

Introducing {gtreg}: an R package to produce regulatory tables for clinical research

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These slides are best viewed from the url
<https://shannonpileggi.github.io/gtreg-talk-phuse-2023>

Introduction

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Checklist

✓ Install recent R release

I am on version 4.2.1

✓ Install RStudio

I am on version 2022.12.0+353

✓ Install packages

```
1 install.packages(c("gtreg", "gtsummary", "tidyverse", "labelled", "usethis"))
```

✓ Ensure you can knit Rmarkdown files

Overview

gtreg



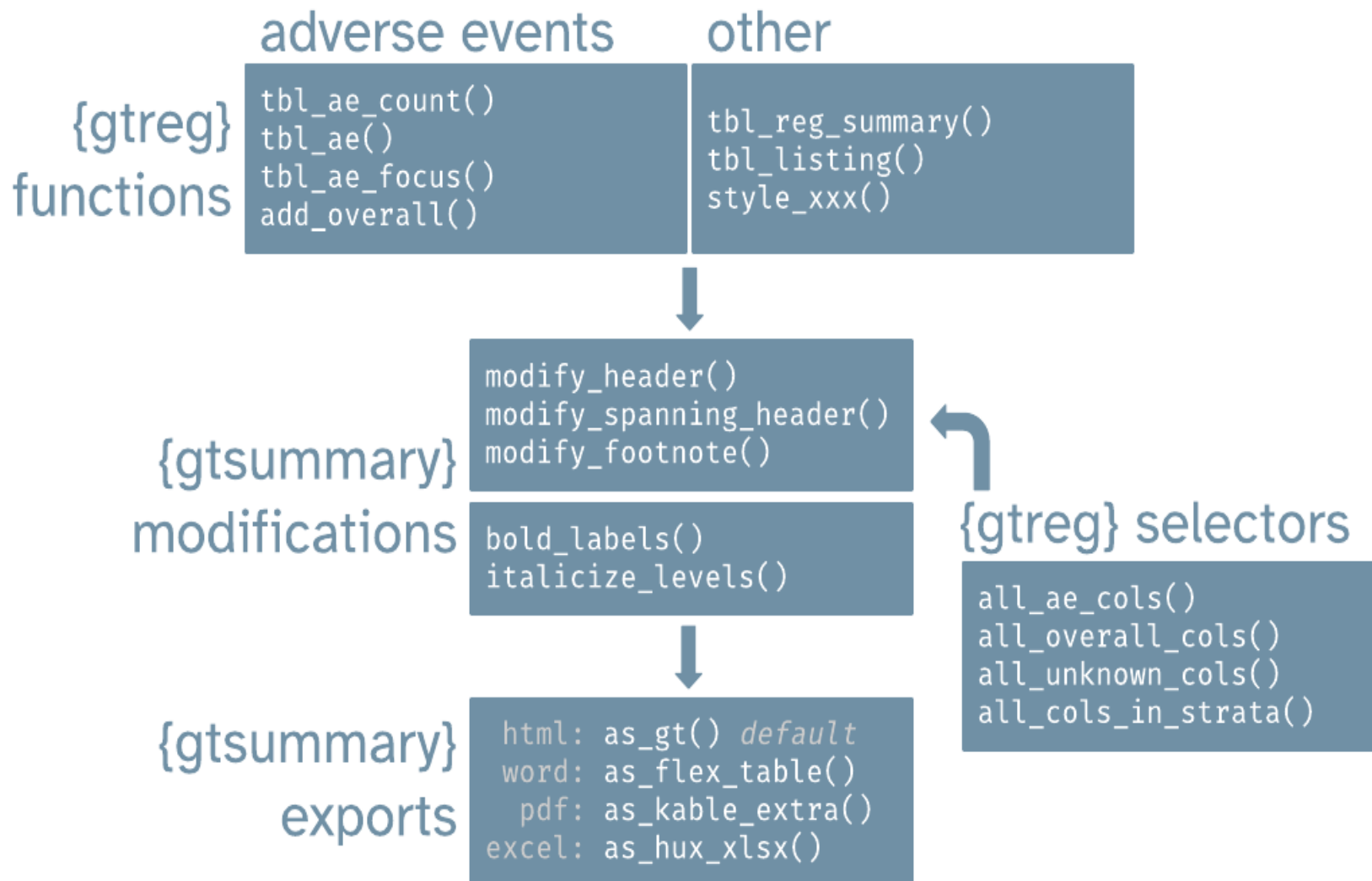
<https://shannonpileggi.github.io/gtreg/>

{gtreg} is built on

{gtsummary} is built on

{gt}

{gtreg} overview



About adverse events

Adverse events

patient_id	trt	system_organ_class	adverse_event	grade	drug_attribution
ID 1	Drug B	Blood and lymphatic system disorders	Anaemia	4	Unrelated
ID 1	Drug B	Blood and lymphatic system disorders	Increased tendency to bruise	5	Unrelated
ID 1	Drug B	Blood and lymphatic system disorders	Increased tendency to bruise	4	Unlikely
ID 1	Drug B	Blood and lymphatic system disorders	Thrombocytopenia	1	Probably
ID 1	Drug B	Blood and lymphatic system disorders	Thrombocytopenia	3	Definite

- An adverse event (AE) is a medical issue that occurs during the course of treatment or observation.
- AEs are classified according to a [hierarchy](#), and we typically report lower level terms within a system organ class.
- AEs also record severity / grade and likelihood of attribution to treatment.

