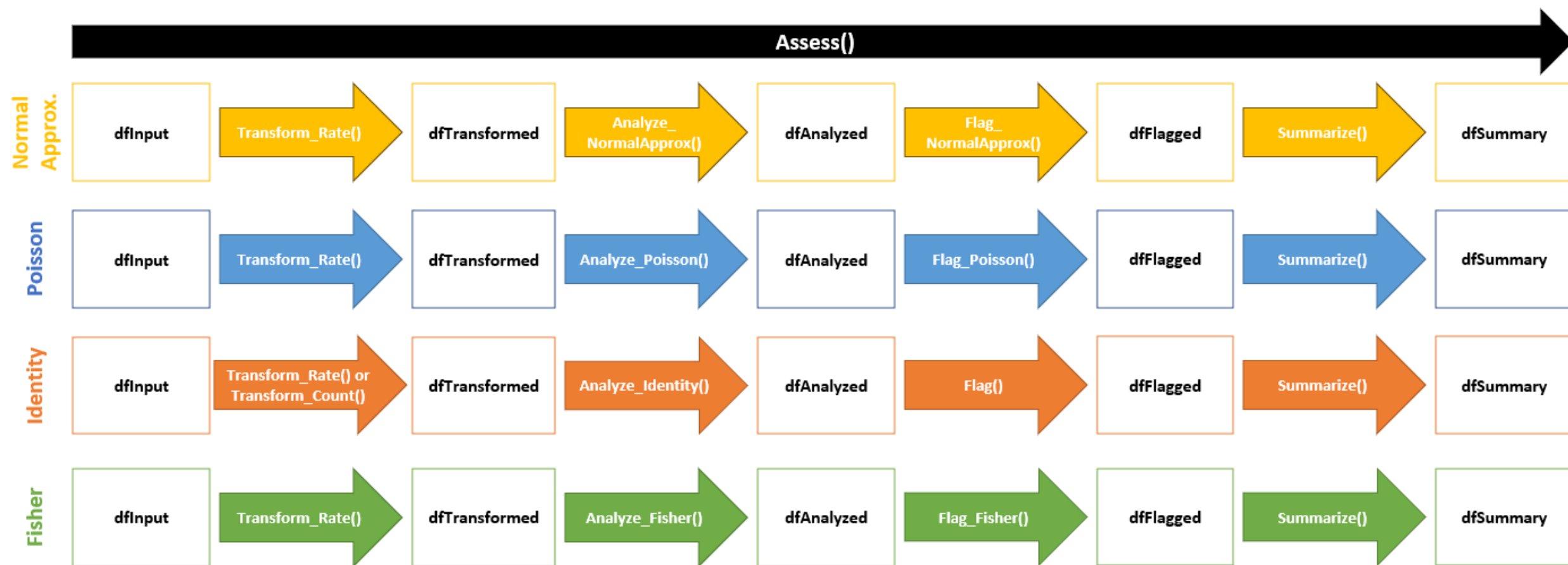
**Raw+** (1gb)Standardized
Study Data**Input** (100kb)Cross-domain
Participant-level data**Transformed**Site-level
derived data**Analyzed**Site-level
analysis results**Flagged**Site-level
with flags**Summary**Site-level
aggregated*Map()**Transform()**Analyze()**Flag()**Summarize()***Custom Mapping**

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

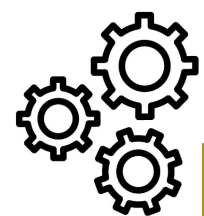
Analytics Modules

- Normal Approximation (Default)
- Entity
- Linear Regression
- Logistic Regression
- ML?!

Link: [Data Pipeline Vignette](#)



* Note that the Normal Approx. analysis method is the default for all KRIs.



Workflow

RunWorkflow()

