MWSUG 2017 - Paper SY02

Patient Safety with SAS® Visual Analytics

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ABSTRACT

In clinical trials, ensuring patient safety is the supreme priority. Stringent monitoring of safety outcomes is a key regulatory consideration. A trial may coincide with unacceptable patient safety within a given indication and needs to be captured as early as possible to save time and money. Monitoring is done by generating various reports to identify any adverse event, checking its severity, identifying its reason etc. These reports can be huge and may take a lot of time and effort to put them together to come to an outcome.

In this paper we will explain how SAS® Visual Analytics can play a vital role in generation of reports to enable easy and deep down monitoring of the patient safety. Its features not only helps in quick generation of reports but also help the monitoring committees to answer their queries , draw inferences and give a complete view of the safety outcome of the trial.

INTRODUCTION

Patient safety has always been the one of the most important factors for successful execution of a trial. In fact, if we talk about the study phases the major focus of an initial phase of a study is safety and it remains throughout the life cycle of the drug along with other factors like efficacy. If an efficient a drug significantly hampers the patient safety with severe side effects overweighing the benefits, it is not approved by the regulatory bodies. Capturing safety issues later in the trial cycle not only leads to loss of time and money but may also put the life of trail subjects into risk. Sometimes regulatory bodies like FDA can remove the researchers from conducting clinical trials if they do not abide by the safety rules repeatedly.

Monitoring and analyzing patient safety is not limited to the trial being conducted. The historical data for other trials under the same compound, similar sample population (demographics), similar study procedures, and sites etc. help in discover insights. Additionally, the ongoing drugs in the market also help to draw inferences regarding safety measures. SAS Visual Analytics enables to identify such patterns with the help of its easy to use interactive Business Intelligence and reporting capabilities. In this paper, we will discuss how patient safety can be easily monitored and controlled using SAS Visual Analytics.

Majorly we will discuss following types:

- Ongoing Trials
- Historical Trials
- Post-marketing Surveillance

1. ONGOING TRIALS

Monitoring patient safety for ongoing trials is a mandate from Regulatory authorities. Reports need to be submitted to FDA and other regulatory agencies on timely basis with the defined format. The duration of submission may vary depending on the type of trial. However, the trial data needs to be continuously monitored for any safety concerns. Following are the major reports to help the monitoring committees:

1. Number of Adverse Event by System Organ Class/ Preferred Term
2. Number of Adverse Event by Severity
3. Number of Adverse Event by Site

4. Number of Abnormal Labs by Site
5. Number of Adverse Event by Reason
6. Discontinuation of Subjects due to Adverse Event
7. Listing of Subjects with Adverse Event

1.1 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. If the count of AEs is above the threshold value defined for the respective preferred term it demands for an attention. SAS Visual Analytics creates an interactive dashboard which highlights the values above the threshold count to easily draw attention of monitoring committees.

1.2 NUMBER OF ADVERSE EVENTS BY SEVERITY

This dashboard generates the count of AEs within a severity. In case the number of AEs under a high severity increases the cause of AEs needs to be analyzed to understand the reason and take mitigation steps if possible. With the help of SAS Visual Analytics it can be made very interactive and can be combined with the number of AEs by SOC or PT, to see if a specific SOC/PT has high severity AEs.

1.3 NUMBER OF ADVERSE EVENTS BY SITE

This report generates the count of adverse events within each site of the trial. High values of counts help in focusing the specific site and analyzing the root cause for more adverse events if under a specific site. This helps in monitoring and regulating the site procedures and its data quality. If multiple sites under the same region encounters such issues it helps in analyzing the specific geographical factors.

With the help of SAS VA this report can be well integrated with the AE counts by Preferred Term and severity under each site to drill down the actual area of concern. Especially in case of large studies it becomes quite cumbersome for the analyst to bring attention at a site with a low AE count of much higher severity when there are multiple sites with high AE counts of quite lower severities.

1.4 NUMBER OF ABNORMAL LABS BY SITE

This report generates the count of abnormal labs by site. The Lab reference ranges are defined based on the demographics of a healthy person. These values act as threshold for marking the lab results values as normal or abnormal. If majority number of patients has abnormal values under a site it raises an alarm to reassess the lab procedures, devices, treatment procedure or dosage depending on the causal.

1.5 NUMBER OF ADVERSE EVENT BY REASON

This report generates the count of adverse event by the predefined set of possible reasons. This report is very helpful in defining the next steps if any of the reports discussed above is in amber. It can help in identifying site issues if any when combined with the count by site. Reports prepared in SAS VA are interactive enough to evaluate the reports by multiple dimensions together to draw inferences for safety outcome.

1.6 DISPOSITION OF SUBJECTS DUE TO ADVERSE EVENT

This report explains the number of subjects who left treatment phase or trial due to any Adverse Event. If the count of subjects discontinued is high then it may lead to failure of the trail being conducted. The monitoring committees ensure the accuracy of data by crosschecking the Disposition data with the reported Adverse Events.

1.7 LISTING OF SUBJECTS WITH ADVERSE EVENT

This report contains the whole list of subjects with and Adverse Event along all the associated detail.

