

Modular programming  
approach to create mean  
plot and adverse events  
frequency plot

# Who are we

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# Abstract

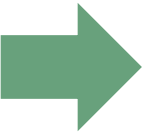
- Clear **data visualization** can be achieved when the same clinical data are represented **both as a table and a plot**. This way, the viewer can get a quick overview from the plot and can examine the detailed data in the table if they are interested in specific values.
- To accomplish this, a **modular programming approach** can be applied to ensure that the **same numbers** are displayed both in the tabular and pictorial format.
- In this presentation, we explore two common types of plots in clinical trials
  - the **mean plot**
  - the **most frequent adverse events plot**
  - We will demonstrate the use of modular **macros** for creating these outputs.
  - The macros are built using the **SG** and the TEMPLATE/SGRENDER (**GTL**) procedures with the possibility for the user to adjust the layout.
  - Furthermore, we discuss **the pros and cons** of the modular approach to output programming.

# Same data –two outputs!

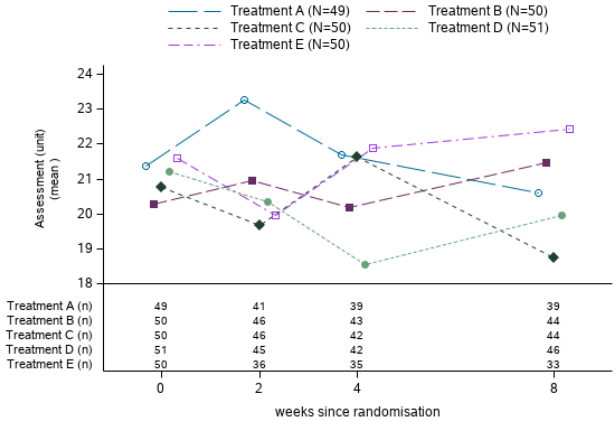
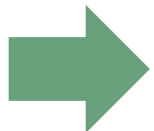
- Two programs two outputs?
- One program for two outputs?

ADaMs

Single program



Single program



Abbreviation: This is abbreviation1, This is abbreviation2, This is abbreviation3  
Note: This is note1, This is note2, This is note3

08MAY21:13:44:50-f\_meanplot\_bds.sas/example2.png

|                     | Treat A<br>1 mg/g<br>(N=49) | Treat B<br>3 mg/g<br>(N=50) | Treat C<br>8 mg/g<br>(N=50) | Treat D<br>20 mg/g<br>(N=52) | Treat E<br>Vehicle<br>(N=50) |
|---------------------|-----------------------------|-----------------------------|-----------------------------|------------------------------|------------------------------|
| Total extent        |                             |                             |                             |                              |                              |
| n                   | 48                          | 50                          | 50                          | 51                           | 50                           |
| Mean (SD)           | 13.03 (8.30)                | 16.51 (14.29)               | 11.76 (7.82)                | 14.84 (12.68)                | 15.78 (11.76)                |
| Median              | 10.00                       | 11.00                       | 10.50                       | 9.00                         | 10.90                        |
| Q1;Q3               | (8.00;16.25)                | (7.50;18.00)                | (6.00;15.00)                | (6.00;18.00)                 | (7.60;19.00)                 |
| Min;max             | 5.0;38.0                    | 5.0;59.0                    | 5.0;48.5                    | 2.5;49.1                     | 5.0;49.9                     |
| Total intensity sum |                             |                             |                             |                              |                              |
| n                   | 49                          | 50                          | 50                          | 51                           | 50                           |
| Mean (SD)           | 8.8 (3.3)                   | 8.4 (3.2)                   | 8.0 (2.6)                   | 9.3 (3.4)                    | 8.3 (3.4)                    |
| Median              | 9.0                         | 9.0                         | 8.0                         | 9.0                          | 8.0                          |
| Q1;Q3               | (7.0;10.0)                  | (6.0;10.0)                  | (6.0;10.0)                  | (7.0;12.0)                   | (6.0;11.0)                   |
| Min;max             | 3;18                        | 3;16                        | 4;16                        | 3;16                         | 3;18                         |
| Total VAS sum       |                             |                             |                             |                              |                              |
| n                   | 49                          | 50                          | 50                          | 51                           | 50                           |
| Mean (SD)           | 11.67 (4.79)                | 11.52 (4.45)                | 10.68 (5.10)                | 11.85 (5.17)                 | 11.00 (4.81)                 |
| Median              | 12.30                       | 11.45                       | 10.85                       | 12.90                        | 11.05                        |
| Q1;Q3               | (7.60;14.50)                | (8.50;15.10)                | (6.60;14.60)                | (8.50;16.10)                 | (8.10;14.80)                 |
| Min;max             | 1.0;19.9                    | 2.0;19.7                    | 0.2;19.0                    | 0.3;20.0                     | 1.7;20.0                     |
| SCORAD score        |                             |                             |                             |                              |                              |
| n                   | 48                          | 50                          | 50                          | 51                           | 50                           |
| Mean (SD)           | 45.363 (13.322)             | 44.293 (14.093)             | 41.036 (12.193)             | 47.213 (14.232)              | 42.761 (15.209)              |
| Median              | 44.400                      | 43.860                      | 41.470                      | 44.500                       | 40.020                       |
| Q1;Q3               | (35.900;56.350)             | (32.400;52.400)             | (32.040;49.000)             | (38.000;58.940)              | (31.300;50.900)              |

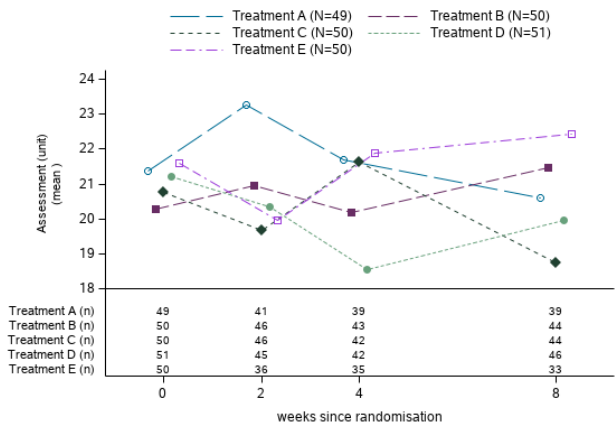
# Same data –two outputs!

- Two programs two outputs?
- One program for two outputs?

ADaMs



Modular programming

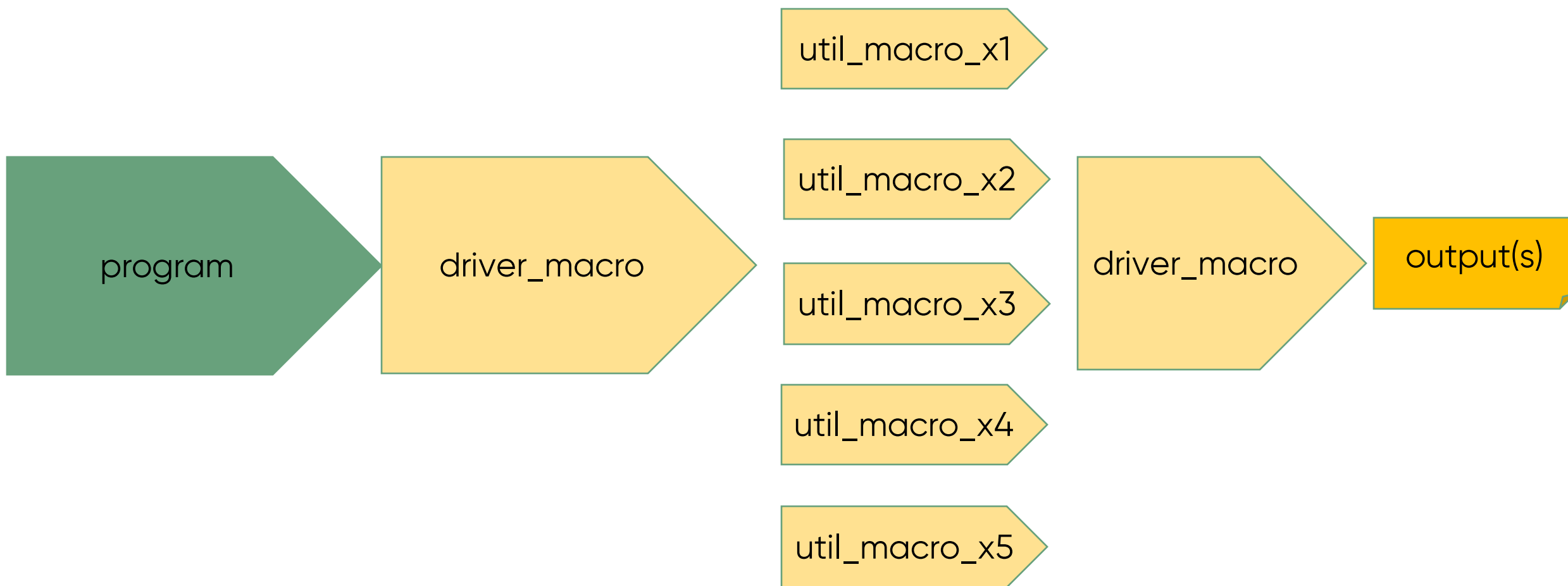


Abbreviation: This is abbreviation1, This is abbreviation2, This is abbreviation3  
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06MAY21:13:44:50-f\_meanplot\_bds.sas/example2.png

