Risk Based Management with SAS® Visual Analytics

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ABSTRACT

Risk based monitoring is an approach defined by regulatory services which not only helps in oversight of clinical trial to ensure efficient conduction of trial.

It not only prevents the risks to data quality, subject safety etc. but also tracks the progress of the study as per the plan. SAS® Visual Analytics plays a vital role in generating graphs and figures for monitoring the data and easily identifying the area of concern.

In this paper, we will discuss how SAS® Visual Analytics can help us generate the major key performance Indicators like Subject enrolment, data quality and management, subject safety and compliance etc. easily to perform central monitoring.

INTRODUCTION

Risk Based Monitoring is one of the responsibilities of effective monitoring of clinical trials. Clinical trials are required to provide an oversight to ensure quality of data and safety of the subjects. It focuses on the oversight activities on preventing or mitigating important and likely risks to data quality and to processes critical to human subject protection. During the past two-three decades the complexity of trials has accelerated. The standards of health care have increased and the population is more graphically dispersed with high variability of infrastructure and treatment choices. To handle all the variant factors centralized monitoring has played an important role in ensuring data quality, tracking trial progress and checking human safety There are a wide range of Key Performance Indicators (KPIs) covered by Risk Based Monitoring categories. . In this paper we will be generating various reports quickly via SAS® Visual Analytics to analyze those metrics. Following are few major categories'

- Site Performance
- Subject Enrolment
- Study Progression
- Safety Profile

1. SITE PERFORMANCE

This involves monitoring the site for its quality data (e.g. Duplicate records, incorrect entries) and missing data. Evaluating the Issues reported by On-site monitoring helps in tracking the progress and provides a sense of quality of overall conduct. Below are some Performance Indicators to help evaluate site performance.

1.1 QUERIES

It covers the number of queries entered to resolve the data issues raised for every site. Example includes

- ➢ Missing data
- ➢ Incorrect data
- ➢ Data out of standard range
- ➢ Data Inconsistency
- ➢ Unusual Data distribution between Study Sites

A centralized monitor should evaluate at least the following matrices with Queries:

1.1.1 NUMBER OF QUERIES IN A STUDY

It indicates the total count of data errors encountered within a study. It helps in reflecting the data quality of a study. A high quality data is always helpful in easy monitoring and tracking. In case the data quality is low it makes the study analysis very difficult and may give incorrect outcome.

1.1.2 NUMBER OF QUERIES PER SITE

Count of data errors for each site helps in comparing the site performance in terms of data quality. Better quality always supports the accuracy of study outcome.

1.1.3 NUMBER OF QUERIES BY TIME

Count of data errors by time helps in identifying the issues associated with a specific phase or CRF. The number of issues may arise if a specific Epoch or CRF of the study is complex.

1.1.4 NUMBER OF QUERIES BY CATEGORY

It helps in drilling down the major cause of data errors.

1.1.5 NUMBER OF QUERIES BY STATUS

It indicates the number of closed and open data errors and need immediate attention.

1.1.6 TIME OF QUERIES RESOLUTION

It presents the average turnaround time of a site to resolve the open errors.

1.1.7 NUMBER OF QUERIES REOPENED

It gives the number of queries reopened due to incorrect resolution.it indicates the accuracy of a site in closing the data errors.

1.1.8 LISTING OF QUERIES

List of data errors helps in analyzing the details to take corrective measures.