Summary table challenges

patient_id	trt	system_organ_class	adverse_event	grade	drug_attribution
ID 1	Drug B	Blood and lymphatic system disorders	Anaemia	4	Unrelated
ID 1	Drug B	Blood and lymphatic system disorders	Increased tendency to bruise	5	Unrelated
ID 1	Drug B	Blood and lymphatic system disorders	Increased tendency to bruise	4	Unlikely
ID 1	Drug B	Blood and lymphatic system disorders	Thrombocytopenia	1	Probably
ID 1	Drug B	Blood and lymphatic system disorders	Thrombocytopenia	3	Definite

- Subjects experience multiple adverse events.
- Not all enrolled subjects experience an adverse event.
- The percent of subjects experiencing specific AEs is of interest; typically AEs are counted by maximum grade per event per subject.
- Multiple AE tables are often required (treatment emergent AEs, AEs on specific treatment cycles, serious AEs, etc.).

Counting by maximum grade

patient_id	system_organ_class	adverse_event	grade
ID 1	Blood and lymphatic system disorders	Anaemia	4
ID 1	Blood and lymphatic system disorders	Increased tendency to bruise	5
ID 1	Blood and lymphatic system disorders	Increased tendency to bruise	4
ID 1	Blood and lymphatic system disorders	Thrombocytopenia	1
ID 1	Blood and lymphatic system disorders	Thrombocytopenia	3

Counting by maximum grade

Patient ID	System Organ Class	Adverse Event	Grade
Term 1			
ID 1	Blood and lymphatic system disorders	Anaemia	4
Term 2			
ID 1	Blood and lymphatic system disorders	Increased tendency to bruise	5
ID 1	Blood and lymphatic system disorders	Increased tendency to bruise	4
Term 3			
ID 1	Blood and lymphatic system disorders	Thrombocytopenia	1
ID 1	Blood and lymphatic system disorders	Thrombocytopenia	3

Counting by maximum grade

Patient ID	System Organ Class	Adverse Event	Grade
Term 1			
ID 1	Blood and lymphatic system disorders	Anaemia	4
Term 2			
ID 1	Blood and lymphatic system disorders	Increased tendency to bruise	5
ID 1	Blood and lymphatic system disorders	Increased tendency to bruise	4
Term 3			
ID 1	Blood and lymphatic system disorders	Thrombocytopenia	1
ID 1	Blood and lymphatic system disorders	Thrombocytopenia	3

Similar logic applies when counting by severity (e.g. mild, moderate, severe) - if stored as a factor, the highest factor level is retained (severe).

First adverse event tables

Data

Adverse Events

Patients

df_adverse_events

- 10 unique subjects
- multiple rows per subject

patient_id	trt	system_organ_class	adverse_event	grade	drug_attribution	any_complication	grade3_complication
ID 1	Drug B	Blood and lymphatic system disorders	Anaemia	4	Unrelated	TRUE	TRUE
ID 1	Drug B	Blood and lymphatic system disorders	Increased tendency to bruise	5	Unrelated	TRUE	TRUE
ID 1	Drug B	Blood and lymphatic system disorders	Increased tendency to bruise	4	Unlikely	TRUE	TRUE
ID 1	Drug B	Blood and lymphatic system disorders	Thrombocytopenia	1	Probably	TRUE	FALSE
ID 1	Drug B	Blood and lymphatic system disorders	Thrombocytopenia	3	Definite	TRUE	TRUE

Introducing {gtreg}

Variable labels

- A variable label is an attribute of a variable in a data frame.
- Where applicable, *variable labels* (not *variable names*) are printed in {gtsummary} and {gtreg} tables.
- The example data in {gtreg} comes with variable labels; you can also create your own via `labelled::set_variable_labels()`.

```
1 str(df_patient_characteristics)
```

