Paper DV11

Data Visualization for Medical Review

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ABSTRACT

Data Visualization (DV) can be applied effectively to several functional areas in Clinical Research. This paper highlights the applications, techniques and advantages of DV specific to Medical Review function. Medical Experts are the end users of this function who reviews clinical data throughout the duration of study to ensure patient safety and proper study conduct. DV involves creating interactive Subject level and Summary reports of clinical data and then allow end users to review data using several features like Drill down, data highlighting, Subject level filter and many more to get quick insights of data and take prompt actions. Mock Dose Titration data from Cardio Vascular Trial will be used in this paper for demonstration.

INTRODUCTION

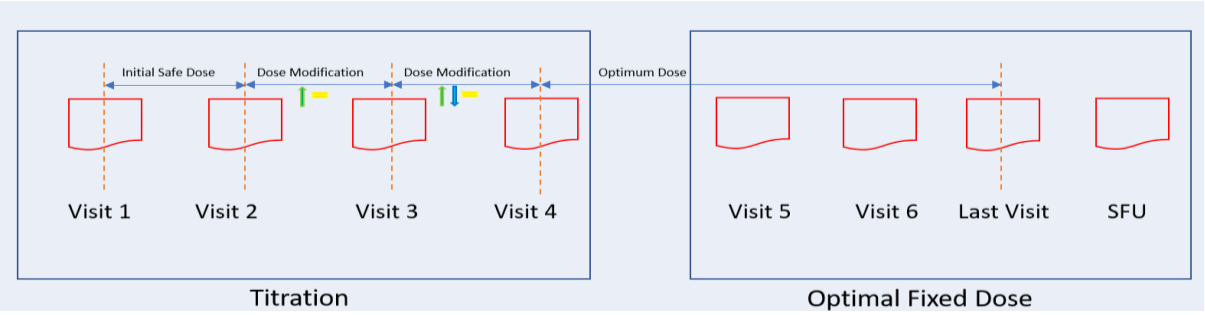
DV is applicable to Data Management, Pharmacovigilance, Medical Review, Risk Based Monitoring, eCOA assessments, Statistical analysis and other areas of Clinical Research. The scope for this paper is to demonstrate the key features of DV and its use for Medical Review process. We will use mock dose titration data and review interactive reports to ensure dose titration procedures are compliant with protocol and also review the reasons for dose modification. For demonstration purpose, interactive reports are created with RStudio® and Shiny® and can be browsed at https://bharath-sunkavalli.shinyapps.io/TitrationDB/.However, similar reports can be reproduced using other DV tools available for Clinical Research.

What is Medical review?

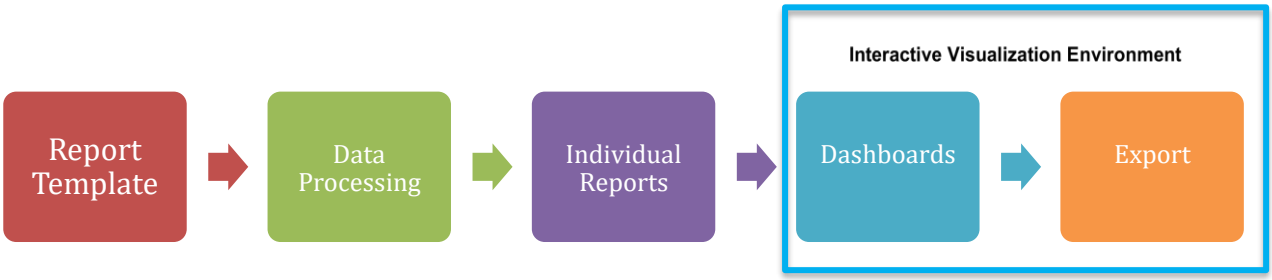
Medical Review is an ongoing process during conduct of the study, this is performed by physicians who are referred as Medical Experts/Medical Reviewers. Medical Review is conducted in accordance to Medical Review Plan which is prepared along with study Protocol and it defines all the key data points to be reviewed during course of study. Primary goal of Medical expert is to ensure patient safety and validity of the data collected. Key data points reviewed from Medical perspective include Protocol Deviations, Patient disposition, study drug exposure, dose titration, premature terminations, Trigger events such as Adverse Events, Death and clinical outcomes, to ensure safety and validity of data collected. In order to facilitate Medical Review, Medical Experts are provided with interactive reports of Subject level and Summary reports. Underlying data for these reports can originate from EDC systems, external sources such as LAB, ECG, eCOA, telemetric devices, coding dictionaries or new derived data.