Assessment Object

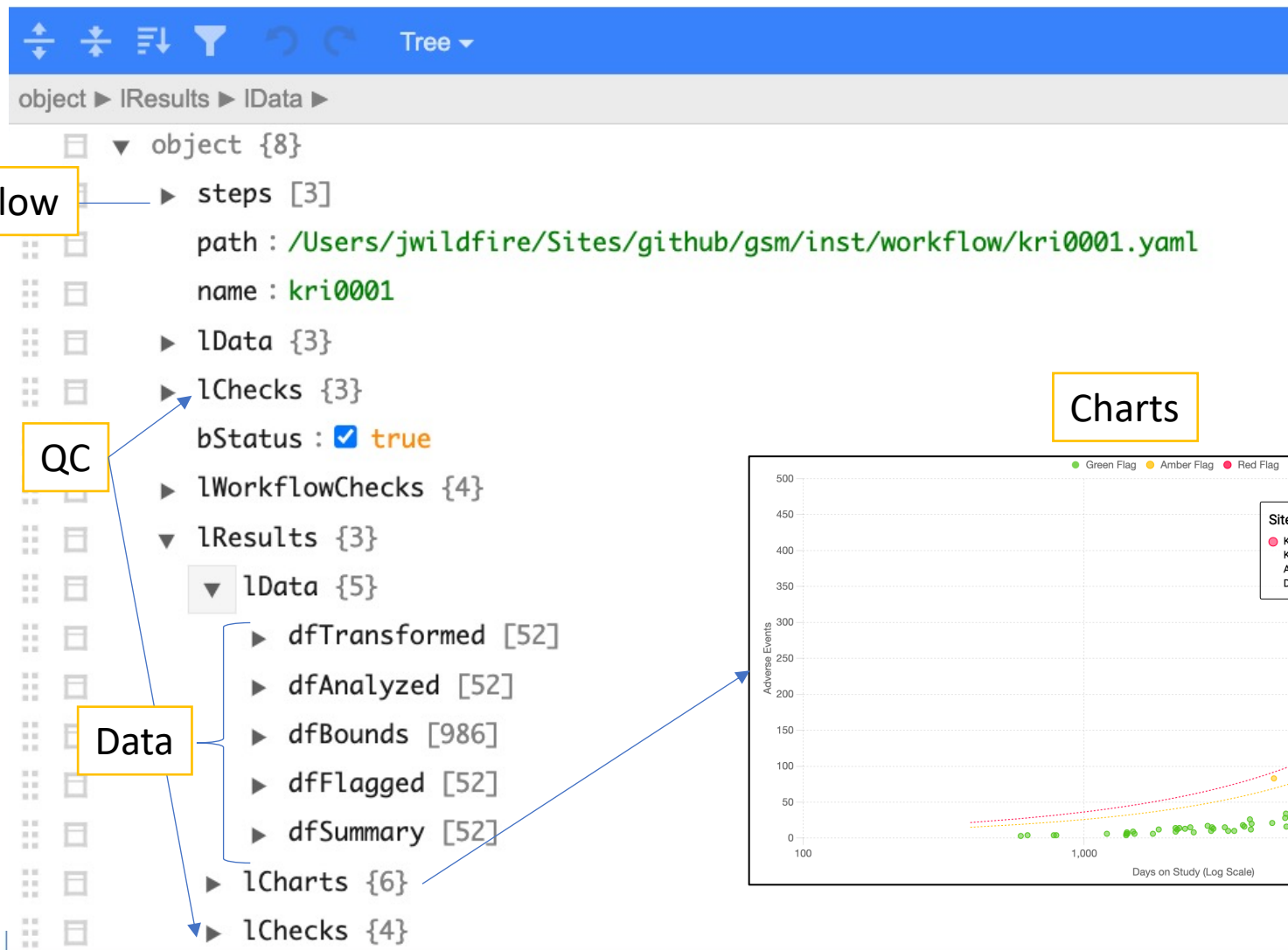
steps:

- name: FilterDomain
inputs: dfSUBJ
output: dfSUBJ
params:
 - strDomain: dfSUBJ
 - strColParam: strEnrollCol
 - strValParam: strEnrollVal
- name: AE_Map_Raw
inputs:
 - dfAE
 - dfSUBJ
output: dfInput
- name: AE_Assess
inputs: dfInput
output: lResults
params:
 - strGroup: "Site"
 - vThreshold: null
 - strMethod: "NormalApprox"
 - nMinDenominator: 30