2. HISTORICAL TRIALS

Historical trial plays a vital role to help identifying the area of concerns. The data of the trials conducted under the same compound reflects the possible adverse events and their root causes. This helps in drawing inferences and making decisions to move forward with the newly planned trials. Let's take an example in a phase III clinical trial of a compound where the trials under the same compound had high safety issues because of one of the study procedure. Following are some examples which help in drawing inferences and taking preventive steps for future.

2.1 NUMBER OF ADVERSE EVENTS BY SITE/COMPOUND

This report describes the count of Adverse Events along with the severity under each site for every compound. It helps to determine the compliance rate of a site to study protocol. The dashboard acts as an input factor for site selection of the upcoming trials and assigning the investigators to those sites.

2.2 NUMBER OF ADVERSE EVENTS RELATED TO INTERVENTIONS BY COMPOUND

This report describes the count of adverse events and serious adverse event related to interventions for the study compound. This gives an insight to the study team to ensure that the interventions are rightly assigned. The report may generate that a specific concomitant medication when given with the study drug may result in severe adverse event. This outcome helps the upcoming trial to avoid similar drug combinations.

2.3 NUMBER OF SERIOUS ADVERSE EVENTS RELATED TO STUDY PROCEDURES BY COMPOUND.

This report describes the count of adverse events and serious adverse event related to study procedures for all the trials conducted under a study compound. This helps the study team to take precautionary measures around such procedures by analyzing their impact in depth.

2.4 DATA QUALITY REPORTS BY SITE.

There can be multiple reports to evaluate the data quality collected from a site. Following are few examples:

- Number of queries generated under a site
- Time to resolve the raised queries
- Number of re-opened queries
- Cases of data redundancy
- Average Time to report study events by site

High quality data gives a clear status and helps in monitoring the patient safety well. It also ensures that the safety incidents are rightly captured without delays for a quick turnaround time.

3. POSTMARKETING SURVILLAINCE

Post marketing surveillance plays an important role in pharmaceutical product development. Even though lots of monitoring and reviews are practiced throughout the clinical trial phase however, concerns about a product's safety may occur when it is widely prescribed. The analysis of real world data bridges the knowledge gap between the real world clinical practices and clinical trials. The outcome of RWE acts as an input in conducting the new clinical trials. It helps to improve the quality and outcome with the learning of new procedures and technologies.

Following factors uncovers the safety risks which may not be encountered during the conduction of a clinical trial:

- Larger population
- Wider range of demographics
- Unplanned comorbid conditions
- Wider range of concomitant drugs
- Variance in the severity of disease

Hence, the reports created on this data are very helpful for understanding the various factors impacting patient safety in the real world. Following are the major reports used for Post-marketing surveillance of real world safety data:

1. Number of Adverse Event by System Organ Class/ Preferred Term
2. Number of Adverse Event by severity
3. Number of Adverse Event by Region
4. Number of Abnormal Labs by Region
5. Number of Adverse Event by Reason
6. Listing of Patients with Adverse Event

These reports are every similar to the one discussed in the ongoing trial section. For report “Number of Adverse Event by Region” the region can be focused depending upon the target areas to be covered by ongoing trials.

STEPS TO CREATE REPORT WITH SAS® VISUAL ANALYTICS

Now, we will see how SAS® Visual Analytics can be used to prepare quick reports. We will create few of combinational reports using the ones discussed above to understand the ease of report designing. The Sample Adverse Event data contains the Subject, Site, Adverse Event Identifier, Severity of Adverse Event, Preferred Term, System Organ Class and Reason for Adverse Event.

