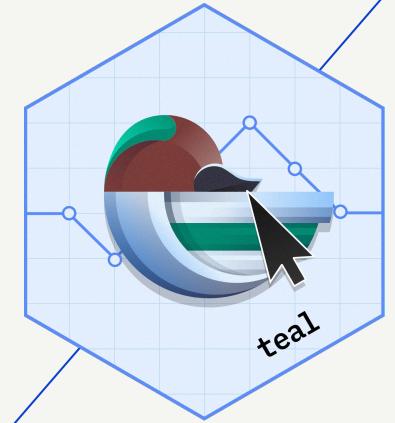


{teal} - an Open Source Framework for Data Exploration in Clinical Trials and Beyond

useR! 2024, Salzburg

Pawel Rucki

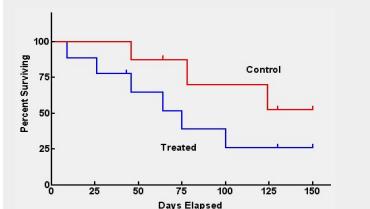
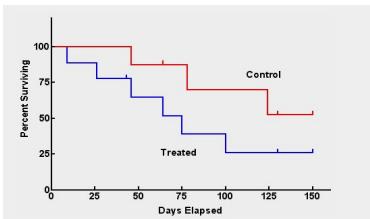
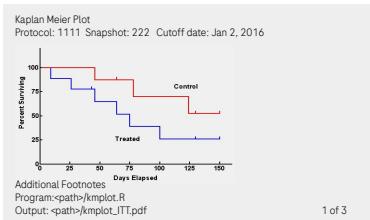


Agenda

- Introduction - what is {teal}
- {teal} core features
- Demo
- Use cases
- Materials

Improve efficiency in the way we work

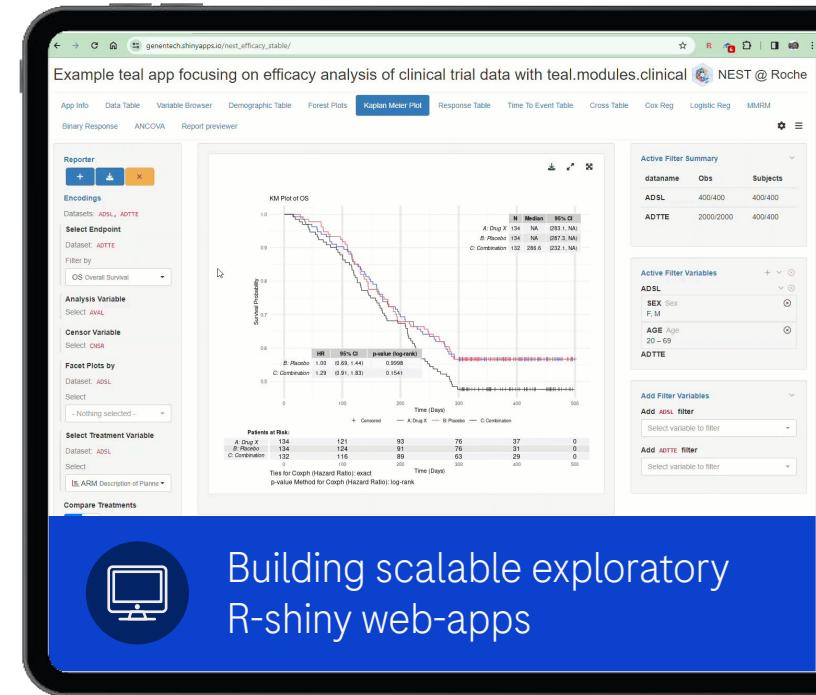
Analyzing clinical trial data requires multiple ways of presenting and interacting with our data



Per-SAP static output
on OS

Ad-hoc analysis
on PFS

Ad-hoc analysis on PFS
in subpopulation



Example teal app focusing on efficacy analysis of clinical trial data with teal.modules.clinical NEST @ Roche

App Info Data Table Variable Browser Demographic Table Forest Plots Kaplan Meier Plot Response Table Time To Event Table Cross Table Cox Reg Logistic Reg MMRM