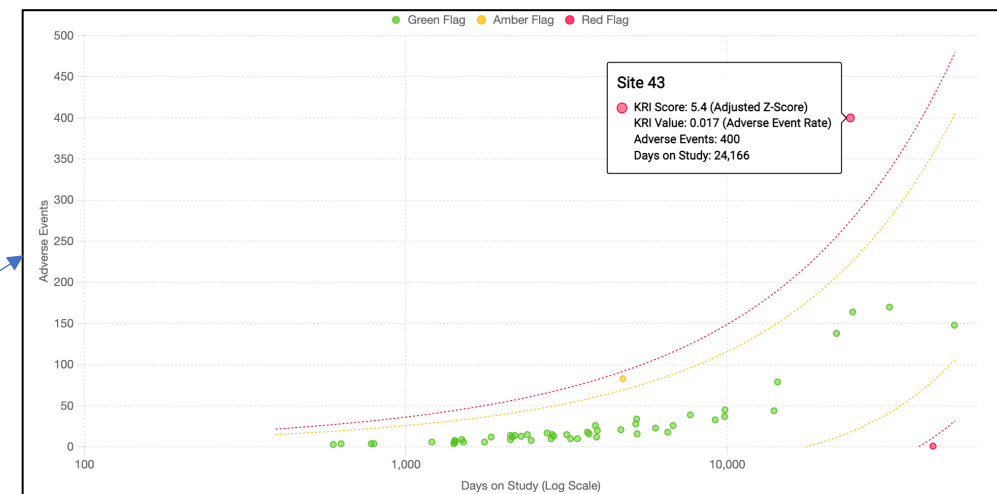
Workflow

QC

Data

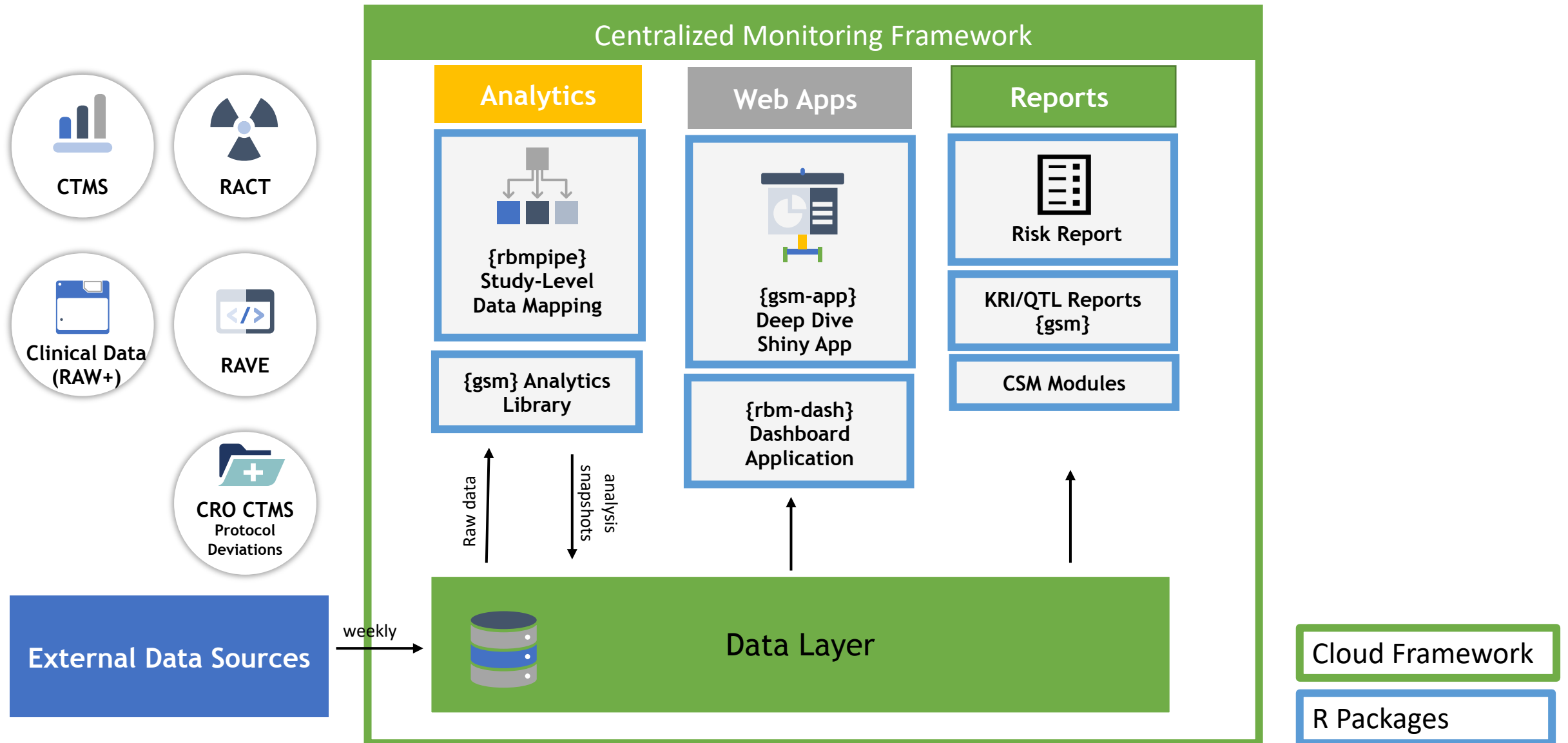


Charts



Link: [Analysis Workflow Vignette](#)

Centralized Monitoring Pipeline @ Gilead



Report Demo - Monthly Study Snapshot

Link: [Sample Report](#)

What is the current KRI profile for the study?