SAMPLE DATA

Subject	Site ID	AEID	Severity	Preferred Term	System Organ Class	Reason of Adverse Event
1000	100	1	2	Nausea	Gastro Intetinal Disorder	Study Procedure
1000	100	2	2	Arrhythmia	Cardiac Disorder	Not related to Study
1000	100	3	3	Cough	Respiratory, thoracic disorde	Study Procedure
1001	100	1	1	Influenza	Respiratory, thoracic disorde	Study Device
1001	100	2	1	Nausea	Gastro Intetinal Disorder	Study Procedure
1004	100	1	2	Arrhythmia	Cardiac Disorder	Study Device
1004	100	2	1	Cough	Respiratory, thoracic disorde	Study Procedure
1004	100	3	3	Influenza	Respiratory, thoracic disorde	Not related to Study
1004	100	4	1	Nausea	Gastro Intetinal Disorder	Study Procedure
1012	100	1	2	Arrhythmia	Cardiac Disorder	Not related to Study
1012	100	2	1	Nausea	Gastro Intetinal Disorder	Study Procedure
1021	100	1	1	Arrhythmia	Cardiac Disorder	Not related to Study
1021	100	2	2	Cough	Respiratory, thoracic disorde	Study Procedure
1021	100	3	3	Nausea	Gastro Intetinal Disorder	Not related to Study
1023	101	1	1	Cough	Respiratory, thoracic disorde	Study Procedure
1023	101	2	2	Nausea	Gastro Intetinal Disorder	Not related to Study
1023	101	3	3	Influenza	Respiratory, thoracic disorde	Not related to Study
1028	101	1	2	Cough	Respiratory, thoracic disorde	Study Procedure
1028	101	2	3	Nausea	Gastro Intetinal Disorder	Not related to Study
1028	101	3	3	Influenza	Respiratory, thoracic disorde	Not related to Study
1026	101	1	2	Cough	Respiratory, thoracic disorde	Not related to Study
1026	101	2	3	Nausea	Gastro Intetinal Disorder	Study Drug
1026	101	3	2	Influenza	Respiratory, thoracic disorde	Study Procedure
1031	101	4	1	Influenza	Respiratory, thoracic disorde	Study Procedure
1035	101	1	3	Nausea	Gastro Intetinal Disorder	Study Drug
1035	101	2	2	Cough	Respiratory, thoracic disorde	Study Procedure
1036	101	3	3	Nausea	Gastro Intetinal Disorder	Not related to Study
1037	101	1	2	Nausea	Gastro Intetinal Disorder	Not related to Study
1037	101	2	1	Cough	Respiratory, thoracic disorde	Not related to Study
1038	101	1	1	Nausea	Gastro Intetinal Disorder	Not related to Study
1078	102	1	1	Cough	Respiratory, thoracic disorde	Not related to Study
1078	102	2	3	Nausea	Gastro Intetinal Disorder	Not related to Study
1078	102	3	3	Arrhythmia	Cardiac Disorder	Not related to Study
1079	102	1	3	Nausea	Gastro Intetinal Disorder	Study Drug
1088	102	1	3	Arrhythmia	Cardiac Disorder	Study Drug
1089	102	1	3	Arrhythmia	Cardiac Disorder	Study Drug
1089	102	2	3	Nausea	Gastro Intetinal Disorder	Study Drug
1089	102	3	1	Cough	Respiratory, thoracic disorde	Not related to Study
1086	102	1	1	Cough	Respiratory, thoracic disorde	Not related to Study
1086	102	2	2	Nausea	Gastro Intetinal Disorder	Not related to Study
1090	102	1	2	Nausea	Gastro Intetinal Disorder	Not related to Study
1090	102	2	2	Cough	Respiratory, thoracic disorde	Not related to Study

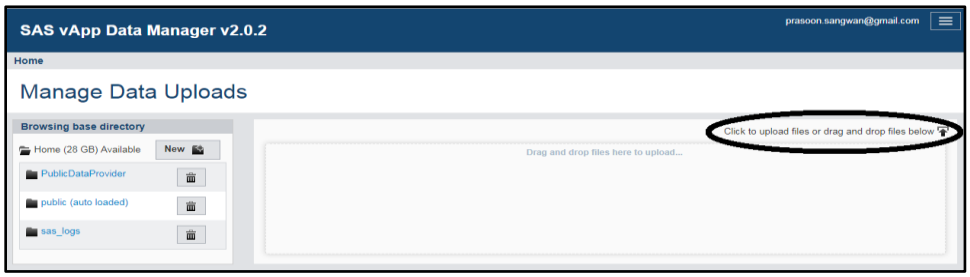
Table 1. Sample Adverse Event data of a trial stored in AE data.xlsx

LOAD DATA INTO SAS VISUAL ANALYTICS

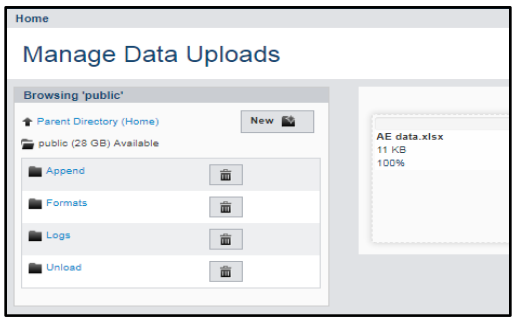
1. To Load data on SAS Cloud for SAS Visual Analytics go to SAS® vApp Data Manager.