Binary Response ANCOVA Report previewer

Reporter + - X

Encodings

Select Endpoint Dataset: ADSL, ADTTE

Dataset: ADTTE

Filter by OS Overall Survival

Analysis Variable Select AVAL

Censor Variable Select: OSNA

Facet Plots by Dataset: ADSL

Select - Nothing selected -

Select Treatment Variable Dataset: ADSL

Select IS ARM Description of Plans

Compare Treatments

KM Plot of OS

Survived Probability

HR 0.95 95% CI 0.91-1.00 p-value (logrank) 0.9598

A Drug X 134 121 93 76 37 0
B placebo 134 124 91 76 31 0
C Combination 132 295.5 232 113 29 0

Time (Days)

Patients at Risk + Gensored - A Drug X - B placebo - C Combination

Ties for Coph (Hazard Ratio): exact p-value Method for Coph (Hazard Ratio): log-rank

Active Filter Summary

dataname	Obs	Subjects
ADSL	400/400	400/400
ADTTE	2000/2000	400/400

Active Filter Variables

- + ADSL
- SEX Sex: F, M
- AGE Age: 20-69
- ADTTE

Add Filter Variables

Add ADSL filter

Select variable to filter

Add ADTTE filter

Select variable to filter

Building scalable exploratory R-shiny web-apps

What is {teal}?



