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Redefining "Interactive" Dashboards to Enhance Safety Data Review

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ABSTRACT

The periodic review of safety data is a critical task throughout clinical trials which can be extremely inefficient and make signal detection difficult. Interactive dashboards developed through close collaboration between programmers and study team members provide an optimized method of reviewing accumulated safety data to minimize subject risk. By avoiding the limitations of static listings and visualizations, dynamic displays allow the reviewer many views of the data without being overwhelmed with many different visualizations or listings. By allowing the reviewer to manipulate views of the data, filter data being fed into the display, and mark data to trigger targeted dynamic supporting displays with relevant data, the reviewer can unleash the full power of the increasing volume of clinical trial data. Through up front study team member and programmer collaboration, these dashboards redefine "interactive" by setting up reviewers to perform their own analysis without needless programmer intervention.

INTRODUCTION

The average phase II study cost ranges from $7.0 million to $19.6 million and the average phase III study cost ranges from $11.5 million to $52.9 million and sponsor monitoring is one of the largest drivers of this cost[1]. This leads to a crucial consideration for clinical trials in balancing effective monitoring while minimizing the cost required.

Given the large volume of data collected throughout a clinical trial and the many responsibilities and limited resources of study team members for the trial, an efficient and efficacious method of reviewing accumulated data is a critical component of trial conduct. There is a myriad of limitations of reviewing this data, such as static listings which display limited information, dashboards that have an overwhelming amount of data and are difficult to navigate within the time constraints study team members are under, or the inability of a study team member to understand trends in safety data for the trial while simultaneously investigating the drivers of these trends.

By having a set of dashboards which were created in Spotfire® through close collaboration between programmer and study team members, it is possible to circumvent these limitations and enhance the effectiveness of safety data review while minimizing the amount of time needed for the review.

ADVERSE EVENT SUMMARY

Interactive dashboards allow study team members the ability to fully comprehend the accumulated safety data without spending extraneous time collecting and organizing the data, however not all interactive dashboards are created equal.

To make interactive dashboards truly effective, the end user must be able to access the information displayed instantaneously when viewing the dashboard, and then be able to investigate further depending on the unique needs of the clinical trial. Since each clinical trial is unique, it is important to have dashboards that account for these uniquities.

Figure 1: Left side of dashboard with relevant adverse event metrics

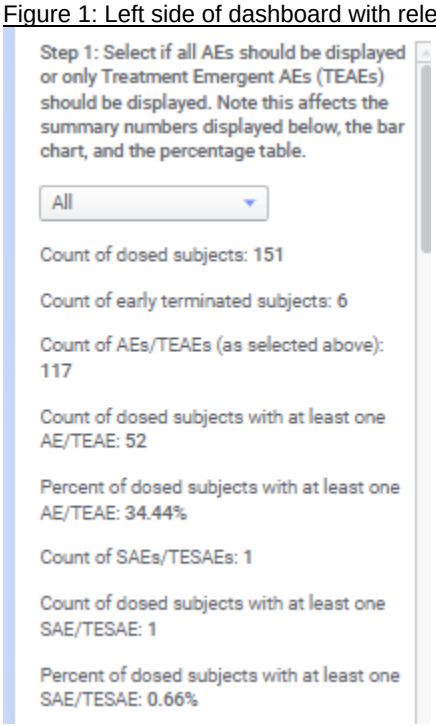


Figure 2: Middle of dashboard - bar chart of adverse event counts

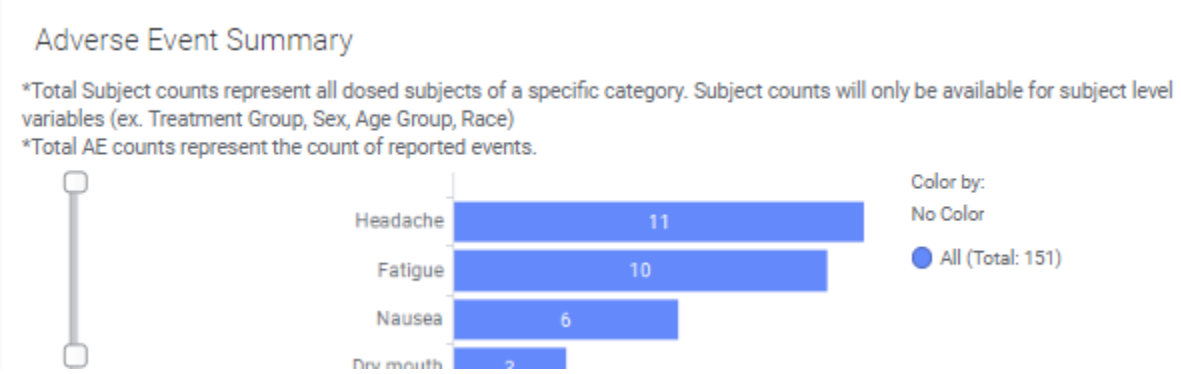


Figure 3: Top right side of dashboard – percentage of subjects and adverse events

Subject Percentage is the percentage of total dosed subjects in the study who reported this value as an AE/TEAE.

