

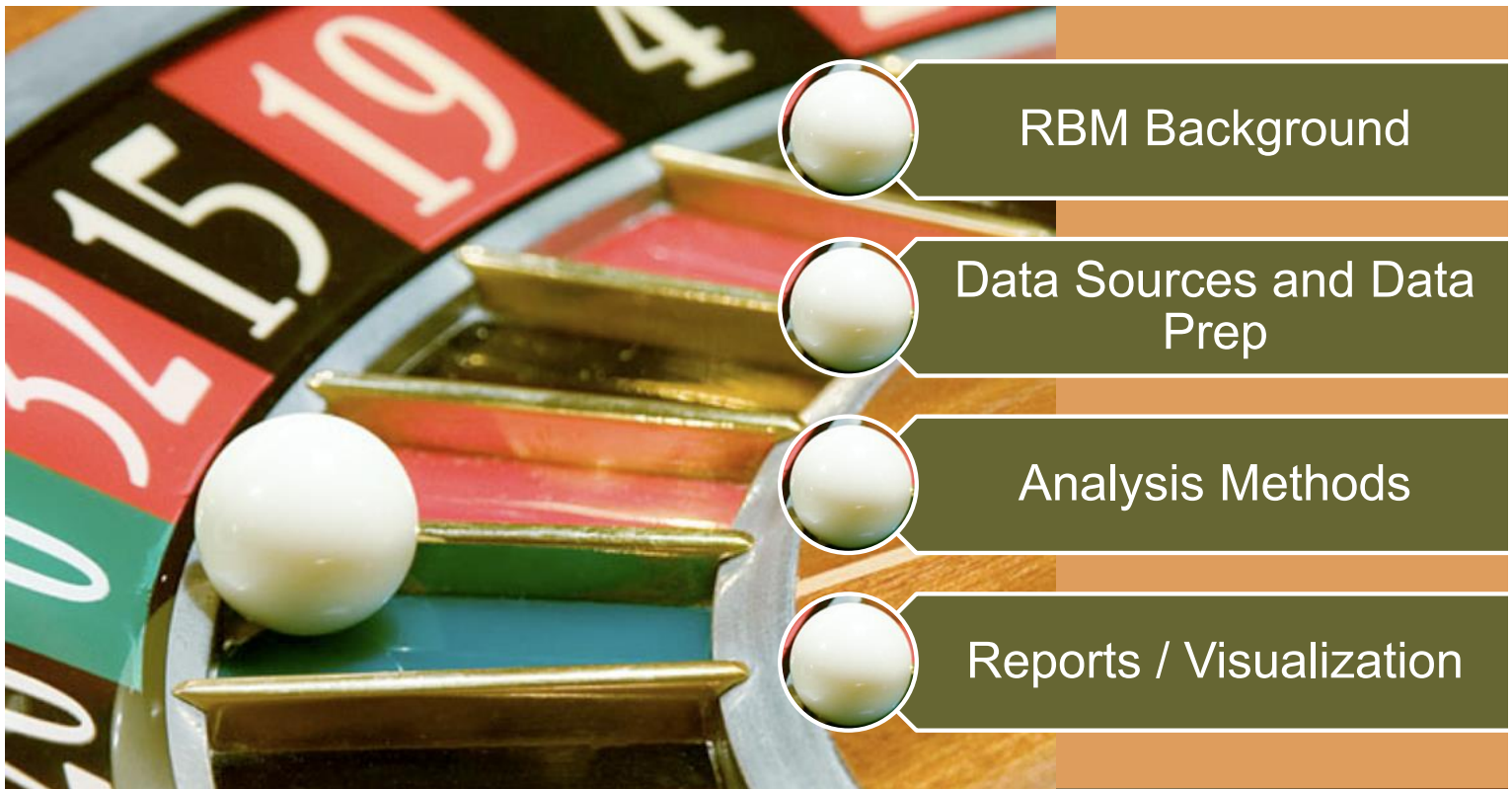
An illustration on a blue background. A hand is shown dropping a white die into a pill container. The die has faces with red dots, a pink face, and two faces with yellow and orange capsules. The pill container is a light blue capsule-shaped container with a green cap, containing three yellow and green capsules and a purple capsule. The title text is overlaid on the container.