A R Shiny-based interactive data exploration framework



Modularized and standardized building blocks

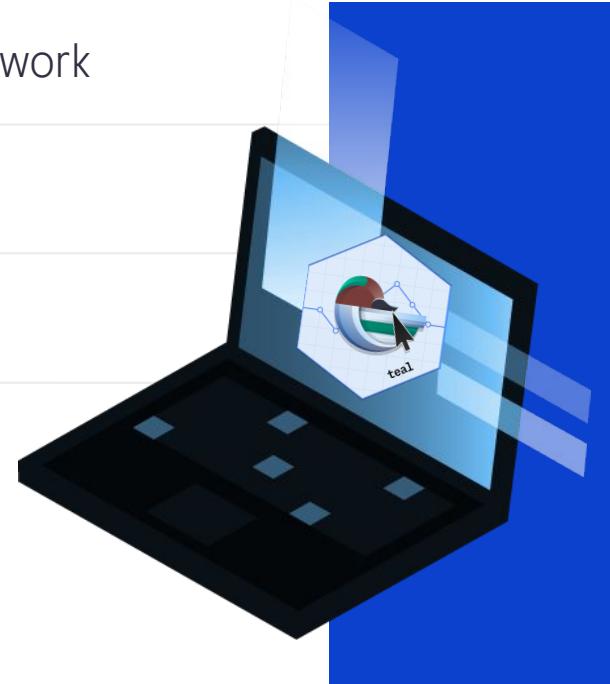


Collection of specialized R packages



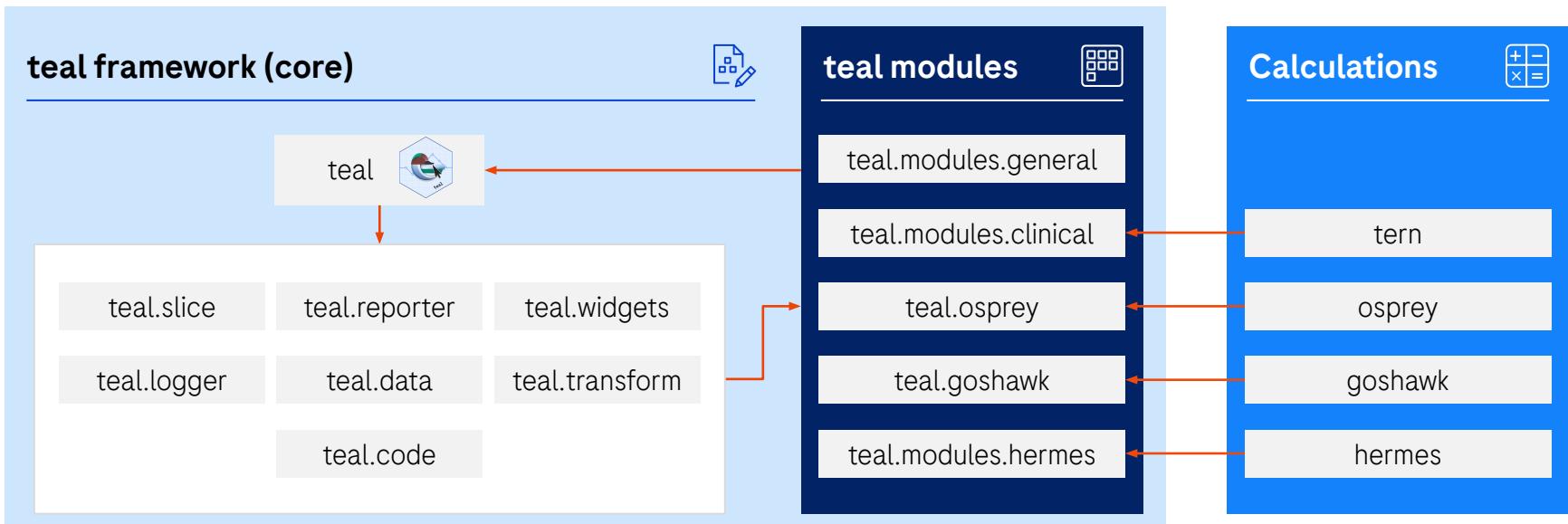
Streamlines creation of web-apps that offers:

- Dynamic filtering facility
- Code reproducibility
- Reporting engine
- Many data summarization and visualizations



{teal} Universe Products Map

The screenshot shows a software application window titled "Example App with teal.modules.clinical modules". The interface includes a navigation bar with links like "Study Information", "Data Table", "Variable Browser", "Demographic Table", "Forest Plots", "Kaplan Meier Plot", "Response Table", "Time To Event Table", "Cross Table", "Cox Reg", "Logistic Reg", and "MMRM". The main area displays a table of demographic data for four groups: A: Drug X (N=134), B: Placebo (N=134), C: Combination (N=132), and All Patients (N=400). The table includes columns for Age, Sex, and various statistical measures like Mean, Median, and Min-Max. On the left, there's a "Report" panel with sections for "Encodings", "Dataset: ADSL", "Select Treatment Variable", and "Summary Variables". On the right, there are sections for "Active Filter Summary", "Active Filter Variables", and "Add Filter Variables".



teal Framework R Packages



- ▶ [teal](#): shiny-based interactive exploration framework for analyzing data
- ▶ [teal.widgets](#): shiny components used within teal
- ▶ [teal.reporter](#): allows teal applications to generate reports
- ▶ [teal.slice](#): provides a filtering panel to allow subset of data
- ▶ [teal.data](#): creating and loading the data needed for teal applications
- ▶ [teal.code](#): handles reproducibility of outputs
- ▶ [teal.transform](#): standardizes extracting and merging data
- ▶ [teal.logger](#): standardizes logging within teal framework

teal Modules R Packages



- ▶ [teal.modules.general](#): general analysis modules for exploring any data types
- ▶ [teal.modules.clinical](#): modules for analyzing CDISC data and clinical trial reporting with [tern](#) R package
- ▶ [teal.osprey](#): modules for analyzing and reporting early-phase clinical trial data with [osprey](#) R package
- ▶ [teal.goshawk](#): modules for analyzing and visualizing biomarker data with [goshawk](#) R package
- ▶ [teal.modules.hermes](#): modules for analyzing and visualizing RNAseq data with [hermes](#) R package

Key Features: Filter Panel



Ability to subset your dataset



Out of the box from teal framework



Active filter summary



Pre-defined filter state

The screenshot displays the 'Active Filter Summary' interface, which includes the following sections:

- Active Filter Summary:** A table showing filter counts:

	Obs	Subjects
ADSL	400/400	400/400
ADTTE	1600/1600	400/400
- Active Filter Variables:** A section for **ADSL** containing:
 - RACE:** ASIAN (208), BLACK OR AFRICAN AMERICAN (91), WHITE (74), AI
 - AGE:** A histogram showing the distribution of age with two highlighted points at 20 and 69.
- ADTTE:** A section for **ADTTE** containing:
 - PARAMCD Parameter Code:** CRSD (400), EFS (400), OS (400), PFS (400) (all checked)
- Add Filter Variables:** Two dropdown menus for adding filters:
 - Add **ADSL** filter:** Select variable to filter
 - Add **ADTTE** filter:** Select variable to filter

