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R Shiny Applications within Ophthalmology

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ABSTRACT

With the increasing need for faster and more efficient exploratory analysis of clinical trial data, R Shiny provides a framework that does just that. The time consuming task of re-running code to further investigate and report on deliverables is replaced with this interactive web application. This not only makes workflow faster, but it also provides a convenient feature; the ease of access and usage of data and results through a web URL. Through the creation of packages, the R Shiny applications can be streamlined to fit the outputs required for different therapeutic areas. In this paper, the work presented will cover a package created for Ophthalmology. This package will contain reproducible code containing modules to create tables, listings, and graphs for analyzing Ophthalmology studies in a dynamic setting. Within these modules, dynamic filtering options will allow the user to explore the data with specifications predefined.

1. INTRODUCTION

At Roche, introducing more R based programming in everyday tasks as programmers has allowed us to create agile solutions to complex problems caused by the growing complexity of studies. One of these solutions is the use of R Shiny. Why do we need an R Shiny application for our study work? It is a great way for quick data exploration and quality control. Roche has been using R Shiny applications for this purpose. This has allowed us to share insights in a more intuitive, interactive way that enables self-service analysis.

Roche has developed an R package, known as “TEAL”, which is based on R Shiny to create interactive data exploration web applications. This framework provides us with a standard template for data exploration that allows us to have code reproducibility and interactive dynamic filtering. The main three components of every TEAL application are: the encoding panel on the left, filter panel on the right, and the output in the center panel.

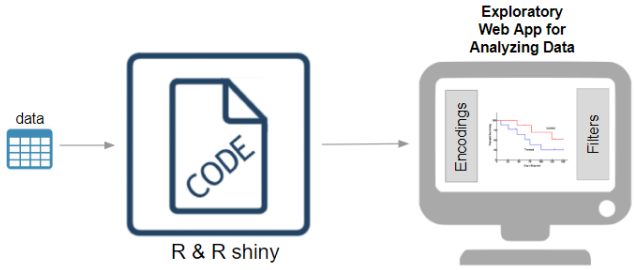

Figure 1: Teal Development Roadmap

The encoding panel on the left allows the user to adjust the output in the center interactively. The filter panel on the right allows the user to subset the data interactively. The TEAL module defines the output in the center. Through the creation of different packages, the applications can be streamline to fit the outputs required for a specific therapeutic area. In this paper, a package designed for Ophthalmology studies is presented. This package will contain a set of modules that will allow the user to dynamically explore the data within predefined specifications. This application uses two dummy BDS ADaM datasets; Subject Level Analysis Dataset (ADSL) and Ophthalmic Examinations Analysis Dataset (ADOE).

2. APPLICATION LAYOUT

2.1 THE MODULES

This application contains four main modules: Data Table, Variable Browser, Demographics and Efficacy. The Data Table module, **Figure 2**, lists all the data available in the dataset. The Variable Browser, **Figure 3**, allows you to visually display one specific variable within a dataset. The demographics table, **Figure 4**, summarizes the demographics variables of interest for your dataset. This may include age, sex, race, and ethnicity of the patients within your study.