MONITORING CLINICAL TRIALS WITH A SAS RISK-BASED APPROACH

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PhUSE 2014, London

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RBM Background

Data Sources and Data
Prep

Analysis Methods

Reports / Visualization

RISK-BASED MONITORING

REGULATORS' RECOMMENDATIONS


EUROPEAN MEDICINES AGENCY
SCIENCE · MEDICINES · HEALTH

18 November 2013
EMA/269919/2013
Compliance and Inspection

Reflection paper on risk based quality management in clinical trials

Draft Agreed by the Clinical Trial Facilitation Group (CTFG) for release for consultation	31 May 2011
Draft Adopted by the Good Clinical Practice (GCP) Inspectors Working Group for consultation	14 June 2011
Start of public consultation	5 August 2011
End of consultation (deadline for comments)	15 February 2012
Agreed by the Clinical Trial Facilitation Group (CTFG) for publication	13 September 2013
Adopted by GCP Inspectors Working Group	12 September 2013

Keywords: Quality Management, Risk Management, Quality Tolerance Limit, Risk Control, Clinical Trial

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2013/11/WC500155491.pdf



EMA

“...**identification of the risks** on a continuous basis for risk-bearing activities **throughout the design, conduct, evaluation and reporting** of clinical trials.”

FDA

...“**consensus that risk-based approaches** to monitoring... are more likely than routine visits to all clinical sites and 100% data verification to **ensure subject protection and overall study quality**.”



Guidance for Industry

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

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
Office of Good Clinical Practice (OGCP)
Office of Regulatory Affairs (ORA)
August 2013
Procedural

OMB Control No. 0910-0733
Expiration Date: 03/31/2016
See additional PRA statement in section VII of this guidance.

<http://www.fda.gov/downloads/Drugs/.../Guidances/UCM269919.pdf>

RISK-BASED MONITORING

THE DRIVERS

Meet regulatory requirement to monitor the progress and conduct of clinical investigations

Optimize traditional on-site monitoring and centralized monitoring

Leverage technology to assess risk related to a study

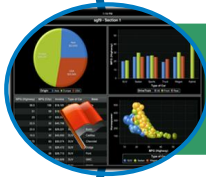
Maintain patient safety and study integrity