Higher number of queries may indicate significant error in data collection and reporting at a site. Display 1 shows two line graphs showing the type of data errors (query types) raised for each site and number of queries open and closed by time (month).These help in tracking the data error type and phase of the study impacted. Similarly the bar chart showing the current status of queries makes it easy for the monitors to follow up on the open queries and evaluate the performance.
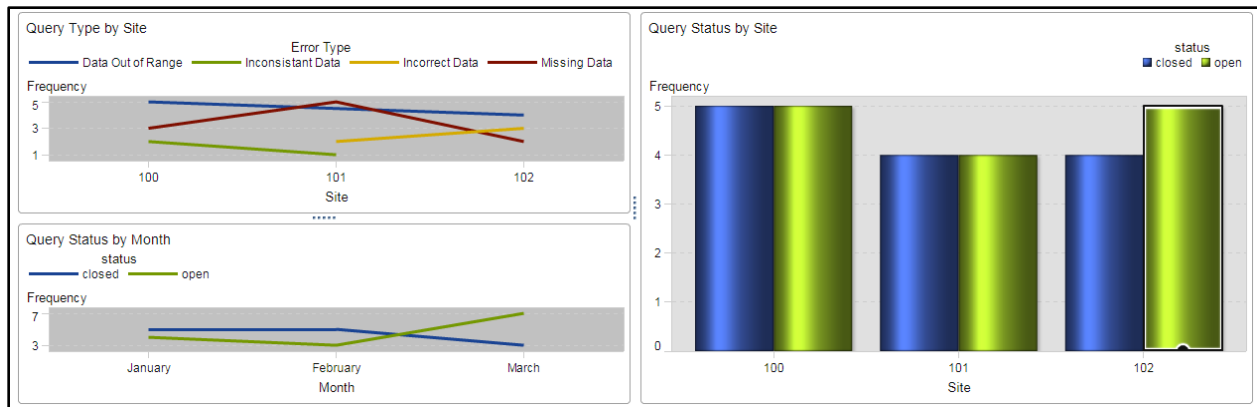
Display 1. Reports to analyze Queries.

1.2 SITE ISSUES

It evaluates the issues encountered in site procedure like flaw in equipment, documentation, approvals, missed training, incompliance with study protocol. Once the data is collected it is analyzed to see how sites are performing for a study. High number of issues can be threatening to the clinical trial and may lead to a demand of On-site monitoring or clarification of protocol processes. Following are few important performance indicators of site issues.

1.2.1   NUMBER OF ISSUES REPORTED IN STUDY
It indicates the total count of issues encountered within a study. It helps in reflecting the execution status of a study.

1.2.2   NUMBER OF ISSUES REPORTED PER SITE
Count of issues for each site helps in comparing the site performance in terms of trial procedures.

1.2.3   NUMBER OF ISSUES REPORTED PER TIME
It explains the number of issues by a time period such as month. It may indicate an external factor like weather impacting the study procedures and help sponsor to plan accordingly.

1.2.4   NUMBER OF ISSUES REPORTED PER CATEGORY
It gives the count by the type of issues. This helps in identifying the risk associated with the study procedures of specific phase and its impact.

1.2.5   NUMBER OF ISSUES REPORTED PER STATUS
Count of issues open and closed gives a clear state of Trial.

1.2.6   TIME OF ISSUES RESOLUTION.
This states the average time to resolve issues per site.

1.2.7   NUMBER OF ISSUES REOPENED.
It indicates the count of issues reopened, showing the accuracy of actions taken by sites. The list of issues facilitates the monitoring committee to get to the details of the issue.

These indicators help to monitor the total number of issues in a study, comparing sites, identifying the risk associated with the study procedures of specific phase and its impact on subject safety and integrity of trial. Display 2 shows a pie chart representing the number of open, reopen, and closed by study ad bar graphs further segregating these by month and site for detailed monitoring. The Line chart shows the average time taken by sites to resolves
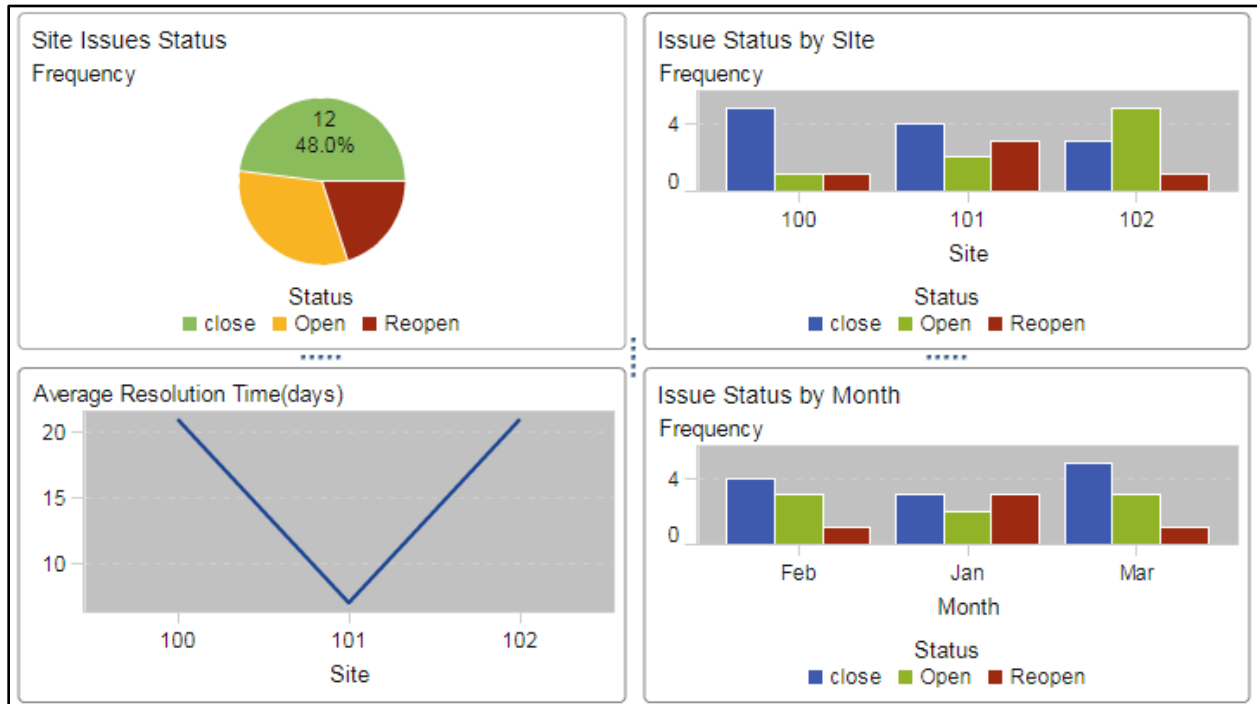
Display 2 Graphs presenting Issue with different dimensions.

