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Leveraging Data Visualization

&

R Shiny for Efficient Subgroup Analysis

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Agenda

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Introduction

DATA   VISUALIZATION   R Shiny   EFFICIENT?

Introduction

Presenting adverse event data across subgroups from complex studies that range over years are vital for assessing patient safety.
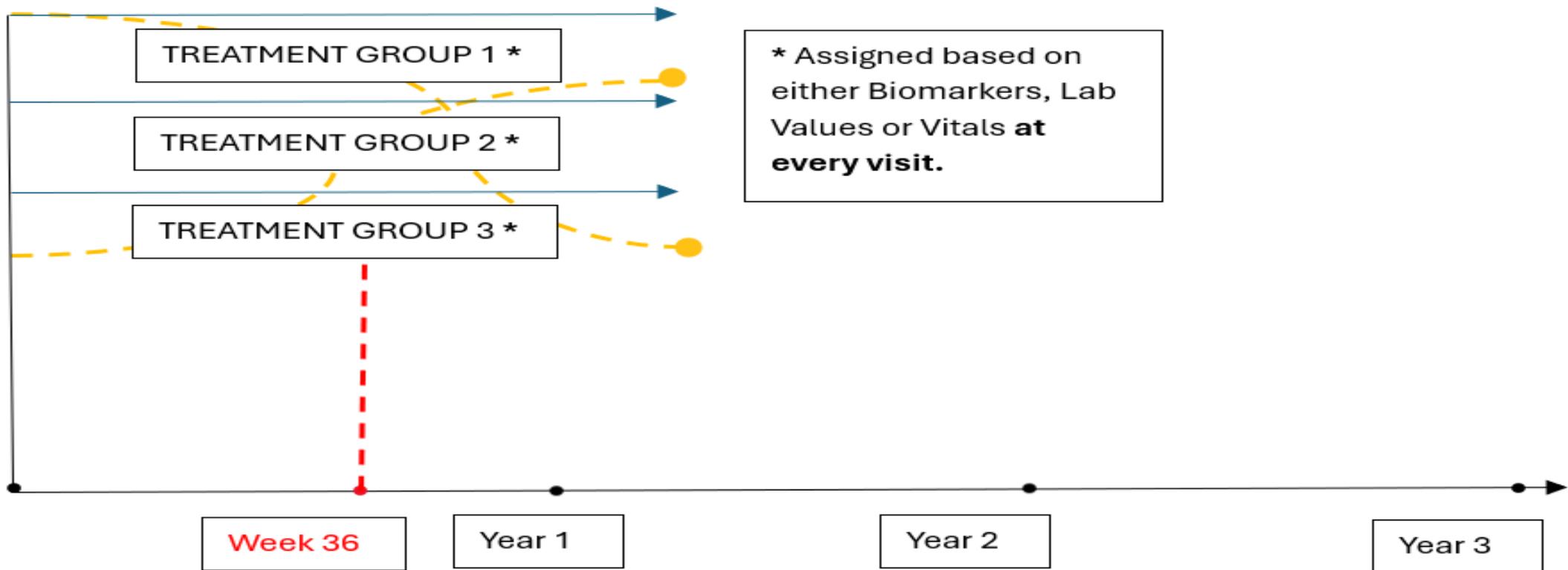
While Tables & Listings remain foundational in regulatory submissions, visualizations like Heatmaps through R Shiny can be helpful in data reviewing when studies involve the concept of dynamic dosing.

Combining these visuals with metadata-driven, traceable formats ensures regulatory compliance while improving efficiency in understanding safety data.

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Let us consider an example

Figure 1: A Dummy Study Schema

TREATMENT GROUP 1 *

TREATMENT GROUP 2 *

TREATMENT GROUP 3 *

* Assigned based on either Biomarkers, Lab Values or Vitals **at every visit.**

Week 36

Year 1

Year 2

Year 3

The Concept of Dynamic N

- As the doses are based on parameters and can change at every visit, the actual count of subjects assigned to one treatment group at a particular timepoint keep changing.

- Using denominator directly from ADaM.ADSL based on initial treatment assignment may not be precise at every timepoint.

