Reproducible Analyses & Literate Programming

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What is Reproducibility?

A data analysis is **reproducible** if all the information (data, files, etc.) needed to compute results is available for someone else to re-do your entire analysis and get the same results.

- All data processing steps from `raw data` to `cleaned data` are available and documented
- All analysis decisions made are documented and available in code
- Results don't depend on your specific computational environment (e.g. no hard coded file paths, seeds set for stochastic computations)

Why is Reproducibility Important?

- Allows you to show evidence of your results
- Encourages transparency about decisions made during analysis
- Enables others to check and use/extend your methods and results
- Enables FUTURE YOU to check and use/extend your methods and results

"You mostly collaborate with yourself, and me-from-two-months-ago never responds to email"

Dr. Mark Holder, Computational Biologist

Why is Reproducibility Important?

Dangers of writing code that is hard to double-check or confirm:

- The New York Times

The New York Times

How Bright Promise in Cancer Testing Fell Apart

First, though, he asked two statisticians at M. D. Anderson, Keith Baggerly and Kevin Coombes, to check the work. Several other doctors approached them with the same request.

Dr. Baggerly and Dr. Coombes found errors almost immediately. Some seemed careless — moving a row or a column over by one in a giant spreadsheet — while others seemed inexplicable. The Duke team shrugged them off as "clerical errors."

Updated NIH Guidelines

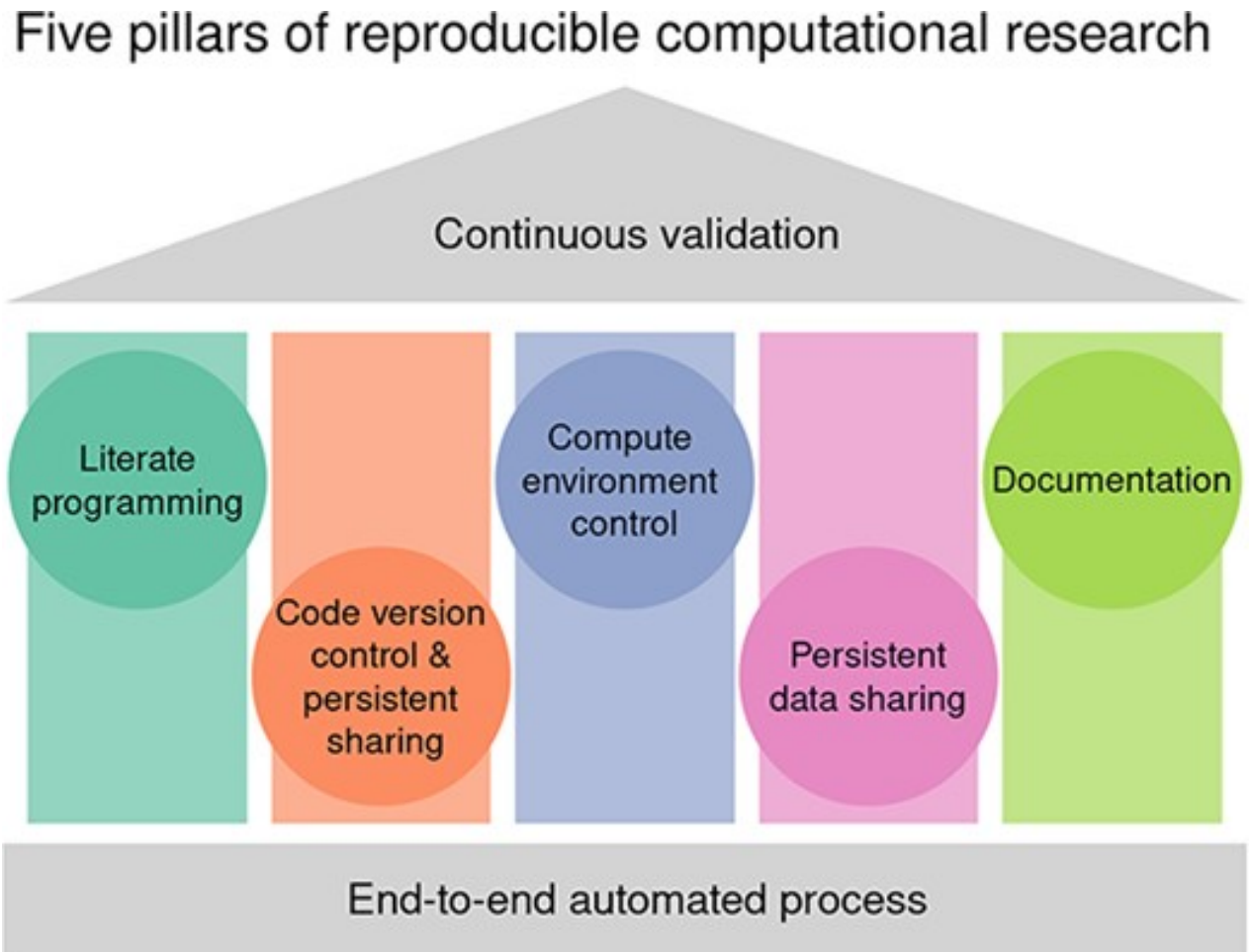
NIH Data Management & Sharing Policy Updates

