

# Development of a Risk-Based Monitoring (RBM) Visualization Application Interface using JMP Scripting Language (JSL)

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Atsumi, living with epilepsy



Inspired by **patients.**  
Driven by **science.**

# Outline

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- **Background**
- **Objectives**
- **Application Interface - KRI Analyzer**
- **Demo**

# Traditional Monitoring Approach

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- ✓ **On-site monitoring**
- ✓ **Implemented by regular site visits**
- ✓ **Costly - multiple sites**
- ✓ **Negligible effect**

# **RBM is a Risk-Based Approach**

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## **Application of Systematic Quality Risk Management to Clinical Trials**

- **Identification of risks**
- **Assessment of the risks represented by KRI**
- **Execution of monitoring and risk-mitigation plan**

# Centralized Monitoring is the Key to RBM

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- ✓ **Centralized monitoring is a remote evaluation carried out by sponsor personnel at a location other than the sites at which the clinical investigation is being conducted.**
  - 1. Provide many of the capabilities of on-site monitoring as well as additional capabilities**
  - 2. Reduce errors**
  - 3. Low cost – minimize the site visits**
  - 4. Helps in early identification and mitigation of data quality risk/issue(s)**

# Guidelines on RBM

The regulatory environment is changing

EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

Reflection paper on risk based quality management in clinical trials

“... Any analysis of trends should be done in relation to the overall impact on the scientific merits and usability of the generated data as established through **priority setting and identification of risks**.



**Guidance for Industry  
(August 2013)**

**Oversight of Clinical Investigations —  
A Risk-Based Approach to Monitoring**

“... certain data anomalies (e.g., fraud, including fabrication of data, and other non-random data distributions) may be more readily detected by **centralized monitoring techniques** than by on-site monitoring.”

ICH Guideline for GCP E6(R2)

Revision of the 1996 GCP Scheduled for Approval in NOV16

**Introduces 3 new significant additions**

**Quality risk management (Based on ICH Q9)  
Oversight**

**Monitoring** :The sponsor should develop a systematic, prioritized, risk-based approach to monitoring clinical trials

- Routine review of submitted data.
- Identification of missing data, inconsistent data, data outliers or unexpected lack of variability and protocol systematic or significant errors in data collection and reporting at a site or across sites, or may be indicative of potential data manipulation or data integrity problems.
- Using statistical analyses to identify data trends within and across sites.
- Analyzing site characteristics and performance metrics.
- Selection of sites and/or processes for targeted on-site monitoring

# **JMP is an Interactive Visualization Tool to Evaluate Clinical Data**

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- ✓ **Provide Interactive Tools to Create and Customize a Variety of Graphs to Explore Data**
- ✓ **Perform Statistical Analysis**
- ✓ **JMP Scripting Language (JSL) Customize, Repackage or Extend JMP Functionalities**
- ✓ **JSL Can Integrate with Powerful SAS, R Capabilities**

# Objectives

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## Use JSL to Create an Application Interface to

- ✓ **Analyze and visualize ongoing data to identify the site at the risk in an efficient manner**
  - **Allow access to the snapshots of multiple studies simultaneously**
  - **Provide an interactive monitoring dashboard allowing for quick glimpse of the status of study sites**
  - **Allow for drilldown to the detailed analysis of individual KRI**

# Risk Assessment

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- ✓ **Risk Identification - Key Risk Indicators**
  - Based on the critical data and critical process
  - **Subject Safety:** Informed consent violation, AE underreporting
  - Data quality: missing primary end point data
- ✓ **Risk analysis**
- ✓ **Risk evaluation**

# Application Interface

## - Study Snapshots Selection

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Key Risk Indicator - Analysis Interface - JMP

### KRI Visualization Tool

Choose study, batch and week

Current study:  Current batch:  Current week:

Reports

Please click a category

- KRI Drill Down
- Dashboard
- Site Profile
- Data Quality & Validity
- Patient Safety
- Site Compliance and Performance
- KRI Documentation