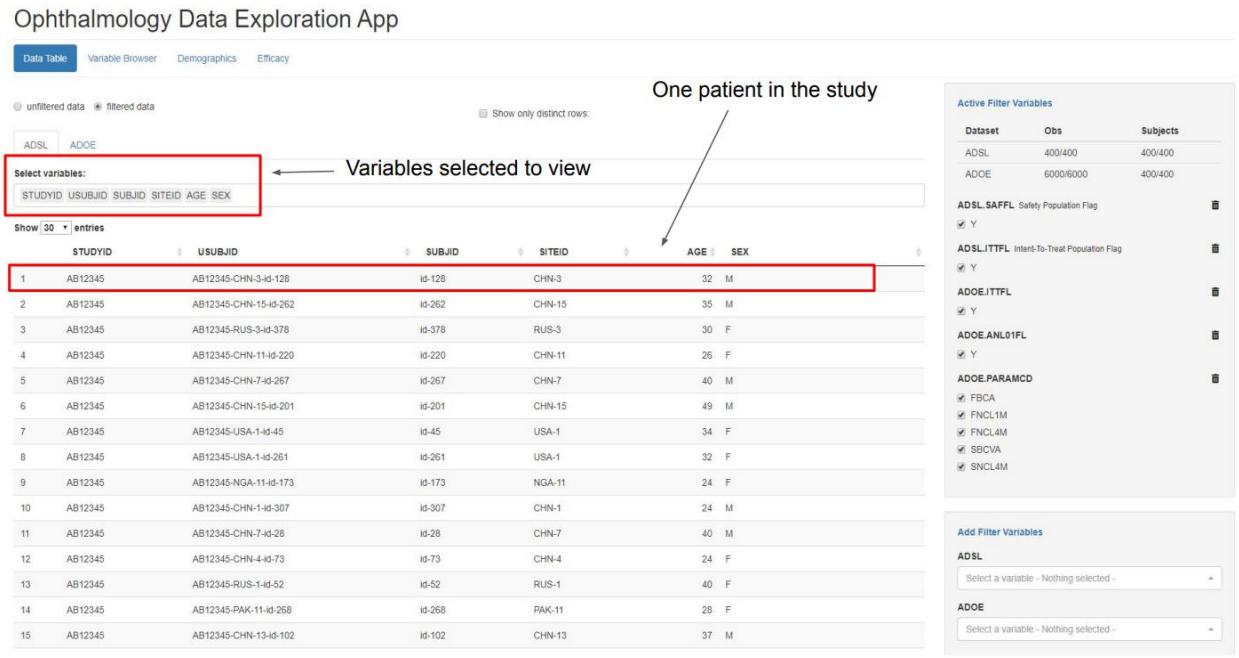

Figure 2: Data Table Module

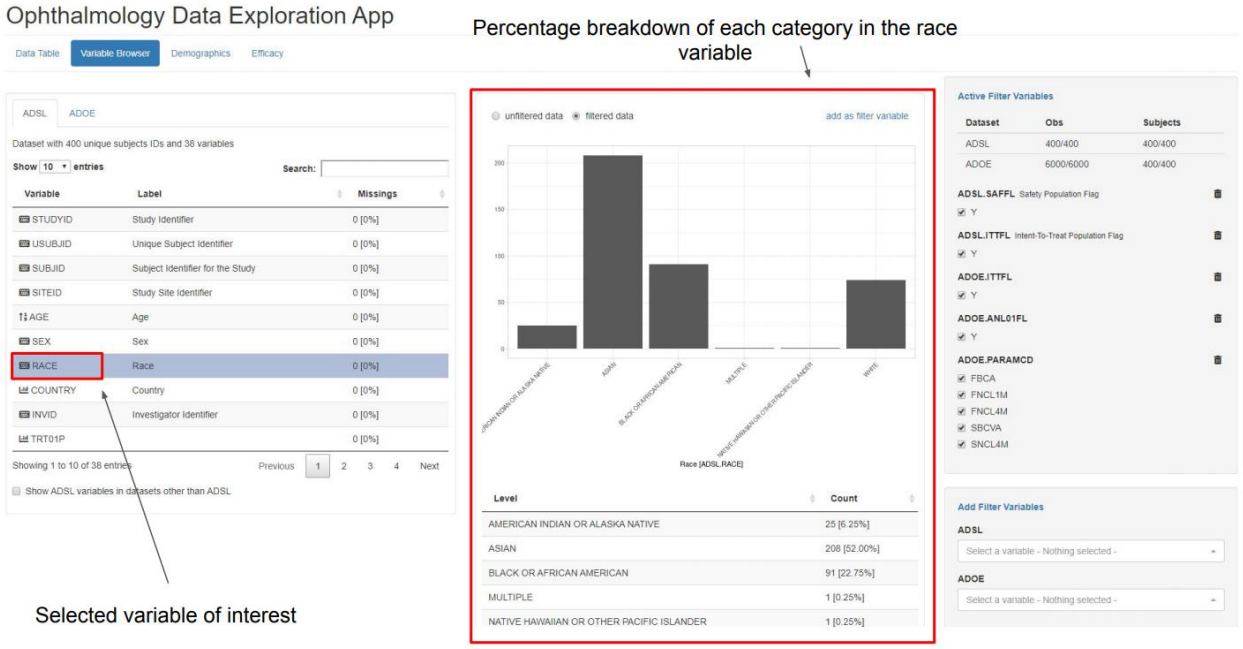

Figure 3: Variable Browser Module

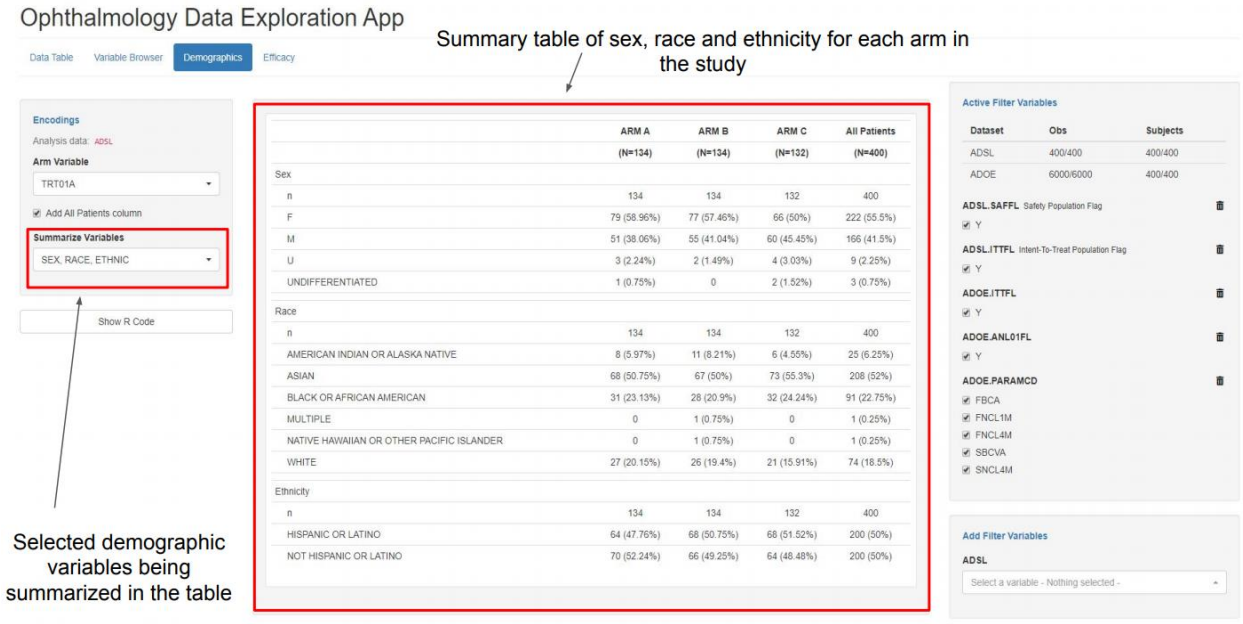

Figure 4: Demographic Table Module

Within the Efficacy module, there are five tabs displaying different analyses. There is a summary table, summary plot, spaghetti plot, ancova table and a mixed model repeated measures table. The summary