Case Scenario for DV:

Let's consider a double blinded study with titration phase. During titration phase each subject starts with safe dose at baseline visit and is increased gradually in following visits until optimal dose is reached. Optimal dose can be maximum dose set by sponsor or maximum tolerable dose without adverse effects. Dose modification is decided by investigators when subject meets certain criteria defined in protocol. The objective of Medical expert in this case is to monitor dose titration phase and ensure dose adjustments are done as per protocol. Incase Medical Experts find that the reason for dose modification does not comply with protocol, then a query is raised to investigator in EDC application.



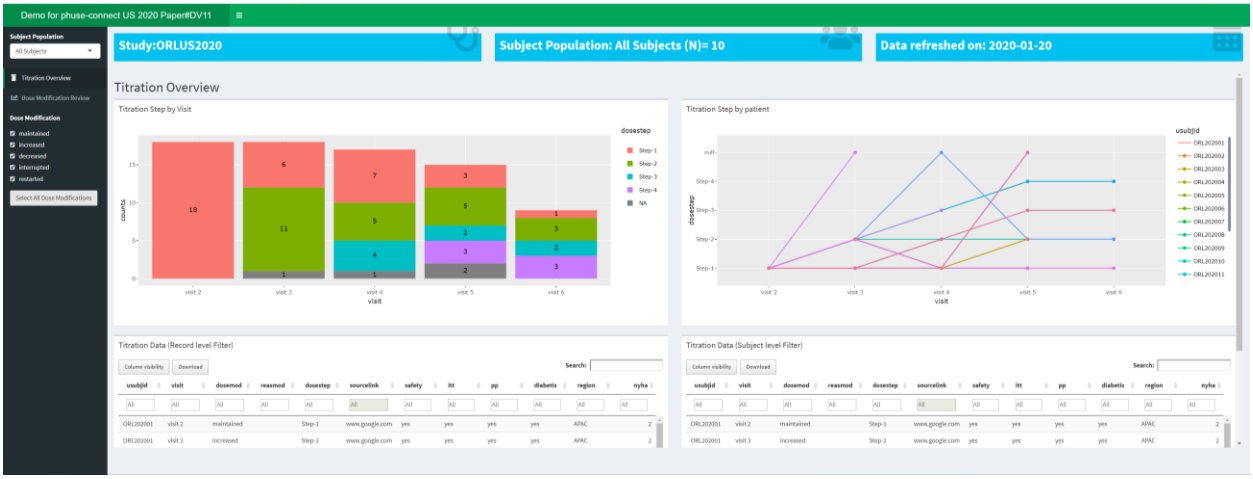
Approach for DV:
Below flow chart is an approach for creating reports and **I**nteractive **V**isualization **E**nvironment (IVE)



Below are the steps for case scenario:

- Prepare Report Template: Discuss with Medical Experts and design a template for each report and dashboard
  - monitor dose titration, a *Bar chart with titration dose steps by visit* and Subject listing with Exposure data is requested
  - review the reasons for dose adjustments, a *Bar chart with dose modification by visit* and Adverse Event listing is requested
- Process data: Process required data needed for report using statistical tool
  - Data used for case scenario is Study drug exposure, Adverse Events and Demographics
- Create Reports: Render reports using DV tool
  - Bar charts of *dose step by visit* and *dose modification by visit*, and data listings
- Dashboards: Assemble relevant reports into one view and make them interactive;
  - Assemble Bar Chart and listing in one view and link together to user controls
- Export: Provision to export reports and data listing for sharing or further investigation
  - Add additional buttons to export bar chart or download data

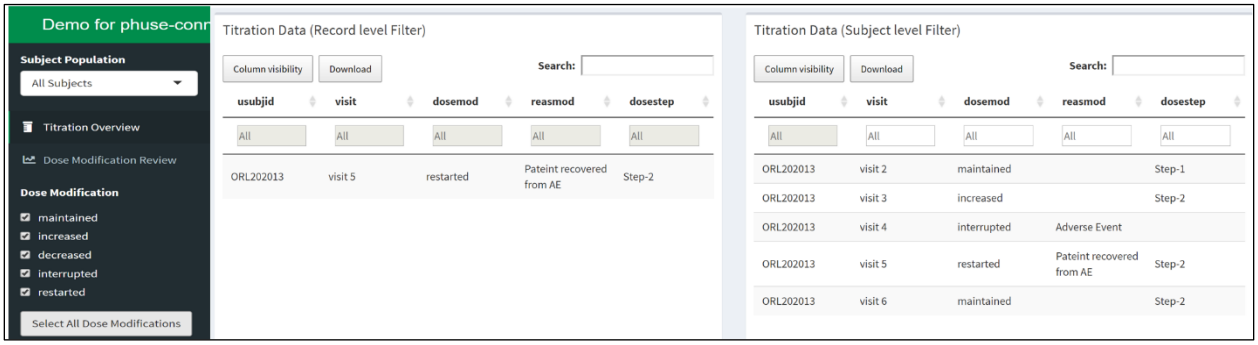
Interactive Visualization Environment (IVE):
An Interactive Visualization Environment is a GUI of dashboards with built-in interactivity.Below is a screenshot of a Dashboard,you can access the IVE created for case scenario at https://bharath-sunkavalli.shinyapps.io/TitrationDB/