- Effective Date: January 25, 2023
- Purpose: Enhance data sharing to advance research transparency & reproducibility

Key Requirements:

- As of 1/2023, all NIH Grants must create and adhere to a Data Management Plan (DMP)
- This plan will likely requires sharing of research data, and in some cases, code.
- You may be asked to provide your cleaned analysis data (and possibly code) at time of publication or end of grant.

Five Pillars Of Reproducibility



How Do We Ensure Our Code is Reproducible?

- **Compute Environment Control**
  - Virtual environments, avoid absolute file paths (e.g. `~/Users/Whiting/Projects...`)
- **Code Version Control**
  - Document changes you make, or use git/Github
- **Documentation**
  - Comment and document your code
  - Invest in a good `README.md`
- **Data Integrity** - more details later
- **Literate Programming**
  - Have a clear project structure, avoid 'by hand' steps

Literate Programming

Avoid ‘by hand’ steps used in the analysis

- Don’t clean by hand in Excel. All analysis steps should be done in code and saved in well-documented scripts.
- If any ‘non-scriptable’ steps are unavoidable, document those steps very clearly
- DNR (Do Not Repeat) - if you do it more than 3 times, consider writing a function
- Use **reproducible reporting** practices for analyses (e.g. Rmd, quarto, Jupyter notebook, inline text stats)

Reproducible Reporting

Reproducible Reporting

- **R Markdown**, **Quarto** and **Jupyter** are tools for integrating code and narrative text into a single executable document
- Can be rendered into various **output formats** (HTML, PDF, Word, and slides)
- Detailed code and data analysis steps are included in one document, encouraging **transparency** and providing a complete record of the research process
- Documents automatically update when data or code changes, **reducing errors** and **maintaining consistency**.
- Version-control compatible

Quarto Features: Callouts and Comments

Sometimes you need to draw attention to something in your report. You can do this using `{.callout-note}`

```
::: {.callout-note}
Note that there are five types of callouts, including:
`note`, `warning`, `important`, `tip`, and `caution`.
:::
```

Note

Note that there are five types of callouts, including: `note`, `warning`, `important`, `tip`, and `caution`.

```
::: {.callout-warning}
Here is an example of a warning
:::
```

Warning

Here is an example of a warning

Quarto Features: Tabs

```
---
title: Use tabs to organize content
output: html_document
---

You can turn parallel sections to tabs in `html_document` output.

## Results {.tabset}

### Plots

We show a scatter plot in this section.

```{r, fig.dim=c(5, 3)}
par(mar = c(4, 4, .5, .1))
plot(mpg ~ hp, data = mtcars, pch = 19)
```

Tables

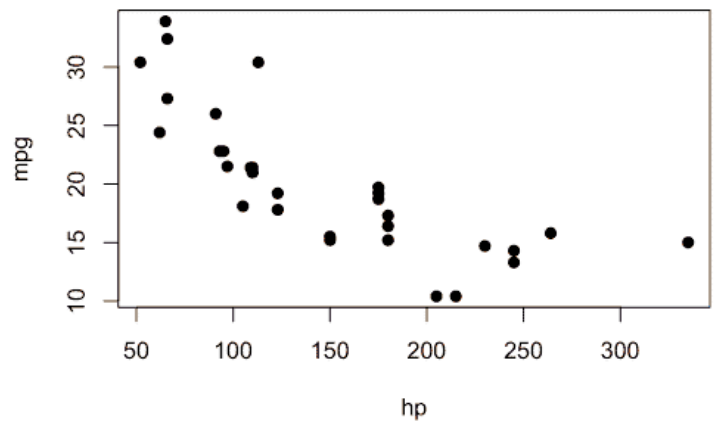
We show the data in this tab.