table, **Figure 5**, gives a summary of the mean, standard deviation, median, and minimum and maximum for a variable of interest at each visit time point for the patients in the study.

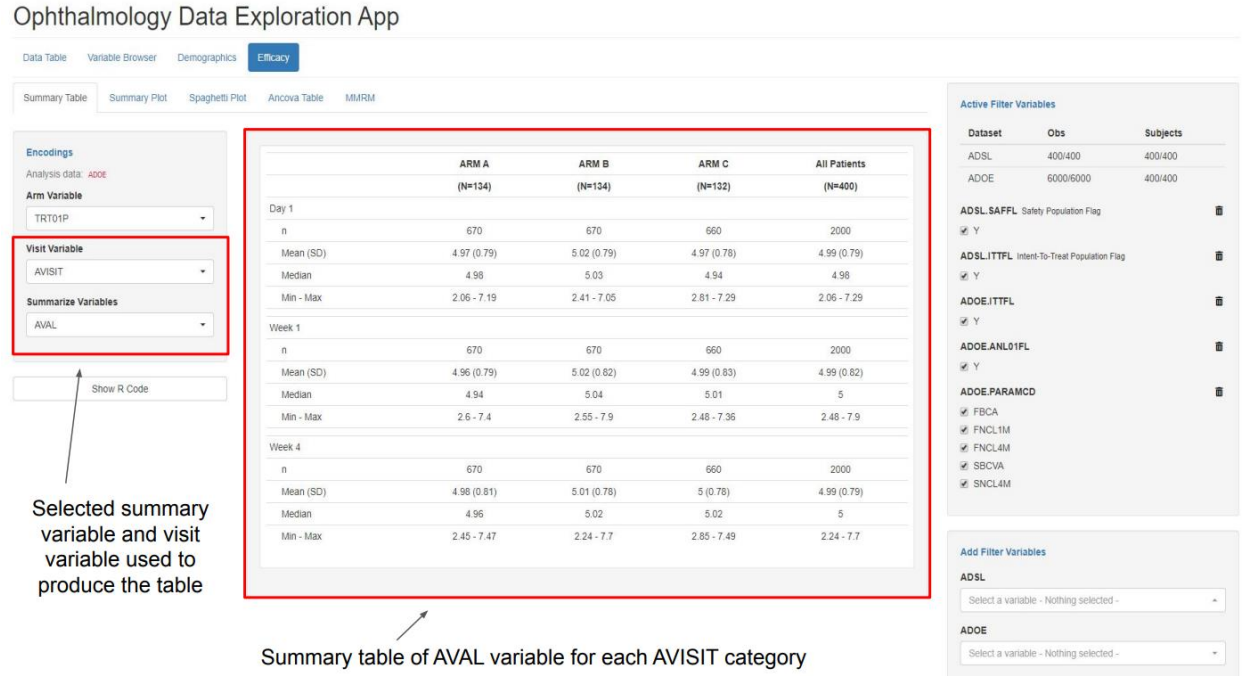

Figure 5: Summary Table Module

In Ophthalmology studies, the variable of interest could be, for example, AVAL or CHG and this would be summarized across the visit variable (AVISIT or AVISTN).