Key Features:

Show R Code



Reproducible code when you see the desired output in analysis



Include any filters added



Include library () calls

Show R code

```

## and might have omitted this step for some reason. Please reach
## out to the app developer for details.

# ADSL MD5 hash at the time of analysis: 01965f31841821489767446baaff0ad2
# ADTTE MD5 hash at the time of analysis: af41fb660390618275fbcba67c82a563

ADTTE <- dplyr::inner_join(x = ADTTE, y = ADSL[, c("STUDYID", "USUBJID"), drop = FALSE], by = c("STUDYID", "USUBJID"))

# Description of Planned Analysis
ANL_1 <- ADTTE %>% dplyr::select(STUDYID, USUBJID, PARAMCD, AVAL, CNSR, AVALU)
ANL_2 <- ADSL %>% dplyr::select(STUDYID, USUBJID, ARM, STRATA1, AGEGR1)
ANL_3 <- ADTTE %>%
  dplyr::filter(PARAMCD == "OS") %>%
  dplyr::select(STUDYID, USUBJID, PARAMCD)
ANL <- ANL_1
ANL <- dplyr::inner_join(ANL, ANL_2, by = c("STUDYID", "USUBJID"))
ANL <- dplyr::inner_join(ANL, ANL_3, by = c("STUDYID", "USUBJID", "PARAMCD"))
ANL <- ANL %>% formatters::var_relabel(AVAL = "Analysis Value", CNSR = "Censor", ARM = "Description of Planned Analysis")

anl <- ANL %>%
  dplyr::filter(ARM %in% c("A: Drug X", "B: Placebo", "C: Combination")) %>%
  dplyr::mutate(ARM = stats::relevel(ARM, ref = "A: Drug X")) %>%
  dplyr::mutate(ARM = droplevels(ARM)) %>%
  dplyr::mutate(is_event = CNSR == 0)
variables <- list(tte = "AVAL", is_event = "is_event", arm = "ARM", strat = "STRATA1")
grid::grid.newpage()
lyt <- grid::grid.layout(nrow = nlevels(ANL$AGEGR1), ncol = 1) %>%
  grid::viewport(layout = .)
grid::pushViewport()
result <- mapply(df = split(anl, f = anl$AGEGR1), nrow = seq_along(levels(anl$AGEGR1)), FUN = function(df_i, r) {
  if (nrow(df_i) == 0) {
    grid::grid.text("No data found for a given facet value.", x = 0.5, y = 0.5, vp = grid::viewport(layout.pos.col = 1))
  } else {
    g_km(df = df_i, variables = variables, font_size = 8L, xlab = paste0("Time", " (", gsub("(^|[[:space:]])", "", r), ")"),
        conf_level = 0.95,
        pval_method = "log-rank", ties = "exact"
      ), ci_ribbon = FALSE, vp = grid::viewport(layout.pos.row = nrow_i, layout.pos.col = 1), draw = TRUE)
  }
}, SIMPLIFY = FALSE)
km_grobs <- tern::stack_grobs(grobs = result)
km_grobs

```

Copy to Clipboard
Dismiss

Key Features: teal Reporter



Create a report for your analysis



Zip file that contains:

- .Rmd
- .rds
- .png
- And the requested report type
(html, pdf, or ppt)

The screenshot displays the teal Reporter application interface. At the top, there are three large buttons: a blue '+' button, a blue download icon button, and an orange 'X' button. Below these are sections for 'Report previewer' and 'Download the Report'. The 'Report previewer' shows a 'Kaplan Meier Plot' card, which is described as a non-parametric method used to estimate the survival function from lifetime data. It includes a 'Filter State' section with detailed filtering options for datasets ADSL, AGE, and ADTTE. To the right of the plot is a table with columns for 'BLACK OR AFRICAN AMERICAN', 'WHITE', and 'AMERICAN INDIA'. Below the plot is a 'Plot' section showing a Kaplan-Meier survival curve with four groups: A (Drug), B (Placebo), C (Combination), and D (Control). The 'File Browser' at the bottom shows a folder named 'report_202301232356403062' containing four files: 'file15a41d15fea8f2.rds', 'file15a41d60ef42dc.png', 'input_20230123235640313.html', and 'input_20230123235640313.Rmd'. The files were all modified at 11:56 PM.