AE Percentage is the SOC/PT/Reported Term percentage out of the count of SOC/PT/Reported events.

Preferred Term	Overall Subject Percentage	AE Percentage
Abdominal distension	1.32%	1.71%
Abdominal Pain	0.66%	0.85%
Abdominal pain upper	0.66%	0.85%
Allergy to arthropod sting	0.66%	0.85%
Amenorrhoea	0.66%	0.85%
Ankle fracture	0.66%	0.85%
Application site pain	0.66%	0.85%

Figure 4: Bottom right side of dashboard – details of selected adverse events

Details on Demand

Subject ID	Site	Treatment Group	Sex	Age	Age Group	Race	Start Day	Start Date	End Day	End Date	Duration	Reported Term	Preferred Term
05-401	05 - Nashville Study Center (Pogba)	Placebo	Male	52	>= Median Age (49)	Black or African American	1	06-Dec-2020	6	11-Dec-2020	5	FATIGUE	Fatigue
07-401	07 - Franklin and Marshall Researc...	Placebo	Female	33	< Median Age (49)	Black or African American	13	12-Mar-2021				FATIGUE	Fatigue

For example, in the Adverse Event Summary dashboard above, the study team member can instantly view key safety metrics, such as the percent of dosed participants with an adverse event or percent of dosed participants with a serious adverse event. The study team member can also clearly see the adverse events most prevalent in the study, as well as the percentage of participants with a given adverse event and the percentage of the event out of the total adverse events.

From this initial view, the study team member can then investigate further depending on what the safety analysis for the clinical trial demands. For example, the study team member can choose to limit the display to only treatment emergent adverse events to investigate further. Or if the study team member is interested in the breakdown of events based on system organ class (SOC), they can view the events categorized by SOC rather than the preferred term. From there, the study team member can see the breakdown of adverse events occurring in different subsets of the population, such as by sex, race, or treatment group for open label studies or studies which have their treatment assignments available after unblinding. For ongoing trials where the study team member is familiar with the existing adverse event profile, they can toggle the displays to only view adverse events that are new or have been revised since their last review. After this, the study team member can use any of the views of the data combined with filtering by variables such as the clinical study site, start day, relationship, or any other variable the study team member requested be available for the trial.

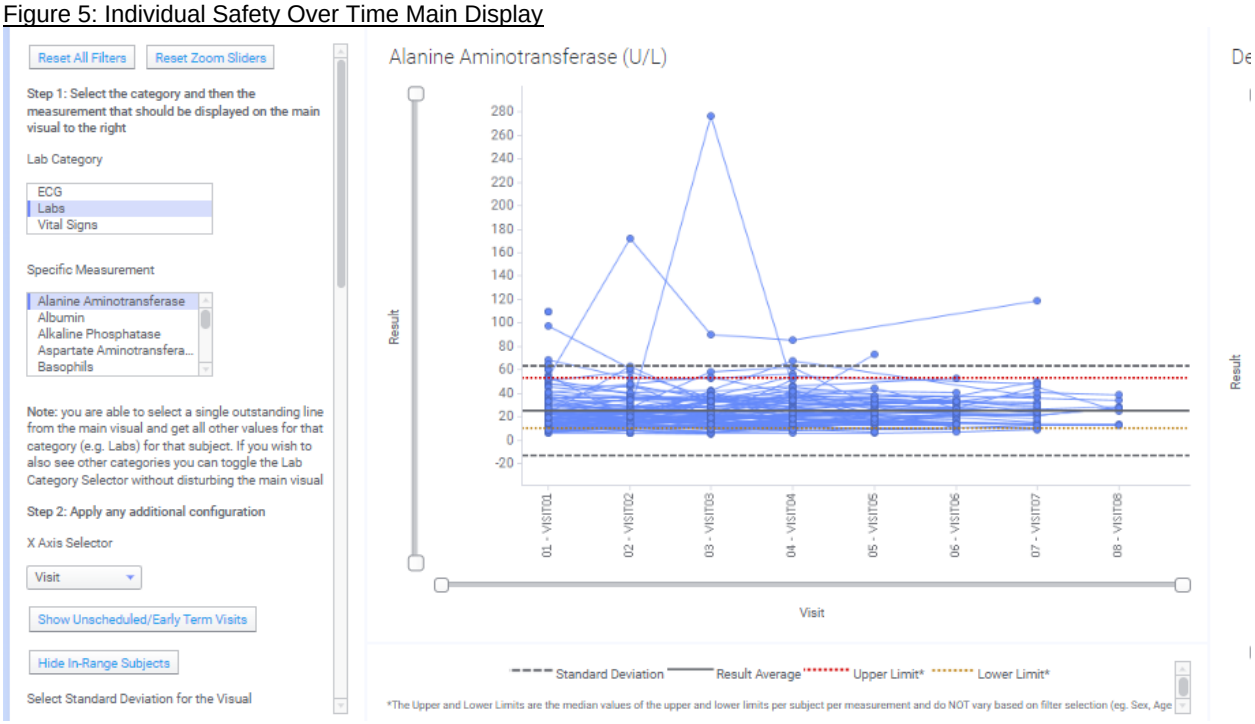
Inevitably as the study team member reviews the accumulated adverse event data, there will be events the study team member would like to view in more detail. From any of the views above, the study team member can select adverse events of interest and view relevant data about the event (outcome, relationship, participant characteristics) to investigate further at the event level.