```{r}
head(mtcars)
```
```

Plots Tables

We show a scatter plot in this section.

```
par(mar = c(4, 4, 0.5, 0.1))
plot(mpg ~ hp, data = mtcars, pch = 19)
```



Plots Tables

We show the data in this tab.

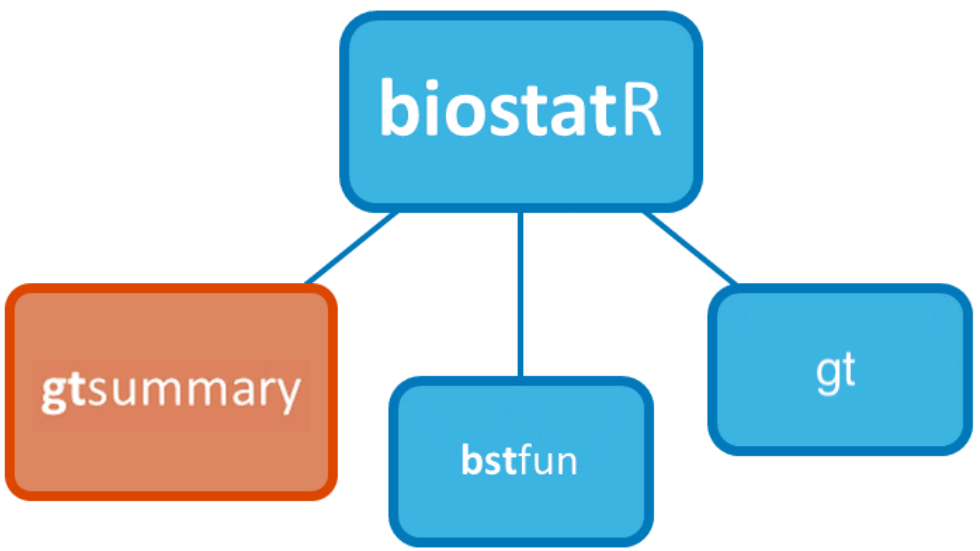
```
head(mtcars)
```

```
##                   mpg cyl disp  hp drat    wt  qsec vs am gear carb
## Mazda RX4         21.0   6  160 110 3.90 2.620 16.46  0  1    4    4
## Mazda RX4 Wag     21.0   6  160 110 3.90 2.875 17.02  0  1    4    4
## Datsun 710        22.8   4  108  93 3.85 2.320 18.61  1  1    4    1
## Hornet 4 Drive    21.4   6  258 110 3.08 3.215 19.44  1  0    3    1
## Hornet Sportabout 18.7   8  360 175 3.15 3.440 17.02  0  0    3    2
## Valiant           18.1   6  225 105 2.76 3.460 20.22  1  0    3    1
```

What Goes In Your Report?

gtsummary

- {gtsummary} - Tools to create publication-ready analytical and summary tables using the R programming language.
- Summarizes data sets, regression models, and more, using sensible defaults with highly customizable capabilities.



{gtsummary} overview

- Create **tabular summaries** including:
  - "Table 1"
  - Cross-tabulation
  - Regression models summaries
  - Survival data summaries
- Report statistics from {gtsummary} tables **inline** in R Markdown
- **Stack or merge** any table type
- Use **themes** to standardize across tables
- Choose from different **print engines**

Basic tbl_summary()

```
1  sm_trial <- trial %>%
2    select(trt, age, grade, response)
3
4  sm_trial %>%
5    select(-trt) %>%
6    tbl_summary()
```

Characteristic	N = 200[1]
Age	47 (38, 57)
Unknown	11
Grade	
I	68 (34%)
II	68 (34%)
III	64 (32%)
Tumor Response	61 (32%)
Unknown	7

[1] Median (Q1, Q3); n (%)

- Four types of summaries: `continuous`, `continuous2`, `categorical`, and `dichotomous`
- Variables coded `0/1`, `TRUE/FALSE`, `Yes/No` treated as dichotomous
- Statistics are `median (IQR)` for continuous, `n (%)` for categorical/dichotomous
- Lists `NA` values under “Unknown”
- Label attributes are printed automatically

Survival outcomes with tbl_survfit()

```
library(survival)
fit <- survfit(Surv(ttdeath, death) ~ trt, trial)
tbl_survfit(
  fit,
  times = c(12, 24),
  label_header = "**{time} Month**"
) %>%
  add_p()
```