Study Overview

Results

AE Reporting Rate

SAE Reporting Rate

Non-important PD Rate

Important PD Rate

G3+ Lab Abnormality Rate

Study Discontinuation Rate

Treatment Discontinuation Rate

Query Rate

Outstanding Query Rate

Outstanding Data Entry Rate

Data Change Rate

Screen Failure Rate

KRI Glossary

Error Log

Inactive KRI's

AA-AA-000-0000 Assessment Overview

Generated with the Good Statistical Monitoring {gsm} package

Snapshot Date: 2023-11-02

Select Site
None ▾

Study Status

☐ Show Details

Parameter	Value
Unique Study ID	AA-AA-000-0000
Protocol title	Protocol Title
Protocol nickname	Protocol Nickname
Sites (Enrolled / Planned)	176 / 190
Participants (Enrolled / Planned)	1301 / 1300

Study Overview

24 Red KRIs

65 Amber KRIs

Sites Containing

Red ▾

 Flags

16 of 176 sites with at least one red KRI (9.1% of total).

60 of 176 sites with at least one red or amber KRI (34.1% of total).

Site	Country	Status	Subjects	Red KRIs	Amber KRIs	AE	SAE	PD	IPD	LB	SDSC	TDSC	QRY	OQRY	ODAT	CDAT	SF
28	US	Active	5	4	0	✓	⬆	✓	✓	⬆	⬆	⬆	✓	✓	✓	✓	✓
173	US	Active	27	2	1	✓	✓	⬆	⬆	✓	✓	✓	✓	✓	✓	✓	⬇
42	US	Active	22	0	1	⬆	✓	✓	✓	✓	✓	✓	⬇	✓	⬆	✓	✓



App Demo - Deep Dive Application

What are the underlying details for a flagged KRI at a given site?

GSM Deep Dive App

Study Overview Metric Details Site Details Participant Details

2022-03-01

Indication

Protocol Indication

TA

Therapeutic Area

Phase

p3

Sites

190

Subjects

1301

Metric

AE Reporting Rate (Site)