Key Features:

Curated sets of teal modules for targeted purposes



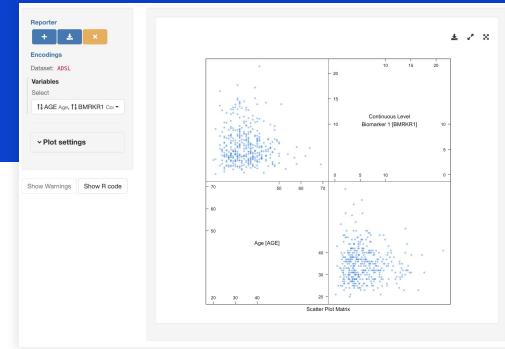
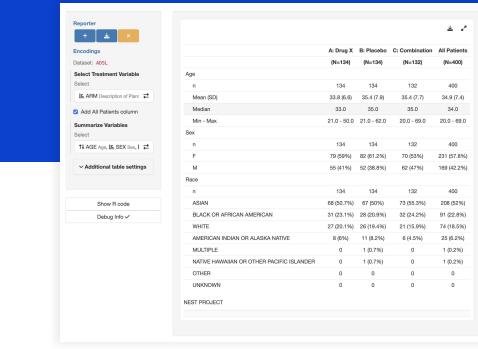
Actively developed and maintained centrally by a dedicated team



Purposefully designed, e.g. for clinical trials reporting or biomarker analysis



50+ common analysis modules available for use



Creating a teal App

```
library(teal)

app <- init(
  data = teal_data(
    IRIS = iris,
    MTCARS = mtcars
  ),
  modules = list(example_module()),
  header = "My first teal application"
)

runApp(app)
```

My first teal application

example teal module

Choose a dataset

IRIS

	Sepal.Length	Sepal.Width	Petal.Length	Petal.Width	Species
1	5.1	3.5	1.4	0.2	setosa
2	4.9	3.0	1.4	0.2	setosa
3	4.7	3.2	1.3	0.2	setosa
4	4.6	3.1	1.5	0.2	setosa
5	5.0	3.6	1.4	0.2	setosa
6	5.4	3.9	1.7	0.4	setosa
7	4.6	3.4	1.4	0.3	setosa
8	5.0	3.4	1.5	0.2	setosa
9	4.4	2.9	1.4	0.2	setosa
10	4.9	3.1	1.5	0.1	setosa
11	5.4	3.7	1.5	0.2	setosa
12	4.8	3.4	1.6	0.2	setosa
13	4.8	3.0	1.4	0.1	setosa
14	4.3	3.0	1.1	0.1	setosa
15	5.8	4.0	1.2	0.2	setosa
16	5.7	4.4	1.5	0.4	setosa
17	5.4	3.9	1.3	0.4	setosa
18	5.1	3.5	1.4	0.3	setosa
19	5.7	3.8	1.7	0.3	setosa
20	5.1	3.8	1.5	0.3	setosa
21	5.4	3.4	1.7	0.2	setosa
22	5.1	3.7	1.5	0.4	setosa
23	4.6	3.6	1.0	0.2	setosa
24	5.1	3.3	1.7	0.5	setosa
25	4.8	3.4	1.9	0.2	setosa
26	5.0	3.0	1.6	0.2	setosa
27	5.0	3.4	1.6	0.4	setosa
28	5.2	3.5	1.5	0.2	setosa
29	5.2	3.4	1.4	0.2	setosa
30	4.7	3.2	1.6	0.2	setosa
31	4.8	3.1	1.6	0.2	setosa
32	5.4	3.4	1.5	0.4	setosa
33	5.2	4.1	1.5	0.1	setosa
34	5.5	4.2	1.4	0.2	setosa
35	4.9	3.1	1.5	0.2	setosa