Characteristic	12 Month	24 Month	p-value[1]
Chemotherapy Treatment			0.2
Drug A	91% (85%, 97%)	47% (38%, 58%)	
Drug B	86% (80%, 93%)	41% (33%, 52%)	

[1] Log-rank test

- Also, regression (and more) models with `tbl_regression()` and `tbl_uvregression()`

{gtsummary} + formulas

select variables

give instructions

```
sm_trial %>%
tbl_summary(
  label      =          age          ~ "Patient Age",
  type       =    c(age, marker)     ~ "continuous",
  digits     = starts_with("age")    ~      0,
  statistic  =  all_continuous()     ~ "{mean} ({sd})"
)
```

Use `lists` to pass ≥2 sets of instruction:

```
label = list(age ~ "Patient Age", marker ~ "Marker Level")
```

Customize Using Add-on Functions

Summary tables can be further updated using **helper functions**:

- **add_*()** add additional column of statistics or information, e.g. p-values, q-values, overall statistics, treatment differences, N obs., and more
- **modify_*()** modify table headers, spanning headers, footnotes, and more
- **bold_*()/italicize_*()** style labels, variable levels, significant p-values

Advanced Tips: Update tbl_summary() with modify_*()

```
sm_trial %>%
  tbl_summary(
    by = trt, missing = "no"
  ) %>%
  modify_header(
      stat_1 ~ "**Group A**",
      stat_2 ~ "**Group B**"
  ) %>%
  modify_spanning_header(
    all_stat_cols() ~ "**Drug**") %>%
  modify_footnote(
    all_stat_cols() ~
      paste("median (IQR) for continuous;",
            "n (%) for categorical")
  )
```

Characteristic	Drug	
	Group A[1]	Group B[1]
Age	46 (37, 60)	48 (39, 56)
Grade		
I	35 (36%)	33 (32%)
II	32 (33%)	36 (35%)
III	31 (32%)	33 (32%)
Tumor Response	28 (29%)	33 (34%)

[1] median (IQR) for continuous; n (%) for categorical

- Use `show_header_names()` to see the internal header names available for use in `modify_header()`

Advanced Tips: continuous2 & digits

```
tbl_summary(
  sm_trial,
  by = trt,
  type = age ~ "continuous2",
  statistic =
    list(
      age ~ c("{mean} ({sd})",
              "{min}, {max}"),
      response ~ "{n} / {N} ({p}%)"
    ),
  label =
    grade ~ "Pathologic tumor grade",
  digits = age ~ 1
)
```

Characteristic	Drug A N = 98[1]	Drug B N = 102[1]
Age		
Mean (SD)	47.0 (14.7)	47.4 (14.0)
Min, Max	6.0, 78.0	9.0, 83.0
Unknown	7	4
Pathologic tumor grade		
I	35 (36%)	33 (32%)
II	32 (33%)	36 (35%)
III	31 (32%)	33 (32%)
Tumor Response	28 / 95 (29%)	33 / 98 (34%)
Unknown	3	4

[1] n (%); n / N (%)

- `type`: specifies the summary type as `continuous2`
- `digits`: specify the number of decimal places for rounding

Advanced Tips: tbl_continuous()

Summarize a continuous variable within categories and across different strata.

```
tbl_continuous(
  data = trial,
  variable = age,
  by = trt,
  include = c(grade, response)
)
```

Characteristic	**Drug A** N = 98[1]	**Drug B** N = 102[1]
Grade		
I	46 (36, 60)	48 (42, 55)
II	45 (31, 55)	51 (42, 58)
III	52 (42, 61)	45 (36, 52)
Tumor Response		
0	46 (36, 60)	47 (37, 54)
1	48 (41, 61)	49 (43, 59)

[1] Age: Median (Q1, Q3)

Advanced Tips: Custom p-value functions

- Many tests available by default: https://www.danieldsjoberg.com/gtsummary/reference/tests.html
- If you need one not on the list, create a custom function (use broom tidy at the end)

```
# define function (need to use these argume
calculate_prop_test <- function(data, varia
  data <- tidyr::drop_na(data, dplyr::all_o
  prop.trend.test(
    x = table(data[[variable]], data[[by]])
    n = table(data[[by]])) |>
    broom::tidy()
}

trial[c("grade", "trt")] %>%
  tbl_summary(by = trt) %>%
  add_p(test = grade ~ "calculate_prop_test
```