SAS RISK-BASED MONITORING

SAS APPROACH



Acquire and Prepare Data



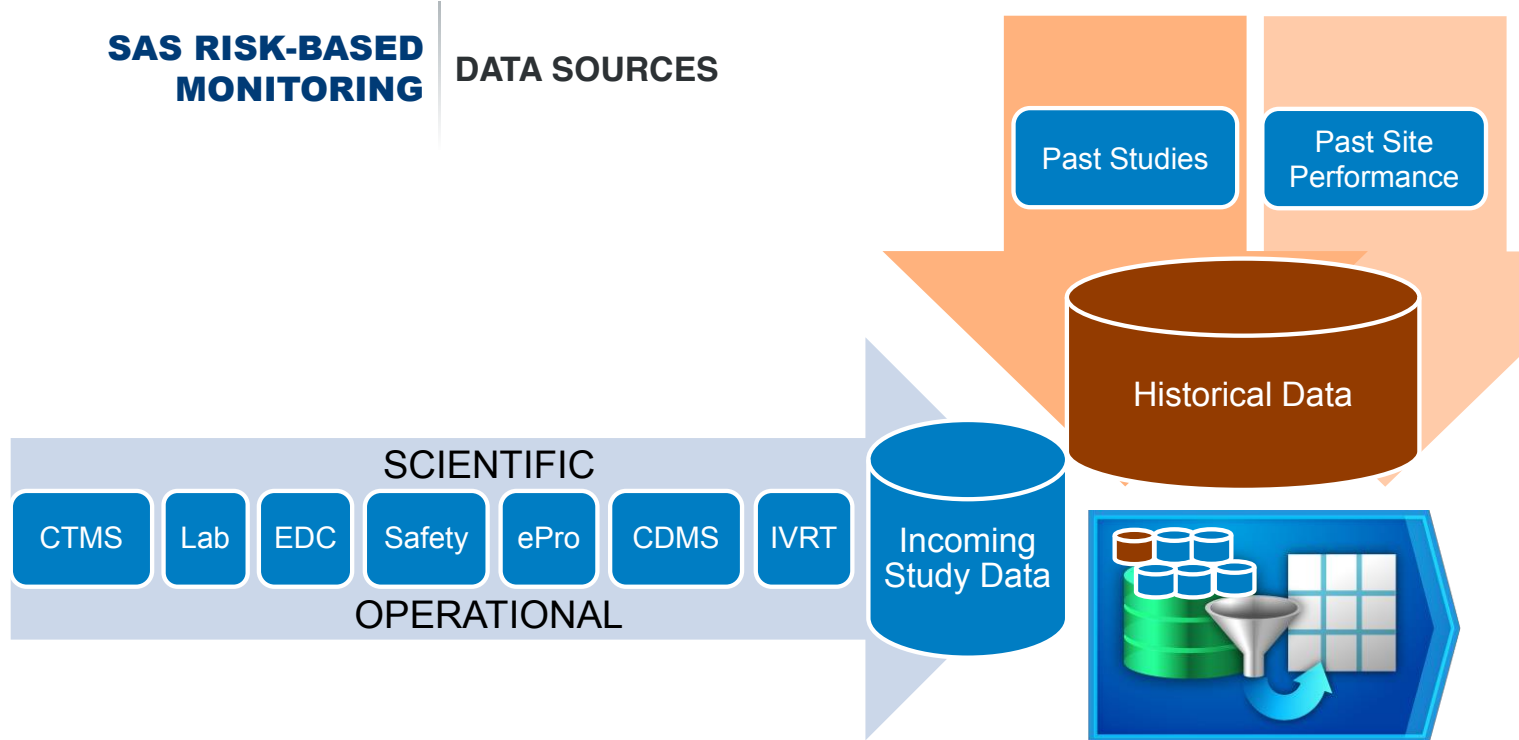
Assess Risk



Report / Visualize

SAS RISK-BASED MONITORING

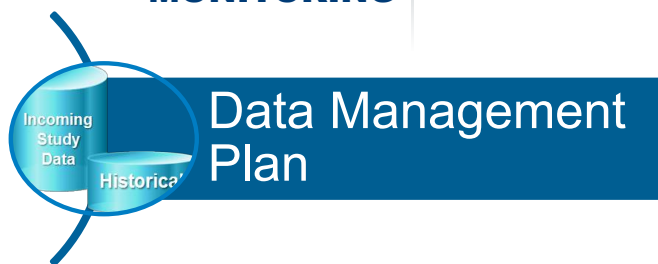
DATA SOURCES



PREPARE FOR INSIGHT

SAS RISK-BASED MONITORING

PREPARE FOR INSIGHT

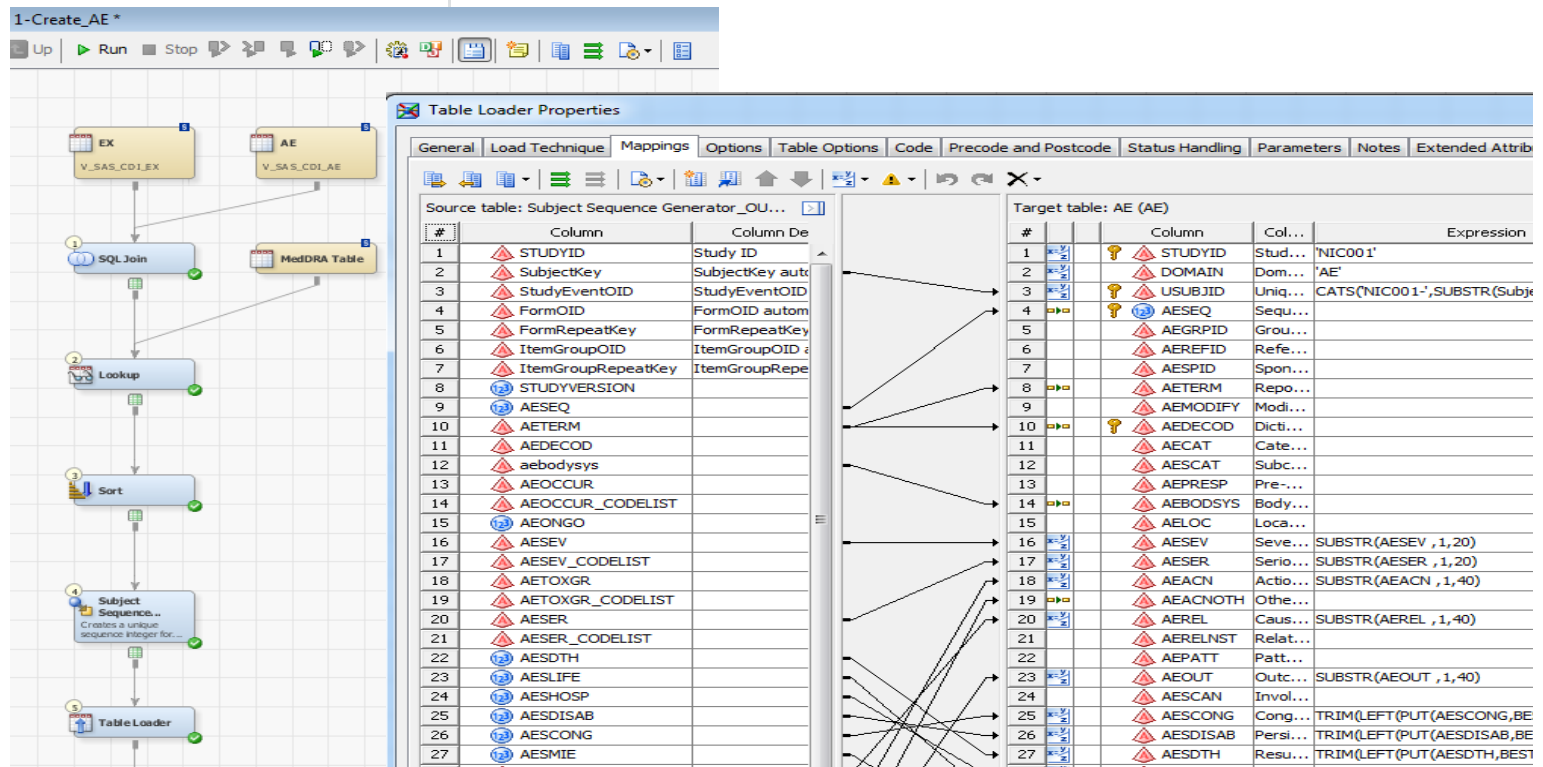


- Data collection procedures
- Edit checks and validations
- Update frequency
- Project scope
- How much data?



- **Automate Collection & Refresh**
 - Filter sources to determine appropriate data elements
- **Aggregate and Filter**
 - Integrate clinical and operational data from past studies with current data
- **Standardize Data – CDISC**
- **Reconcile Sources**