|                     | Treat A<br>1 mg/g<br>(N=49) | Treat B<br>3 mg/g<br>(N=50) | Treat C<br>8 mg/g<br>(N=50) | Treat D<br>20 mg/g<br>(N=52) | Treat E<br>Vehicle<br>(N=50) |
|---------------------|-----------------------------|-----------------------------|-----------------------------|------------------------------|------------------------------|
| Total extent        |                             |                             |                             |                              |                              |
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| n                   | 49                          | 50                          | 50                          | 51                           | 50                           |
| Mean (SD)           | 8.8 (3.3)                   | 8.4 (3.2)                   | 8.0 (2.6)                   | 9.3 (3.4)                    | 8.3 (3.4)                    |
| Median              | 9.0                         | 9.0                         | 8.0                         | 9.0                          | 8.0                          |
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| Min;max             | 3;18                        | 3;16                        | 4;16                        | 3;16                         | 3;18                         |
| Total VAS sum       |                             |                             |                             |                              |                              |
| n                   | 49                          | 50                          | 50                          | 51                           | 50                           |
| Mean (SD)           | 11.67 (4.79)                | 11.52 (4.45)                | 10.68 (5.10)                | 11.85 (5.17)                 | 11.00 (4.81)                 |
| Median              | 12.30                       | 11.45                       | 10.85                       | 12.90                        | 11.05                        |
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| SCORAD score        |                             |                             |                             |                              |                              |
| n                   | 48                          | 50                          | 50                          | 51                           | 50                           |
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| Median              | 44.400                      | 43.800                      | 41.470                      | 44.500                       | 40.020                       |
| Q1;Q3               | (35.900;56.350)             | (32.400;52.400)             | (32.040;49.000)             | (38.000;58.940)              | (31.300;50.900)              |

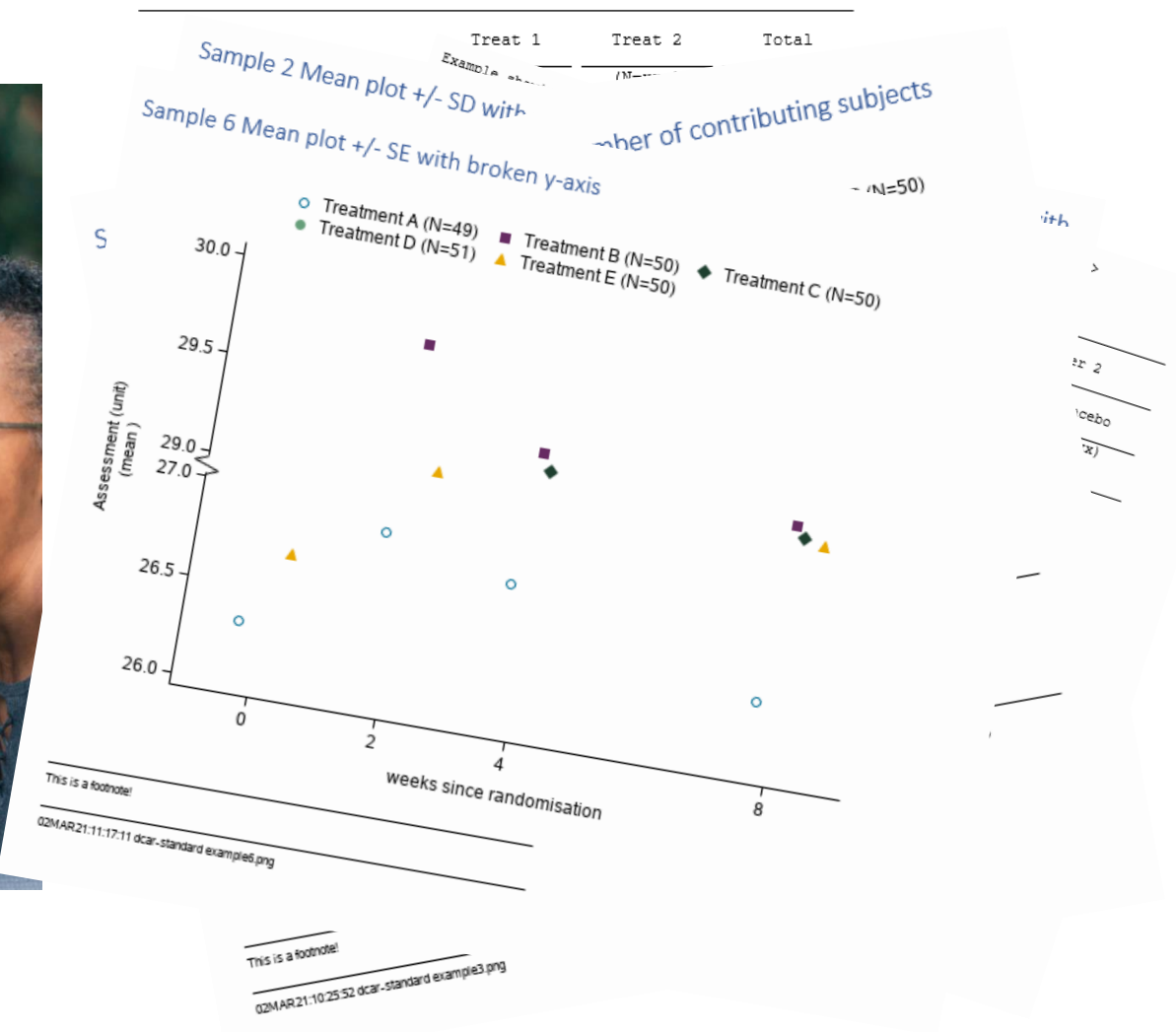
# Modular programming at LEO Pharma



# Development of new standard TFL programs and shells

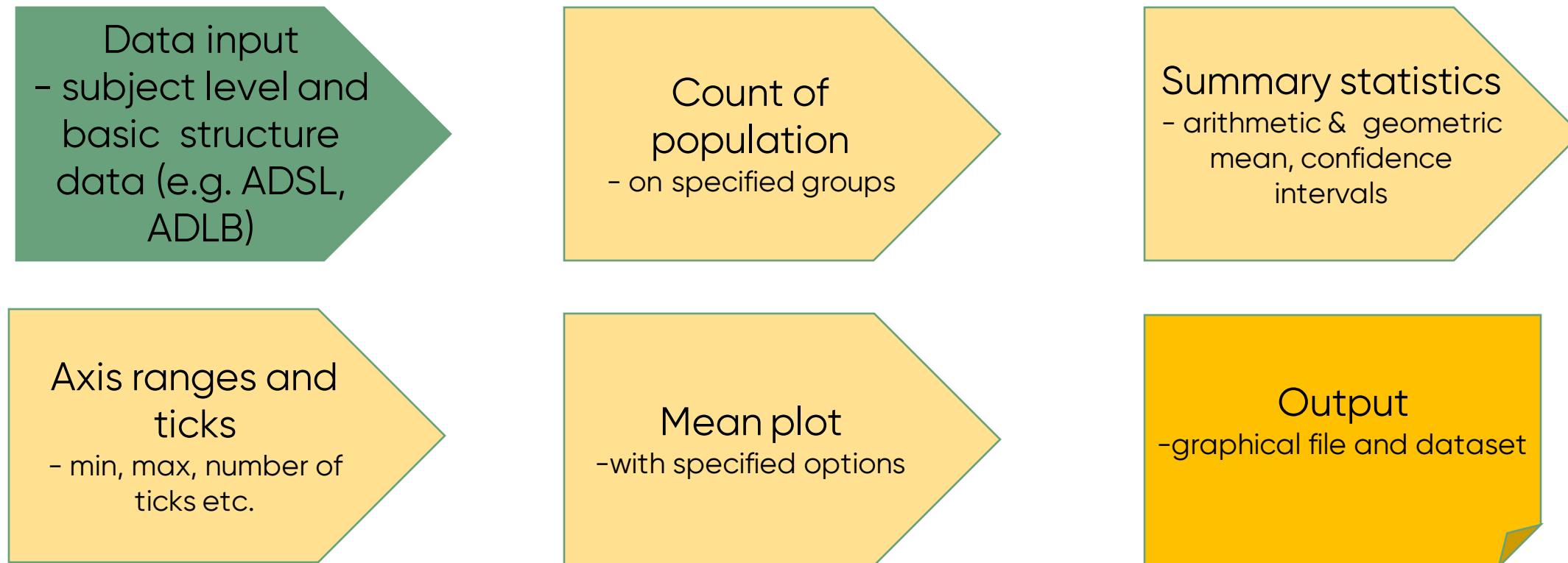


Template for summary statistics for categorical and continuous variables - <Analysis population set>