2   SUBJECT ENROLMENT

Enrolment of subjects in a study is a critical process. This needs to be thoroughly monitored; efficacious enrolment of subjects is a major achievement in the success of clinical trial.

2.1 SCREENING RATIO

It states the number of subjects planned to screen to number of subjects screened. This ratio is calculated for a study, drilling down to its region and sites.

2.2 RANDOMIZATION RATIO

It states the number of subjects planned to be randomized to number of subjects randomized. This ratio is calculated for a study, drilling down to its region and sites.

2.3 NUMBER OF SCREEN FAILURES

It states the count of subjects screen failed. This report helps in determining the probability of enrolment failure.

2.4 NUMBER OF DISPOSITION BY REASON.

It states count of subjects discontinued by the reason of discontinuation. It helps to evaluate the factors forcing subjects to discontinue the study without completion.

2.5 NUMBER OF ELIGIBILITY VIOLATIONS

It shows the count of violations to entry criteria; highlights the issues with the enrolment procedures.

Display 3 shows the randomization ratio by site. It explains the uniformity of assignment of subjects to different treatment arms to ensure the integrity of randomization at site level.
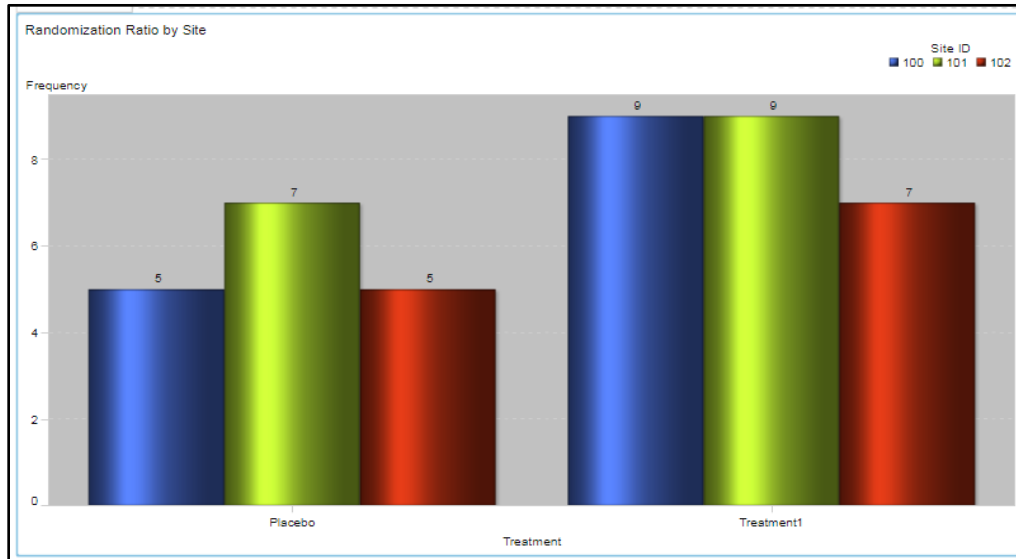
Display 3. Bar Chart with Site level Randomization Ratio