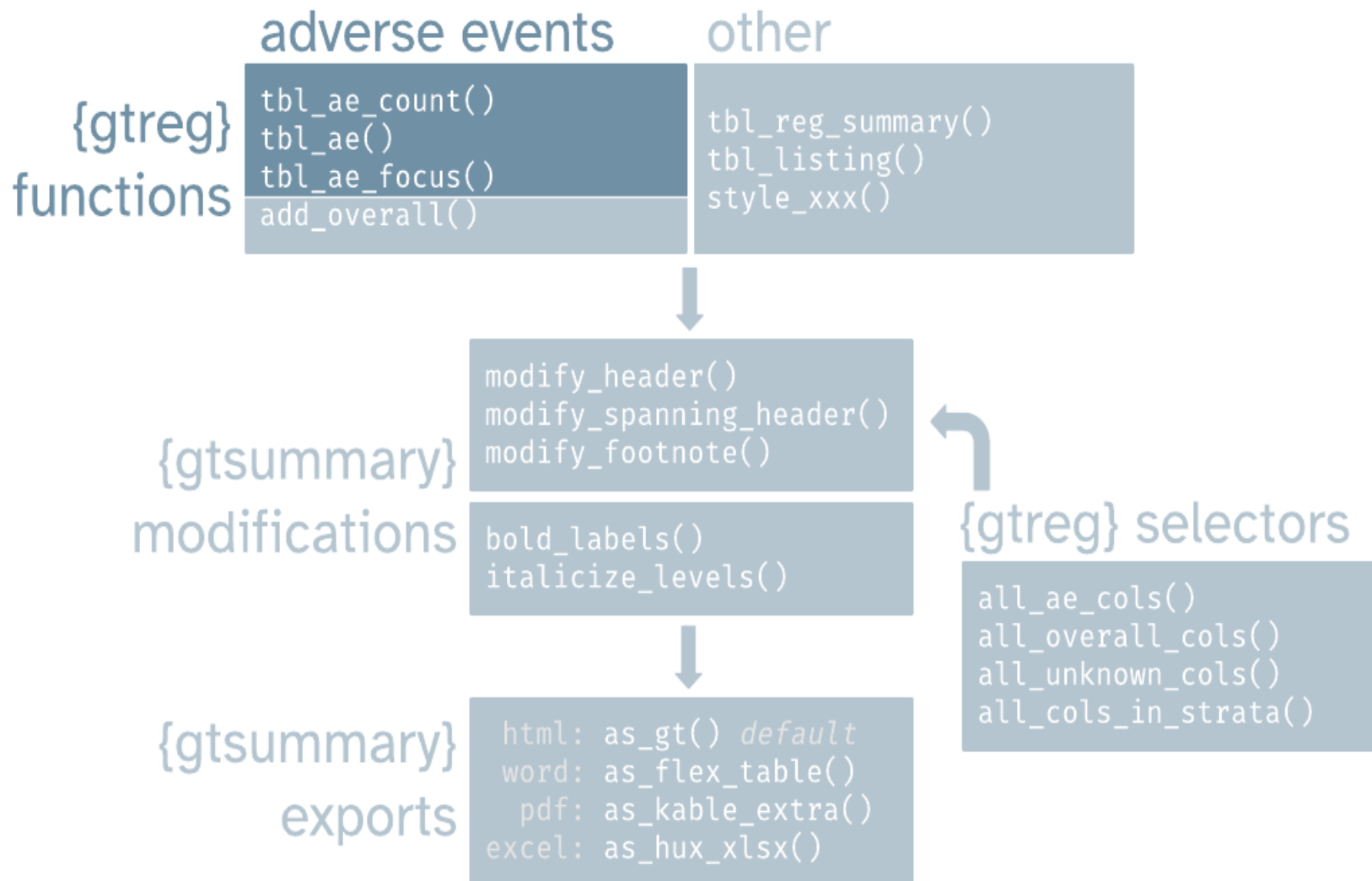
```
tibble [100 × 7] (S3: tbl_df/tbl/data.frame)
 $ patient_id : chr [1:100] "ID 1" "ID 2" "ID 3" "ID 4" ...
 $ trt        : chr [1:100] "Drug B" "Drug B" "Drug B" "Drug B" ...
 $ age       : num [1:100] 28 47 39 45 58 42 57 23 41 49 ...
 $ marker     : num [1:100] 4.81 7.71 6.45 6.32 5.79 ...
 $ status     : Factor w/ 6 levels "Completed Study",...: 2 1 1 5 4 1 4 2 6 2 ...
 $ discontinued: chr [1:100] "Yes" "No" "No" "Yes" ...
 $ off_trt_ae : chr [1:100] "Intestinal dilatation" NA NA NA ...
```

```
1 View(df_patient_characteristics)
```

	patient_id Patient ID	trt Treatment Group	age Patient Age	marker Biological Marker	status Study Status	discontinued Discontinued from Study	off_trt_ae Off Treatment Adverse Event
1	ID 1	Drug B	28	4.807148	Adverse Event	Yes	Intestinal dilatation
2	ID 2	Drug B	47	7.714544	Completed Study	No	NA
3	ID 3	Drug B	39	6.449793	Completed Study	No	NA
4	ID 4	Drug B	45	6.319944	Subject Withdrew	Yes	NA
5	ID 5	Drug B	58	5.785283	Physician Decision	Yes	NA
6	ID 6	Drug A	42	5.630501	Completed Study	No	NA
7	ID 7	Drug A	57	4.635768	Physician Decision	Yes	NA
8	ID 8	Drug B	23	5.183005	Adverse Event	Yes	Intestinal dilatation
9	ID 9	Drug A	41	5.874626	Active	No	NA
10	ID 10	Drug B	49	5.421306	Adverse Event	Yes	Intestinal dilatation

Showing 1 to 10 of 100 entries, 7 total columns

First adverse event tables



tbl_ae_count()

- Count *all* AEs (not by maximum grade).