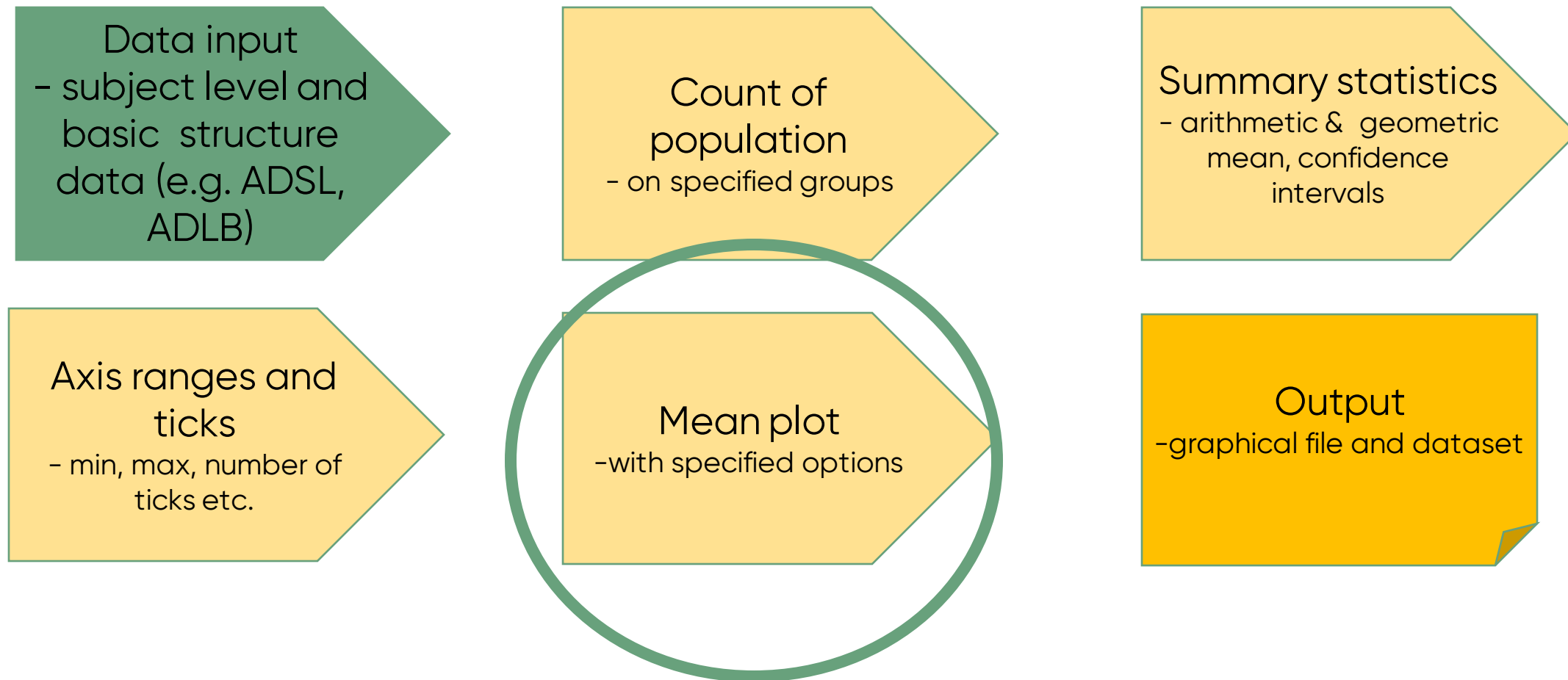
# Driver for the mean plot macro

## - the structure



# Driver for the mean plot macro

## - the structure

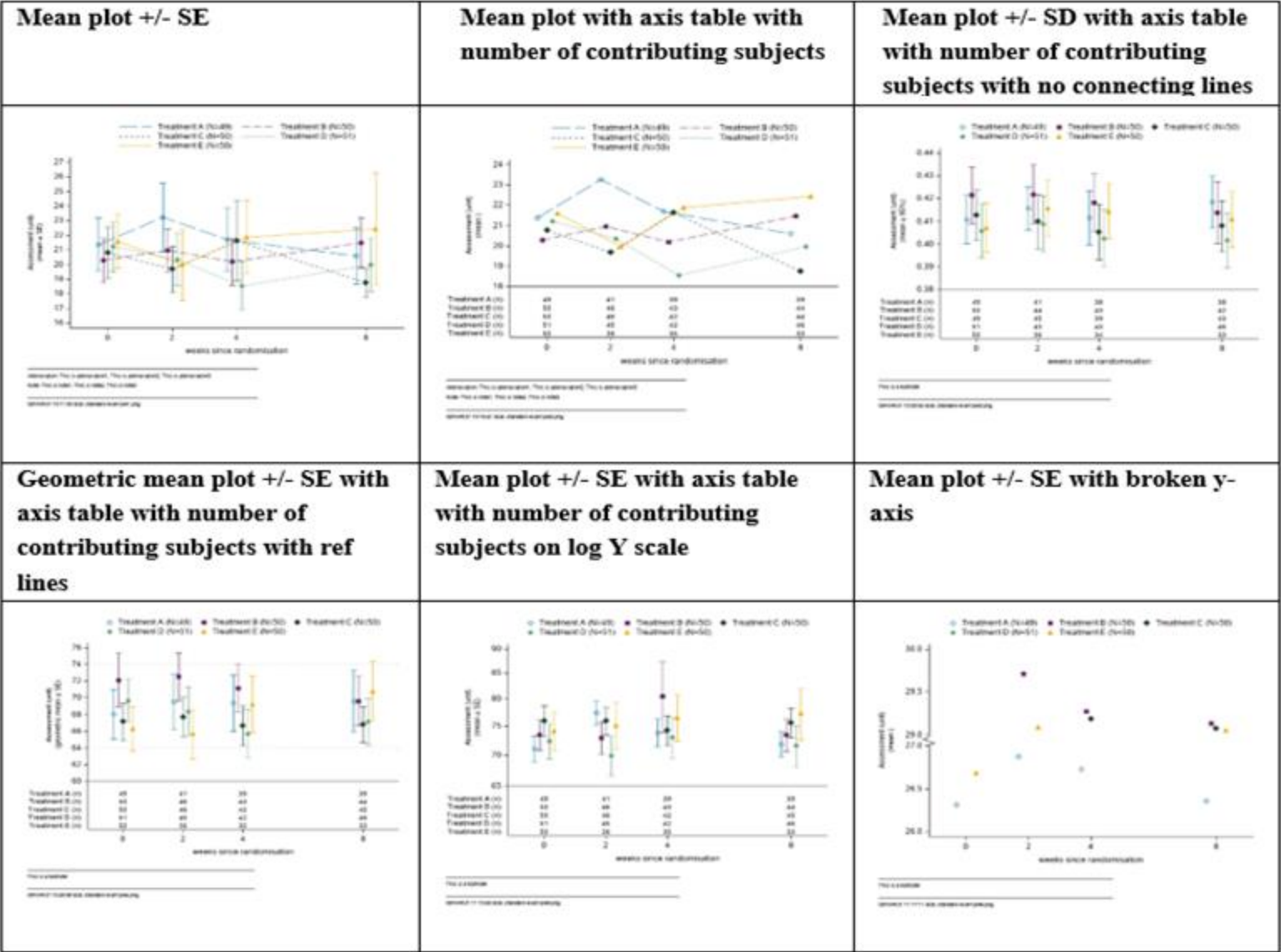


# Full code and examples available at Github

- [https://github.com/clausstenberg/phuse\\_2021\\_DV02](https://github.com/clausstenberg/phuse_2021_DV02)