Display 1. My Applications

2. To upload the file click on the upper right corner or drag and drop the file in the righter portion.



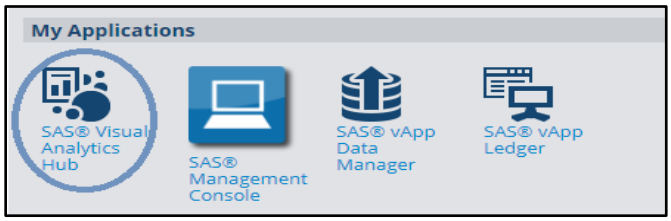
Display 2. SAS vApp Data Manager



Display 3. Uploaded File AE data.xls

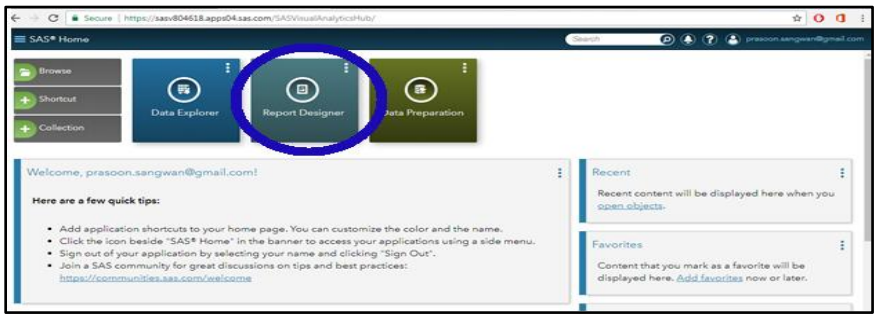
CREATE REPORT WITH SAS VISUAL ANALYTICS

1. Go to SAS Visual Analytics and Select Report Designer.



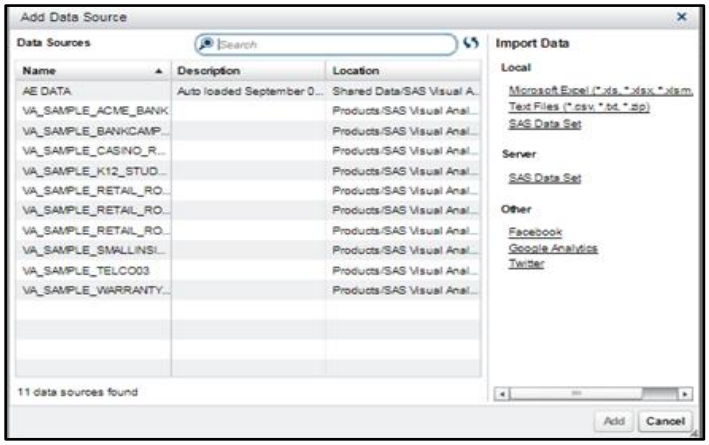
Display 4. My Applications –SAS Visual Analytics Hub

2. Go to SAS Visual Analytics and Select Report Designer.



Display 5. Report Designer

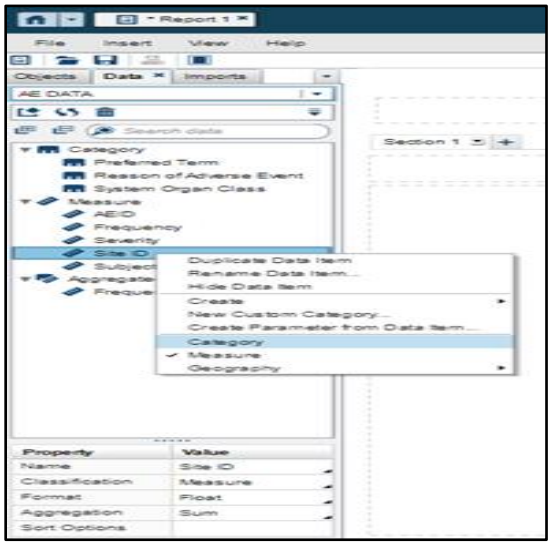
3. Add the Data Source “AE DATA” to create reports through Data tab and click “Select a data source”.



Display 6. Select Data Source

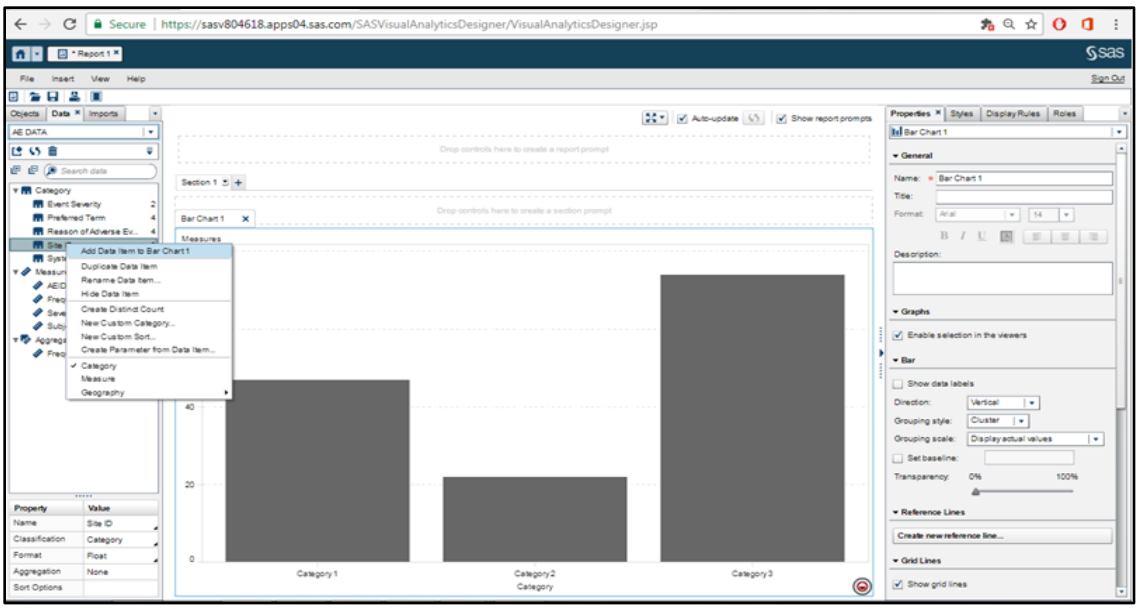
4. SAS VA automatically read the attributes and distributes them among Category and Measures. However, if needed we can move any attribute from “category” to “measure” with a right click.