Characteristic	Drug A N = 98[1]	Drug B N = 102[1]	p-value[2]
Grade			0.7
I	35 (36%)	33 (32%)	
II	32 (33%)	36 (35%)	
III	31 (32%)	33 (32%)	

[1] n (%)

[2] Chi-squared Test for Trend in Proportions

Advanced Tips: tbl_uvregression() with formula

- `formula` argument is powerful! You can adjust for variables, or pass mixed model formats (e.g. `"{y} ~ {x} + (1 | gear)"`)
- Additionally, `add_global_p()` can be useful

```
tbl_uvreg <- sm_trial %>%
  tbl_uvregression(
    method = glm,
    y = response,
    method.args = list(family = binomial),
    formula = "{y} ~ {x} + age",
    include = -c(age),
    exponentiate = TRUE
  ) %>%
  bold_labels() %>%
  add_global_p()

tbl_uvreg
```

Characteristic	N	OR[1]	95% CI[1]	p-value
Chemotherapy Treatment	183			0.7
Drug A		—	—	
Drug B		1.13	0.60, 2.13	
Grade	183			0.9
I		—	—	
II		0.85	0.39, 1.85	
III		1.01	0.47, 2.16	

[1] OR = Odds Ratio, CI = Confidence Interval

Advanced Tip: tbl_merge()

Often it's useful to put summary stats and model estimates side by side

```
t3 <- trial[c("age", "grade", "response")]
  tbl_summary(missing = "no") %>%
  add_n() %>%
  modify_header(stat_0 ~ "**Summary Statist

t4 <- tbl_uvregression(
    trial[c("ttdeath", "death", "age", "gra
    method = coxph,
    y = Surv(ttdeath, death),
    exponentiate = TRUE,
    hide_n = TRUE)

tbl_merge(tbls = list(t3, t4)) %>%
  modify_spanning_header(everything() ~ NA_
```

Characteristic	N	Summary Statistics[1]	HR[2]	95% CI[2]	p-value
Age	189	47 (38, 57)	1.01	0.99, 1.02	0.3
Grade	200				
I		68 (34%)	—	—	
II		68 (34%)	1.28	0.80, 2.05	0.3
III		64 (32%)	1.69	1.07, 2.66	0.024
Tumor Response	193	61 (32%)	0.50	0.31, 0.78	0.003

[1] Median (Q1, Q3); n (%)

[2] HR = Hazard Ratio, CI = Confidence Interval

Advanced Tip: gtsummary Themes

- Themes control many aspects of how a table is printed. Function defaults can be controlled with themes, as well as other aspects that are not modifiable with function arguments.
- The {gtsummary} package comes with a few themes, and we welcome user-contributed themes as well!
- Most commonly used theme: `gtsummary::theme_gtsummary_compact()`
- More info: https://www.danieldsjoberg.com/gtsummary/articles/themes.html

Other Useful Functions

tbl_listing()

Problem: You <3 {gtsummary} themes, but you have a non-{gtsummary} table included your analysis report and it doesn't match your beautiful {gtsummary} tables.

Solution: tbl_listing() from the {gtreg} package turns any table into a {gtsummary} class table. Now {gtsummary} themes can be applied to any table in your report.

```
trial %>%
      select(trt, age, marker) %>%
      head(n = 4) %>%
      gt::gt()
```

```
trial %>%
      select(trt, age, marker) %>%
      head(n = 4) %>%
      gtreg::tbl_listing() %>%
      gtsummary::as_gt()
```

Other Useful Functions

gtreg::tbl_listing()

```
theme_gtsummary_compact()
```

```
Setting theme `Compact`
```

gtsummary table

```
trial %>%
  select(grade, marker) %>%
  tbl_summary()
```

Characteristic	N = 200[1]
Grade	
I	68 (34%)
II	68 (34%)
III	64 (32%)
Marker Level (ng/mL)	0.64 (0.22, 1.39)
Unknown	10

[1] n (%); Median (IQR)

non-gtsummary table

```
trial %>%
  select(trt, age, marker) %>%
  head(n = 4) %>%
  gt()
```

trt	age	marker
Drug A	23	0.160
Drug B	9	1.107
Drug A	31	0.277
Drug A	NA	2.067


```
theme_gtsummary_compact()
```

```
Setting theme `Compact`
```

gtsummary table

```
trial %>%
  select(grade, marker) %>%
  tbl_summary()
```

Characteristic	N = 200[1]
Grade	
I	68 (34%)
II	68 (34%)
III	64 (32%)
Marker Level (ng/mL)	0.64 (0.22, 1.39)
Unknown	10

[1] n (%); Median (IQR)

non-gtsummary table

```
trial %>%
  select(trt, age, marker) %>%
  head(n = 4) %>%
  tbl_listing() %>%
  as_gt()
```

Chemotherapy Treatment	Age	Marker Level (ng/mL)
Drug A	23	0.160
Drug B	9	1.107
Drug A	31	0.277
Drug A		2.067

Other Customizations

Many more customization available!