The summary plot, **Figure 6**, allows the user to graphically view the mean number of patients at each visit for the summary variable of interest. It also provides a 95% confidence interval for the mean at each visit. The plot displays this for each arm using different colours. Underneath the plot, there is a table that lists the number of subjects at each visit for each arm.

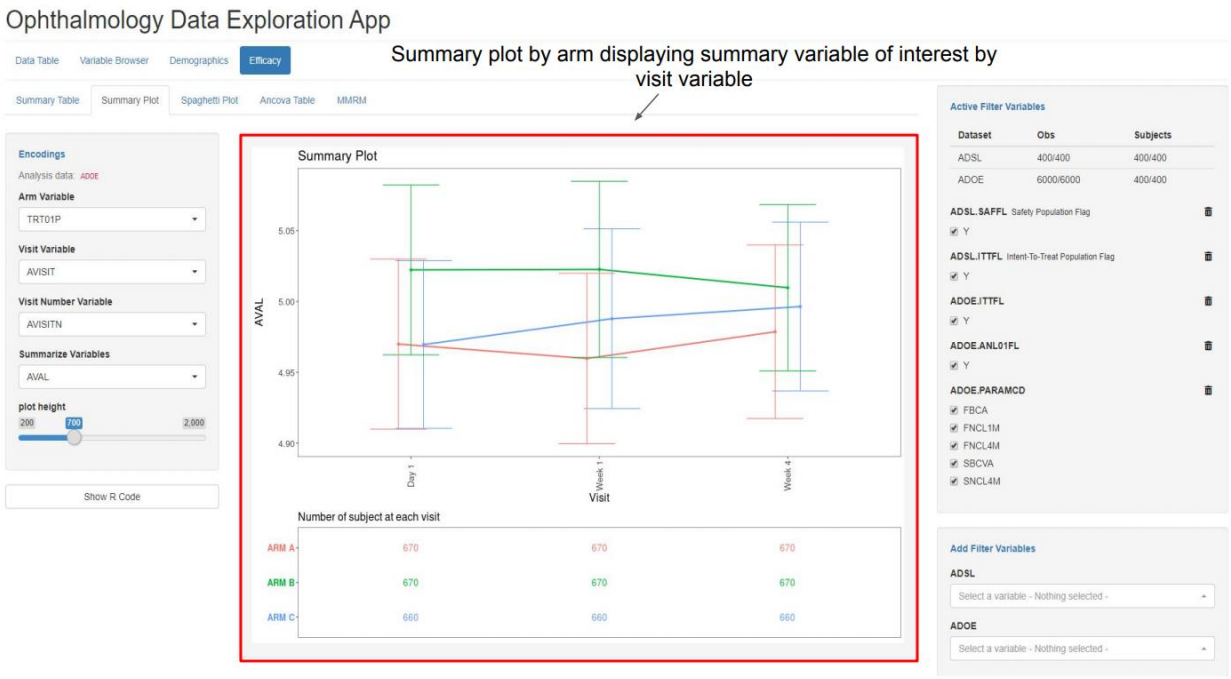

Figure 6: Summary Plot Module

The spaghetti plot, **Figure 7**, displays the summary variable values for each patient at each visit. There is also a brushing feature which allows the user to click over a certain point on the plot which then populates a table with the corresponding subject ID, visit number and summary variable value for that brushed point.