- **Create Profiles**
 - Geography, Sites, Subjects

ADD DATA SOURCED FROM EDC



**SAS RISK-BASED
MONITORING**

ASSESS RISK / MONITOR PERFORMANCE & QUALITY



Risk Analysis



SAS RISK-BASED MONITORING

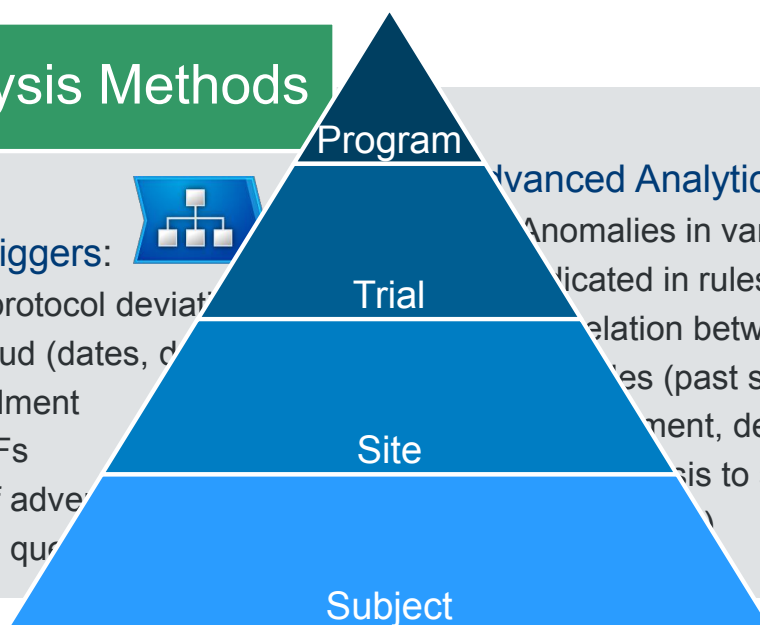
HYBRID ANALYTICS



Analysis Methods

Rule Based Triggers:

- Number of protocol deviations
- Potential fraud (dates, dates)
- Target enrollment
- Missing CRFs
- Incidence of adverse events
- Outstanding queries



Advanced Analytical Triggers:

- Anomalies in variables NOT included in rules
- Correlation between multiple variables (past screening errors, rate of enrollment, demographics)
- Analysis to spot variability (visit dates, etc.)