Figure 2: Dummy Template to represent AE data

Overview of Adverse Events at timepoint i

TREATMENT GROUP 1	TREATMENT GROUP 2	TREATMENT GROUP 3
N_i	N_i	N_i

Problem Statement

Challenge	Opportunity
Adverse Event Data **+** **Visit Information** **+** **Changing Treatment Information** **+** **Subgroups**	**R Shiny** **+** **Visualization** **+** **Embed output generation**

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AEs (AEDECOD,AESOC,AESEV)

VISITS & Treatments.

Subgroups

Regions , Countries
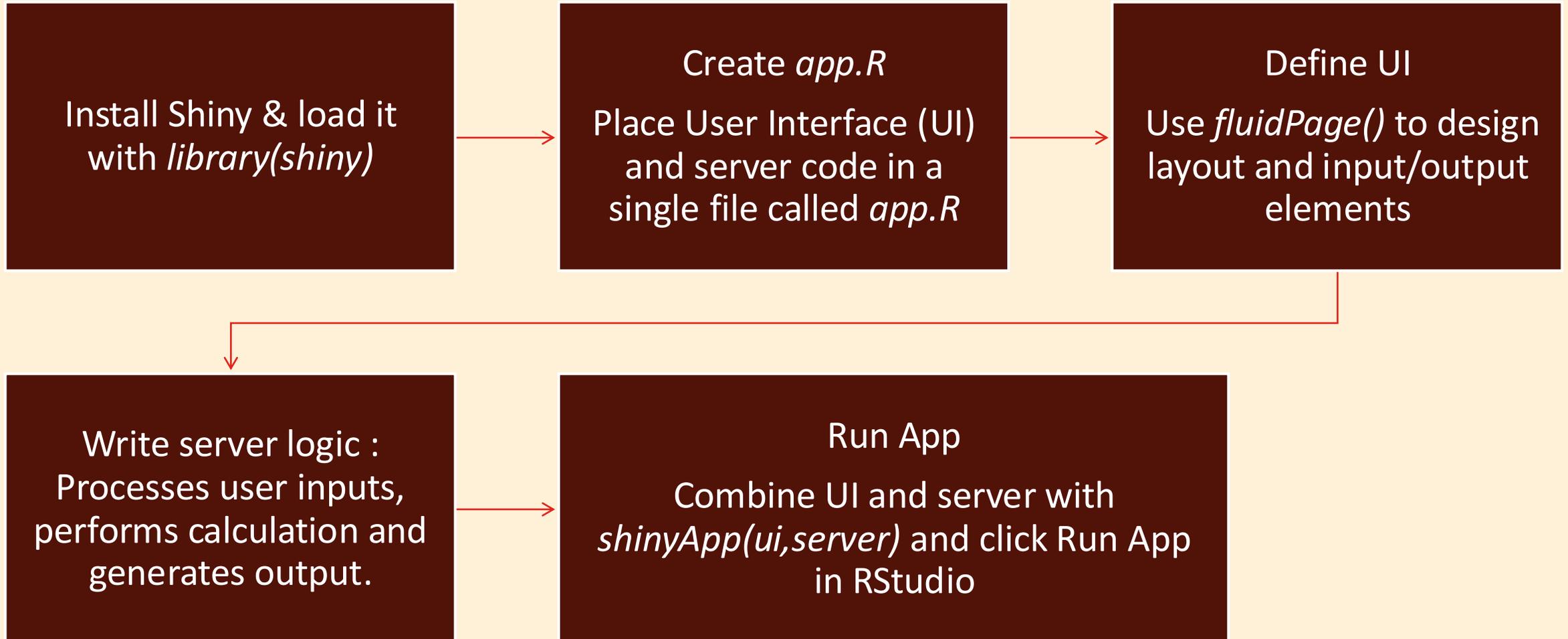
Prior Therapy / Rescue Therapy Status

Baseline Conditions

How Does our Data Look?

- Includes AE information, Corresponding Visit & Treatment Information.