INDIVIDUAL SAFETY OVER TIME

Another important component of safety data review is the quantitative safety data of individual trial participants. This review spans multiple domains, categories, and tests for each subject, and can be a large time investment, especially when not done efficiently.

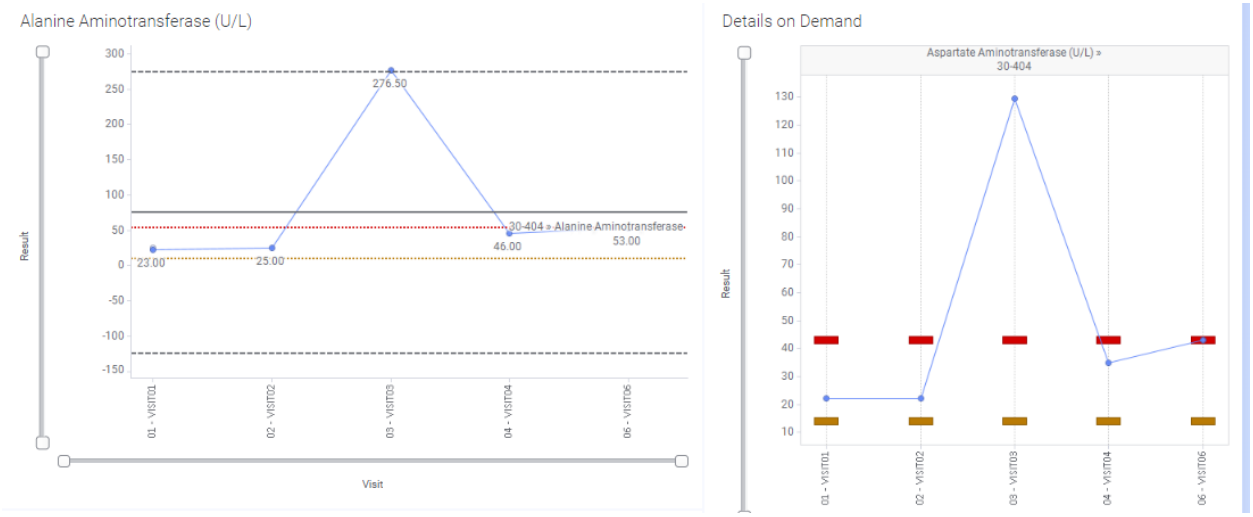
To facilitate the review of individual participant safety data, the study team member needs the ability to view accumulated safety data for multiple subjects in the trial, and then drill down to identify individual participants with safety concerns based on this initial review.