Please pick a button

Drill Downs from Dataset

- OverallRank
- OverallRank Log

Drill Downs from KRI

- Overall Rank Cell Plot

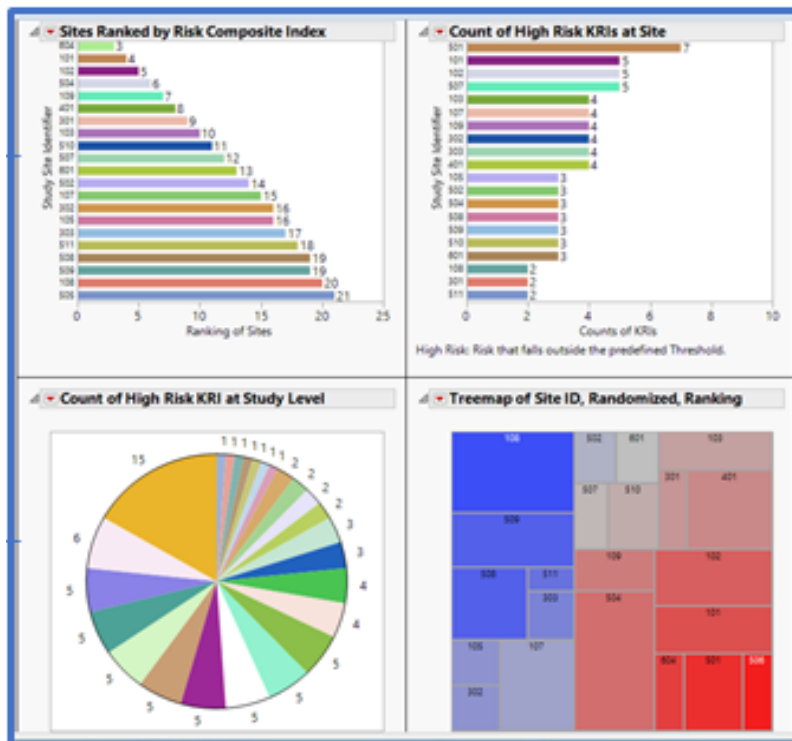
Open KRI Family Based on KRI

- KRI Family
- Close All

Connected to SAS Server "Local".