5. Similarly, you can create a new custom category by grouping the values together.



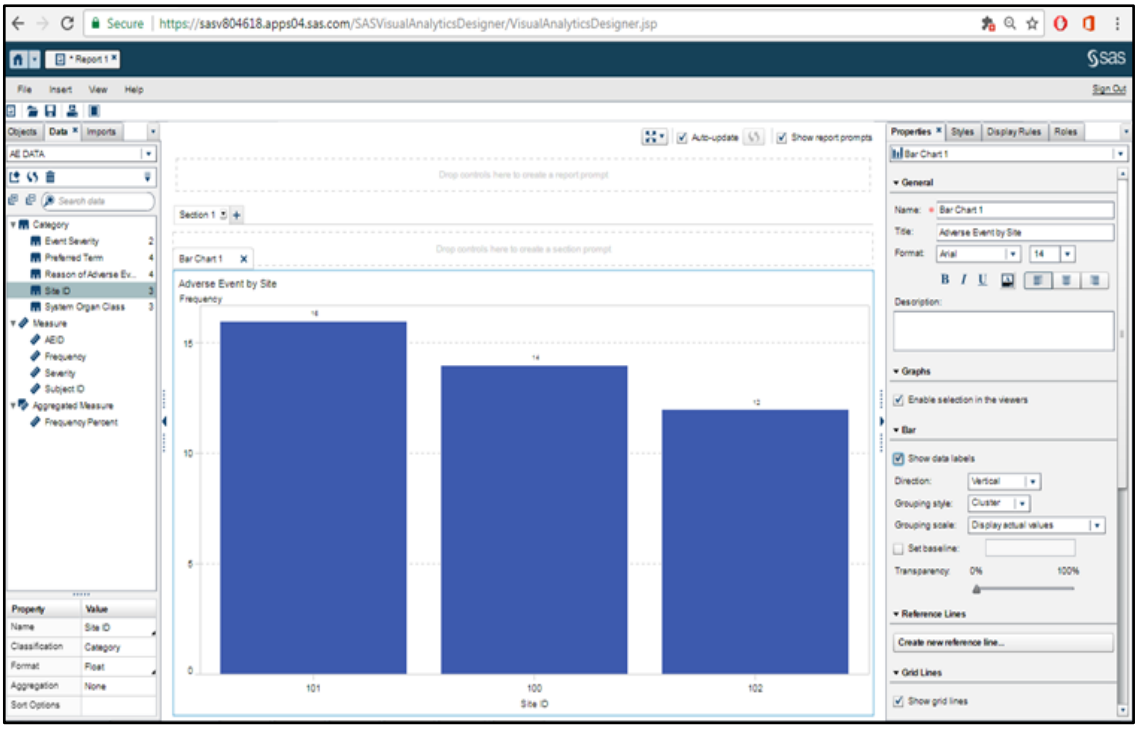
Display 7. Define Measures Categories and Custom Categories