Figure 5: Individual Safety Over Time Main Display



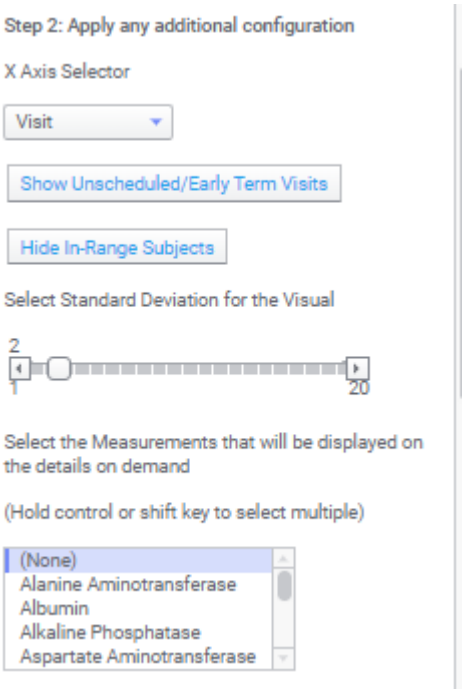
In Figure 5, the study team member can select the lab category and measurements, which are dynamically populated depending on the available numeric safety measures applicable to the trial. Once the study team member has made their selection, the main line chart will display dynamically with the data from the selected test for all subjects, chronologically ordered by the participant's study visit on the y-axis. The study team member can instantly see any extremely high or low values for the subject, and whether this is consistent with the participant's results throughout the trial, or if this is an outlier for the participant which needs to be addressed. The average, standard deviation, and upper/lower limits for the lab test are clearly indicated on the chart to give the study team member a reference for the values. Additionally, when there is a large number of study visits or a large range for the results, the study team member can use the sliders next to either axis to enlarge a specific section of the chart.

Figure 6: Individual Safety Over Time Filtered View



Shown in Figure 6, once the study team member has selected a particular subject (or subjects), they are able to also select other tests of interest to compare to the test displayed on the main line chart. This allows the study team member to easily compare if any abnormal values follow the same pattern in related tests. For more information, the study team member can hover over specific data points on the charts to view any queries issued on the data points, whether the lab value was central or local, and patient demographic characteristics.

Figure 7: Individual Safety Over Time Additional Configuration Options



The options in Figure 7 show the ability of the study team member to alter the display based on the category (ex. Vital signs, laboratory tests, ECG results) and test selected for the main display. The study team member can change between viewing the line chart by visit or study day to see the results aligned by visit when viewing multiple subjects, or to see the study day of the results when it is necessary to know the proximity of the timing of results for a participant. They can then also choose to alter the standard deviation displayed on the line chart to see results

outside of varying standard deviations depending on how many results are falling inside or outside the default of two standard deviations displayed. The buttons above also allow the study team member to easily hide or show unscheduled and early termination visits and in-range subjects (any subject where all results are within lower and upper limit for test). Showing unscheduled visits can be helpful if a study team member is trying to view if an outlier test result had a repeated confirmatory measurement and if the test returned to a normal range. As seen in Figure 5, when larger volumes of data are present, hiding in-range participants can be particularly helpful in only viewing participants with results outside of the expected range.

GROUPED SAFETY OVER TIME

Monitoring safety data trends across participants is as vitally important as monitoring the safety data for individual participants in the trial for study team members. Therefore, a complete set of safety dashboards requires a view of trends across participants in safety measures. This view needs to allow study team members to discern any trends quickly and effectively in test values over the study which may impact the safety of the trial participants.