Code

Table

Data

```
1 df_adverse_events |>
2   tbl_ae_count(
3     ae = adverse_event,
4     soc = system_organ_class,
5     by = grade
6   )
```

tbl_ae()

- Count AEs per subject by maximum grade.

Code

Table

Data

```
1 df_adverse_events |>
2   tbl_ae(
3     id = patient_id,
4     ae = adverse_event,
5     soc = system_organ_class,
6     by = grade
7   )
```

tbl_ae()

- Count AEs per subject by maximum grade.
- Supply `id_df` to achieve subject denominator.

Code	Table	Data
------	-------	------

```
1 df_adverse_events |>
2   tbl_ae(
3     id = patient_id,
4     id_df = df_patient_characteristics,
5     ae = adverse_event,
6     soc = system_organ_class,
7     by = grade
8   )
```

tbl_ae() with strata

Code	Table	Data
------	-------	------

```
1 df_adverse_events |>
2   tbl_ae(
3     id = patient_id,
4     id_df = df_patient_characteristics,
5     strata = trt,
6     ae = adverse_event,
7     soc = system_organ_class,
8     by = grade
9   )
```

tbl_ae_focus()

- Count dichotomous AE attributes via `include`.
- Supply `id_df` to achieve subject denominator.

Code

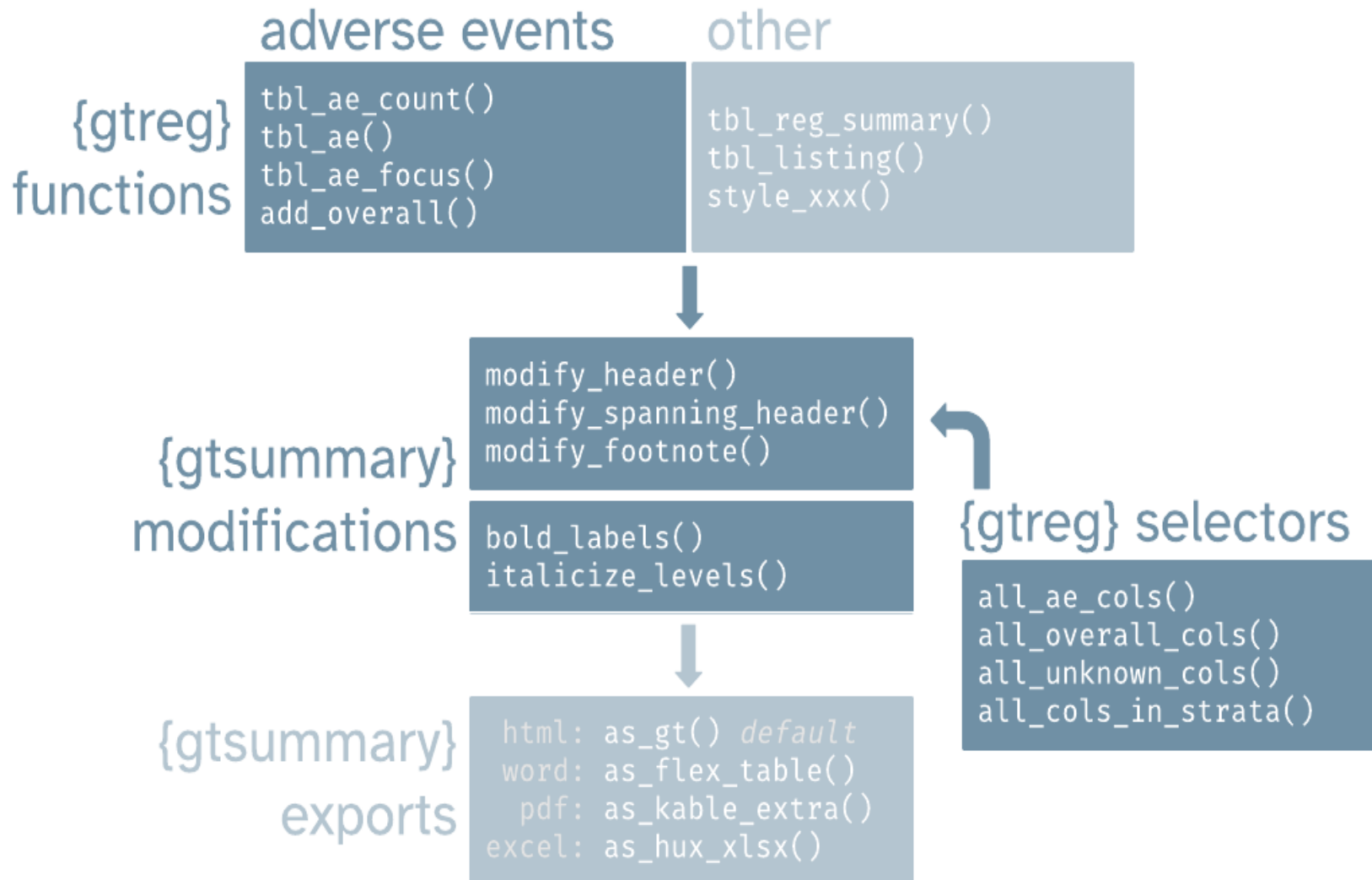
Table

Data

```
1 df_adverse_events |>
2   tbl_ae_focus(
3     id = patient_id,
4     id_df = df_patient_characteristics,
5     ae = adverse_event,
6     soc = system_organ_class,
7     include = c(any_complication, grade3_complication)
8   )
```

Modified adverse event tables

Modified adverse event tables



tbl_ae() with add_overall()

See [documentation](#) for more `add_overall()` functionality.