UNDERSTANDING THE ANALYSIS



Report / Visualize



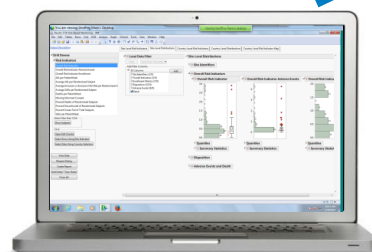
Geocoded
Maps

Dashboards

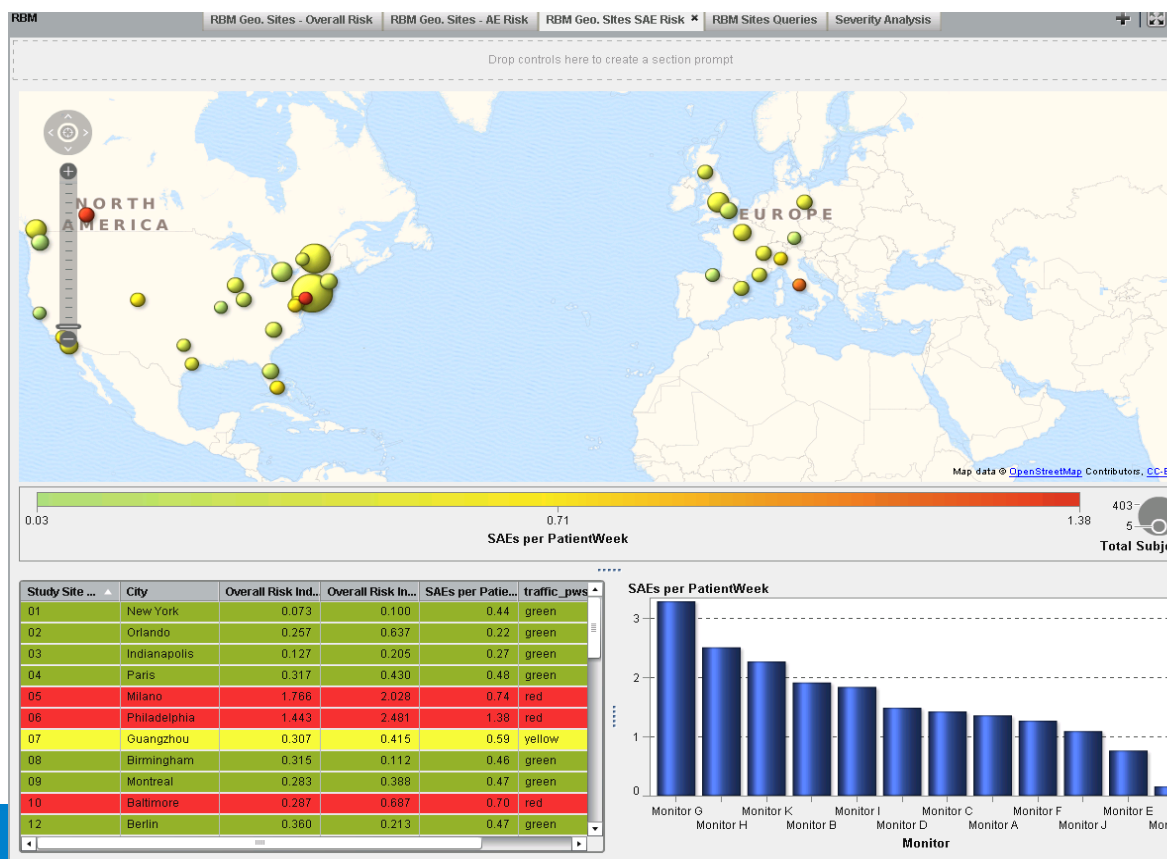
Tables &