Site

None

Participant

None

Reset All

Overview

20 Red KRIs 40 Amber KRIs

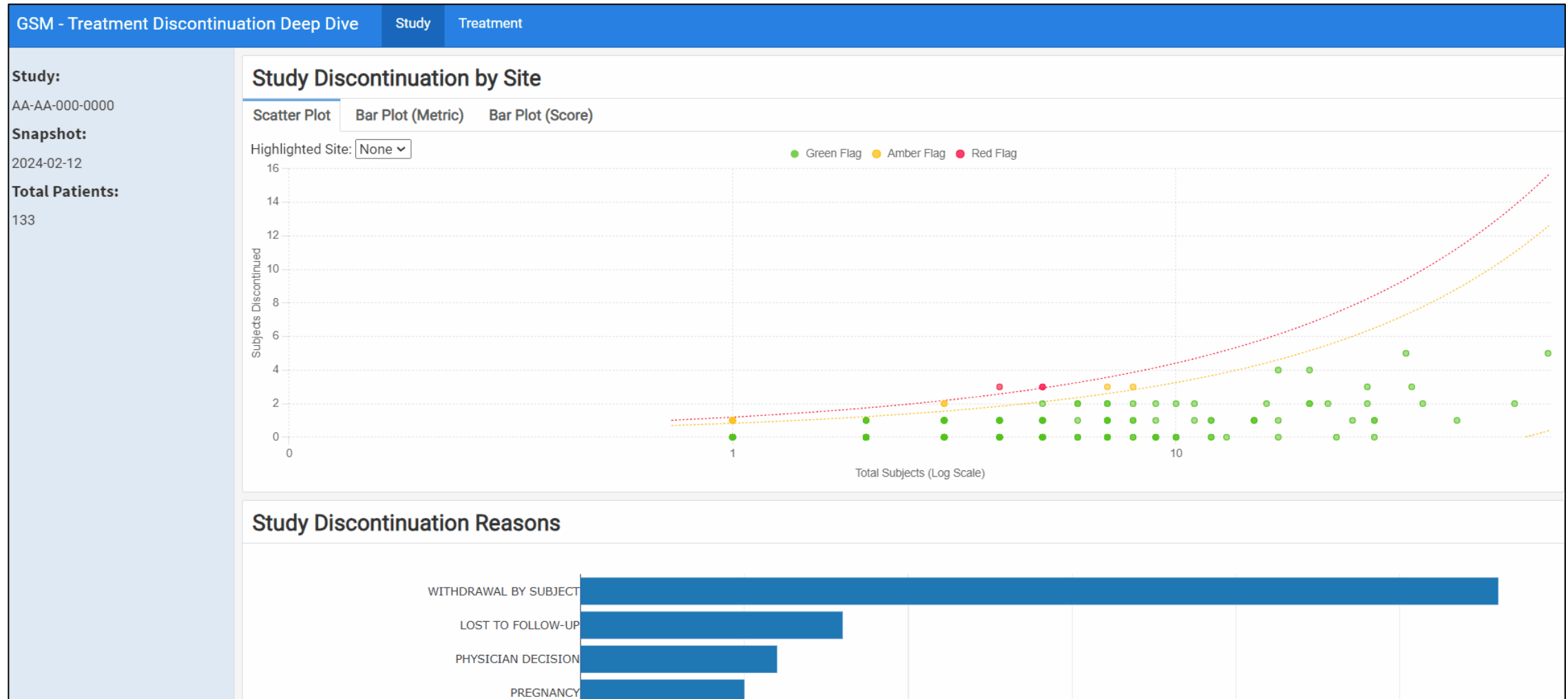
Sites Containing Red Flags

Site	Country	Status	Subjects	Red KRIs	Amber KRIs	AE	SAE	PD	IPD	SDSC	TDSC	OQRY	SF
28	US	Active	5	3	0	✓	⬆	✓	✓	⬆	⬆	✓	✓
173	US	Active	27	2	1	✓	✓	⬆	⬆	✓	✓	✓	⬇
75	China	Active	10	2	1	⬆	✓	⬆	⬆	✓	✓	✓	✓
161	Japan	Active	5	2	0	✓	✓	✓	✓	⬆	⬆	✓	✓
114	US	Active	7	1	1	✓	✓	⬆	⬆	✓	✓	✓	✓
186	US	Active	5	1	1	✓	✓	⬆	⬆	✓	✓	✓	✓
20	US	Active	1	1	1	✓	✓	✓	⬆	—	—	—	⬆
60	US	Active	4	1	1	✓	✓	✓	✓	⬆	⬆	✓	✓
145	US	Active	1	1	0	✓	✓	✓	⬆	—	—	—	✓



Report Demo - KRI Covariate Analysis

How are key covariate distributed for each KRI?





GSM Quality Control Framework

- QC Report Generated on release ([vignette](#))
- 171 Qualification Tests ([vignette](#))
- ~1500 Unit tests
- Contributor Guidelines ([vignette](#))
- Full Code Review via PR
- Release Process w/ Regression Testing ([vignette](#))
- Code Formatting via {styler}
- All implemented via GitHub Actions ([vignette](#))



Qualification Report for the {gsm} R Package

Report Run Date: 2023-11-02

Source: `vignettes/articles/Qualification.Rmd`

Introduction

Risk-Based Quality Monitoring (RBQM) is a proactive approach to clinical trial monitoring that focuses on identifying and addressing the most critical risks to the integrity of study data and patient safety. This approach aims to ensure that study data are accurate, reliable, and credible while optimizing the use of resources and minimizing the burden on study sites.

The `gsm` R package supports RBQM by performing risk assessments primarily focused on detecting differences in quality at the site level. This approach is intended to detect potential issues related to critical data or process(es) across the major risk categories of safety, efficacy, disposition, treatment, and general quality. Each category consists of one or more risk assessment(s). Each risk assessment analyzes the data to flag sites with potential outliers and provides a visualization to help the user understand the issue.

Scope

Qualification testing ensures that core functions execute as expected on a system-wide scale. Qualification includes executing various functional, performance, and usability testing. Qualification tests are designed to provide developers with a repeatable process that is easy to update and document. This document summarizes the qualification testing performed on `gsm` functions essential to the analytics workflow.