6. Select Bar Chart from Objects tab. Add the category (Site ID) to the bar chart.



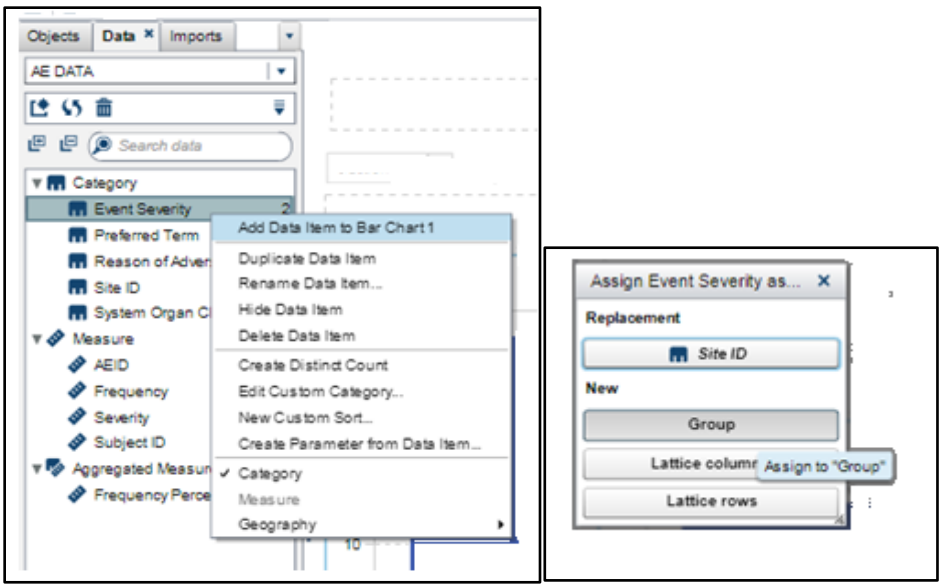
Display 8. Creating Bar Chart

7. Below report is created, showing the number of adverse events encountered by each site.



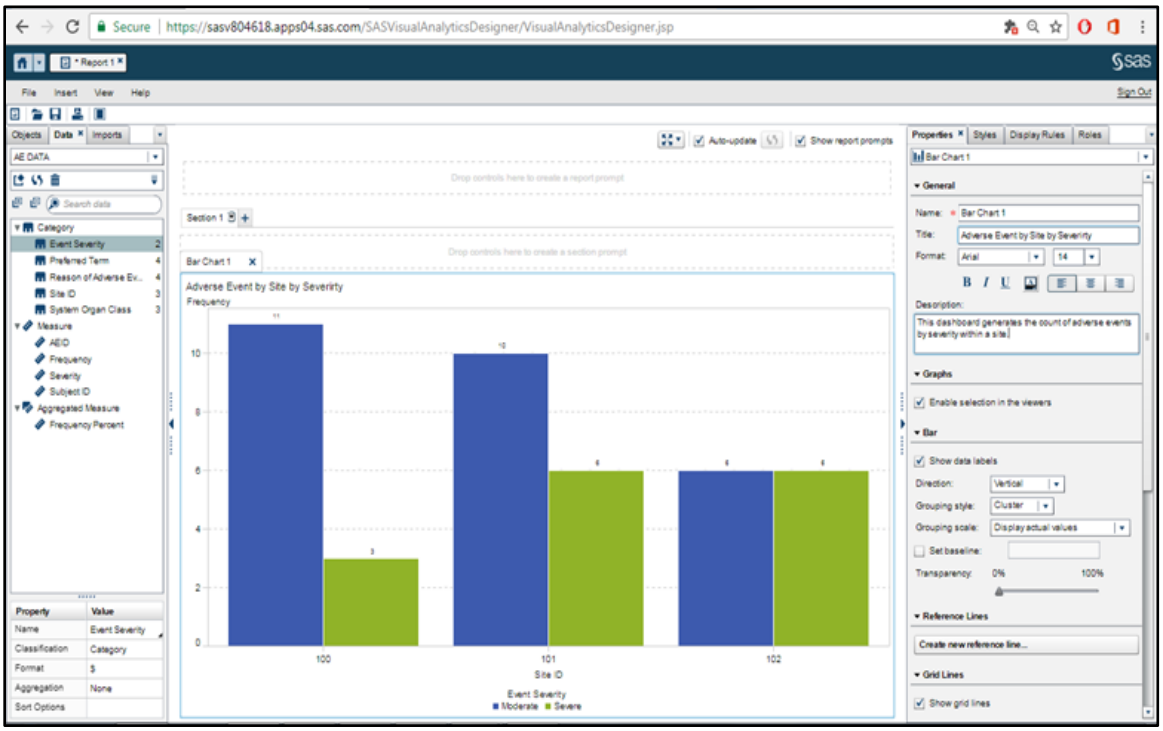
Display 9. AE Frequency Bar Chart for Site

8. Now to create another report of Number of AE by Event Severity; the new customized category. Add Event Severity to Bar Chart and small window will pop up where we will add Event Severity as a Group and the report will be created.



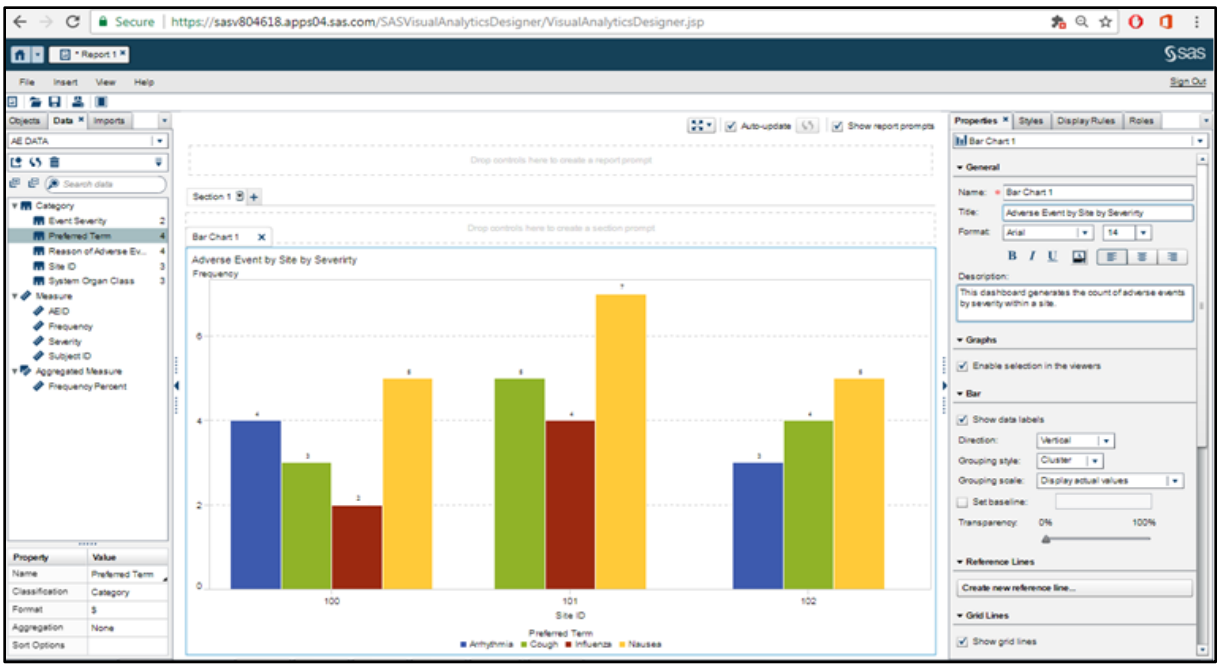
Display 10. Adding Event Severity Dimension to Bar Chart for Site