# Dashboard Monitoring

## - Overview



Click a Button to View

Data Table

Select a KRI, then Click

Launch KRI Analysis

Cancel

Select a Site, then Click

Site Profile

Cancel

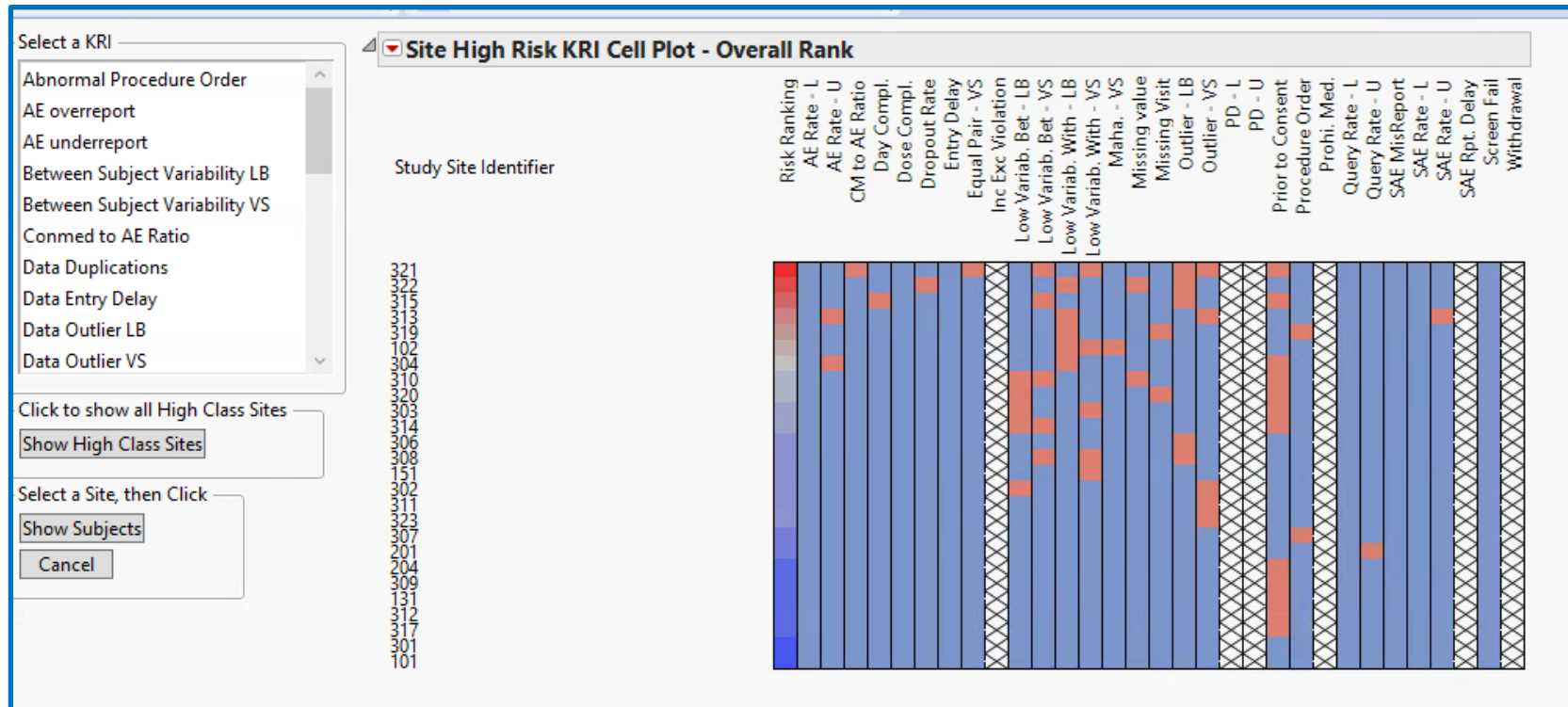
Choose Study Snapshot to Compare

Select a snapshot 201703 Week 2

OK

Cancel

# Cell Plot of Site Risk Rank and KRI Fired



# Dashboard Monitoring

## – KRI Trend

**KRI Trend Analysis**

Select KRI and Site to View KRI over time

Select KRIs

- Adverse Event Rate - High
- Adverse Event Rate - Low
- Between Subjects Variability - FA
- Between Subjects Variability - LB
- Between Subjects Variability - VS
- Conmed to AE Ratio
- Delayed Data Entry
- Dosing Compliance (Admin. Ratio) - I