Display 4 shows the enrollment count by region. This chart easily identifies the zip codes and then provides a pictorial view of the regions where the enrolment is high.
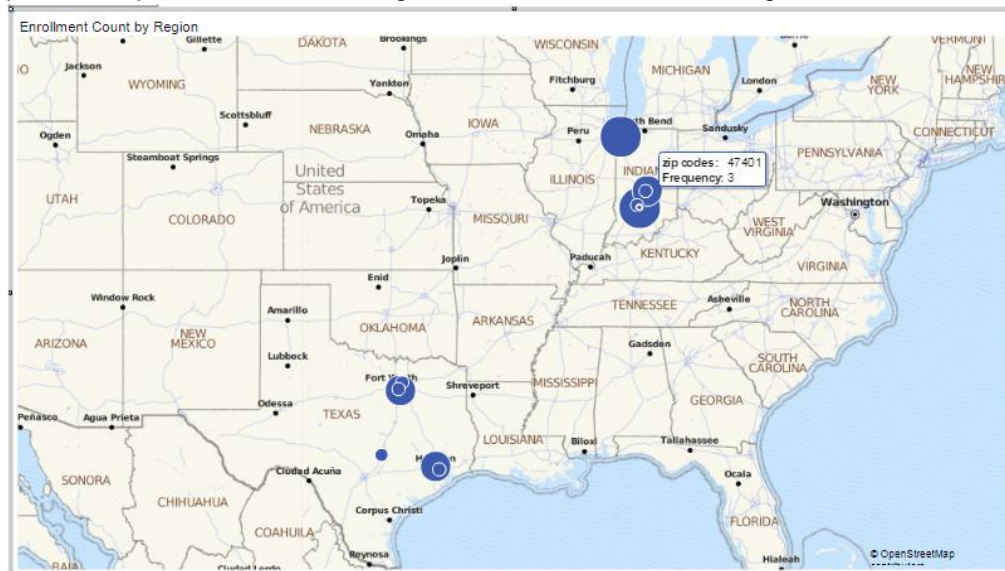
Display 4. Geo Bubble Map showing Enrolment count by zip code

3   STUDY PROGRESSION

Study progression involves tracking the progress of the study as per the Investigation plan. Investigation plan is an inseparable part of study and needs to be followed at each site. Every study has planned dates, protocol approval, enrolment, screening, start of treatment and so on. Tracking the actual events to planned dates monitors the overall progress of the study. Following are the major report used in monitoring study progression.

3.1 PLANNED TO ACTUAL VISIT RATIO
Comparison of counts between the planned and actual visits tracks the progress of the investigation plan.

3.2 FORECASTING VISITS
Forecasting the visits based on the actual visits and investigation plan helps site foresee the upcoming visits and study progress.

3.3 NUMBER OF VISITS BY MONTH
It gives the count of monthly visits, this report can be analyzed at both study and site level. It helps to track the budget and other requirements of the study by the sites. It also ensures that the trial is progressing as planned.

3.4 TIME TO STUDY END POINTS (MILESTONES)
Comparing the study end points with their planned date ensure the study progression is on course.

3.5 SUBJECT PROGRESSION
The number of patients in each epoch defines the progress of study as per the investigation plan.

3.6 COMPLIANCE RATIO
This report shows the percentage of study compliance and non-compliance cases. These can be further drilled down to violations within each epoch of the study.