9. Report of Adverse Event by severity within sites created by grouping Event severity and site. Title, description, Format and other properties can be assigned through the right pane.



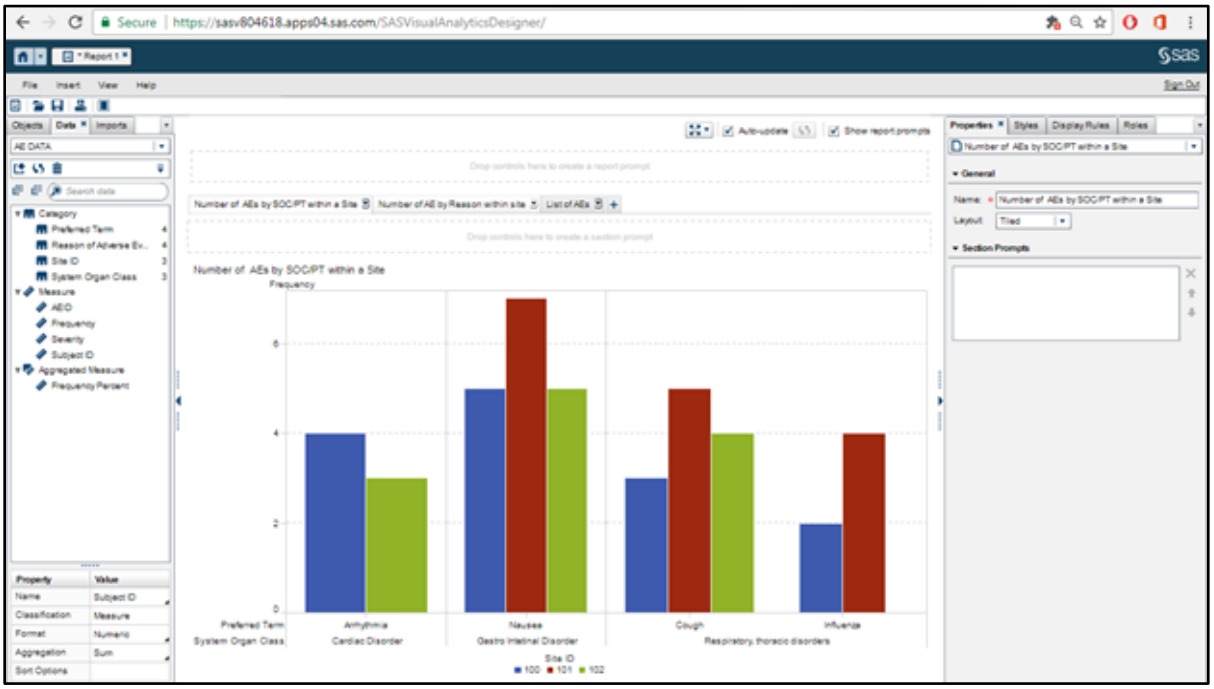
Display 11. Frequency Bar Chart with Site and Event Severity Dimensions