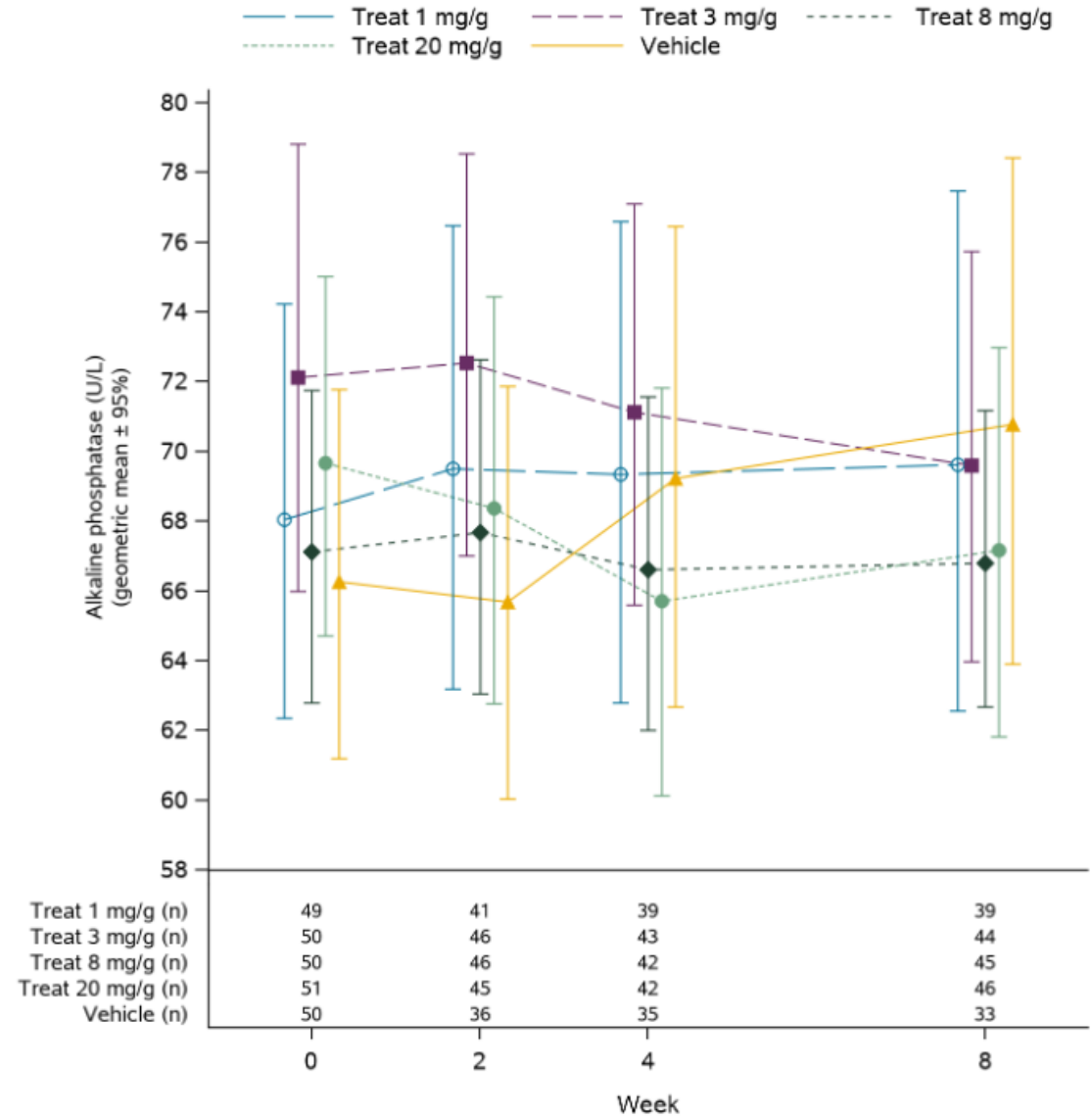


# Mean plot



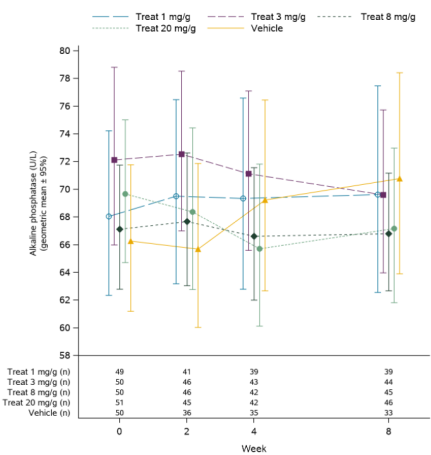
# Mean plot

- Want:
  - Geometric mean plot for Alkaline phosphatase by week with 95% confidence intervals and x-axis table with contributing subjects by treatment group.
- How:
  - Make SAS programs that
    - Select data
    - Call driver macro for mean plot
      - Count population number
      - Do summary statistics
      - Set Axis ranges and ticks
      - Do mean plot



# Mean plot

- Input data to mean plot macro:



| # | ⊕ mean    | ⊕ up_ci    | ⊕ low_ci   | ⊕ nsubj | ⊕ npop | ⚠ treatgrp    | ⊕ treatgrpn | ⊕ weekn | ⚠ PARAMCD | ⚠ PARAM                    | ⚠ group |
|---|-----------|------------|------------|---------|--------|---------------|-------------|---------|-----------|----------------------------|---------|
| 1 | 65.720961 | 71.8263554 | 60.1345379 | 42      | 51     | Treat 20 mg/g | 20          | 4       | ALP       | Alkaline phosphatase (U/L) | 4-20    |
| 2 | 70.792907 | 78.4281471 | 63.9009827 | 33      | 50     | Vehicle       | 90          | 8       | ALP       | Alkaline phosphatase (U/L) | 8-90    |
| 3 | 69.519222 | 76.4692674 | 63.2008441 | 41      | 49     | Treat 1 mg/g  | 1           | 2       | ALP       | Alkaline phosphatase (U/L) | 2-1     |
| 4 | 66.628917 | 71.5791949 | 62.0209900 | 42      | 50     | Treat 8 mg/g  | 8           | 4       | ALP       | Alkaline phosphatase (U/L) | 4-8     |
| 5 | 69.605673 | 75.7286115 | 63.9777972 | 44      | 50     | Treat 3 mg/g  | 3           | 8       | ALP       | Alkaline phosphatase (U/L) | 8-3     |
| 6 | 65.685085 | 71.8641006 | 60.0373530 | 36      | 50     | Vehicle       | 90          | 2       | ALP       | Alkaline phosphatase (U/L) | 2-90    |
| 7 | 69.359423 | 76.6028356 | 62.8009340 | 39      | 49     | Treat 1 mg/g  | 1           | 4       | ALP       | Alkaline phosphatase (U/L) | 4-1     |
| 8 | 72.120261 | 78.8142618 | 65.0047244 | 50      | 50     | Treat 3 mg/g  | 3           | 0       | ALP       | Alkaline phosphatase (U/L) | 0-3     |