Display 5. is a bar chart stating the compliance ratio in all three epochs of trial..
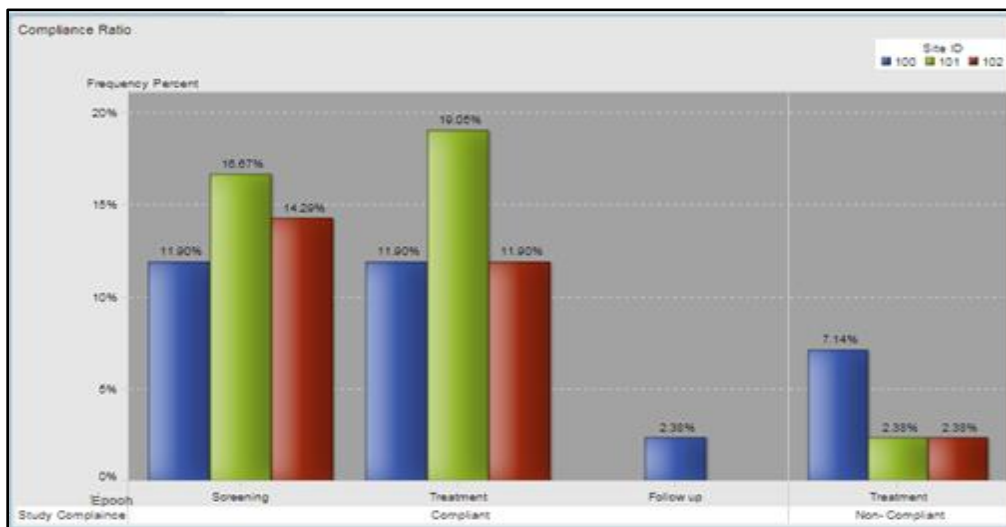

Display 5. Bar chart explains study compliance within epochs by each site.

Display 6 The bar Graph shows the number of actual visits by site within each month. The visit numbers are directly tagged to study epochs hence gives a view of study progress.
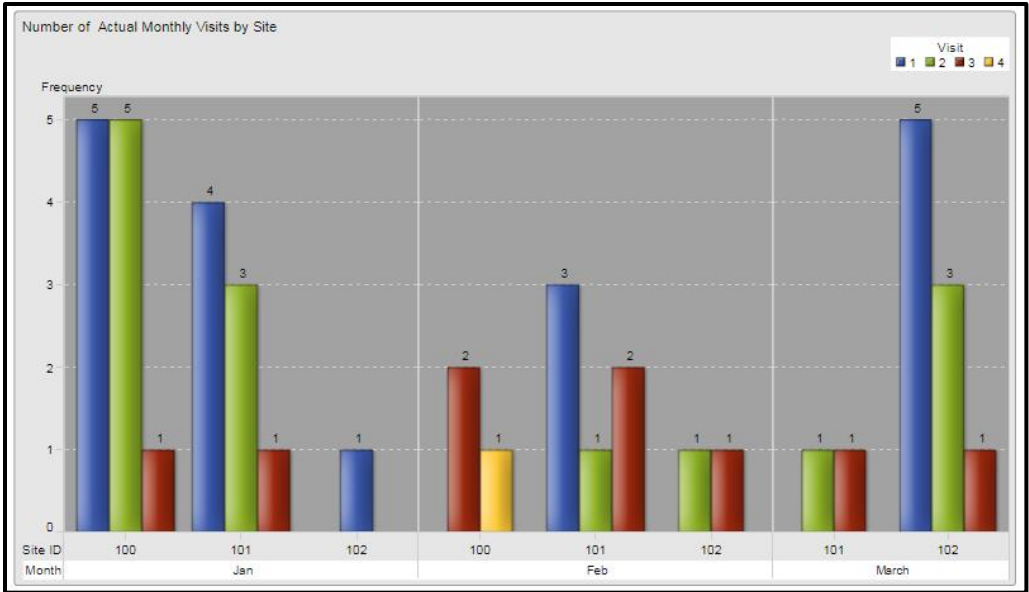
Display 6. Bar chart explains the actual visits by month within each site.