- As ADAM.ADAE follows OCCDS structure, a custom dataset for the Shiny app that includes visit information is created.
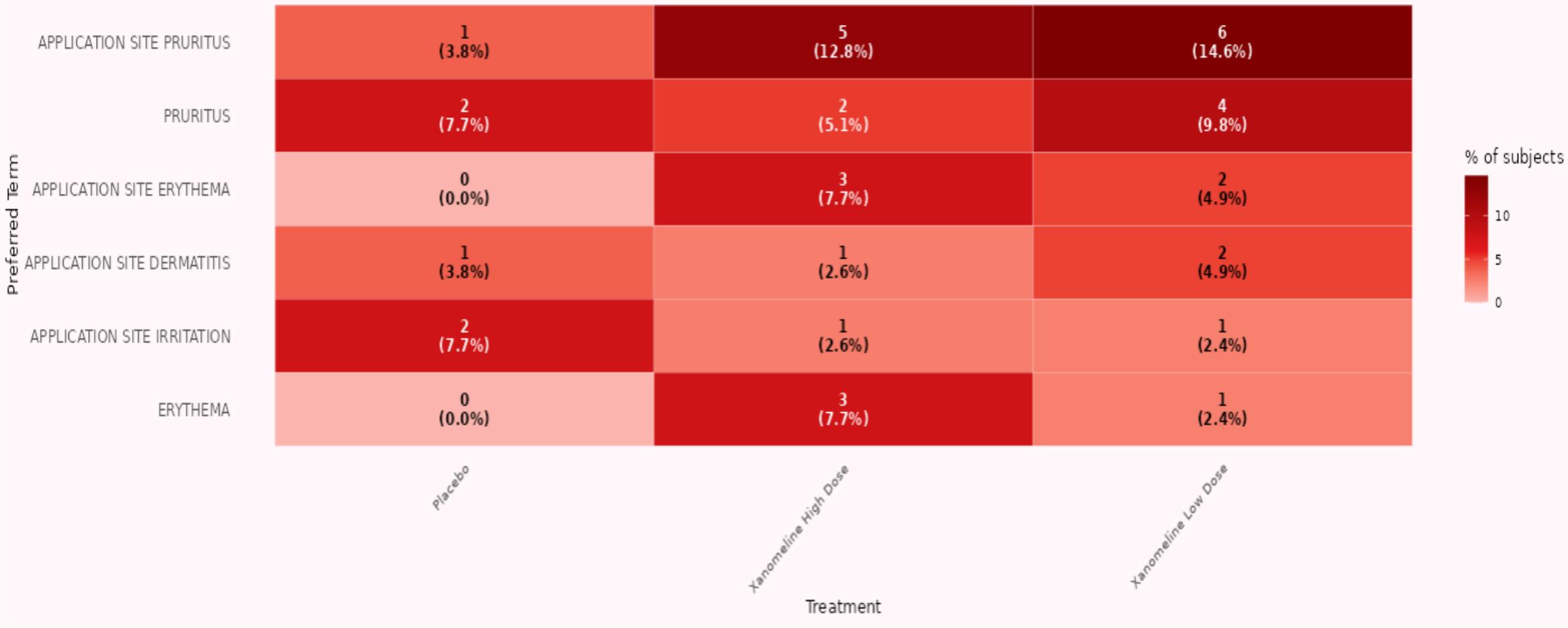
USUBJID	AEDECOD	AESEV	TRTA	SEX	WEIGHTGR	ASTDT	VN
Unique Subject Identifier	Dictionary-Derived Term	Severity/Intensity	Actual Treatment	Sex	Weight Group	Analysis Start Date	Visit Number
01-701-1034	APPLICATION SITE PRURITUS	MILD	Xanomeline High Dose	F	25-<30	27-08-2014	8
01-701-1028	**APPLICATION SITE ERYTHEMA**	**MILD**	**Xanomeline High Dose**	**M**	**>=30**	**21-07-2013**	**3**
01-701-1028	**APPLICATION SITE PRURITUS**	**MILD**	**Xanomeline Low Dose**	**M**	**<30**	**08-10-2013**	**5**
01-701-1023	ERYTHEMA	MILD	Placebo	M	>=30	07-08-2012	3
01-701-1023	ERYTHEMA	MILD	Placebo	M	>=30	07-08-2012	3
01-701-1023	ERYTHEMA	MODERATE	Placebo	M	>=30	07-08-2012	3
01-701-1023	ATRIOVENTRICULAR BLOCK SECOND DEGREE	MILD	Placebo	M	>=30	26-08-2012	3.5
01-701-1015	APPLICATION SITE ERYTHEMA	MILD	Placebo	F	25-<30	03-01-2014	3
01-701-1015	APPLICATION SITE PRURITUS	MILD	Placebo	F	25-<30	03-01-2014	3
01-701-1015	DIARRHOEA	MILD	Placebo	F	25-<30	09-01-2014	3.5

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R Shiny

Install Shiny & load it with *library(shiny)*

Create *app.R*

Place User Interface (UI) and server code in a single file called *app.R*

Define UI

Use *fluidPage()* to design layout and input/output elements

Write server logic : Processes user inputs, performs calculation and generates output.

