



An Initiative to Use R in Takeda SQS Japan

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Better Health, Brighter Future



What is “SQS” ?



- SQS = Statistical & Quantitative Sciences
- SQS Japan is under Global SQS
 - Lead drug development for Japan portfolio with innovative statistical designs and analysis methodologies through pre-clinical, clinical and post marketing cycle as a part of global SQS
 - Consists of Statistical Programmers (hereinafter called stat programmers) and Biostatisticians (including me)

 Encounter in 2000

 Thorough investigation for 3 months in 2003

 External activities since 2004

 A has-been, but “official” internal activities since 2024

-  SQS Japan should stay updated with industry trends, increase literacy, and proactively strategize the introduction of R (or Python). This will ensure the capability to perform bio-statistical tasks in clinical development, even if SAS becomes unavailable tomorrow.

An Initiative to Use R in Takeda SQS



- Takeda Biostatisticians have used R for several statistical methods, especially the latest statistical methods. For example, multiplicity adjustment (MCP-Mod, graphical approach, gatekeeping, and so on), adaptive design, planning oncology clinical trials, and so on. We also created some Shiny application to conduct statistical calculation.
- On the other hand, R is not commonly used among Takeda stat programmers (At least in Japan), and there are very few cases where R has been applied for the formal deliverables in clinical studies, especially in a confirmatory stage.

An Initiative to Use R in Takeda SQS



- Takeda has been developing R roadmap to strategize the utilization of R in Takeda SQS.
- These days, SQS Global has conducted R trainings and awareness activities for several years.
- The aim is to develop modern standardized platform to further advance the usage of statistical modeling tools beyond SAS, such as R / Python.



Overview of R Trainings by Takeda SQS



- Introduction to R and RStudio
- Manipulate data and create summaries
- Graphics and statistical tests
- Develop your own functions and simulations
- R Markdown and Quarto
- R Shiny
- Create tables using “gt” package
- Etc.

55 min per lecture

Overview of R Trainings by Takeda SQS **Japan** (it's me)



- Introduction to R / RStudio
- Develop your own functions and programming
- Introduction to matrix and R traditional graphics
- Data handling with base R and tidyverse package
- Create tables for clinical studies using rtables + tern package
- Introduction to ggplot2 package
- Statistical methods and simulation
- How to develop Shiny application
- R Tips

55 min x 22 lectures

An Initiative to Use R in Takeda SQS Japan (Programmer)



FY2024

- R trainings
 - For SQS Global and SQS Japan
 - Additional training collaborated with CRO (ICON)
- Collaboration with global team
- Develop Shiny application

Challenges

- R grammar is hard for SAS users to understand.
- Motivation to learn R even though SAS exists.



An Initiative to Use R in Takeda SQS Japan (Biostatistician)



FY2024

- R trainings for Japanese
- Using R in our operation process
 - Develop Shiny application
 - Statistical approach using R

FY2025

- Investigation for Shiny & teal package
- Implementation of Shiny application
- External presentation of statistical approach using R



Reference Documents for R Training



R Basics & Data Handling

- 改訂2 版 Rユーザのための RStudio [実践] 入門 (in Japanese): <https://www.amazon.co.jp/dp/4297121700>
- The R Tips , 3rd edition : <https://www.amazon.co.jp/dp/B0719QS6KG>

Clinical TLGs

- Tables in Clinical Trials with R: <https://rconsortium.github.io/rtrs-wg/>
- rtables: <https://github.com/insightsengineering/rtables>
- tern: <https://insightsengineering.github.io/tern/latest-tag/>
- rlistings: <https://insightsengineering.github.io/rlistings/latest-tag/>
- TLG Catalog: <https://insightsengineering.github.io/tlg-catalog/stable/>

ggplot2

- The R Tips + R Graphics Cookbook, 2nd edition: <https://r-graphics.org/>

R shiny

- See below for further details

Pharmaverse & Tables for Clinical Studies



- **sdtmchecks**: identify common data issues in SDTM data
- **admiral**: develop ADaM datasets in R.
- **rtables**: create and display complex tables with R.
 - Tomoyuki Namai and Yumi Nishimoto (2023) "Creating Clinical Tables in R with rtables Package", PharmaSUG SDE Japan 2023.
- **tern**: create tables and graphs used for clinical trial reporting.
- **logrx**: facilitate logging in a clinical environment with the goal of making code easily traceable and reproducible.
- **xportr**: help get xpt files ready for transport either to a clinical data set validator application or to a regulatory agency.
- Other packages for tables: gt, flextable, tfrmt, tables, tidytlg, etc.
 - **flextable + officer**: Nobuo Funao (2018) "Automated Generation of PowerPoint Presentations Using R in Clinical Studies", PharmaSUG SDE 2018
 - **ReporteRs**: Nobuo Funao (201X) "ReporteRs - How to output analysis results to PowerPoint using R"



Why do you use tern, not other packages?