See the documentation at
http://www.danieldsjoberg.com/gtsummary/reference/index.html

And a detailed `tbl_summary()` vignette at
http://www.danieldsjoberg.com/gtsummary/articles/tbl_summary.html

Report Reproducbile Statistics with gtsummary::inline_text()

- Tables are important, but we often need to report results in-line in a report.
- Any statistic reported in a {gtsummary} table can be extracted and reported in-line in an R Markdown document with the `inline_text()` function.
- The pattern of what is reported can be modified with the `pattern =` argument.
- Default is `pattern = "{estimate} ({conf.level*100}% CI {conf.low}, {conf.high}; {p.value})"`

Report Reproducbile Statistics with gtsummary::inline_text()

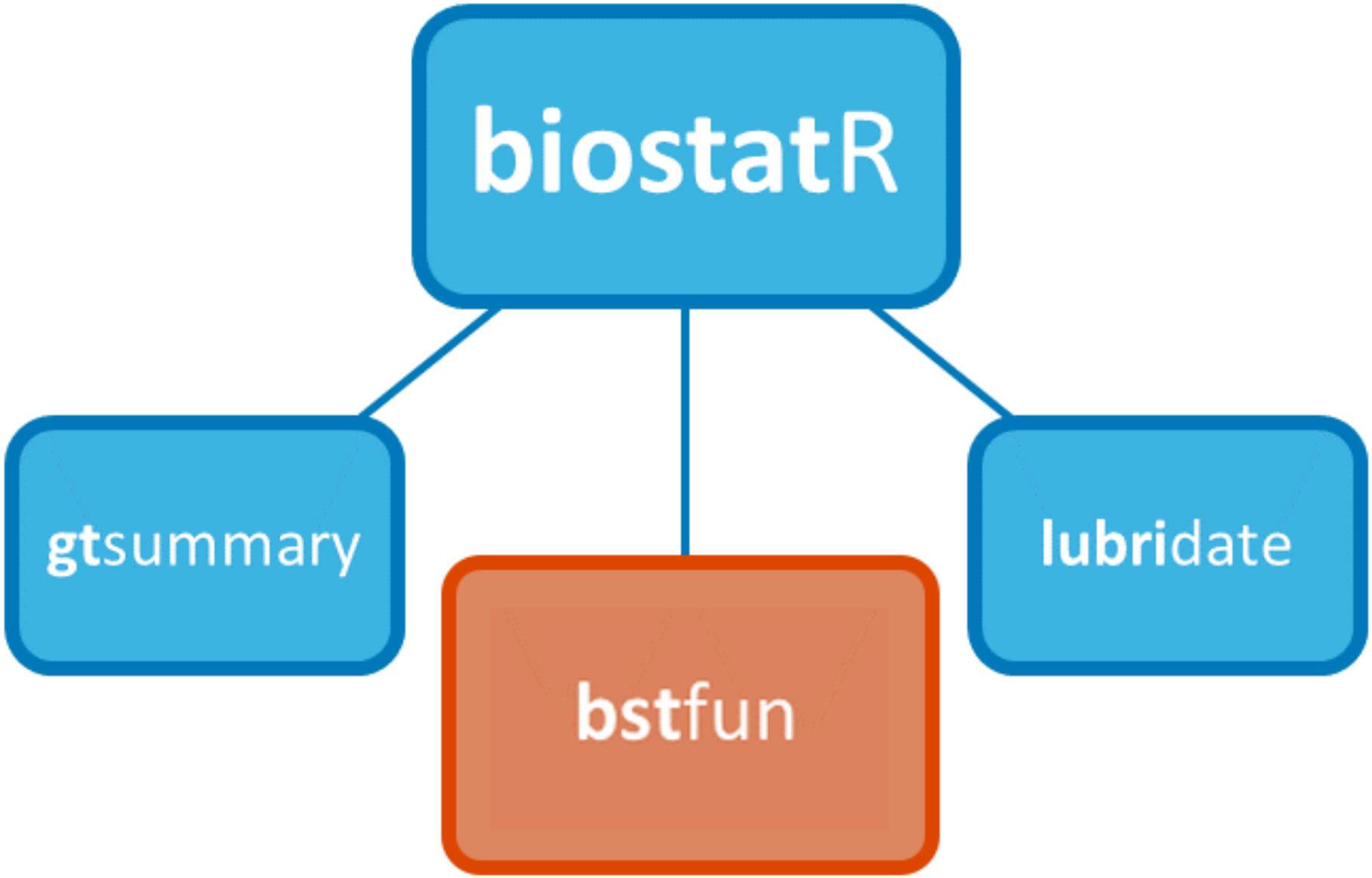
```r
library(gtsummary)

tbl_uvreg <- sm_trial %>%
  tbl_uvregression(
    method = glm,
    y = response,
    method.args = list(family = binomial),
    exponentiate = TRUE
  ) %>%
  bold_labels()

tbl_uvreg
```