Select Sites

- 101
- 102
- 103
- 105
- 107

Cast Selected KRIs and Site IDs into Roles

KRI

Site

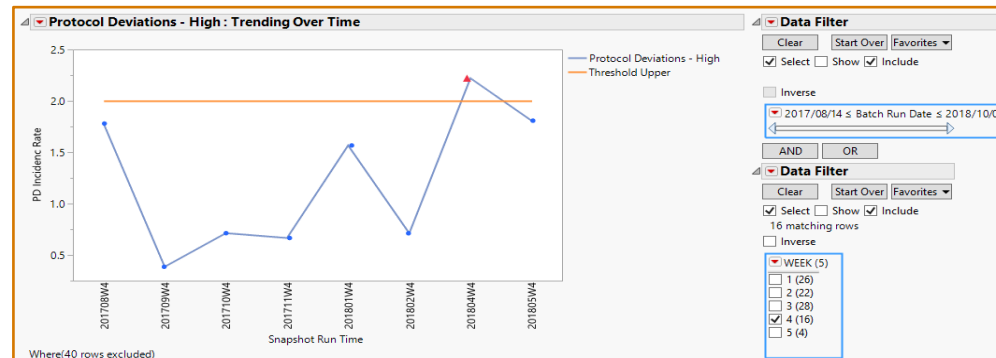
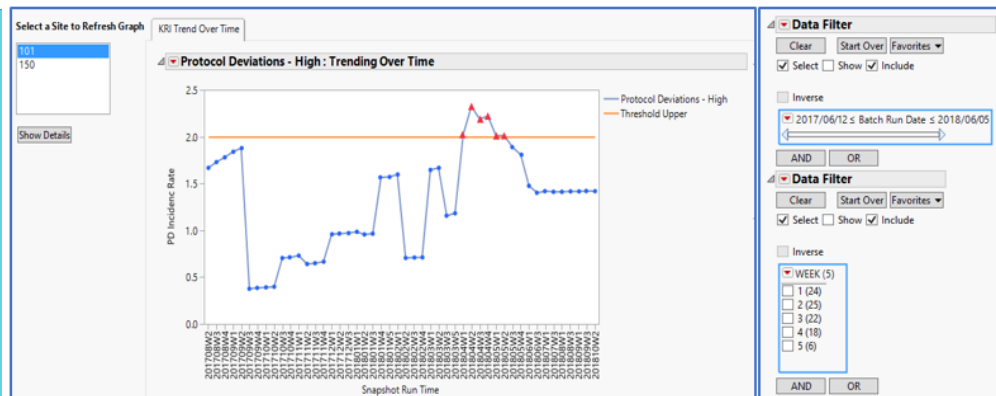
Action