Active Filter Summary

	Obs	Subjects
IRIS	150/150	
MTCARS	32/32	

Active Filter Variables

	Variables
	IRIS
	MTCARS

Add Filter Variables

Add IRIS filter

Select variable to filter

Add MTCARS filter

Select variable to filter

Try it out in shinylive!

```
library(teal.modules.clinical)
library(random.cdisc.data) # a package containing sample data in the ADaM format
```

```
data <- teal_data() |>
  within({
    ADSL <- rads1(cached = TRUE)
    ADAE <- radae(cached = TRUE)
  })
```

```
datanames(data) <- c("ADSL", "ADAE")
```

```
join_keys(data) <- default_cdisc_join_keys[datanames(data)]
```

```
adae <- data[["ADAE"]]
```

```
app <- init(
  data = data,
  modules = list(
    tm_t_events(
      label = "Adverse Event Table",
      dataname = "ADAE",
      arm_var = choices_selected(c("ARM", "ARMCB", "ARM"),
        llt = choices_selected(
          choices = variable_choices(adae, c("AETERM", "AEDECOD")),
          selected = c("AEDECOD")
        ),
        hlt = choices_selected(
          choices = variable_choices(adae, c("AEBODSYS", "AESOC")),
          selected = "AEBODSYS"
        ),
        add_total = TRUE,
        event_type = "adverse event"
      )
    ),
    header = "My teal App 2"
  ),
  runApp(app)
```

My Teal App 2

Adverse Event Table Report previewer



Encodings

Datasets: **ADSL**, **ADAE**

Select Treatment Variable

Dataset: **ADSL**

Select

ARM

Event High Level Term

Dataset: **ADAE**

Select

AEBODSYS

Event Low Level Term

Dataset: **ADAE**

Select

AEDECOD

Add All Patients columns

Additional table settings

Event Summary by Term : Body System or Organ Class and Dictionary-Derived Term				
Body System or Organ Class	A: Drug X	B: Placebo	C: Combination	All Patients
Dictionary-Derived Term	(N=134)	(N=134)	(N=132)	(N=400)
Total number of patients with at least one adverse event	122 (91%)	123 (91.8%)	120 (90.9%)	365 (91.2%)
Overall total number of adverse events	609	622	703	1934

cl A.1

Total number of patients with at least one adverse event	78 (58.2%)	75 (56%)	89 (67.4%)	242 (60.5%)
Overall total number of adverse events	132	130	160	422

ddc A.1.1.1.1

ddc A.1.1.1.1	50 (37.3%)	45 (33.6%)	63 (47.7%)	158 (39.5%)
ddc A.1.1.1.2	48 (35.8%)	48 (35.8%)	50 (37.9%)	146 (36.5%)

cl B.2

Total number of patients with at least one adverse event	79 (59%)	74 (55.2%)	85 (64.4%)	238 (59.5%)
Overall total number of adverse events	129	138	143	410

ddc B.2.2.3.1

ddc B.2.2.3.1	48 (35.8%)	54 (40.3%)	51 (38.6%)	153 (38.2%)
ddc B.2.1.2.1	49 (36.6%)	44 (32.8%)	52 (39.4%)	145 (36.2%)

cl D.1

Total number of patients with at least one adverse event	70 (50%)	87 (60%)	80 (50%)	237 (59%)
Overall total number of adverse events	120	137	140	400

Active Filter Summary	
Obs	Subjects
ADSL	400/400
ADAE	1934/1934

Active Filter Variables	
Add ADSL filter	Select variable to filter

Add Filter Variables	
Add ADSL filter	Select variable to filter

Add ADAE filter

Select variable to filter

Try it out in shinylive!

Demo Apps via teal Gallery

<https://insightsengineering.github.io/teal.gallery/demo.html>

Links on shinyapps.io

- | > | <u>Exploratory analysis on general data frames</u> | APP_NAME |
|-------|--|---------------|
| ————— | | ————— |
| > | <u>Safety analysis on clinical trial data</u> | "exploratory" |
| ————— | | ————— |
| > | <u>Efficacy analysis on clinical trial data</u> | "safety" |
| ————— | | ————— |
| > | <u>Efficacy analysis on clinical trial data</u> | "efficacy" |
| ————— | | ————— |



Use cases:

Clinical Trials



Data exploration:

- Data summarisation
 - Data preview
 - Missing data
 - Simple 1 or 2 dimensional visualizations
 - ...
-



Study applications:

- Adverse events
- Demographics
- Efficacy
- Safety
- Patient profile
- ...

