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

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Introduction

Developers

Overview

gtreg

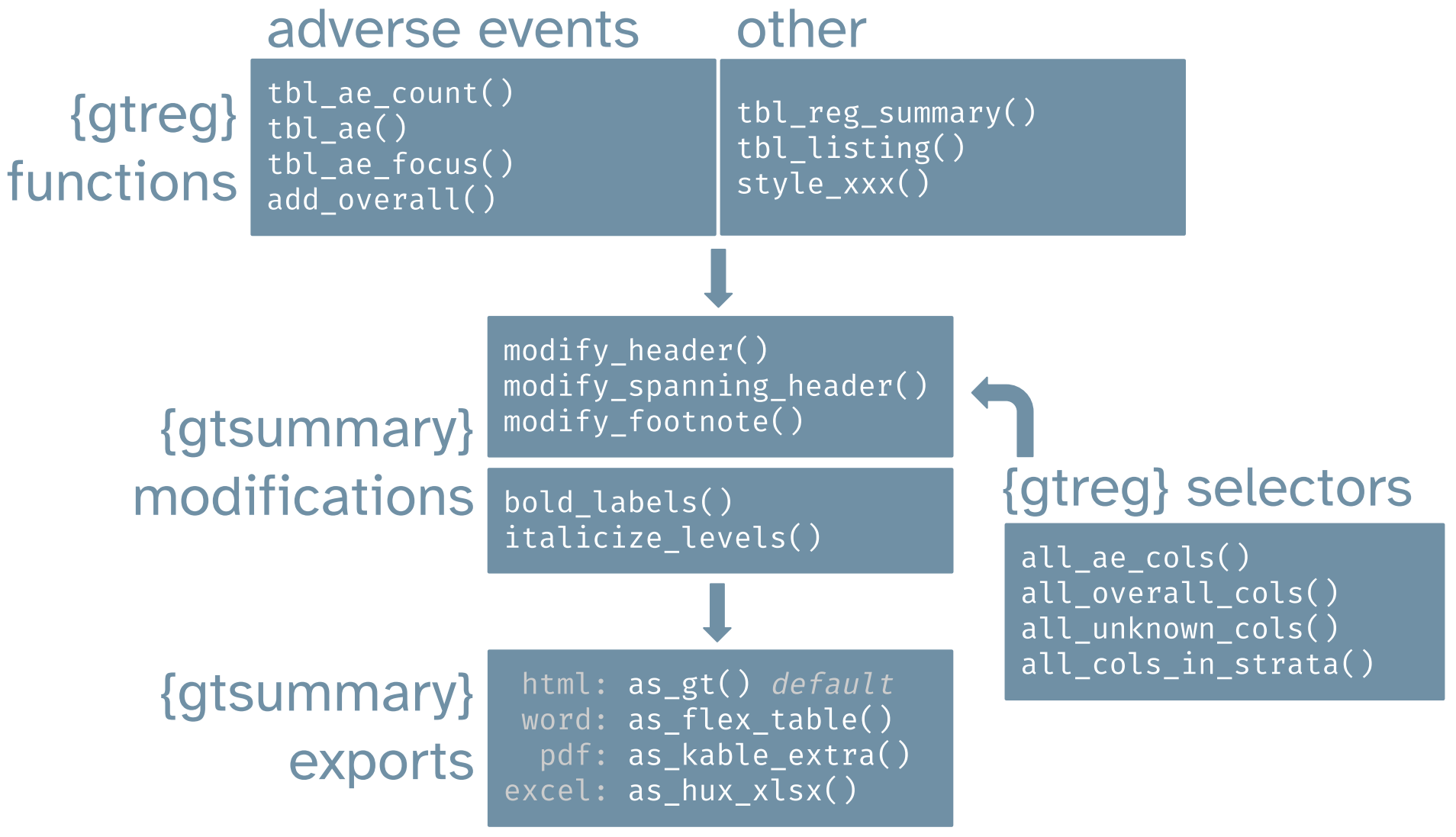
https://shannonpileggi.github.io/gtreg/

{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

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" ...
  ..- attr(*, "label")= chr "Patient ID"
 $ trt         : chr [1:100] "Drug B" "Drug B" "Drug B" "Drug B" ...
  ..- attr(*, "label")= chr "Treatment Group"
 $ age         : num [1:100] 28 47 39 45 58 42 57 23 41 49 ...
  ..- attr(*, "label")= chr "Patient Age"
 $ marker      : num [1:100] 4.81 7.71 6.45 6.32 5.79 ...