OK

Cancel

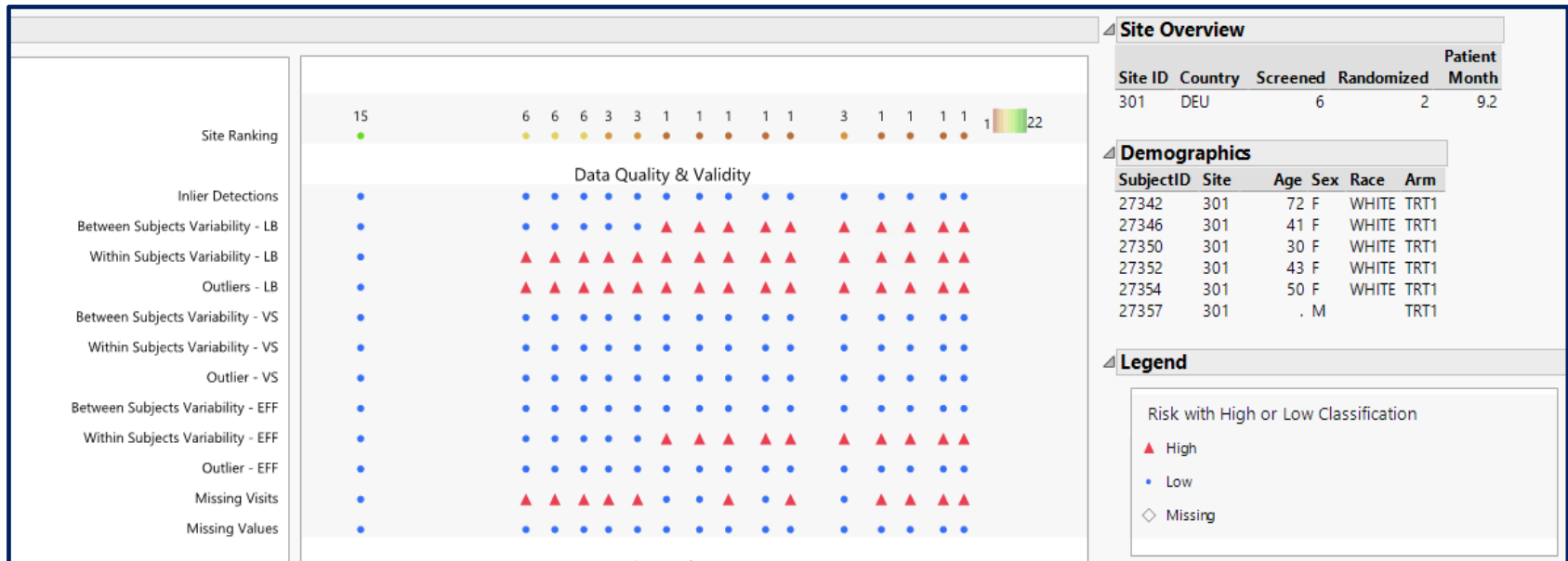
Remove

Help



# Dashboard Monitoring

## - Site Profile



## Classification of KRI over Time

▲ = fired

# Dashboard Monitoring

## – snapshot comparison

Select a Review Flag then Click OK

☐ New  
☐ Modified  
☐ Stable  
☐ Dropped

OK Cancel

Select a Row

Add Comments

Save File

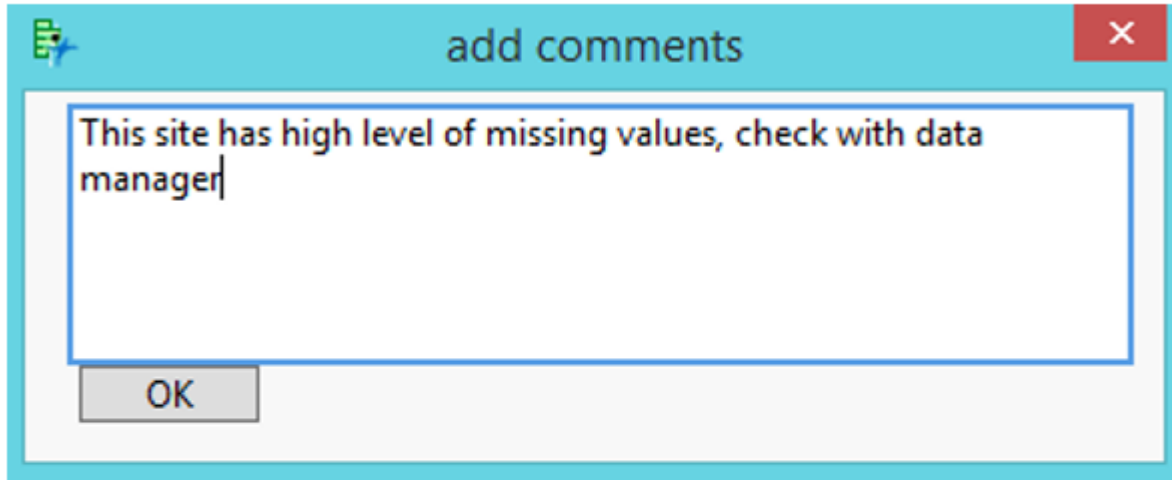
|   | Study | Site ID | Key Risk Indicator | Snapshot Date                      | Previous Deviation Value | Previous Snapshot Date | Review Flag         |
|---|-------|---------|--------------------|------------------------------------|--------------------------|------------------------|---------------------|
| • | 1     | XYZ0001 | 101                | Inclusion/Exclusion Violation      | 2018/09/17               | 5                      | 2017/12/06 Modified |
| • | 2     | XYZ0001 | 101                | Mahalanobis Distance - VS          | •                        | 1.135                  | 2017/12/06 Dropped  |
| • | 3     | XYZ0001 | 101                | Low Variability Betwn. Subj. - LB  | 2018/09/17               | 567.056                | 2017/12/06 Stable   |
| • | 4     | XYZ0001 | 101                | Outlier - FA                       | •                        | 6.871                  | 2017/12/06 Dropped  |
| • | 5     | XYZ0001 | 101                | Outlier - VS                       | 2018/09/17               |                        | • New               |
| • | 6     | XYZ0001 | 101                | Low Variability Within Subj. - EFF | 2018/09/17               |                        | • New               |
| • | 7     | XYZ0001 | 101                | Low Variability Within Subj. - VS  | 2018/09/17               | 11.769                 | 2017/12/06 Modified |
| • | 8     | XYZ0001 | 102                | Dropout Rate                       | 2018/09/17               |                        | • New               |
| • | 9     | XYZ0001 | 102                | Inclusion/Exclusion Violation      | 2018/09/17               | 6                      | 2017/12/06 Stable   |
| • | 10    | XYZ0001 | 102                | Mahalanobis Distance - LB          | 2018/09/17               | 4.254                  | 2017/12/06 Stable   |
| • | 11    | XYZ0001 | 102                | Missing Values                     | 2018/09/17               |                        | • New               |
| • | 12    | XYZ0001 | 102                | SAE Rate - Upper                   | 2018/09/17               |                        | • New               |
| • | 13    | XYZ0001 | 103                | AE Rate - Lower                    | 2018/09/17               |                        | • New               |