Code

Table

Data

```
1 df_adverse_events |>
2   tbl_ae(
3     id = patient_id,
4     id_df = df_patient_characteristics,
5     strata = trt,
6     ae = adverse_event,
7     soc = system_organ_class,
8     by = grade
9   ) |>
10  add_overall(across = 'by') |>
11  bold_labels()
```

tbl_ae() with modified headers

Code	Table	Data
------	-------	------

```
1 df_adverse_events |>
2   tbl_ae(
3     id = patient_id,
4     id_df = df_patient_characteristics,
5     strata = trt,
6     ae = adverse_event,
7     soc = system_organ_class,
8     by = grade
9   ) |>
10  add_overall(across = 'by') |>
11  bold_labels() |>
12  modify_header(
13    all_ae_cols() ~ "***Grade {by}***"
14  ) %>%
15  modify_spanning_header(
16    all_ae_cols(TRUE, TRUE) ~ "{strata}" \nN = {n}"
17  )
```

Table modifications

<https://shannonpileggi.github.io/gtreg/articles/table-modifications.html>

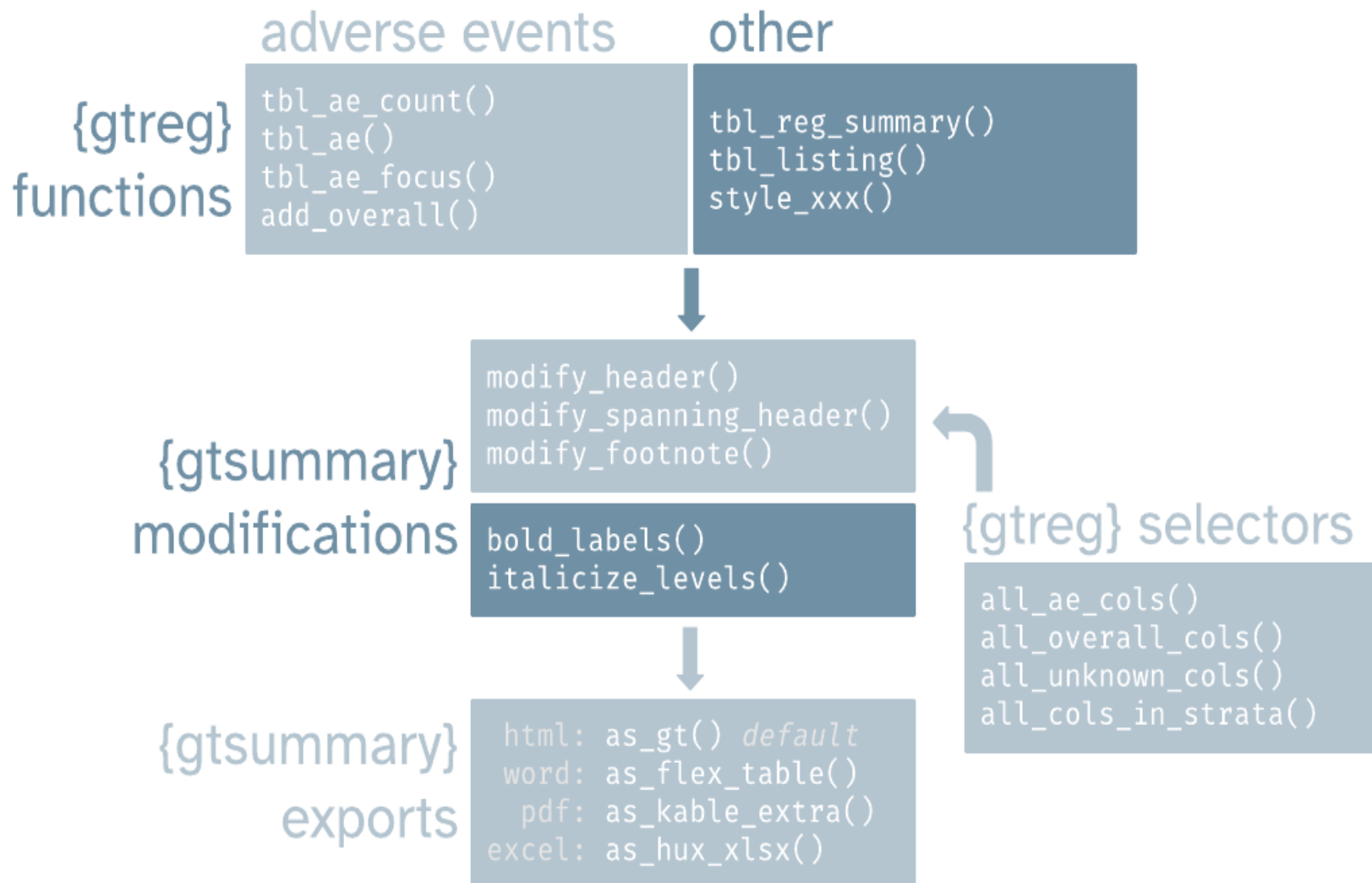
Use `modify_header()` and `modify_spanning_header()` with `all_` column selectors.