Screenshot 1: Dashboard of Titration Overview

Below are the highlights of IVE:

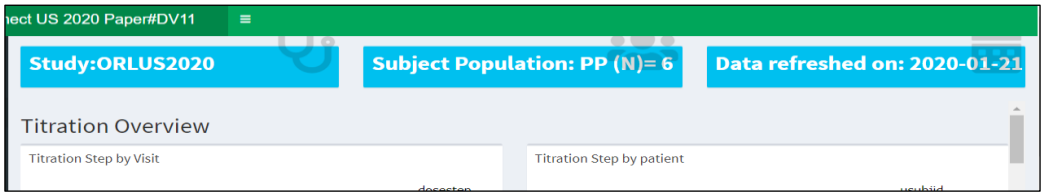
- User controlled filters: The data used for reports can be controlled using filters
    - Subject level filters: These filters selects all data for subjects that meet the criteria
        - Population flags(drop down list in side menu)
        - Other examples, subjects who reached certain visit, screen failures, subjects with diabetes etc.
    - Record level filters: These filter selects all observations that meet the criteria.
        - Dose modification (check box in side menu)
        - filters can be Serious AE, abnormal findings



Screenshot 2: User controlled filters

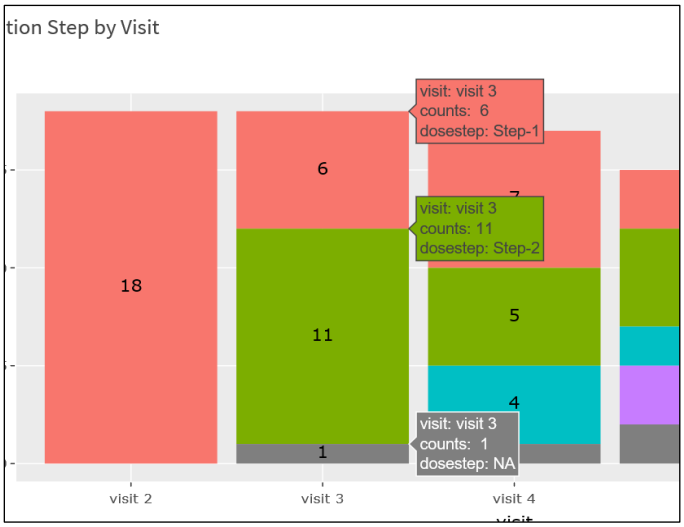
- Interactive tables: Perform data browsing operations like sort, filter, search, Hide columns, select rows/columns in tabular reports

- Add dynamic content to dashboard header (blue highlighted cells)



Screenshot 3: Dynamic information cells

- Interactive Graphs: Select, Hover and zoom over graphs to read underlying data points



Screenshot 4: Graph displaying data points

- Drill down: All the reports in dashboard can be linked to allow drill down between summary reports and subject level reports, between graphical reports and tabular reports and between two subject level tabular reports
- Export report in standard file formats for sharing and reporting
- Application can be developed, hosted, and published online using web technologies, this allows end users to review and analyze data without the need of having the application installed in local hardware

CONCLUSION

As demonstrated in this paper, provision of interactive data visualization reports will allow Medical Experts to quickly visualize, interact and gain insights of data and take necessary action, much faster than providing them with static reports. It not only improves the efficiency of review process but also enhances user experience with intuitive user interface and user defined controls. A similar approach can be applied for other functional areas in clinical research where data is reviewed, analyzed and reported.

REFERENCES

Interactive visualizations used for demonstration are developed with RStudio® and Shiny® and are deployed on *https://www.shinyapps.io/*

Winston Chang, Joe Cheng, JJ Allaire, Yihui Xie and Jonathan McPherson (2019). shiny: Web Application Framework for R. R package version 1.4.0. http://shiny.rstudio.com

Graphs are creating using ggplot2 and plotly

H. Wickham. ggplot2: Elegant Graphics for Data Analysis. Springer-Verlag New York, 2016.
Carson Sievert (2018) plotly for R. https://plotly-r.com

Tables are created using R package DataTables

Yihui Xie, Joe Cheng and Xianying Tan (2019). DT: A Wrapper of the JavaScript Library 'DataTables'. R package version 0.11. https://github.com/rstudio/DT

RECOMMENDED READING

https://shiny.rstudio.com/tutorial/

https://rstudio.github.io/shinydashboard/get_started.html

CONTACT INFORMATION

Your comments and questions are valued and encouraged.

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