**Note:** Red =New Record  
 Yellow = Modified due to a change in KRI ranking  
 Blue = Stable indicating no change in the ranking  
 Green = Dropped

# Dashboard Monitoring

## – snapshot comparison

A.



add comments

This site has high level of missing values, check with data manager

OK

B.

|   | Study   | Site ID | Key Risk Indicator | Review Flag | Notes                                                               | Monitor | Note Date  |
|---|---------|---------|--------------------|-------------|---------------------------------------------------------------------|---------|------------|
| 4 | XYZ0001 | 102     | Missing Values     | New         | This site has high level of missing values, please check with Da... | Wendy S | 2018-11-27 |
| 5 | XYZ0001 | 102     | SAE Rate - Upper   | New         |                                                                     |         |            |

# Analysis of Individual KRI

Key Risk Indicator - Analysis Interface - JMP

## KRI Visualization Tool

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# Analysis of Individual KRI

## Dropout Rate by Site ID

Click to Order by

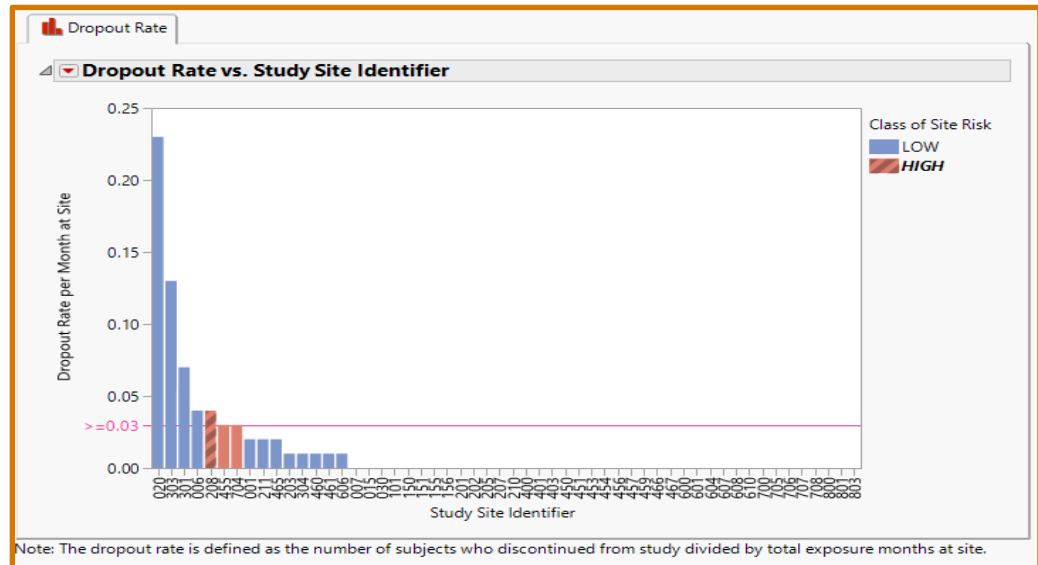
☐ Site ID  
☒ Dropout Rate  
☐ Site Overall Rank