t0

Adverse Event	N = 10						Overall
	Unknown	1	2	3	4	5	
Blood and lymphatic system disorders	—	—	1 (10)	—	2 (20)	7 (70)	10 (100)
Anaemia	1 (10)	—	—	2 (20)	1 (10)	3 (30)	7 (70)
Increased tendency to bruise	—	—	—	—	4 (40)	2 (20)	6 (60)
Iron deficiency anaemia	—	1 (10)	2 (20)	—	2 (20)	2 (20)	7 (70)
Thrombocytopenia	—	—	1 (10)	3 (30)	1 (10)	4 (40)	9 (90)
Gastrointestinal disorders	—	—	—	—	4 (40)	6 (60)	10 (100)
Difficult digestion	—	1 (10)	—	—	3 (30)	1 (10)	5 (50)
Intestinal dilatation	—	2 (20)	1 (10)	—	—	1 (10)	4 (40)
Myochosis	—	—	3 (30)	1 (10)	1 (10)	3 (30)	8 (80)
Non-erosive reflux disease	—	4 (40)	—	—	3 (30)	3 (30)	10 (100)
Pancreatic enzyme abnormality	—	2 (20)	1 (10)	2 (20)	2 (20)	1 (10)	8 (80)

Other tabling functions

Other tabling functions



tbl_reg_summary()

Create summary tables with standard regulatory formatting.

Code

Table

Data

```
1 df_patient_characteristics |>
2   tbl_reg_summary(
3     by = trt,
4     include = c(marker, status)
5   ) |>
6   bold_labels()
```

tbl_listing()

A fancy  way to print grouped data.

Code

Table

Data

```
1 df_adverse_events |>
2   head(n = 10) |>
3   select(system_organ_class, adverse_event, grade, drug_attribution, patient_id) |>
4   arrange(adverse_event, desc(grade)) |>
5   tbl_listing(
6     group_by = system_organ_class
7   ) |>
8   bold_labels()
```

tbl_listing() extensions

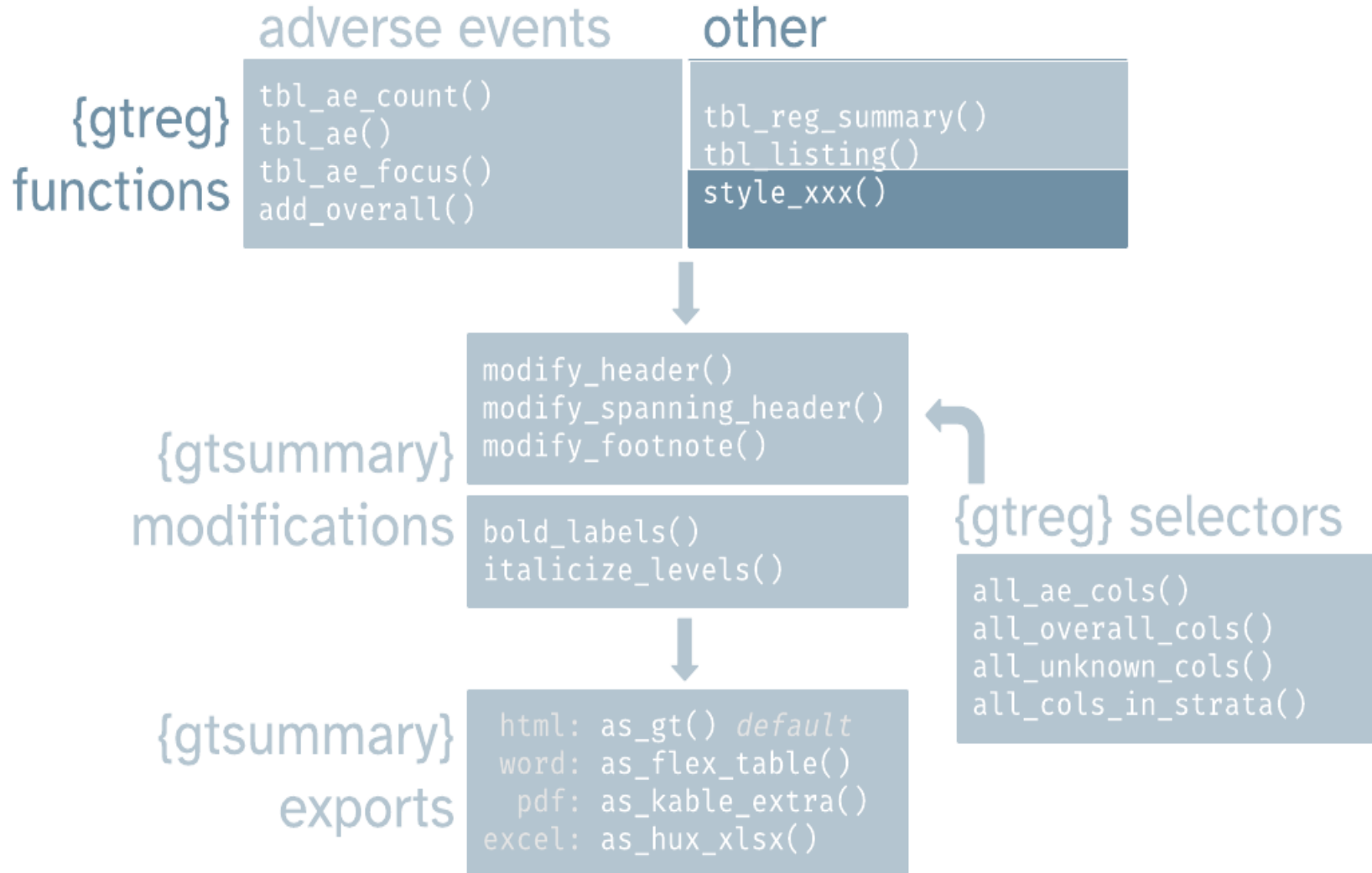
Remember this table?