Run App

Combine UI and server with *shinyApp(ui,server)* and click Run App in RStudio

Heatmap of AEs vs Treatments by VISIT

Adverse Events vs Treatment - Visit 5
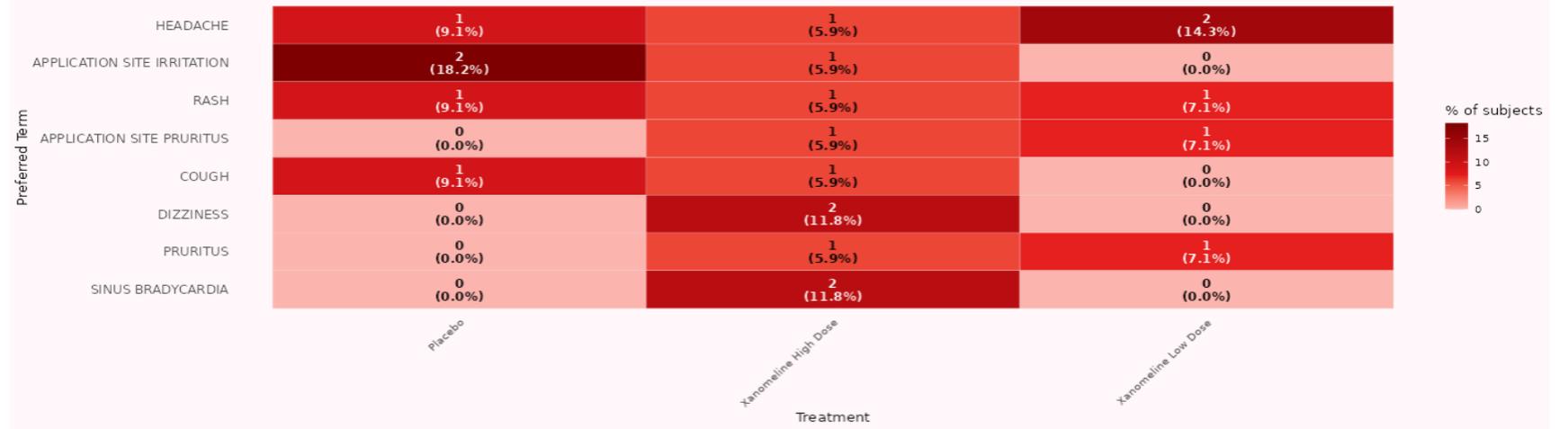
HTML Output of app.R

How can this be used?

- To verify counts generated in Tables, Listings & Figures.

- Different stakeholders can collaborate to efficiently monitor AE data in periodic reviews.

- As it accounts different combinations of subgroups, repetitive report generation is eliminated.

- Furthermore, Box plots and other graphical visualizations can be applied to other safety data, such as vital signs and laboratory results, which are already organized in the ADaM Basic Data Structure (BDS) format. This approach would support efficient data monitoring and enhances interpretability.

Future Enhancements

1. If embedded with **<u>validated</u>** output generation , can contribute to the eventual submission process.

2. Can be used as supporting material to aid regulators for visual review along with the usual outputs.*

* Point 2 is based by referring to a PHUSE White Paper [POS_PP16.pdf] pilot   project published in 2022, that talks about linking the HTML plot along with CSS (cascading style sheets) & the JavaScript being included for submission and R Submissions Working Group Pilot 4 project in 2024 [R:fda-pilot4] where the submission package involved a Web Assembly component through FDA's Electronic Common Technical Document (eCTD).

References

1. https://lexjansen.com/css-us/2020/POS_PP16.pdf

2. https://lexjansen.com/phuse-us/2020/dv/DV13_ppt.pdf

3. https://www.lexjansen.com/phuse/2018/dv/DV11.pdf

4. R Consortium - Using R to Submit Research to the FDA: Pilot 4 Successfully Submitted to FDA Center for Drug Evaluation and Research

5. GitHub - phuse-org/TestDataFactory: All files related to the PhUSE Test Data Factory (TDF) project

6. Archive Page | PHUSE

QnA

Thank you for your time & attention!

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