Listings

Cross Tabs

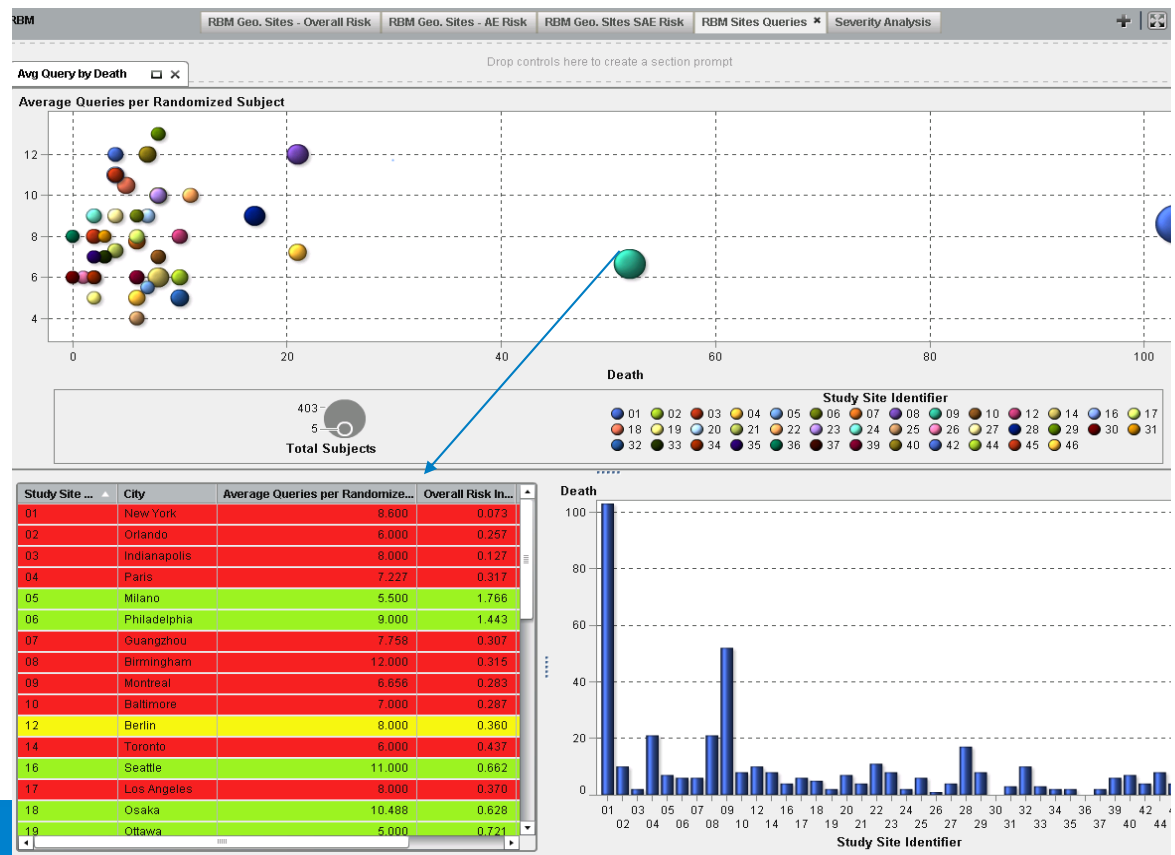
Charts &
Plots



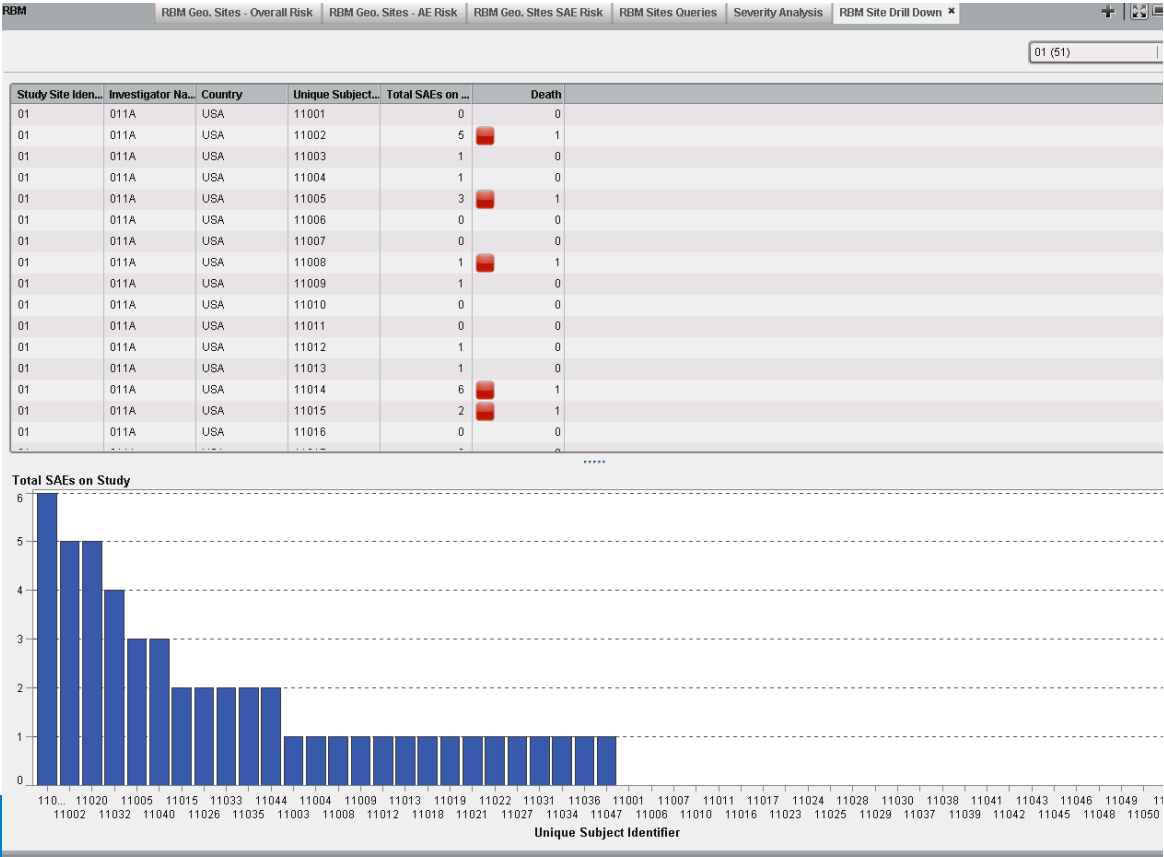
- SAE Risk
- Distribution of AEs by Monitor