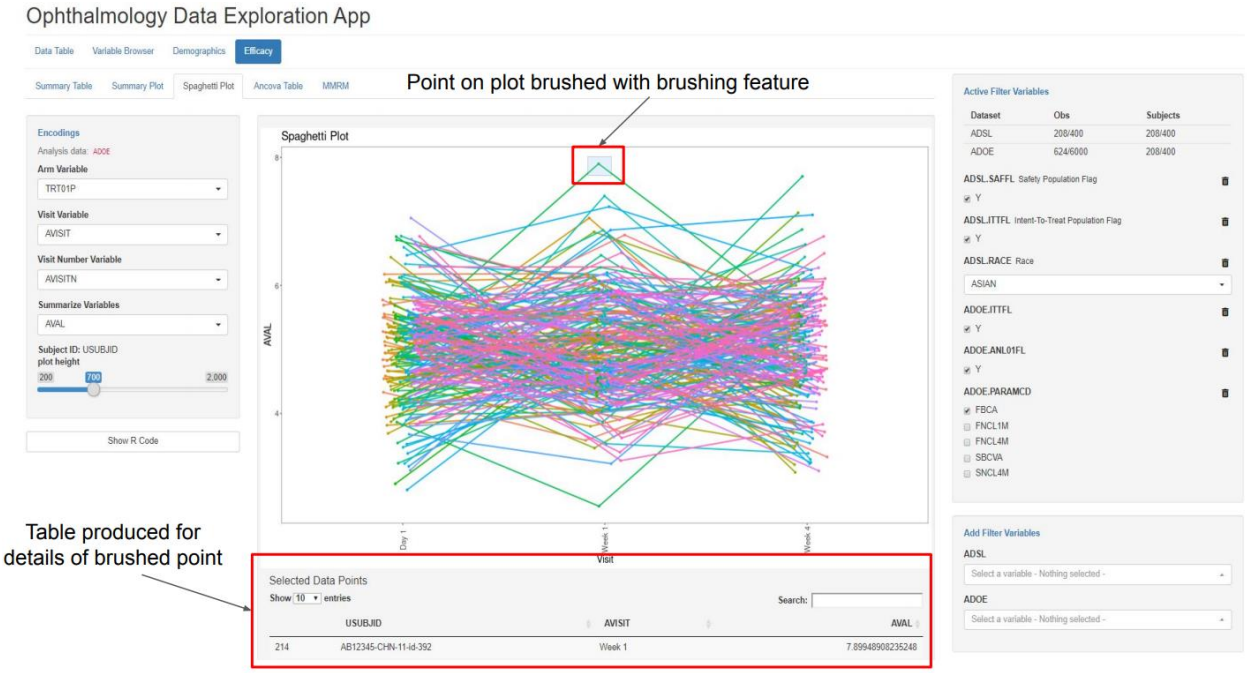

Figure 7: Spaghetti Plot Module

The Analysis of Variance (ANCOVA) table, **Figure 8**, displays the number of patients, the mean (in standard deviations), the standard deviation, the median, and the minimum and maximum of the summary variable at each visit. It also displays the change from baseline analysis at each time point using both the unadjusted analysis and ANCOVA analysis. At the top of the table, the number of patients included in the ANCOVA analysis is indicated for each arm.

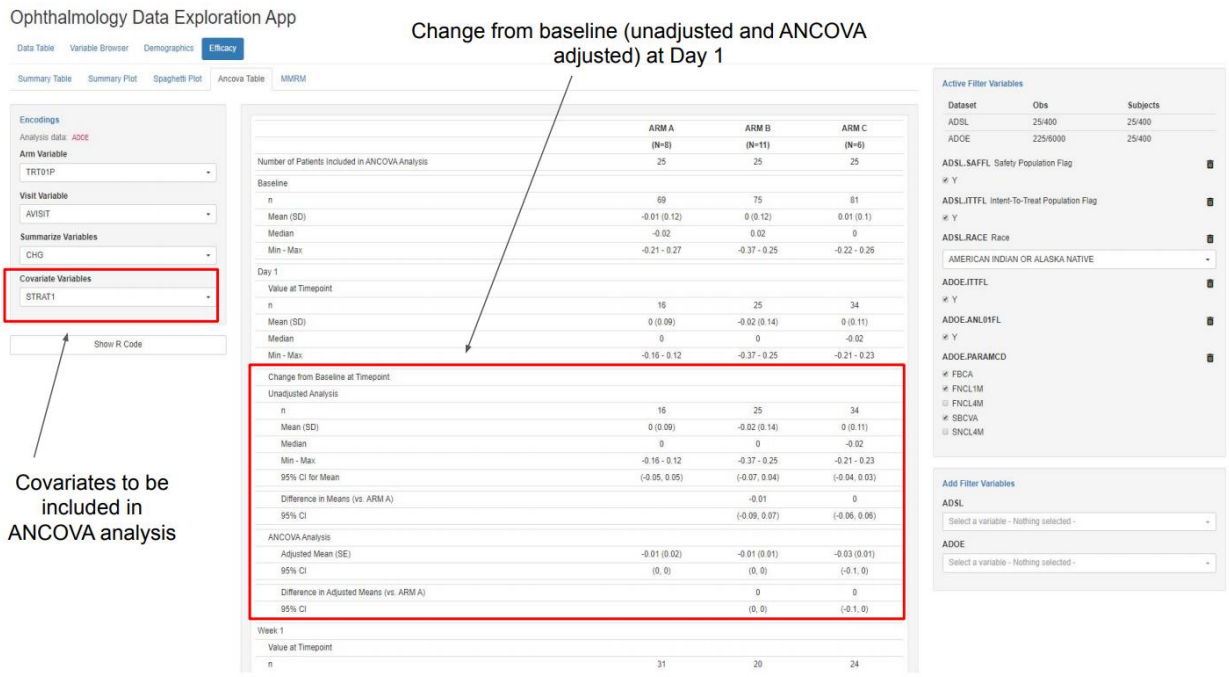

Figure 8: ANCOVA Table Module

The Mixed Model Repeated Measures (MMRM) table, **Figure 9**, is similar to the ANCOVA table except it uses the MMRM for the change from baseline analysis instead of ANCOVA. The MMRM model provides an alternative method to dealing with missing data. It is shown to be a more efficient and reliable method for primary efficacy analysis as it lowers bias and type 1 error while increasing power.[1]