Table	Code	Data
-------	------	------

Patient ID	System Organ Class	Adverse Event	Grade
Term 1			
ID 1	Blood and lymphatic system disorders	Anaemia	4
Term 2			
ID 1	Blood and lymphatic system disorders	Increased tendency to bruise	5
ID 1	Blood and lymphatic system disorders	Increased tendency to bruise	4
Term 3			
ID 1	Blood and lymphatic system disorders	Thrombocytopenia	1
ID 1	Blood and lymphatic system disorders	Thrombocytopenia	3

Table shells

Table shells



Strategy

<https://shannonpileggi.github.io/gtreg/articles/table-shells.html>

Table shells can be generated for any `tbl_ae()` and `tbl_reg_summary()` by:

1. Create dummy data or use your own data.
2. Pass the data to your function of choice.
3. Overwrite the statistic(s) shown to a fixed character string by implementing the `style_xxx()` function in the `digits` argument.

```
1 style_xxx(8:11)
```

```
[1] "xx" "xx" "xx" "xx"
```

```
1 style_xxx(8:11, width = 4, digits = 1)
```

```
[1] "xx.x" "xx.x" "xx.x" "xx.x"
```

Uniform shell for tbl_ae()

Code

Table

Data

```

1 df_adverse_events |>
2   tbl_ae(
3     id = patient_id,
4     id_df = df_patient_characteristics,
5     strata = trt,
6     ae = adverse_event,
7     soc = system_organ_class,
8     by = grade,
9     digits = style_xxx,
10    zero_symbol = NULL
11  ) |>
12  bold_labels() |>
13  modify_header(all_ae_cols() ~ "***Grade {by}**") %>%
14  modify_spanning_header(all_ae_cols(TRUE, TRUE) ~ "***{strata}**  \nN = xx")

```

Custom shell for tbl_ae()