Display 7 shows the number of subjects in each epoch of the study. The bar chart explains the distribution at site level where as the pie chart shows e aggregate at the study level.
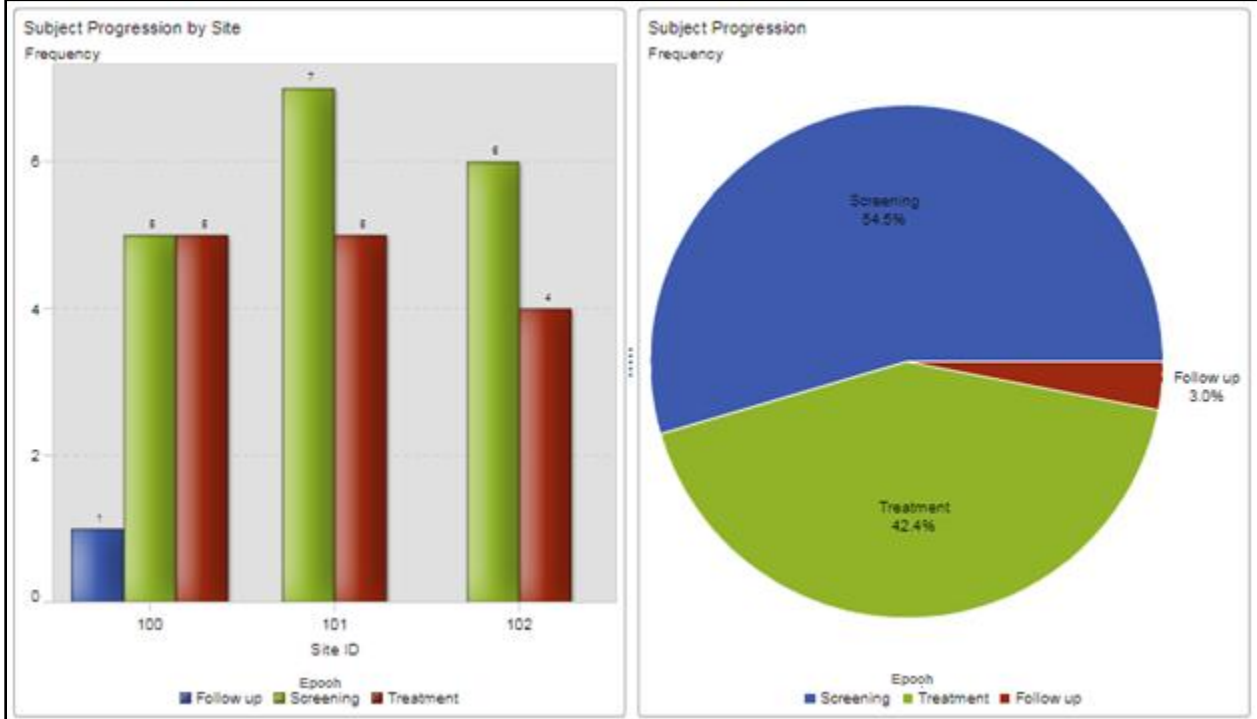
Display 7. Bar chart with subject progression by site and Pie Chart with subject progression by study.

4   SAFETY PROFILE

Subject safety is another very important category of a clinical trial. The major endpoints of a trial are safety and efficacy. Following are few major reports for safety.

4.1 NUMBER OF ADVERSE EVENTS(AES) BY SYSTEM ORGAN CLASS (SOC)/ PREFERRED TERM (PT) .

This report generates the count of adverse events occurred under each preferred term.

4.2 NUMBER OF ADVERSE EVENTS BY SEVERITY.

It generates the count of AEs within a severity. If the numbers of severe incidents are high then it needs immediate root cause analysis.

4.3 NUMBER OF ADVERSE EVENTS BY SITE.

This report generates the count of adverse events within each site of the trial. It also helps in analyzing the specific geographical factors.

4.4 LISTING OF SUBJECTS WITH ADVERSE EVENT.

It gives the complete detail of the adverse events, and help in drilling down to the concerned factors.