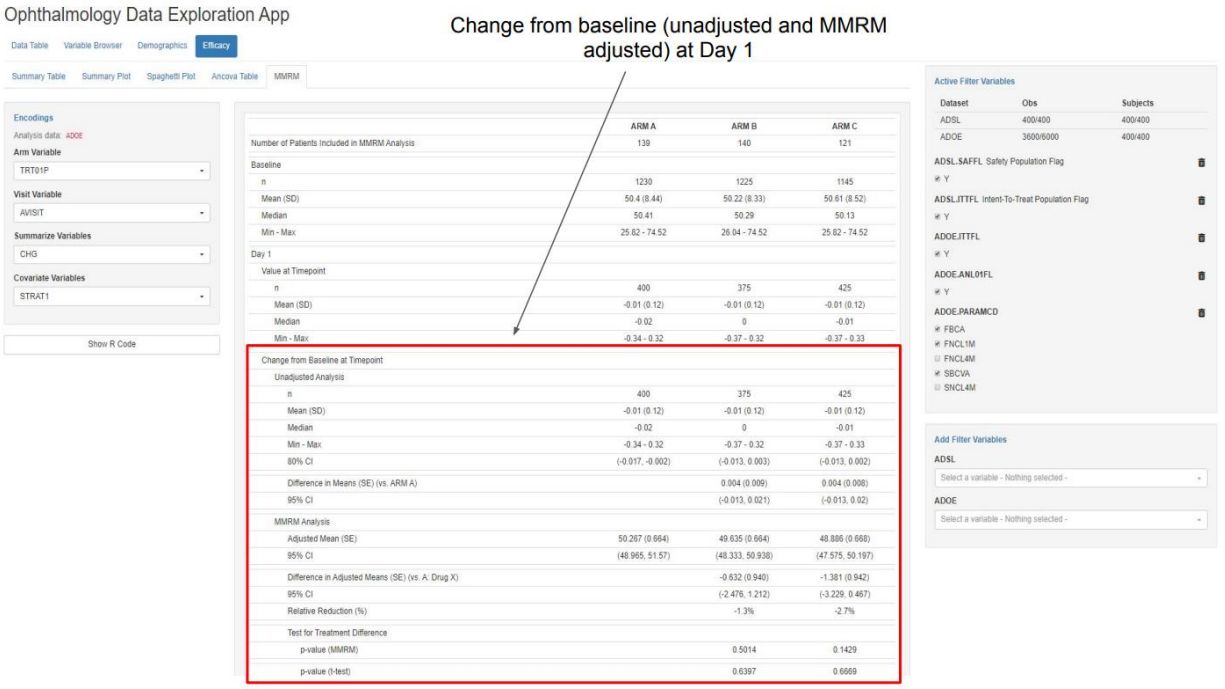

Figure 9: MMRM Table Module

3. APPLICATION FEATURES

3.1 ENCODING AND FILTERING PANEL

The encoding panel can be found on the left side panel of the modules. The items that are displayed in the encoding panel are coded in the user interface object for each module. This allows the user to adjust the output, whether it is a table or plot, using different variables of interest. For example, in the summary table in **Figure 10**, the variable being summarized can be changed from AVAL to CHG using the “Summarize Variables” tab.