  ..- attr(*, "label")= chr "Biological Marker"
 $ status      : Factor w/ 6 levels "Completed Study",..: 2 1 1 5 4 1 4 2 6 2 ...
  ..- attr(*, "label")= chr "Study Status"
 $ discontinued: chr [1:100] "Yes" "No" "No" "Yes" ...
  ..- attr(*, "label")= chr "Discontinued from Study"
 $ off_trt_ae  : chr [1:100] "Intestinal dilatation" NA NA NA ...
  ..- attr(*, "label")= chr "Off Treatment Adverse Event"
```

```
1  View(df_patient_characteristics)
```

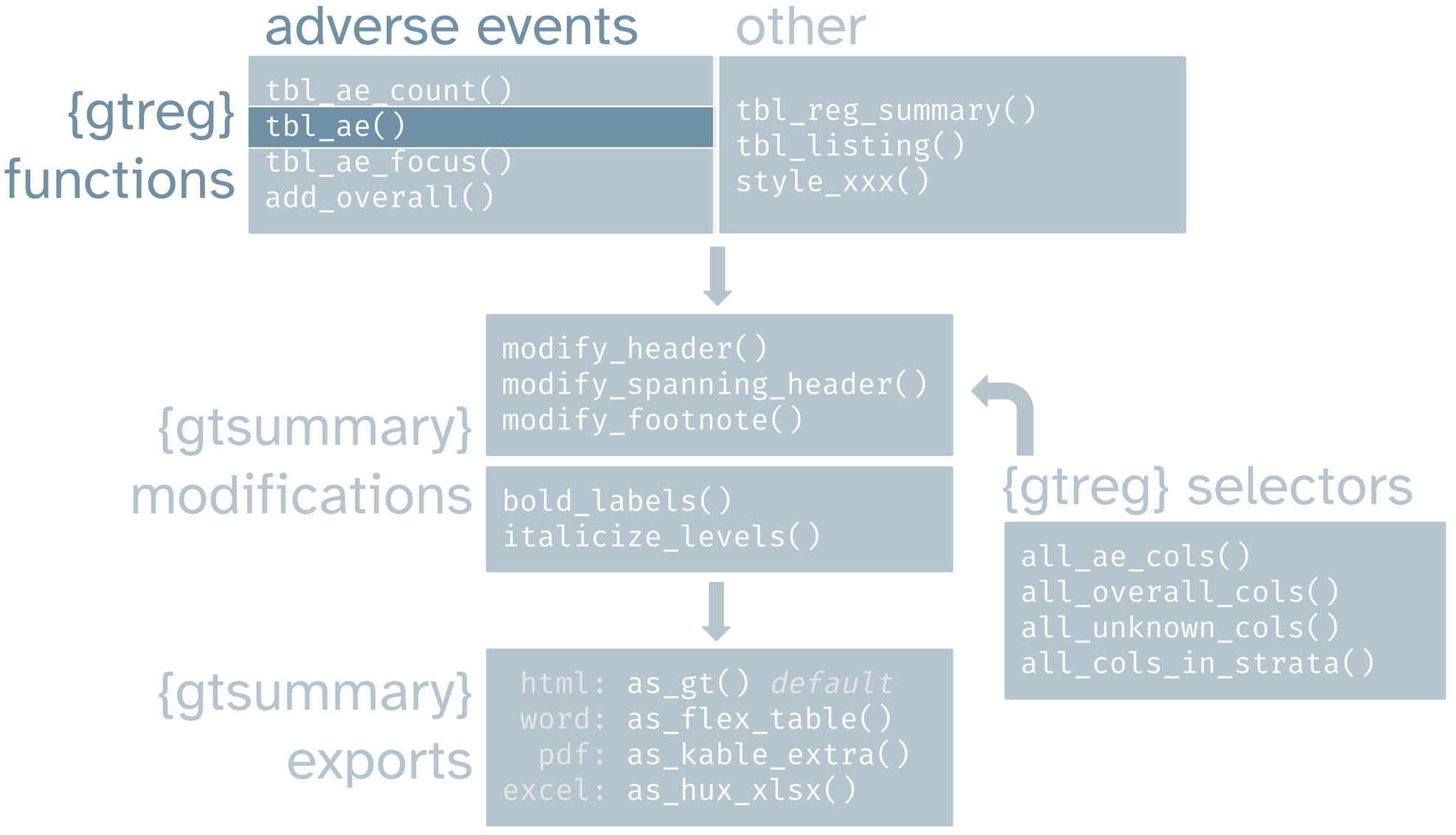
df_patient_characteristics

Filter

	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 AEs per subject by maximum grade.

Code | Table | Data