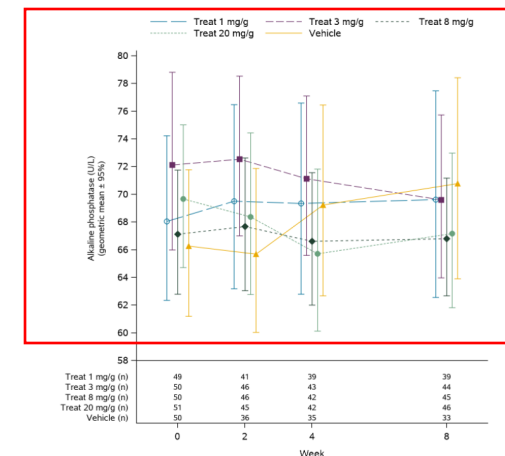
# Mean plot

- proc SGPLOT
- Code for the plot

```
/* plot statement */
proc sgplot data = _data4plot noborder noautolegend dattrmap=_attributemap;
    styleattrs axisbreak=spark;

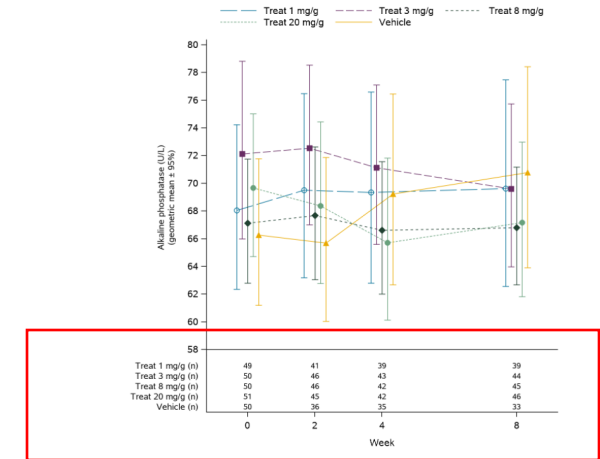
/* plot only with symbols */
    %if %upcase(&only_symbols_meanplot.) = Y %then %do;
        scatter x=&x_var_meanplot y=&y_meanVar_meanplot. / group = _group_name groupdisplay=cluster clusterwidth=&clusterwidth. attrid=&attrid_meanplot. name="symbol"
/* adding confidence intervals if wanted*/
        %if %length(&up_ciVar_meanplot. &low_ciVar_meanplot.) > 0 %then %do;
            yerrorlower=&low_ciVar_meanplot. yerrorupper=&up_ciVar_meanplot.;
        %end;
    %end;

/* plot with connecting lines and symbols */
    %else %do;
/* line */
        series x=&x_var_meanplot y=&y_meanVar_meanplot. / group = _group_name groupdisplay=cluster clusterwidth=&clusterwidth. attrid=&attrid_meanplot. name="mean" ;
/* scatter */
        scatter x=&x_var_meanplot y=&y_meanVar_meanplot. / group = _group_name groupdisplay=cluster clusterwidth=&clusterwidth. attrid=&attrid_meanplot. name="symbol"
/* adding confidence intervals if wanted*/
        %if %length(&up_ciVar_meanplot. &low_ciVar_meanplot.) > 0 %then %do;
            yerrorlower=&low_ciVar_meanplot. yerrorupper=&up_ciVar_meanplot.;
        %end;
    ..
    %end;
```



# Mean plot

- proc SGPLOT
- Code for the x-axis table



```

/* axistable with number of contributing subjects */
%if %upcase(&nsubj_table_meanplot.) = Y %then %do;
    xaxistable _nsubj / location=inside
                    textgroup=_group_name attrid=&attrid_meanplot.
                    class=name_4_xaxis_table
                    NOMISSINGCHAR LABELPOS=&labelpos_nsubj_meanplot.
                    labelattrs=(size=8) ;
/* refline at min to separate the xaxis table */
    refline &reflinesep. / axis=y lineattrs=(thickness=1 color=black) ;
%end;

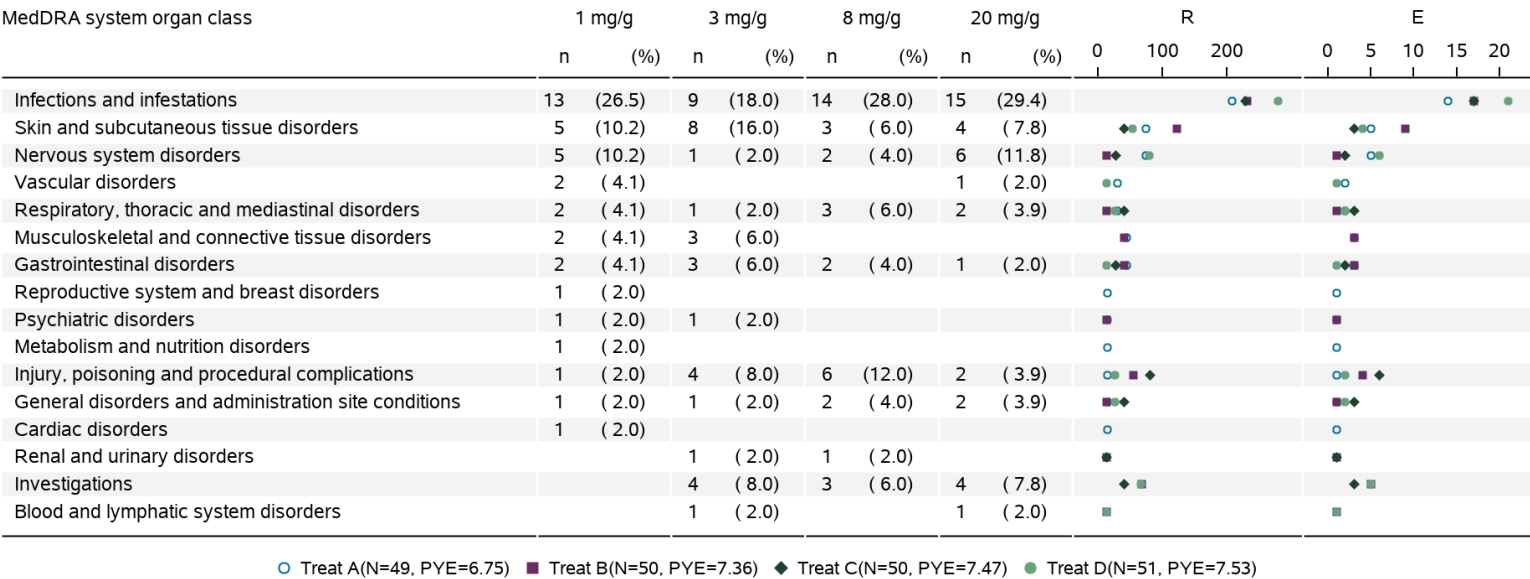
```

## Most frequent adverse events plot

[illegible]

# Most frequent adverse events plot

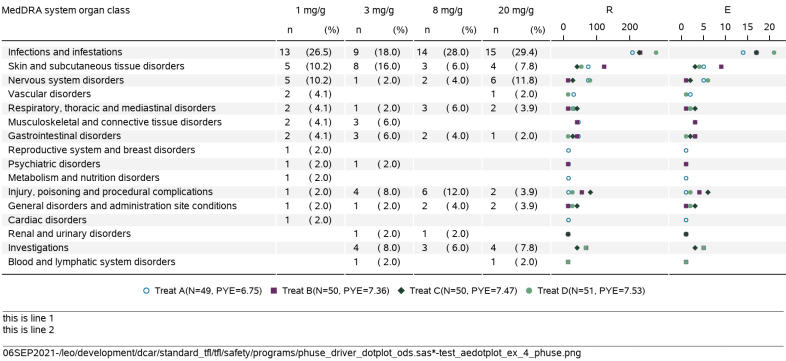
- Want:
  - Frequency on AEs on AEBODSYS with number of subjects (n) and percent (%) as table , rate (R) and events (E) as dotplot by treatment group.
- How:
  - Make SAS programs that
    - Select data
    - Call driver macro for dot plot
      - Count population number
      - Calc exposure year
      - Do summary statistics
      - Do AE dotplot



this is line 1  
this is line 2

06SEP2021-/leo/development/dcar/standard\_tf/tfl/safety/programs/phuse\_driver\_dotplot\_ods.sas\*-test\_aedotplot\_ex\_4\_phuse.png