Click a Button to View

Data Table  
 Dropout Rate at Study/Country Level  
 More Dropout Rate Analysis

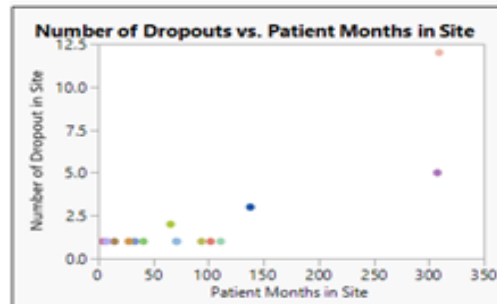
Select a Site then Click

Show Site Ranking  
 View Subjects at Site  
 Cancel Help ?

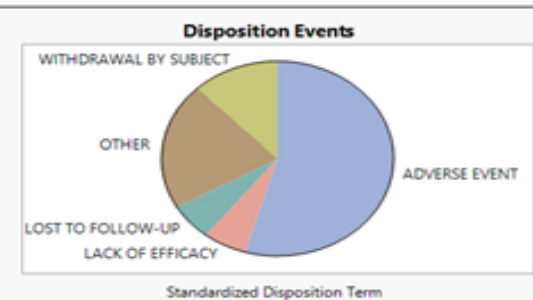


# Dropout Rate Analysis

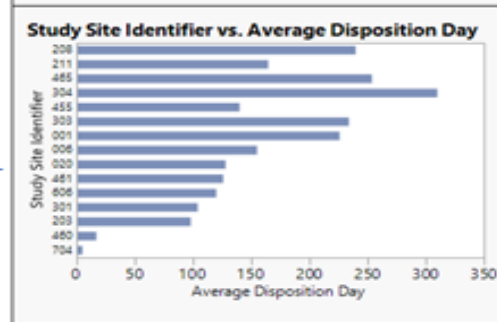
Plot 1



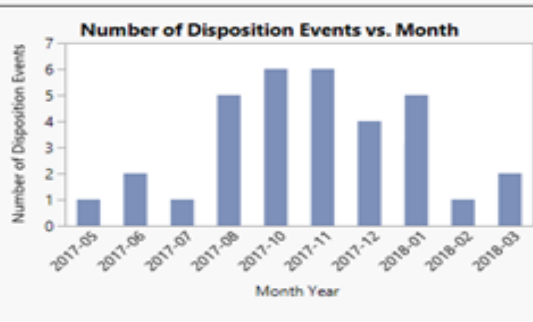
Plot 2



Plot 3



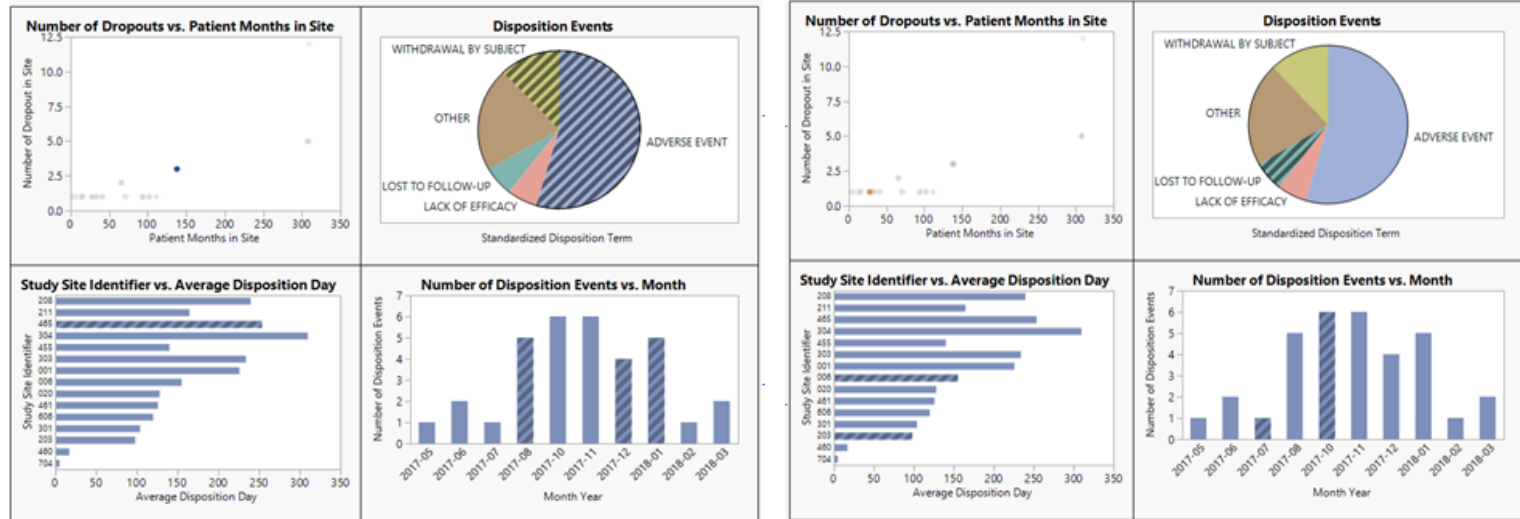
Plot 4



- Plot 1: a scatter plot of Number of Dropouts and Patient Months in Site.
- Plot 2: a pie chart displaying proportions of disposition events (standard terms)
- Plot 3: a bar chart of Average Disposition Day for all sites in the study
- Plot 4: a bar chart of monthly dropouts

# Dropout Rate Analysis

## – Interactive Visualization



- Plot 1: a scatter plot of Number of Dropouts and Patient Months in Site.
- Plot 2: a pie chart displaying proportions of disposition events (standard terms)
- Plot 3: a bar chart of Average Disposition Day for all sites in the study
- Plot 4: a bar chart of monthly dropouts

# Dropout Rate Analysis

## – Subject level data

### Disposition

| Subject Data     |                           |                                  |                       |                   |         |                                    |                                |                                         |                               |                                      |                          |