Characteristic	N	OR[1]	95% CI[1]	p-value
Chemotherapy Treatment	193			
Drug A		—	—	
Drug B		1.21	0.66, 2.24	0.5
Age	183	1.02	1.00, 1.04	0.10
Grade	193			
I		—	—	
II		0.95	0.45, 2.00	0.9
III		1.10	0.52, 2.29	0.8

[1] OR = Odds Ratio, CI = Confidence Interval

In Code: The odds ratio for age is '`inline_text(tbl_uvreg, variable = age)`'

In Report: The odds ratio for age is 1.02 (95% CI 1.00, 1.04; p=0.10)


biostatR
gtsummary
bstfun
lubridate

{bstfun}

- A **shared space** for department members to add functions that may be useful to others
- Houses individual member's **project templates** and function to start projects (`create_bst_project()`: will be discussed in further training)
- Diverse functions for various analysis-related tasks, **{bstfun} Reference Index**: https://mskcc-epi-bio.github.io/bstfun/

{bstfun} Useful Functions

clean_mrn()

MRNs follows specific formatting rules:

- Must be character
- Must contain only numeric components
- Must be eight characters long and include leading zeros.

This function converts numeric MRNs to character and ensures it follows MRN conventions. Character MRNs can also be passed, and leading zeros will be appended and checked for consistency.

```
1 fake_mrn <- c("00100", "100", "0100")
2
3 fake_mrn %>%
4   bstfun::clean_mrn()
```

[1] “00000100” “00000100” “00000100”

{bstfun} Useful Functions

use_varnames_as_labels()

Automatically add labels to your data based on column names

Before:

```
1 mtcars %>%
2   select(mpg, cyl, vs, am) %>%
3   tbl_summary()
```

Characteristic	N = 32[1]
mpg	19.2 (15.4, 22.8)
cyl	
4	11 (34%)
6	7 (22%)
8	14 (44%)
vs	14 (44%)
am	13 (41%)

[1] Median (Q1, Q3); n (%)

After:

```
1 mtcars %>%
2   select(mpg, cyl, vs, am) %>%
3   bstfun::use_varnames_as_labels(caps = c(m
4   tbl_summary()
```

Characteristic	N = 32[1]
MPG	19.2 (15.4, 22.8)
cyl	
4	11 (34%)
6	7 (22%)
8	14 (44%)
VS	14 (44%)
Am	13 (41%)

[1] Median (Q1, Q3); n (%)

{lubridate}

- We work with **a LOT of dates**
- **{lubridate}** helps parse dates from strings, and improves functional operations on date-times
- Data cleaning training will cover this in more depth or see R for Data Science: https://r4ds.had.co.nz/dates-and-times.html

```
1 library(lubridate)
2
3 bday <- dmy("14/10/1940")
4 month(bday)
```