10. Similarly, we have another report of Number of events by preferred Term within each site.



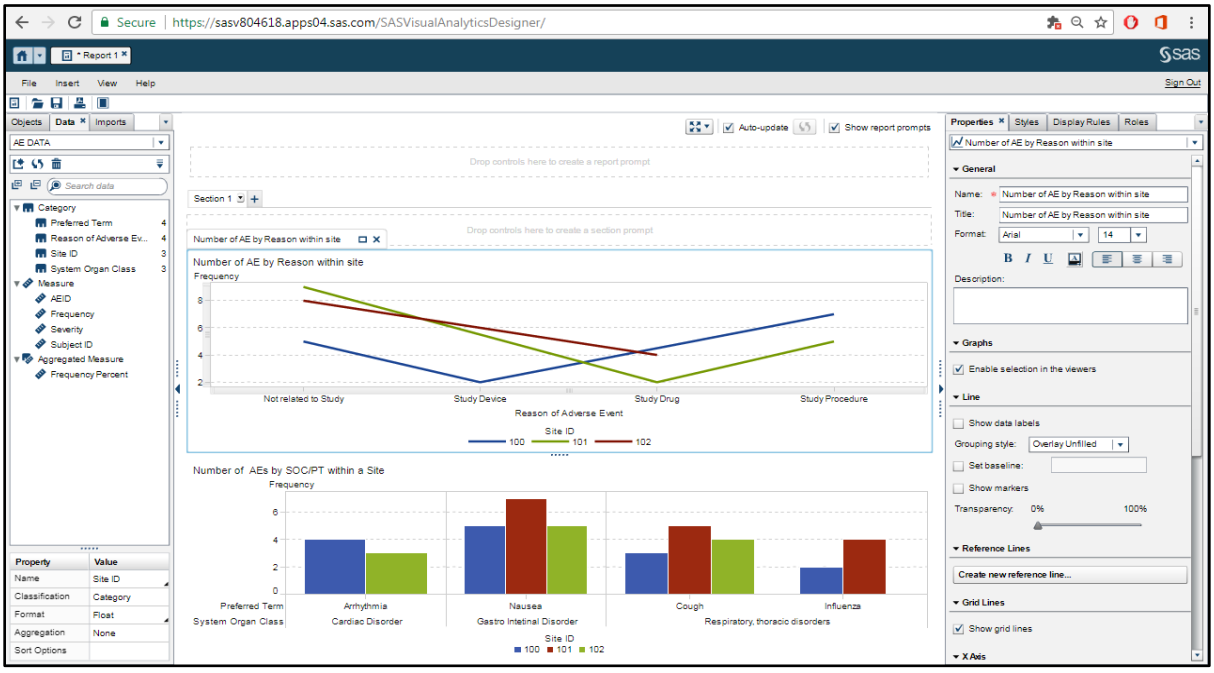
Display 12. Frequency Bar Chart with Site and Preferred Term

11. System Organ Class can be easily embedded for better analysis by “Add Data Item to Bar chart” as Lattice column.



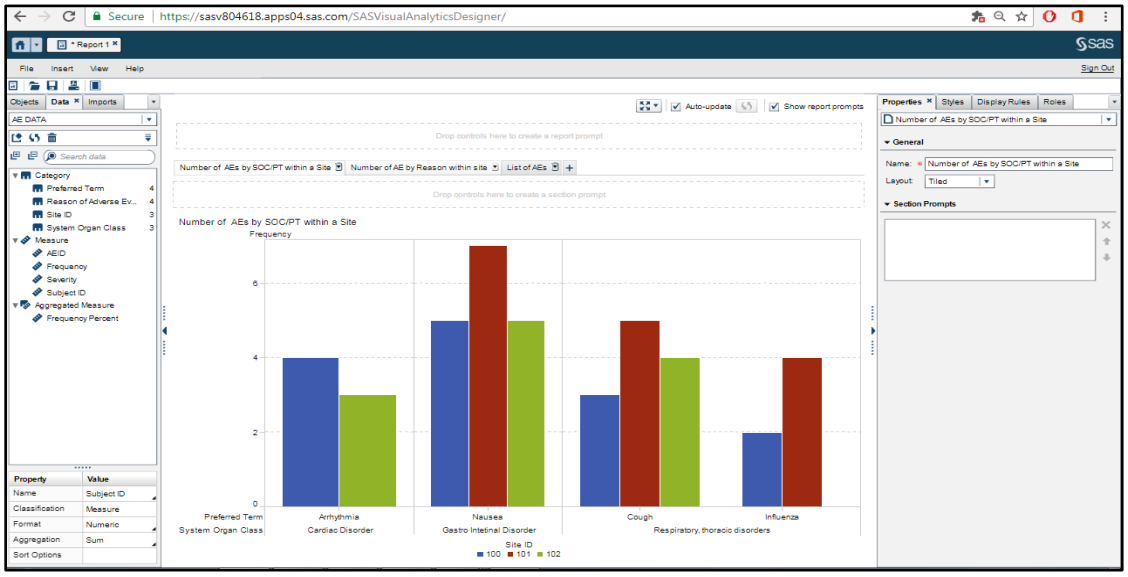
Display 13. Frequency Bar Chart with e-dimensions Site, Preferred Term and System Organ Class

12. Multiple parallel reports can be created to compare and analyze them closely through “Containers”. Here we have created the “Number of AE by Reason “a line graph on the same page as that of Number of AE by PTs/SOCs with in Site.



Display 14. Multiple Graphs in Single Report

13. Sections are created for the related reports to have a complete view. We have “Number of AE by Reason “,” Number of AE by PTs/SOCs with in Site” and listing of AEs as different sections of the reports, which can be navigated back on forth simply with a click.



Display 15. Multiple Sections with Graphs and Listings

CONCLUSION

This paper explained that patient safety is can be monitored and improved by analyzing data from historical trial to the real world drugs. Though the show stoppers are always the ongoing trials and their results acts as the base for approval of a drug but, the historical and prost marketing data contributes a lot in the success stories. This data can be visually explored through faster analytic computations maintaining its integrity and security by SAS Visual Analytics with its wide range of user friendly reporting and BI capabilities.

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RECOMMENDED READING

- *SAS® Visual Analytics – User’s Guide*

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