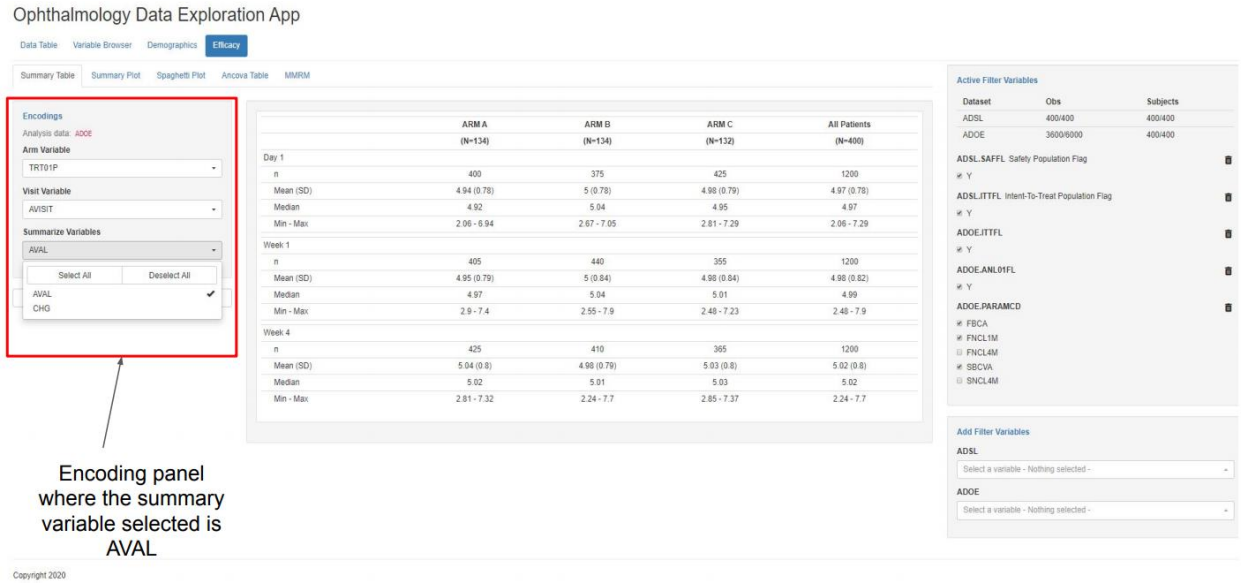

Figure 10: Encoding Panel on Summary Table Module

The filter panel on the right side panel of the modules, standard to the TEAL framework, allows the user to subset the data interactively. Initial preselected subsetting can be initialized in the app.R file. For example, certain flags in ADSL can be initialized for each module when the app runs as seen in **Figure 11**.

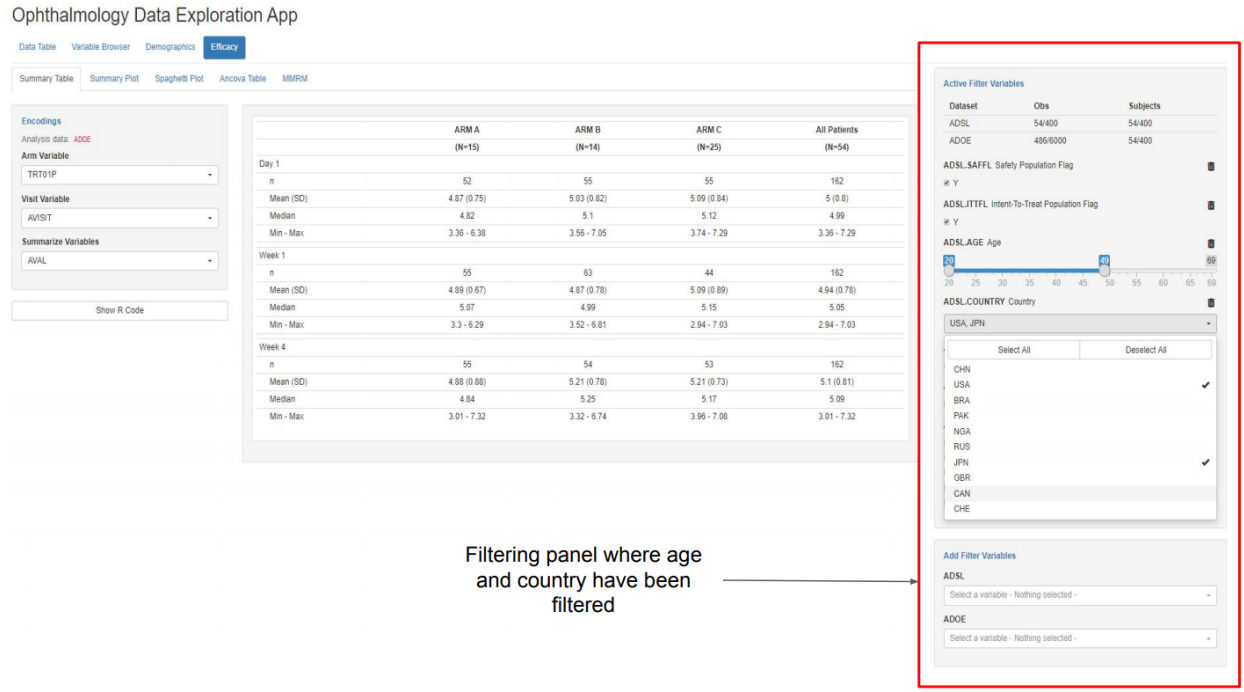

Figure 11: Filtering Panel selection on Summary Table Module

3.2 SHOW R CODE BUTTON

The **Show R Code** button is displayed under the encoding panel of each module. Once clicked, the user sees a pop-up page with the code used to create the current displayed output. This code can be copied using the “copy to clipboard” button. With this copied code, the user can paste it into an R script and produce the static output. This allows for code reproducibility.