Display 8 shows two Bar Charts with the Adverse Events count by reason and severity within each site.
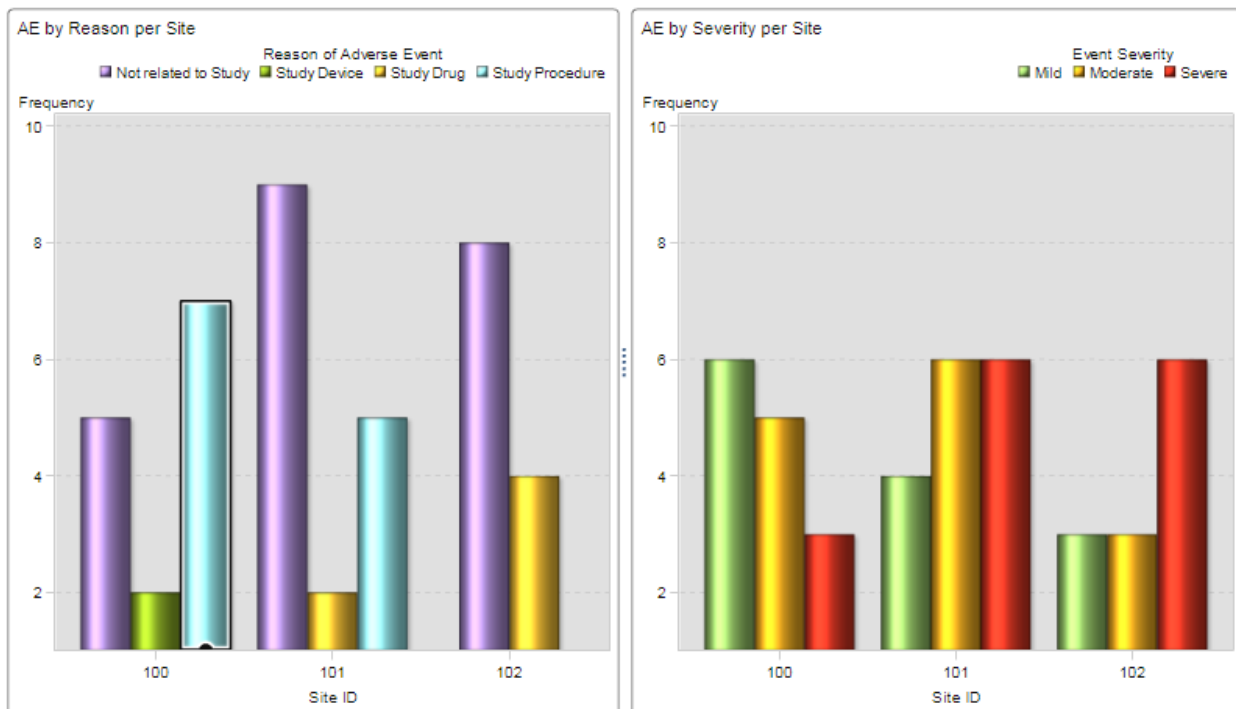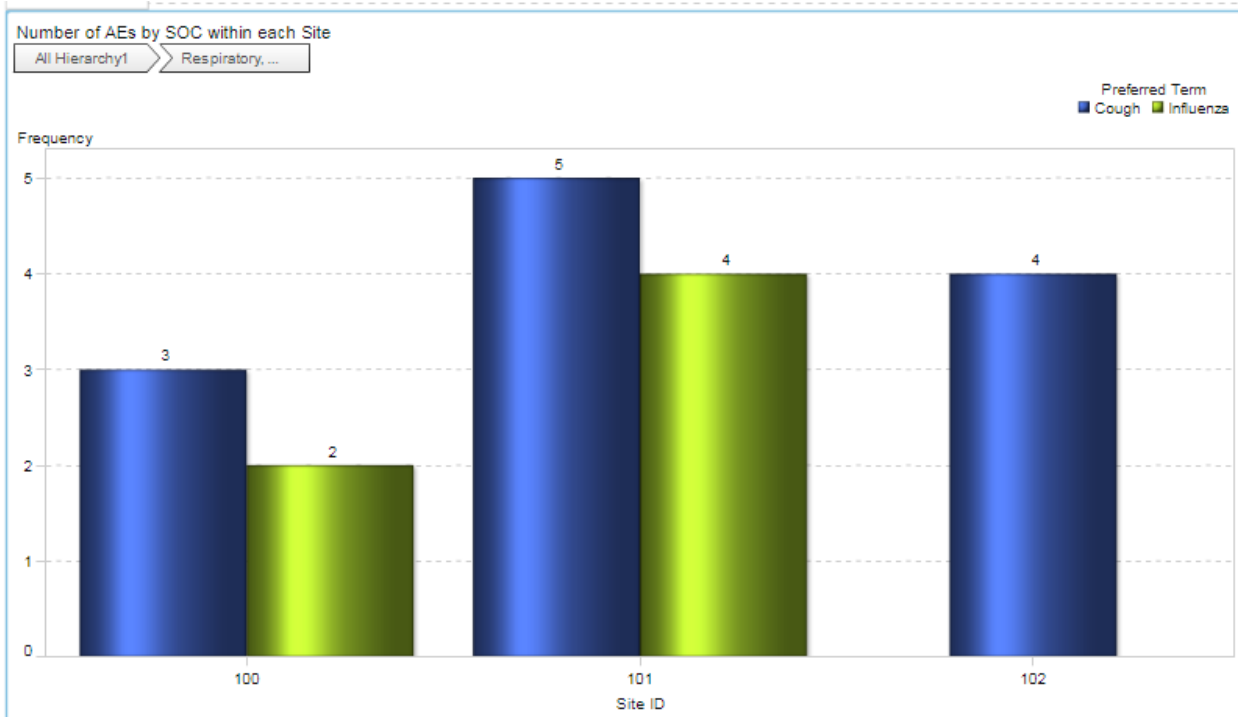

Display 8. Bar Charts with Adverse Event count within Sites by Reason and Severity respectively.