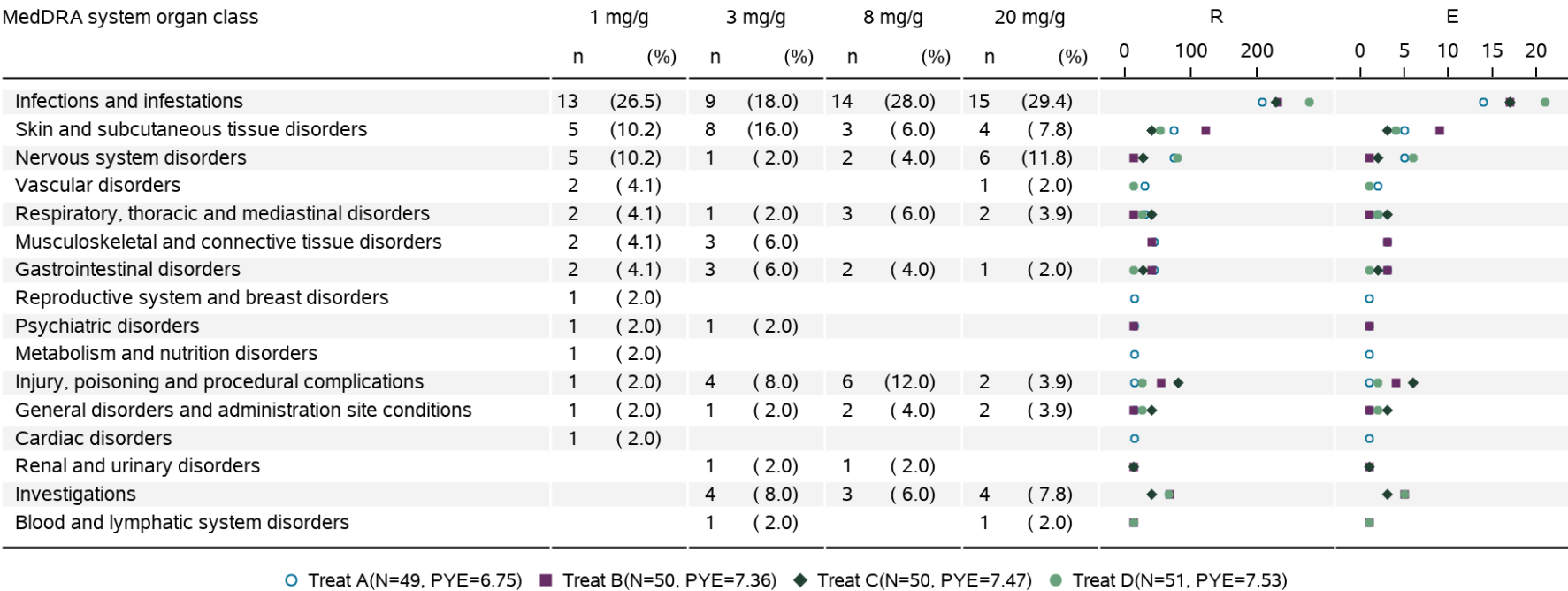
# Most frequent adverse events plot



| ⊕ group | ⊕ POPCOUNT | ⊕ PY         | ⚠ AEBODSYS                                     | ⊕ VALN | ⊕ VALE <sub>↑</sub> | ⚠ LABEL | ⚠ GROUPLABEL             | ⊕ VALP       | ⊕ VALR | ⚠ shorttreat |
|---------|------------|--------------|------------------------------------------------|--------|---------------------|---------|--------------------------|--------------|--------|--------------|
| 3       | 50         | 7.3620807666 | Respiratory, thoracic and mediastinal disor... | 1      | 1                   | Treat B | Treat B (N=50, PYE=7.36) | 2            | 13.58  | 3 mg/g       |
| 3       | 50         | 7.3620807666 | Renal and urinary disorders                    | 1      | 1                   | Treat B | Treat B (N=50, PYE=7.36) | 2            | 13.58  | 3 mg/g       |
| 1       | 49         | 6.7460643395 | General disorders and administration site c... | 1      | 1                   | Treat A | Treat A (N=49, PYE=6.75) | 2.0408163265 | 14.82  | 1 mg/g       |
| 3       | 50         | 7.3620807666 | Blood and lymphatic system disorders           | 1      | 1                   | Treat B | Treat B (N=50, PYE=7.36) | 2            | 13.58  | 3 mg/g       |
| 20      | 51         | 7.5290896646 | Gastrointestinal disorders                     | 1      | 1                   | Treat D | Treat D (N=51, PYE=7.53) | 1.9607843137 | 13.28  | 20 mg/g      |
| 20      | 51         | 7.5290896646 | Blood and lymphatic system disorders           | 1      | 1                   | Treat D | Treat D (N=51, PYE=7.53) | 1.9607843137 | 13.28  | 20 mg/g      |
| 3       | 50         | 7.3620807666 | Nervous system disorders                       | 1      | 1                   | Treat B | Treat B (N=50, PYE=7.36) | 2            | 13.58  | 3 mg/g       |
| 3       | 50         | 7.3620807666 | General disorders and administration site c... | 1      | 1                   | Treat B | Treat B (N=50, PYE=7.36) | 2            | 13.58  | 3 mg/g       |
| 1       | 49         | 6.7460643395 | Cardiac disorders                              | 1      | 1                   | Treat A | Treat A (N=49, PYE=6.75) | 2.0408163265 | 14.82  | 1 mg/g       |
| 1       | 49         | 6.7460643395 | Psychiatric disorders                          | 1      | 1                   | Treat A | Treat A (N=49, PYE=6.75) | 2.0408163265 | 14.82  | 1 mg/g       |
| 20      | 51         | 7.5290896646 | Vascular disorders                             | 1      | 1                   | Treat D | Treat D (N=51, PYE=7.53) | 1.9607843137 | 13.28  | 20 mg/g      |
| 1       | 49         | 6.7460643395 | Injury, poisoning and procedural complicati... | 1      | 1                   | Treat A | Treat A (N=49, PYE=6.75) | 2.0408163265 | 14.82  | 1 mg/g       |
| 1       | 49         | 6.7460643395 | Reproductive system and breast disorders       | 1      | 1                   | Treat A | Treat A (N=49, PYE=6.75) | 2.0408163265 | 14.82  | 1 mg/g       |
| 3       | 50         | 7.3620807666 | Psychiatric disorders                          | 1      | 1                   | Treat B | Treat B (N=50, PYE=7.36) | 2            | 13.58  | 3 mg/g       |
| 1       | 49         | 6.7460643395 | Metabolism and nutrition disorders             | 1      | 1                   | Treat A | Treat A (N=49, PYE=6.75) | 2.0408163265 | 14.82  | 1 mg/g       |
| 8       | 50         | 7.4688569473 | Renal and urinary disorders                    | 1      | 1                   | Treat C | Treat C (N=50, PYE=7.47) | 2            | 13.39  | 8 mg/n       |

# Most frequent adverse events plot

- proc TEMPLATE and SGRENDER (GTL)

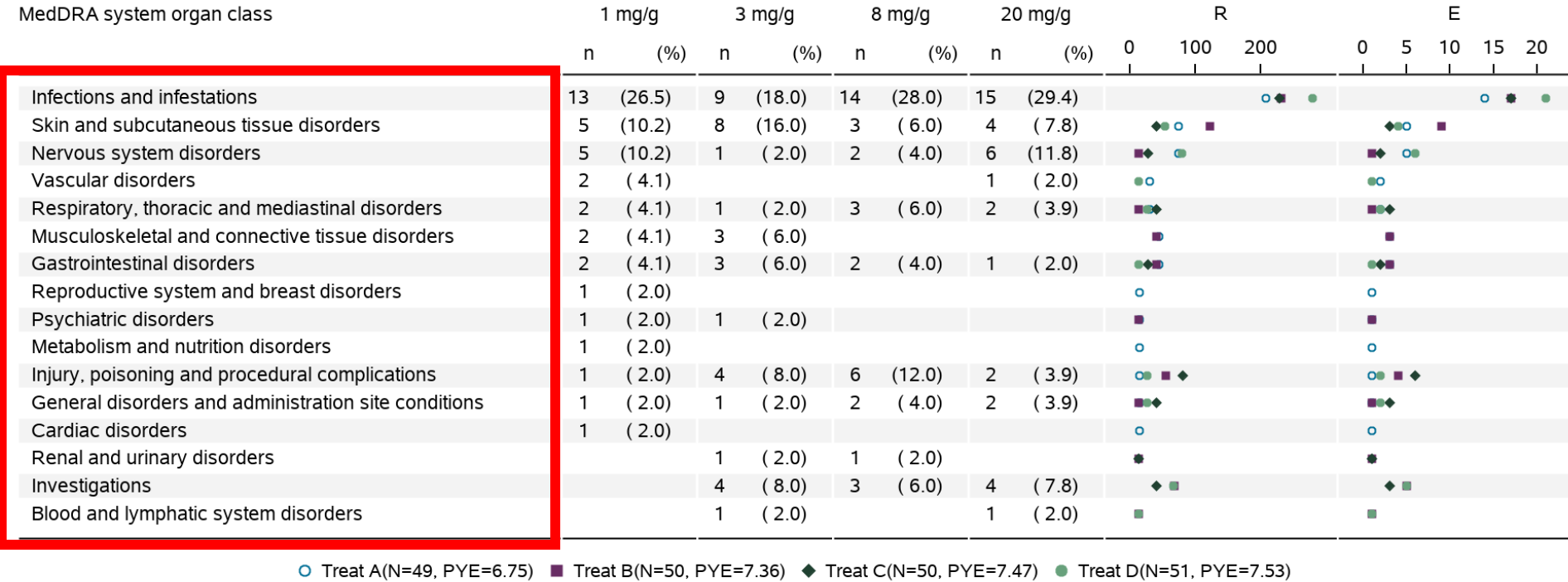


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06SEP2021-/leo/development/dcar/standard\_tfl/tfl/safety/programs/phuse\_driver\_dotplot ods.sas\*-test\_aedotplot\_ex\_4\_phuse.png