! Not yet submission ready!
See: FDA Shiny Submission Pilot
with {teal} included!

Other use cases:



Data review
e.g.: RBQM tool



RNA-seq data
e.g.: `teal.modules.hermes`



Real world data
e.g.: `teal4real`



General data analysis

Additional Resources



New Video Content!

[A Complete Guide to Getting Started with teal](#)



{teal} is part of pharmaverse:
<https://pharmaverse.org/>



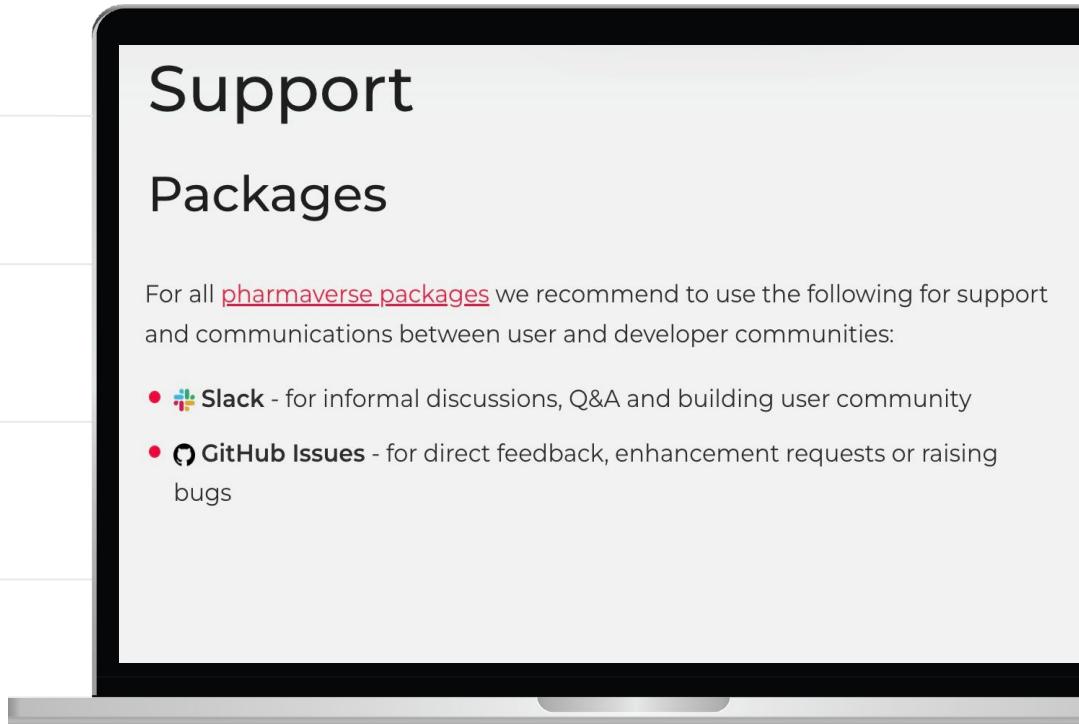
More information about support:
<https://pharmaverse.org/support/>



Slack channel [#teal](#) under
[pharmaverse](#) workspace



Coursera Course is now available!
[Making Data Science Work for Clinical Reporting](#)



Support Packages

For all [pharmaverse packages](#) we recommend to use the following for support and communications between user and developer communities:

-  **Slack** - for informal discussions, Q&A and building user community
-  **GitHub Issues** - for direct feedback, enhancement requests or raising bugs

Collaborating on {teal}



We are looking for collaborators to develop this framework further!



If you're an individual, please contribute on GitHub and join us via [pharmaverse](#) Slack [#teal](#) channel



If you're an organization wanting to adopt {teal} and co-develop, please get in touch with Paweł
pawel.rucki@roche.com



Doing now what patients need next