[1] 10

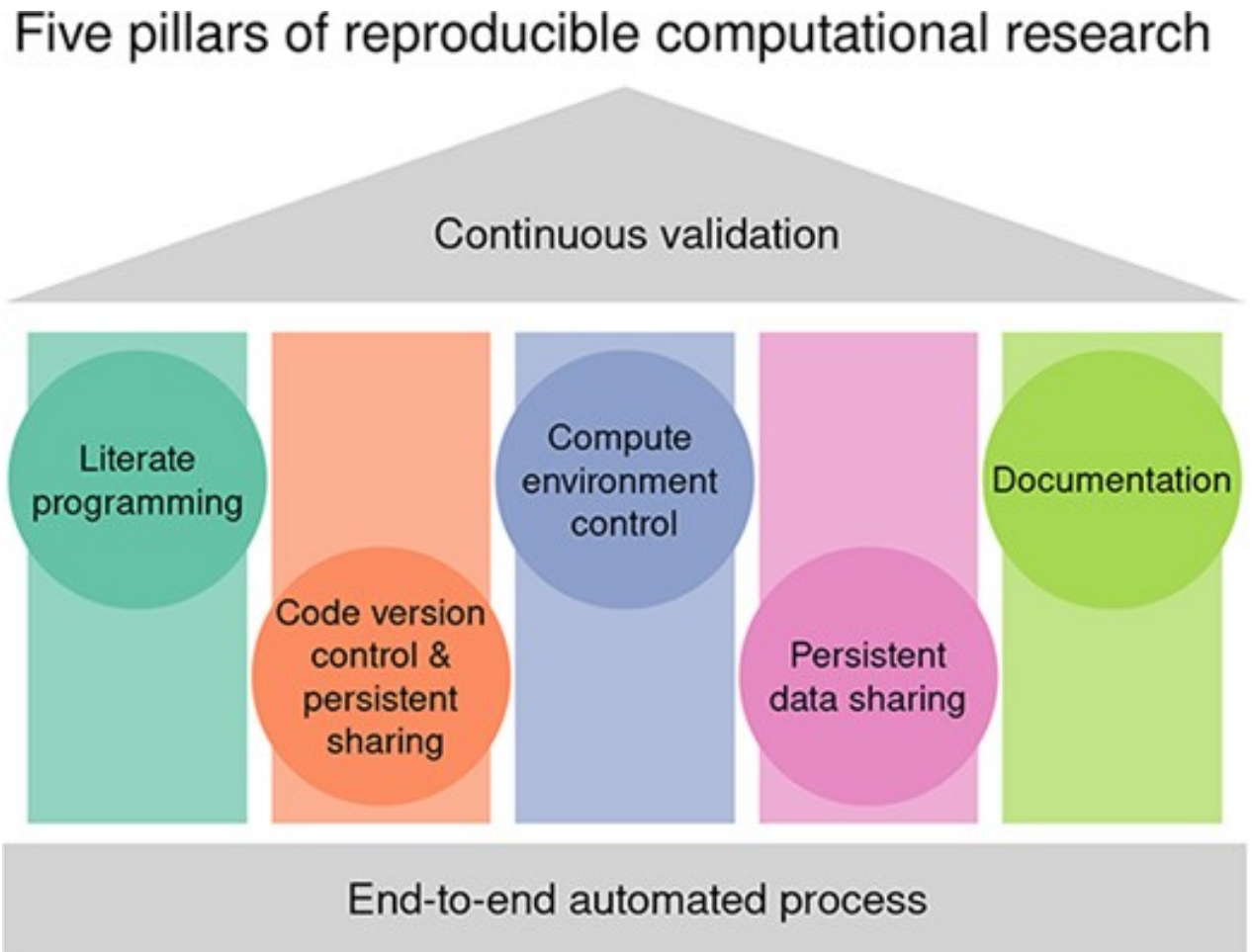
```
1 wday(bday, label = TRUE)
```

[1] Mon Levels: Sun < Mon < Tue < Wed < Thu < Fri < Sat

```
1 year(bday) <- 2016
2 wday(bday, label = TRUE)
```

[1] Fri Levels: Sun < Mon < Tue < Wed < Thu < Fri < Sat

Five Pillars Of Reproducibility



Data Versioning

- How data versions are managed is still highly depending on what service and data types you work with
- For genomic or imaging data, try to use a standardized pipeline
- For clinical data, try to establish a workflow with your service collaborators.
- **Avoid making changes to excel yourself**
- Use the `README` to track

Thank You!!!

Questions?

Resources

- {biostaR} - https://github.mskcc.org/pages/datadojo/biostatR/index.html
- {gtsummary} - https://www.danieldsjoberg.com/gtsummary/
- {bstfun} - https://www.danieldsjoberg.com/bstfun/index.html
- Departmental Resource Guide - https://rconnect.mskcc.org/resource-guide/
- Quarto Docs - https://quarto.org/docs/guide/
- Quarto Blog Post by Alison Hill - https://www.apreshill.com/blog/2022-04-we-dont-talk-about-quarto/