# Most frequent adverse events plot

- proc TEMPLATE and SGRENDER (GTL)

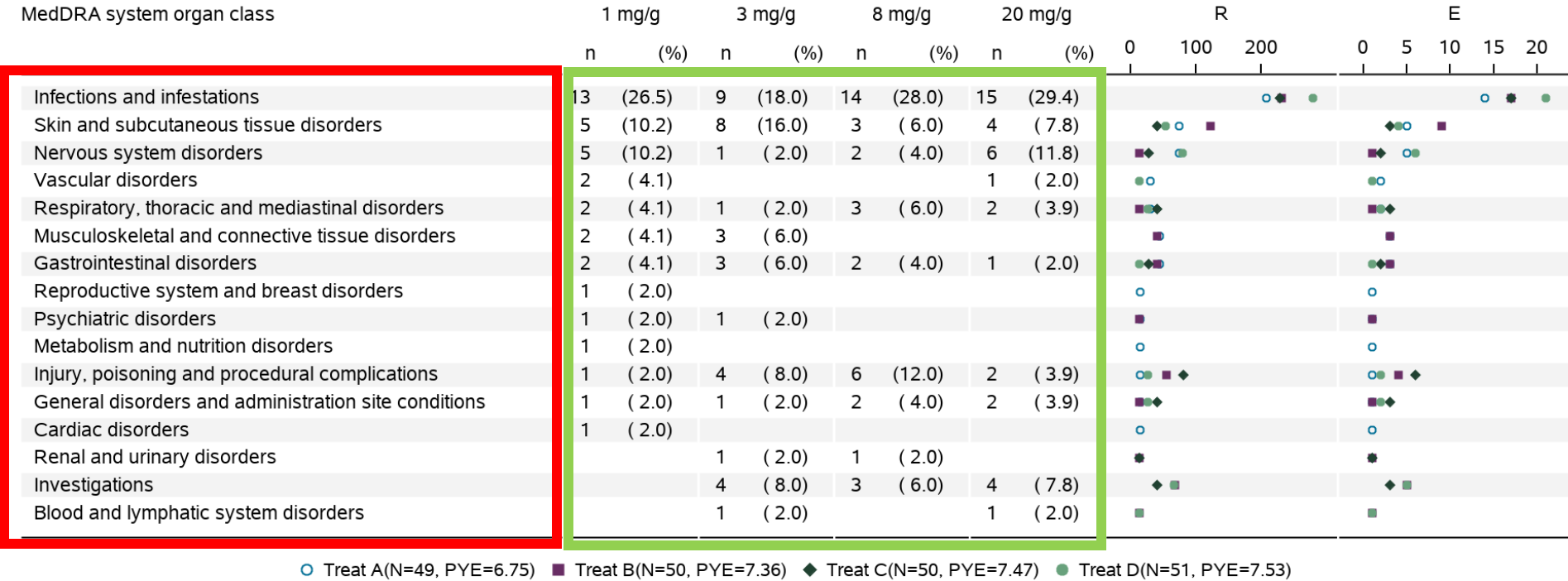


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06SEP2021-/leo/development/dcar/standard\_tfl/tfl/safety/programs/phuse\_driver\_dotplot ods.sas\*-test\_aedotplot\_ex\_4\_phuse.png

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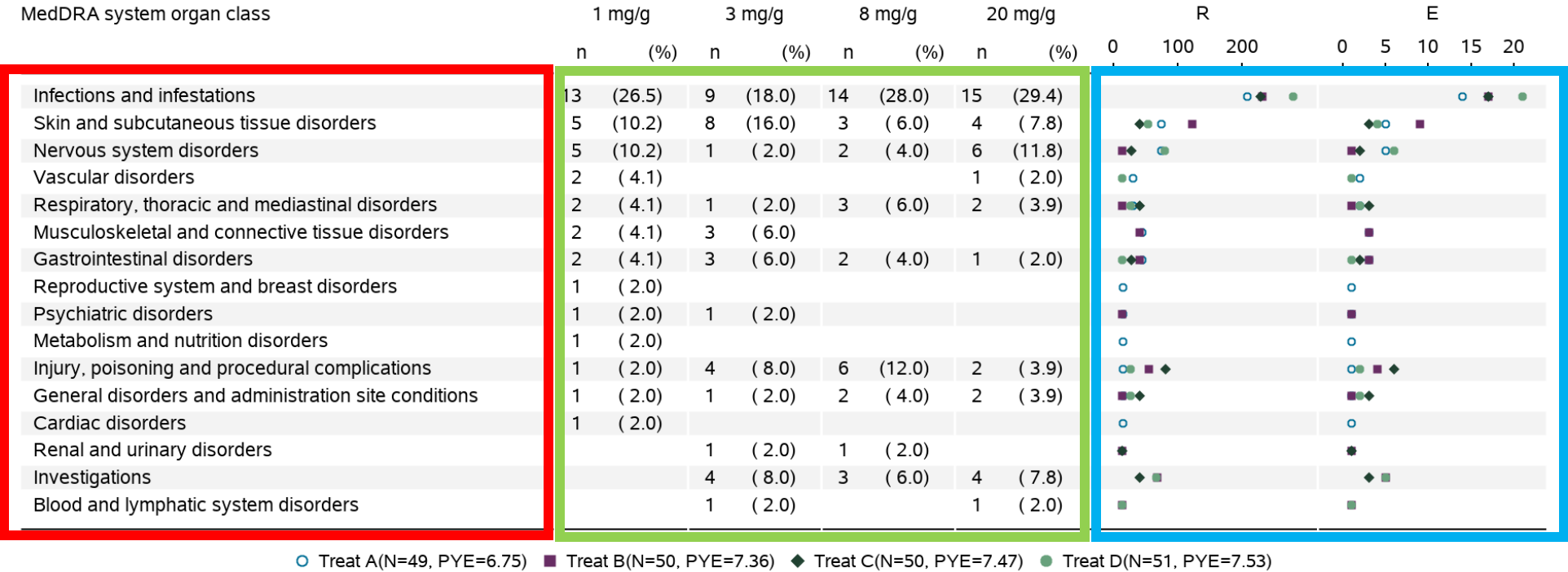


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06SEP2021-/leo/development/dcar/standard\_tfl/tfl/safety/programs/phuse\_driver\_dotplot ods.sas\*-test\_aedotplot\_ex\_4\_phuse.png

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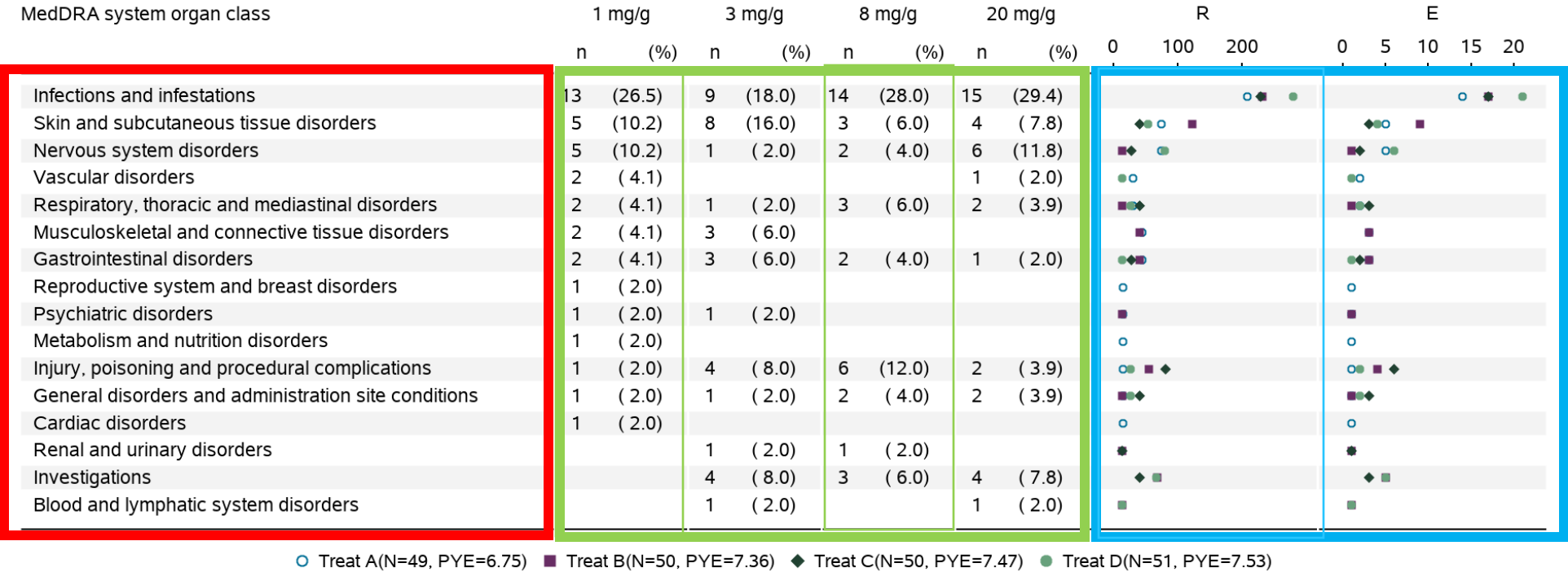