```
df_adverse_events |>
  tbl_ae(
    id = patient_id,
    ae = adverse_event,
    soc = system_organ_class,
    by = grade
  )
```

tbl_ae()

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

Code | Table | Data

```
df_adverse_events |>
  tbl_ae(
    id = patient_id,
    id_df = df_patient_characteristics,
    ae = adverse_event,
    soc = system_organ_class,
    by = grade
  )
```

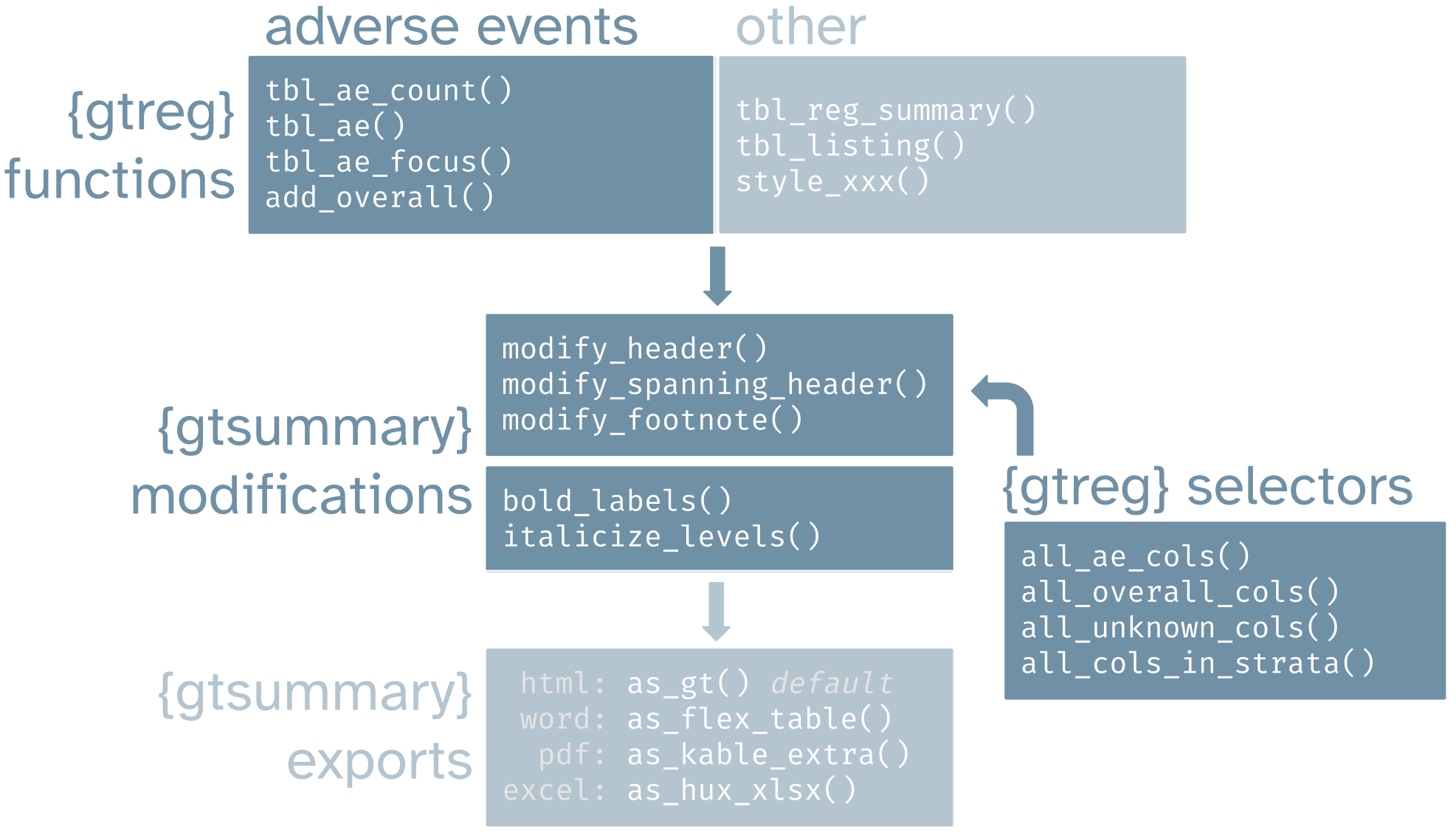
tbl_ae() with strata

Code | Table | Data