Figure 8: Grouped Safety Over Time Boxplots

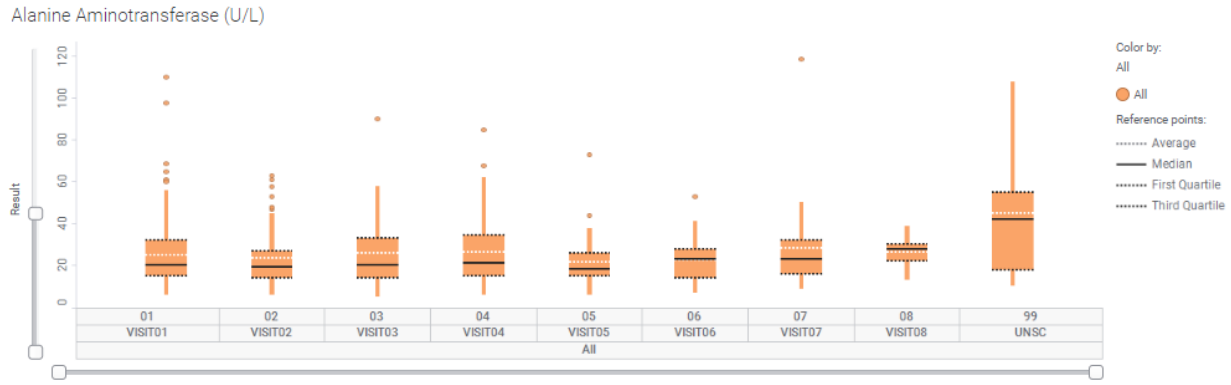


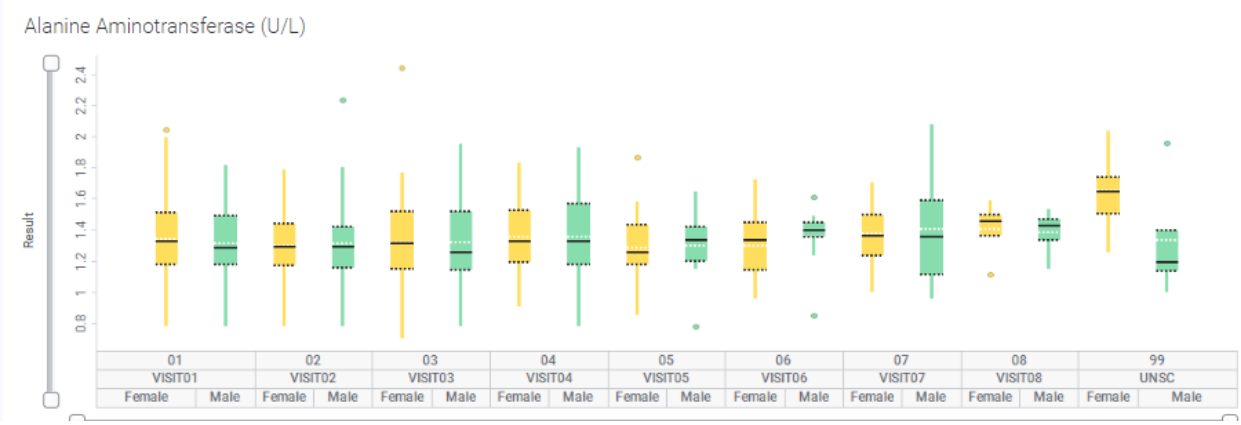
Figure 9: Grouped Safety Over Time Descriptive Statistics

	01 VISIT01 All	02 VISIT02 All	03 VISIT03 All	04 VISIT04 All	05 VISIT05 All	06 VISIT06 All	07 VISIT07 All	08 VISIT08 All	99 UNSC All
Count	137	106	94	84	46	34	29	8	13
StdErr	1.41	1.84	3.03	1.63	1.70	1.69	3.86	3.17	8.52
Max	110.00	172.50	276.50	85.00	73.00	53.00	119.00	39.00	108.00
Avg	25.18	23.73	26.04	26.24	21.70	22.79	28.34	26.25	45.08
Median	20.00	19.50	20.00	21.00	18.50	23.00	23.00	28.00	42.00
Min	6.00	6.00	5.00	6.00	6.00	7.00	9.00	13.00	10.00

The boxplots displayed in Figure 8 allow the study team member to immediately identify obvious changes in test results compared to their baseline value before participation in the trial. Average and median values for each visit are displayed to easily identify trends in results, both when results are skewed, and outliers are present and when results are normalized with fewer outliers. The first and third quartiles are also clearly indicated to allow the study team member to get a clear picture of the range of results at each visit, and whether this range of results is changing throughout trial participation. As with other displays, zoom sliders can be used to focus the display by excluding outliers from the display or looking at specific visits.

Although the visual of the boxplots provides a helpful reference, the descriptive statistics provided in Figure 9 allow for a more thorough investigation. The numeric values for each reference point in the box plots can be found, along with the count of observations to distinguish whether enough observations are present at a visit to warrant concern. The standard error is also present to provide context on how much weight to give a finding.

Figure 10: Grouped Safety Over Time Boxplots by Sex



Another necessary requirement of grouped safety data analysis is viewing results across different cohorts of participants. The boxplots in Figure 10 allow the study team member to easily identify whether trends are prevalent among male or female participants. This provides a wealth of information within the same display as Figure 8 after a single selection made by the study team member. They can quickly pinpoint whether a trend found for all subjects is occurring in both male and female participants, or whether there is a trend in male or female participants that is not easily distinguishable when viewing results for all participants. This option can be modified based on the requirements of the trial to view changes in results across different cohorts, which is another absolute requirement due to the iniquities of each trial.

CONCLUSION

For the accumulated safety data of clinical trials to be reviewed effectively, study team members need to have the ability to perform their review with all necessary data in a way that does not abuse the limited time they have to devote to safety data review, which is one of their many responsibilities throughout a trial.

To have impactful and efficient dashboards, organizations must either commit to the time and effort required for programmers and study team members to combine their expertise and meet the needs of their trials, or they need to rely on an organization who already has the infrastructure in place to meet these needs.

REFERENCES

1. Key cost drivers of pharmaceutical clinical trials in the United States https://pubmed.ncbi.nlm.nih.gov/26908540/

ACKNOWLEDGMENTS

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