Process Overview

Each essential `gsm` workflow function is independently qualified using specifications and test cases compiled in this report. Details are provided below.

Contents

Introduction

Scope

Process Overview

Test Results: Overview

Test Results: Detailed

Unit Tests

Qualification Testing
Environment

Pull Request History

See SM11 for QC Framework details

Overview

`{qcthat}` is a quality control framework for R packages used in Clinical Trials. It has been adopted from the qualification framework used in `{gsm}`.

The benefit of using `{qcthat}` is that you are given a basic scaffold to build out a qualification testing strategy for your R package. This includes:

- A qualification testing folder that lives inside of your `/tests` folder; designed to use with `{testthat}`.
- A basic `.Rmd` report that displays the results of qualification tests.
- A `.github/workflows` folder that includes a templated YAML file, which will automate the creation of a qualification report for every new release of your R package. This can be easily customized to fit your needs.

Read more in the [{qcthat} structure vignette](#).

Contributing

Contributions are welcome! Creating a utility package that is generalizable and extensible to all sorts of repository structures is challenging, and your input is greatly appreciated.

Before submitting a pull request, please ensure it is categorized under one of the following categories:

[{qcthat}](#) is now available as a stand-alone R Package
See Presentation SM11 for QC Framework details

License

[Full license](#)

Apache License (>= 2)

Citation

[Citing qcthat](#)

Developers

Jeremy Wildfire

Author, maintainer

Matt Roumaya

Author 

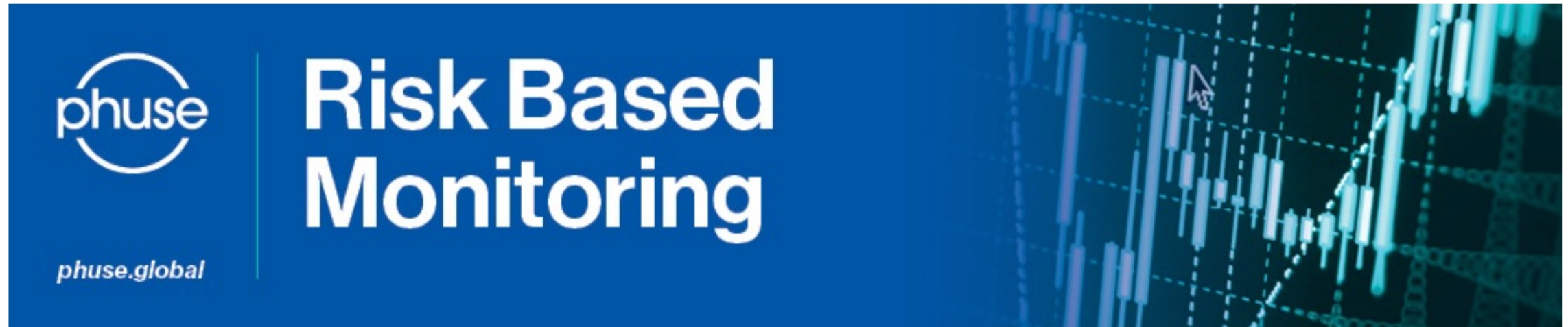
[More about authors...](#)

GSM Timeline @ Gilead

- **Internal Prototype / Proof of Concept**
2020 - Jan 2022
- **Launched "Production" Development Effort**
Jan 2022
- **Fully-Qualified v1.0 Release**
June 2022
- **Deployed Cloud-Based Data-Pipeline**
June 2022 - Mar 2023
- **Live Pilot on 6 studies**
Mar- Sep 2023
- **Open-Source Release**
Aug 2023
- **Live in Business as Usual**
Sep 2023



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.

Open-Source Road Map

- **Upcoming GSM releases**
 - Highlight newly flagged KRIs
 - KRI Distribution Report
 - Expanded QTL Framework
 - Missing Visits/Forms KRIs
 - Expanded QTL Framework
- **Deep Dive Application** - drilldown from Study- to Site- to Subject- details
- **Core CSM / Fraud Detection Framework**
 - Birthday analyses
 - Cluster subjects across/within the sites
 - Multivariate inlier and outliers analyses
 - Digit preference
 - Duplicated records
 - Tests + Visits distribution

Create Phuse RBQM/Open-Source Project for 2024?

Interested in Collaborating?

Contact us directly or sign up [here](#) to receive quarterly updates starting in November.