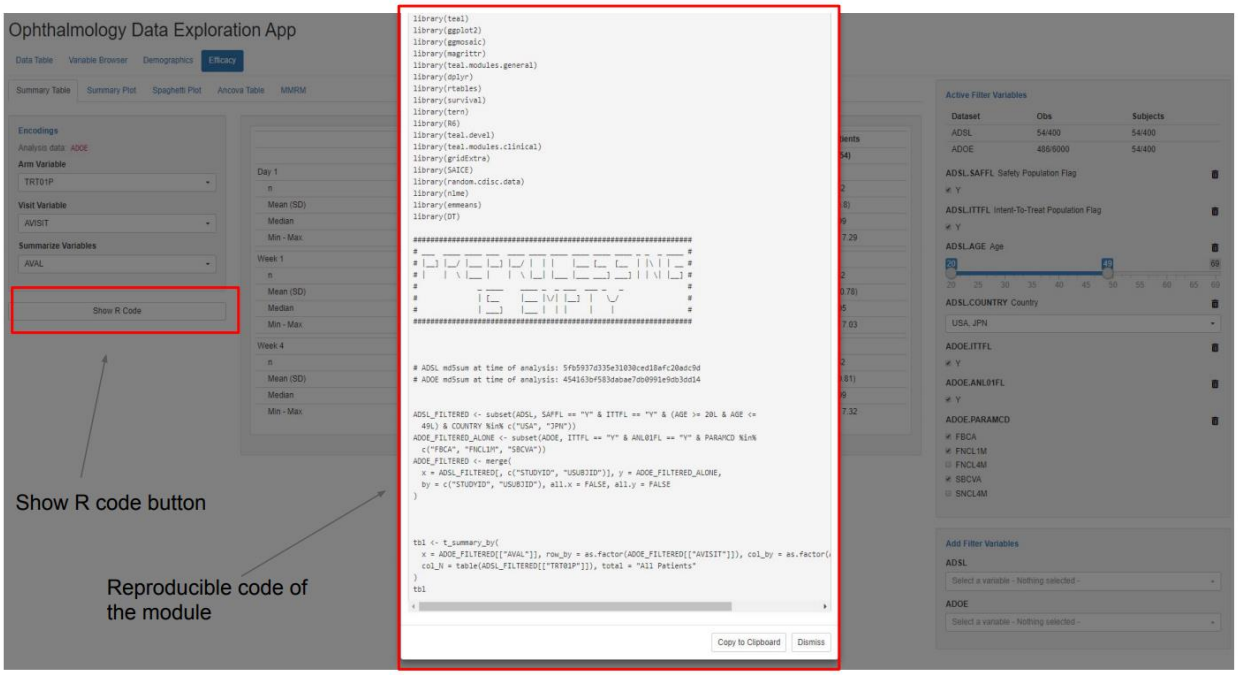

Figure 12: Show R Code Button

4. ADVANTAGES FOR OPHTHALMOLOGY

Some of the advantage of an R shiny application are as follows:

- Provides an agile solutions to problems caused by the growing complexity of studies
- Efficient (automated)
- Easy setup to create tables, listings and graphs (TLGs)
- Tailor for study-specific needs
- Platform-independent
- Transparent analysis environment

Ophthalmology studies can have hundreds of parameters recorded per patient in its Ophthalmology assessment and imaging data. Having the ability to quickly filter out different parameters of interest is a huge advantage. This allows the user to select the parameters of interest within the encoding and filtering panel which then prepopulates the desired output. The user no longer needs to reproduce a static output each time they want to view an output involving new parameters. This provides a great agile solution for quality control and data exploration within Ophthalmology studies.

5. CONCLUSION

With the ability to tailor visualizations through the creation of R packages, R shiny applications can provide a great framework for agile solutions to complex study work needs. In particular, Ophthalmology studies can greatly benefit from these applications due to their large datasets. With hundreds of parameters recorded per patient, the ability to quickly filter and subset the data is done very efficiently within the applications. The above application shows how many TLGs for Ophthalmology studies can be easily produced to fit the needs of the study. Quality control and

exploratory data analysis can become much more efficient since the user no longer needs to reproduce a static output by writing code but rather select the filtering option they are interested in within the application.

6. ACKNOWLEDGMENTS

I would like to acknowledge the NEST - internal scientific software development group at Hoffman-La Roche for the development and guidance of this application. As well, I would like to give a special thank you to Wenyi Liu for all of her guidance and Wes Tarlton for this opportunity.

7. REFERENCES

[1] Mallinckrodt, Craig H., et al. “Recommendations for the Primary Analysis of Continuous Endpoints in Longitudinal Clinical Trials.” *Drug Information Journal*, vol. 42, no. 4, 2008, pp. 303–319.

8. CONTACT INFORMATION

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