```
df_adverse_events |>
  tbl_ae(
    id = patient_id,
    id_df = df_patient_characteristics,
    strata = trt,
    ae = adverse_event,
    soc = system_organ_class,
    by = grade
  )
```

Modified adverse event tables

Modified adverse event tables



tbl_ae() with add_overall()

See documentation for more `add_overall()` functionality.

Code | Table | Data

```
df_adverse_events |>
  tbl_ae(
    id = patient_id,
    id_df = df_patient_characteristics,
    strata = trt,
    ae = adverse_event,
    soc = system_organ_class,
    by = grade
  ) |>
  add_overall(across = 'by') |>
  bold_labels()
```

tbl_ae() with modified headers

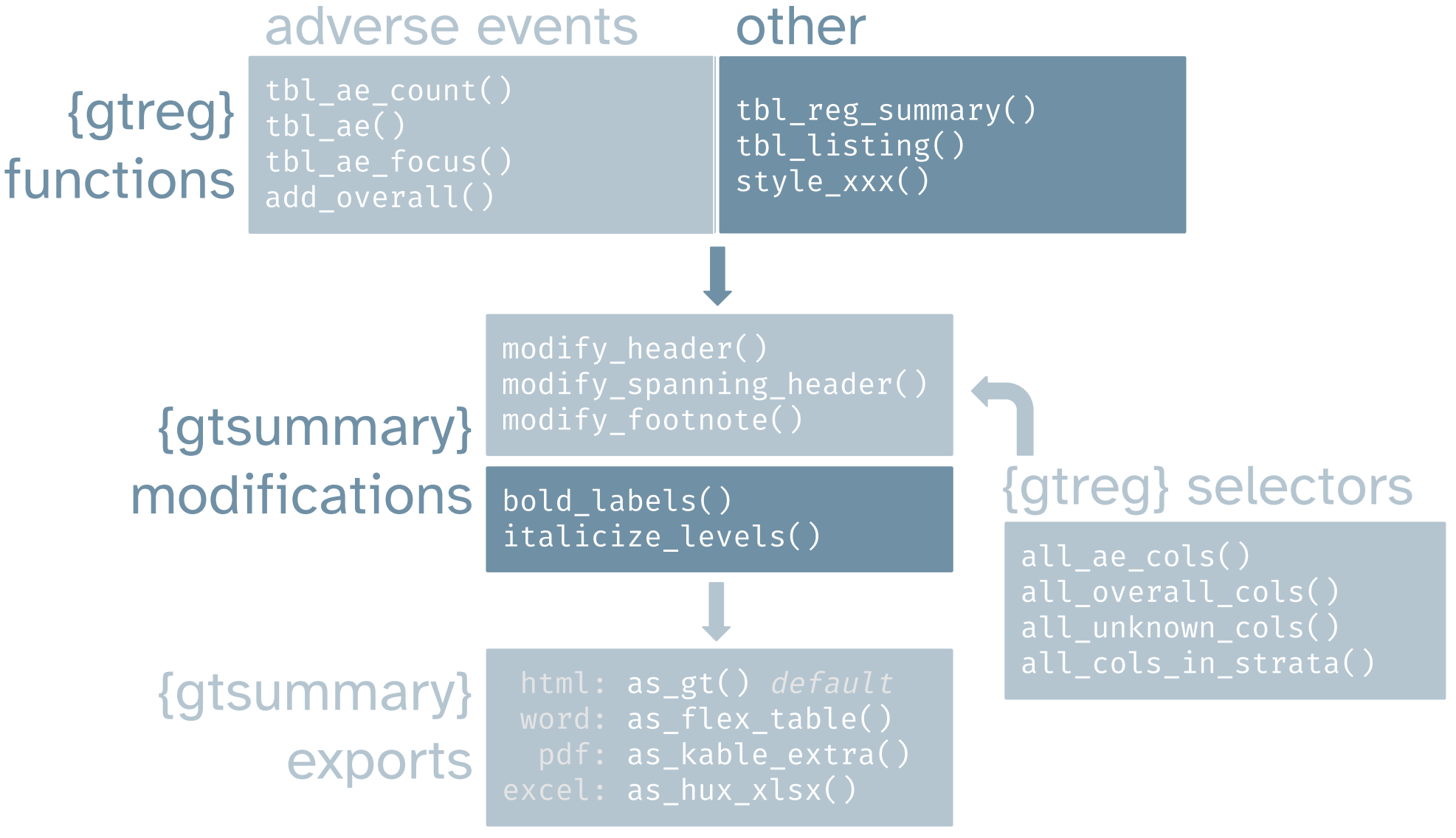
https://shannonpileggi.github.io/gtreg/articles/table-modifications.html

Code | Table | Data

```
df_adverse_events |>
  tbl_ae(
    id = patient_id,
    id_df = df_patient_characteristics,
    strata = trt,
    ae = adverse_event,
    soc = system_organ_class,
    by = grade
  ) |>
 add_overall(across = 'by') |>
 bold_labels() |>
 modify_header(
    all_ae_cols() ~ "**Grade {by}**"
    ) %>%
  modify_spanning_header(
     all_ae_cols(TRUE, TRUE) ~ "**{strata}**  \nN = {n}"
    )
```

Other tabling functions

Other tabling functions



tbl_reg_summary()

Create summary tables with standard regulatory formatting.

Code | Table | Data

```
df_patient_characteristics |>
 select(trt, marker, status) |>
 tbl_reg_summary(
   by = trt
   ) |>
 bold_labels()
```

tbl_listing()

A fancy  way to print grouped data.

Code | Table | Data