|------------------|---------------------------|----------------------------------|-----------------------|-------------------|---------|------------------------------------|--------------------------------|-----------------------------------------|-------------------------------|--------------------------------------|--------------------------|
| Study Identifier | Unique Subject Identifier | Subject Identifier for the Study | Study Site Identifier | Investigator Name | Country | Number of Subjects Treated in Site | Category for Disposition Event | Reported Term for the Disposition Event | Standardized Disposition Term | Start Date/Time of Disposition Event | Day of Disposition Event |
| XYZ0001          | XYZ0001-102-0001          | 00001                            | 102                   | Dr. ABC           | CZE     | 6                                  | DISPOSITION EVENT              | ADVERSE EVENT                           | ADVERSE EVENT                 | 2018-01-29                           | 316                      |
| XYZ0001          | XYZ0001-102-0001          | 00002                            | 102                   | Dr. ABC           | CZE     | 6                                  | DISPOSITION EVENT              | ADVERSE EVENT                           | ADVERSE EVENT                 | 2018-07-11                           | 225                      |

## Summary

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- ✓ **A JMP application is developed to enable an customized analysis of KRIs for multiple studies**
  - **Dashboard monitoring**
  - **Drill down to the subject Level**
  - **Interactive and automatic**
  - **Easy-to-use buttons and list boxes to ensure that the analysis of complex KRI data be conducted in an efficient and effective way**

# Thanks!