Display 9 explains the Adverse Events count by System Organ Class(SOC) within every site and Display 10 shows the drill down to Preferred Term.
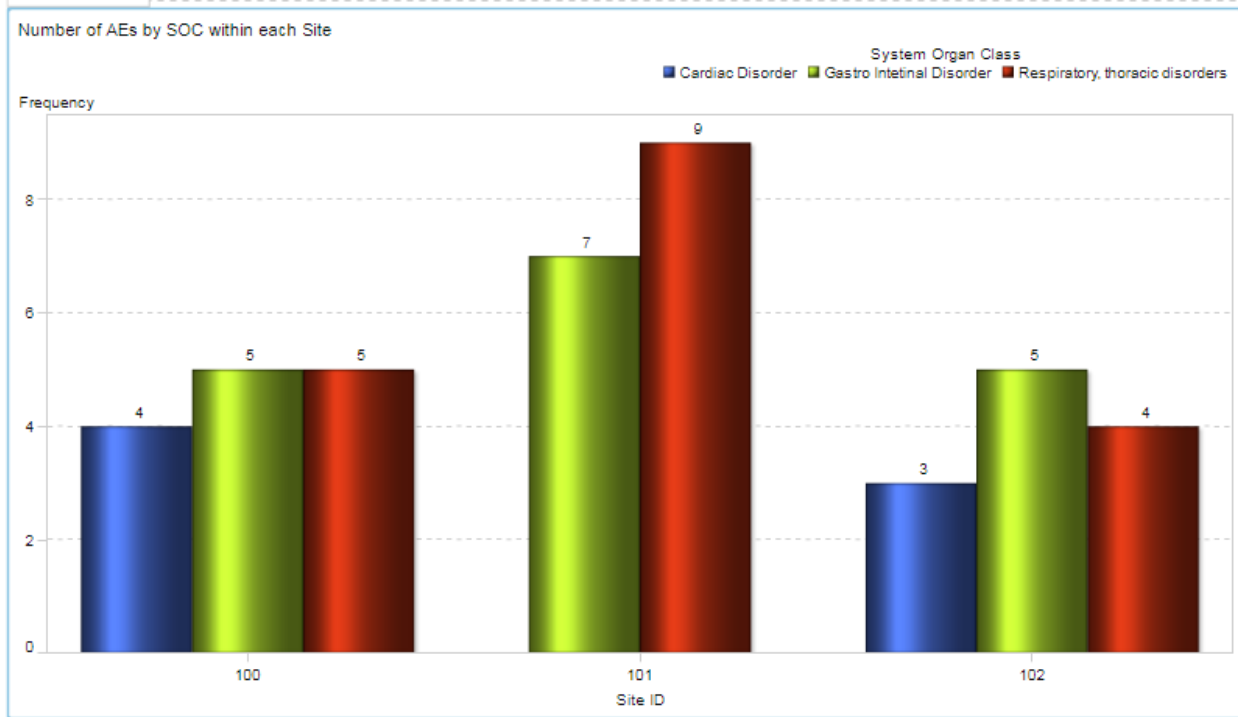
Display 9. Bar Charts with Adverse Event count within Sites by System Organ Class.

Display 10. Drill down to Bar Charts with Adverse Event count within Sites by Preferred Term using hierarchy feature.

CONCLUSION

This paper explains the various reports which helps oversee these risk factors for successful execution of the trial. Risk Based Monitoring keeps an oversight of the important risk-factors with centralized monitoring saving lots of time and money. It also utilizes On-site monitoring in the identified area of concerns for further analysis and mitigation steps SAS® Visual Analytics can make reporting quite user friendly with its wide range of reporting capabilities to generate quick reports consuming data in different formats like SAS files, spread sheets, and text files.

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RECOMMENDED READING

- *SAS® Visual Analytics – User's Guide*
- *FDA Guidelines for Risk Based Monitoring*

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