```
df_adverse_events |>
  head(n = 10) |>
  select(system_organ_class, adverse_event, grade, drug_attribution, patient_id) |>
  arrange(adverse_event, desc(grade)) |>
  tbl_listing(
    group_by = system_organ_class
    ) |>
  bold_labels()
```

tbl extensions

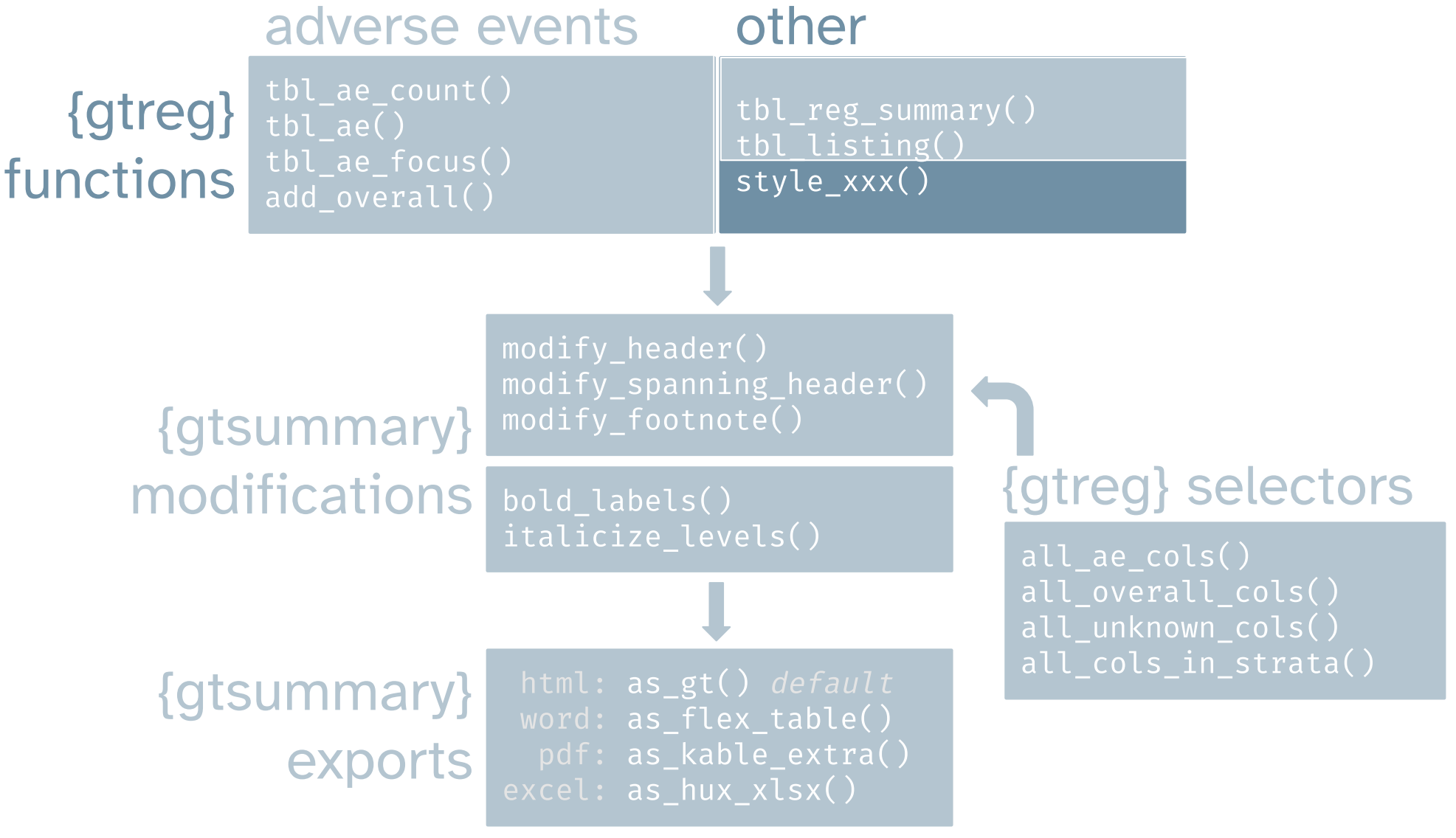
Remember this table?

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()

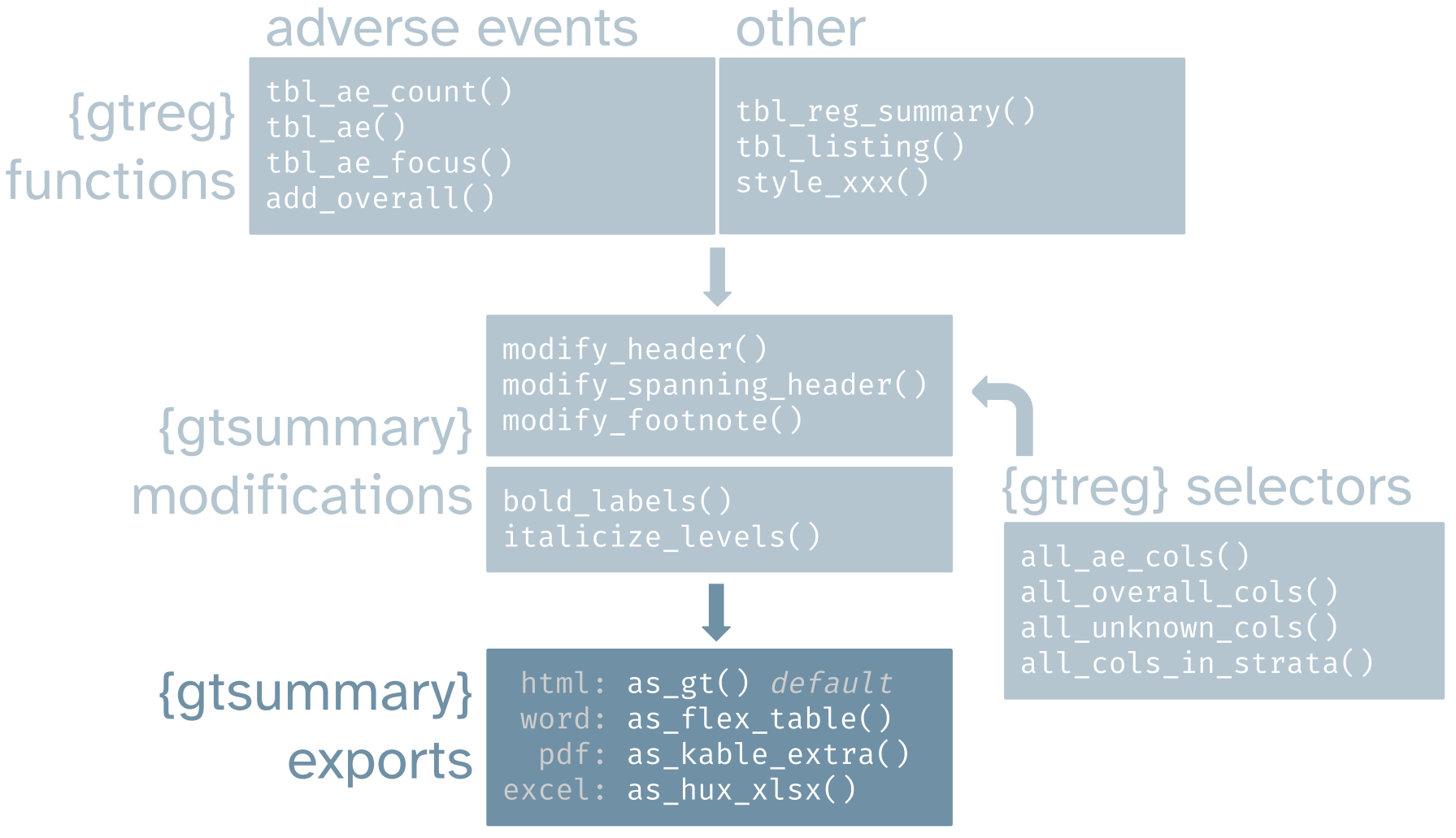
Code | Table | Data

```
df_adverse_events |>
  tbl_ae(
    id = patient_id,
    id_df = df_patient_characteristics,
    strata = trt,
    ae = adverse_event,
    soc = system_organ_class,
    by = grade,
    digits = style_xxx,
    zero_symbol = NULL
  ) |>
 bold_labels() |>
 modify_header(all_ae_cols() ~ "**Grade {by}**") %>%
 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

Thank you!

{gtreg} website

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

{gtreg} installation

```
# install from CRAN
install.packages("gtreg")
# or install development version from github
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