Code

Table

Data

```

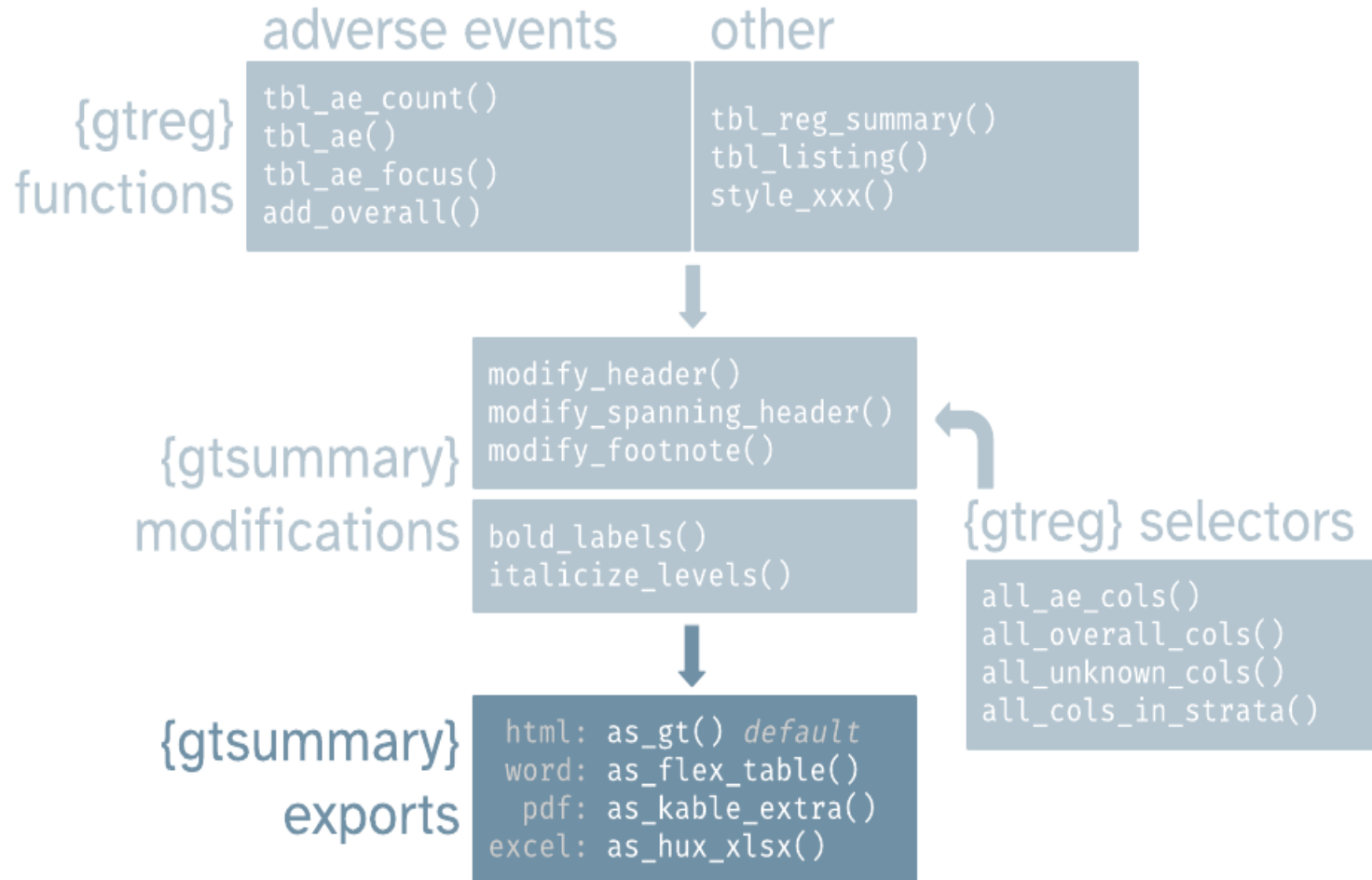
1 df_adverse_events |>
2   tbl_ae(
3     id = patient_id,
4     id_df = df_patient_characteristics,
5     strata = trt,
6     ae = adverse_event,
7     soc = system_organ_class,
8     by = grade,
9     digits = list(
10       style_xxx, # style for n
11       function(x) style_xxx(x, width = 4, digits = 1) # style for %
12     ),
13     zero_symbol = NULL
14   ) |>
15   bold_labels() |>
16   modify_header(all_ae_cols() ~ "***Grade {by}**") %>%
17   modify_spanning_header(all_ae_cols(TRUE, TRUE) ~ "***{strata}** \nN = xx")

```

Exporting options

Exporting options

<https://shannonpileggi.github.io/gtreg/articles/output-gtreg.html>



Exporting options

html

word

excel

pdf

```

1 table1 <- df_adverse_events |>
2   tbl_ae(
3     id = patient_id,
4     id_df = df_patient_characteristics
5     ae = adverse_event,
6     soc = system_organ_class,
7     by = grade
8   ) |>
9   modify_header(
10     all_ae_cols() ~ "***Grade {by}***"
11   ) %>%
12   bold_labels()

```

```
1 table1
```

Adverse Event	N = 100				
	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Blood and lymphatic system disorders					
Anaemia	—	1 (1.0)	—	2 (2.0)	7 (7.0)
Increased tendency to bruise	—	—	—	4 (4.0)	2 (2.0)
Iron deficiency anaemia	1 (1.0)	2 (2.0)	—	2 (2.0)	2 (2.0)
Thrombocytopenia	—	1 (1.0)	3 (3.0)	1 (1.0)	4 (4.0)
Gastrointestinal disorders	—	—	—	4 (4.0)	6 (6.0)
Difficult digestion	1 (1.0)	—	—	3 (3.0)	1 (1.0)
Intestinal dilatation	2 (2.0)	1 (1.0)	—	—	1 (1.0)
Myochosis	—	3 (3.0)	1 (1.0)	1 (1.0)	3 (3.0)
Non-erosive reflux disease	4 (4.0)	—	—	3 (3.0)	3 (3.0)
Pancreatic enzyme abnormality	2 (2.0)	1 (1.0)	2 (2.0)	2 (2.0)	1 (1.0)

Thank you!

 {gtreg} website

<https://shannonpileggi.github.io/gtreg/>

 {gtreg} installation

```
1 # install from CRAN
2 install.packages("gtreg")
3 # or install development version from github
4 devtools::install_github("shannonpileggi/gtreg")
```

 {gtreg} issues

<https://github.com/shannonpileggi/gtreg/issues>

 {gtreg} feature requests or questions: ask on

<https://github.com/shannonpileggi/gtreg/discussions>