- Can output tables “for clinical studies” to WORD file.
- Relatively simple grammar
- RCRSWG adopt rtables in submissions pilot to FDA (demographic table).
- Many sample codes via **TLG Catalog**: <https://insightsengineering.github.io/tlg-catalog/stable/>

Select table, graph, or listing you want

TLG Catalog - Stable



Introduction

Tables ☒

ADA ☐

Adverse Events ☐

Concomitant Medications ☐

Deaths ☐

Demography ☒

DMT01

Disclosures ☐

Disposition ☐

ECG ☐

Efficacy ☐

Exposure ☐

Lab Results ☐

Data Setup

Table with an Additional Study-Specific Continuous Variable

Table with an Additional Study-Specific Categorical Variable

Preview

☒ Code

[Try this using WebR](#)

	A: Drug X (N=134)	B: Placebo (N=134)	C: Combination (N=132)	All Patients (N=400)
Age (yr)				
n	134	134	132	400
Mean (SD)	33.8 (6.6)	35.4 (7.9)	35.4 (7.7)	34.9 (7.4)
Median	33.0	35.0	35.0	34.0
Min - Max	21.0 - 50.0	21.0 - 62.0	20.0 - 69.0	20.0 - 69.0
Age Group				
n	134	134	132	400
18-40	113 (84.3%)	103 (76.9%)	106 (80.3%)	322 (80.5%)
41-64	21 (15.7%)	31 (23.1%)	25 (18.9%)	77 (19.2%)
>=65	0	0	1 (0.8%)	1 (0.2%)
Sex				
n	134	134	132	400
Female	79 (59%)	82 (61.2%)	70 (53%)	231 (57.8%)
Male	55 (41%)	52 (38.8%)	62 (47%)	169 (42.2%)

View R programs for both preprocessing and creating TLGs

- R Package to create a web application, developed by Posit.
- Shiny enables us to easily create web applications without knowledge of web application development. However, once you start creating some apps, you want to customize them, and you need some knowledge of html and javascript.
- Reference
 - **Mastering Shiny:** <https://mastering-shiny.org/index.html>
 - Shiny - GET STARTED: <https://shiny.posit.co/r/getstarted/shiny-basics/lesson1/>
 - bslib: <https://rstudio.github.io/bslib/index.html>
 - DT: <https://rstudio.github.io/DT/shiny.html>
 - Introduction to shinyvalidate:
<https://rstudio.github.io/shinyvalidate/articles/shinyvalidate.html>
 - Shiny for R Gallery: <https://shiny.posit.co/r/gallery/>
 - R Shiny Workshop: <https://github.com/nuitrcs/rshiny>

Shiny Application Demo



Reference: Shiny Assistant

<https://shiny.posit.co/blog/posts/shiny-assistant/>



Hello, I'm Shiny Assistant! I'm here to help you with [Shiny](#), a web framework for data driven apps. You can ask me questions about how to use Shiny, to explain how certain things work in Shiny, or even ask me to build a Shiny app for you.

Here are some examples:

- "How do I add a plot to an application?"
- "Create an app that shows a normal distribution."
- "Show me how make it so a table will update only after a button is clicked."
- Ask me, "Open the editor", then copy and paste your existing Shiny code into the editor, and then ask me to make changes to it.

Let's get started!

Who can see my activity?

Create an app that shows a normal distribution

Certainly! I'll create a Shiny app that displays a normal distribution. This app will allow users to adjust the mean and standard deviation of the distribution and will show both a histogram and a density plot of the resulting normal distribution.

Here's the code for the Shiny app:

Enter a message...

app.R

```
11 ),
12 card(
13   card_header("Normal Distribution Plot"),
14   plotOutput("distPlot")
15 )
16 )
17
18 server <- function(input, output) {
19   output$distPlot <- renderPlot({
20     set.seed(123) # For reproducibility
21     data <- data.frame(x = rnorm(input$n, mean = input$mean, sd = input$sd))
22
23     ggplot(data, aes(x = x)) +
24       geom_histogram(aes(y = ..density..), bins = 30, fill = "skyblue", color = "black") +
25       geom_density(color = "red", size = 1) +
26       stat_function(
27         fun = dnorm,
28         args = list(mean = input$mean, sd = input$sd),
29         color = "blue", size = 1, linetype = "dashed"
30       ) +
31       labs(
32         title = "Normal Distribution",
33         x = "Value",
34         y = "Density"
35       ) +
36       theme_minimal() +
37       theme(plot.title = element_text(hjust = 0.5))
38   })
39 }
40
41 shinyApp(ui, server)
42
```

Downloading webR package: fansi
Downloading webR package: utf8
Downloading webR package: vctrs
Downloading webR package: pillar
Downloading webR package: pkgconfig
Downloading webR package: tibble
Downloading webR package: ggplot2

Attaching package: 'bslib'

The following object is masked from 'package:utils':

page

Warning: Using 'size' aesthetic for lines was deprecated in ggplot2 3.4.0.
i Please use 'linewidth' instead.
Warning: The dot-dot notation ('..density..') was deprecated in ggplot2 3.4.0.
i Please use 'after_stat(density)' instead.
█

Normal Distribution Viewer

Mean:

Standard Deviation:

Number of samples:

Normal Distribution Plot

15

Question ??



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