- Average Queries
- Deaths by Study Identifier



- Study Identifier Details



JMP CLINICAL RBM AND FRAUD

The screenshot displays the JMP Clinical software interface, specifically the 'Clinical Starter - JMP' window. The 'Current Study' is set to 'Nicardipine'. The 'Analytical Process' panel on the left shows a list of categories, with 'Quality and Fraud' selected. The 'Reports' panel on the right shows a list of subcategories, with 'Risk Based Monitoring' and 'Fraud Detection' selected. The 'Click a Button' section contains several buttons for various functions.

Current Study: Nicardipine

Reports

Click a Category: ?

Click a Subcategory: ?

Click a Button: ?

Studies

Risk Based Monitoring

Fraud Detection

Analytical Process

Click a Category: ?

Click a Subcategory: ?

Click a Button: ?

Studies

Workflows

Demographics

Study Visits

Interventions

Events

Findings

Standard Reports

Subject Utilities

Quality and Fraud

Risk Based Monitoring

Update Study Risk Data Set

Define Risk Weight Data Set

Manage Risk Weight Data Sets

Map Geocoding Help

Birthdays and Initials

Cluster Subjects Across Study Sites

Weekdays and Holidays

Perfect Scheduled Attendance

Constant Findings

Duplicate Records

Digit Preference

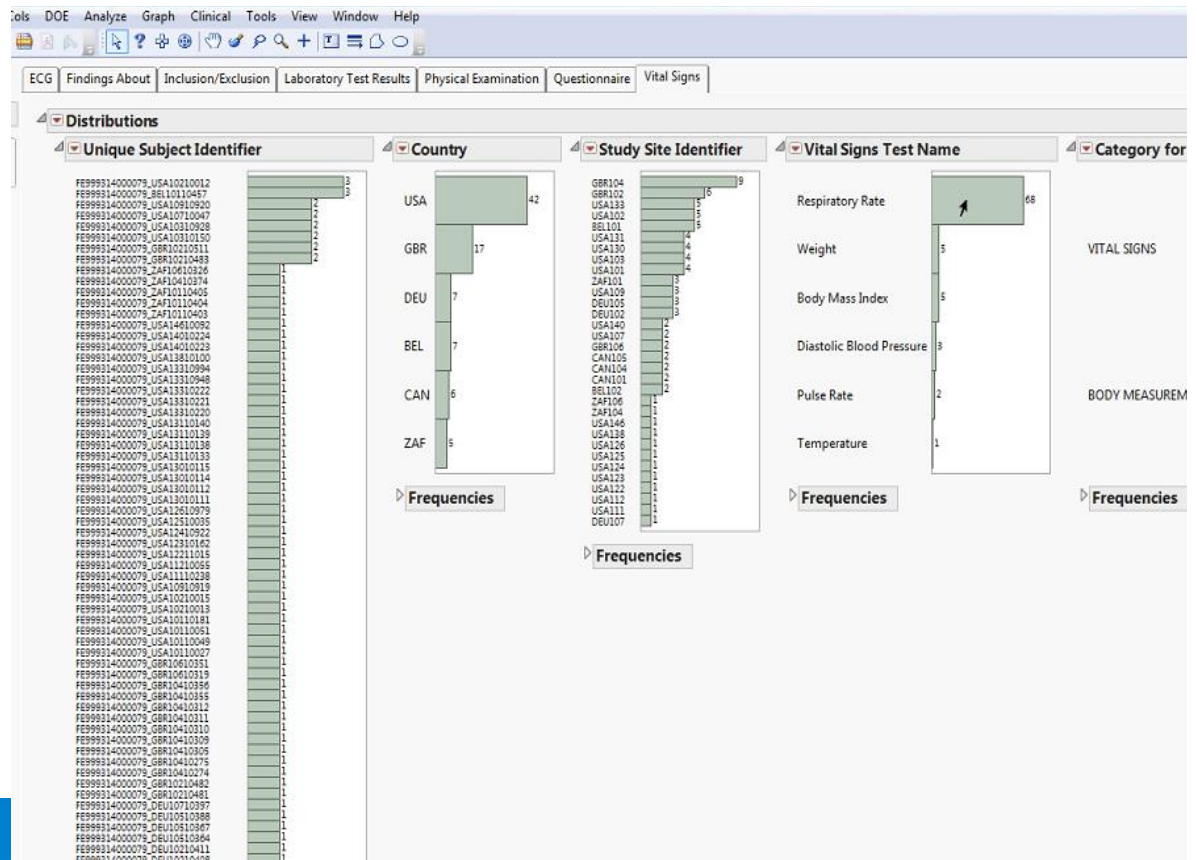
Multivariate Inliers and Outliers

Cluster Subjects Within Study Sites

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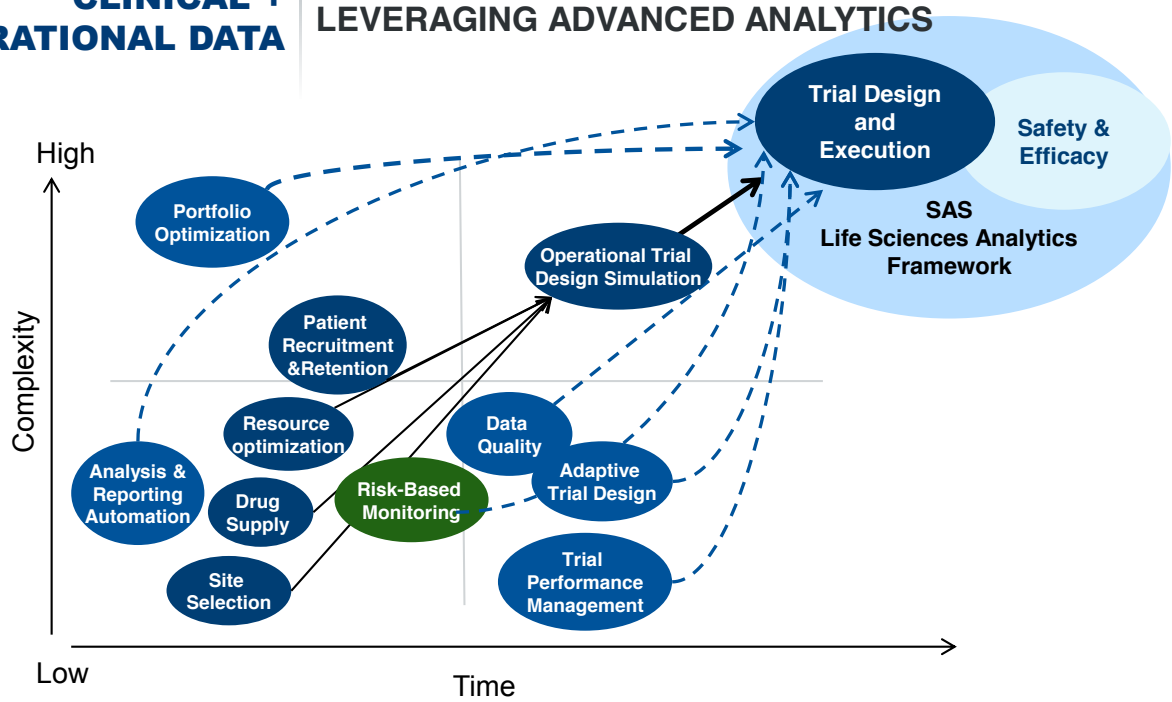
sas THE POWER TO KNOW.

- Subject Level Vitals



**CLINICAL +
OPERATIONAL DATA**

LEVERAGING ADVANCED ANALYTICS



QUESTIONS AND COMMENTS



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