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06SEP2021-/leo/development/dcar/standard\_tfl/tfl/safety/programs/phuse\_driver\_dotplot ods.sas\*-test\_aedotplot\_ex\_4\_phuse.png

# Most frequent adverse events plot

- proc TEMPLATE and SGRENDER (GTL)



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06SEP2021-/leo/development/dcar/standard\_tf/tf/safety/programs/phuse\_driver\_dotplot ods.sas\*-test\_aedotplot\_ex\_4\_phuse.png

# Most frequent adverse events plot

proc TEMPLATE

Code for overall col N  
and first col

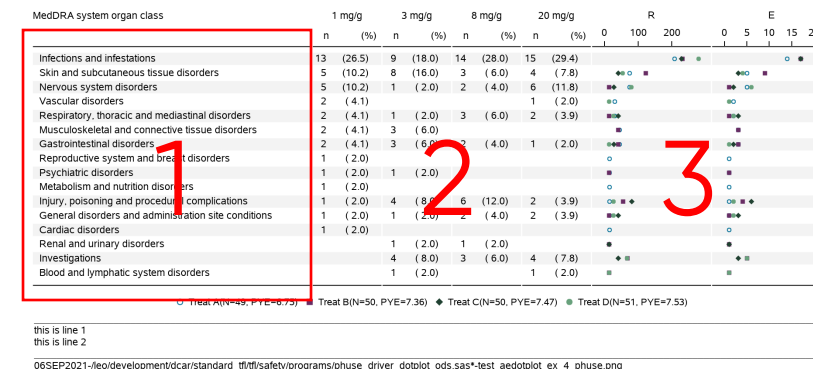
```
proc template;
  define statgraph aedotplot;

    beginnograph ;

      layout lattice /columns=&totcol.
                     columnweights = (&totwidth.)
                     rowdatarange=unionall
                     ;
      /* column for AE's display */
      layout overlay / walldisplay=none
                     border=false
                     x2axisopts=(display=(label line)
                                displaysecondary=(line)
                                labelposition=datacenter
                                label="&display_txt_label_dotplot."
                                labelattrs=(size=&fontsize_axislabel.))
                     yaxisopts=(linearopts = (tickvaluesequence=(start=1 end=&count increment=1))
                                display = none
                                displaysecondary = none)
                                ;

      /*--Draw alternating bands using referenceline--*/
      referenceline y = display_txt2nd/ lineattrs=(thickness=&band_thickness_dotplot.PCT) datatransparency=0.9;
      /* left column with text box */
      scatterplot y=display_txt x=display_col / markercharacter=display_txt
                                                    markercharacterattrs=(size=&fontsize_content.)
                                                    markercharacterposition=right
                                                    yaxis=Y
                                                    xaxis=X2
                                                    markerattrs=(size=0)
                                                    includemissinggroup=true
                                                    ;

    endlayout;
  end;
end;
```



# Most frequent adverse events plot

proc TEMPLATE

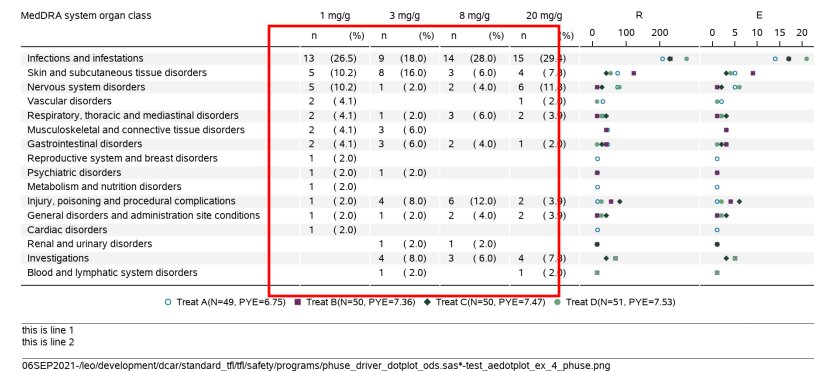
Code for col with stats

```
/* columns for stats - one for each treatment group*/
%if %length(&show_stat_dotplot.)>0 %then %do;

%do i=1 %to &n_treatgrp.;
  layout overlay / walldisplay=none
    border=false
    x2axisopts=(offsetmin=0.2
      display=(label line tickvalues)
      displaysecondary=(line)
      LABELPOSITION=center
      label="&&treatshort&i."
      tickvalueattrs=(size=&fontsize_axisticks.)
      labelattrs=(size=&fontsize_axislabel.))
    yaxisopts=(linearopts=(tickvaluesequence=(start=1 end=&count increment=1))
      display=none
      displaysecondary=none)
    ;
  /*--Draw alternating bands using referenceline--*/
  referenceline y = display_txt2nd/ lineattrs=(thickness=&band_thickness_dotplot.PCT) datatransparency=0.9;

  /*--Draw standard statistics columns--*/
  %if %index(%upcase(&show_stat_dotplot.), N) %then %do;
    scatterplot y=display_txt x=n / markercharacter =nsubj_c_trt_&i. MARKERCHARACTERPOSITION=left markercharacterattrs=(size=&fontsize_content.) xaxis=x2;
  %end;
  %if %index(%upcase(&show_stat_dotplot.), P) %then %do;
    scatterplot y=display_txt x=p / markercharacter =percent_c_trt_&i. MARKERCHARACTERPOSITION=left markercharacterattrs=(size=&fontsize_content.) xaxis=x2;
  %end;
  %if %index(%upcase(&show_stat_dotplot.), E) %then %do;
    scatterplot y=display_txt x=e / markercharacter =event_c_trt_&i. MARKERCHARACTERPOSITION=left markercharacterattrs=(size=&fontsize_content.) xaxis=x2;
  %end;
  %if %index(%upcase(&show_stat_dotplot.), R) %then %do;
    scatterplot y=display_txt x=r / markercharacter =rate_c_trt_&i. MARKERCHARACTERPOSITION=left markercharacterattrs=(size=&fontsize_content.) xaxis=x2;
  %end;

  endlayout;
%end;
```



# Most frequent adverse events plot

proc TEMPLATE

Code for col with plots

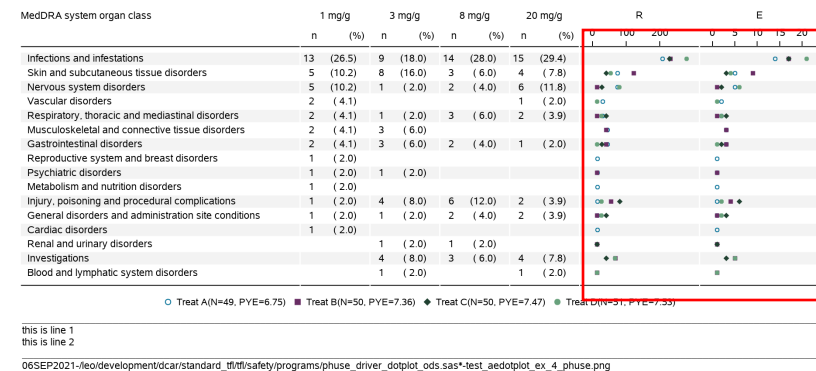
```
/* columns for dot plots */

/* first dotplot */
%if &mk_dotplot.= Y %then %do;

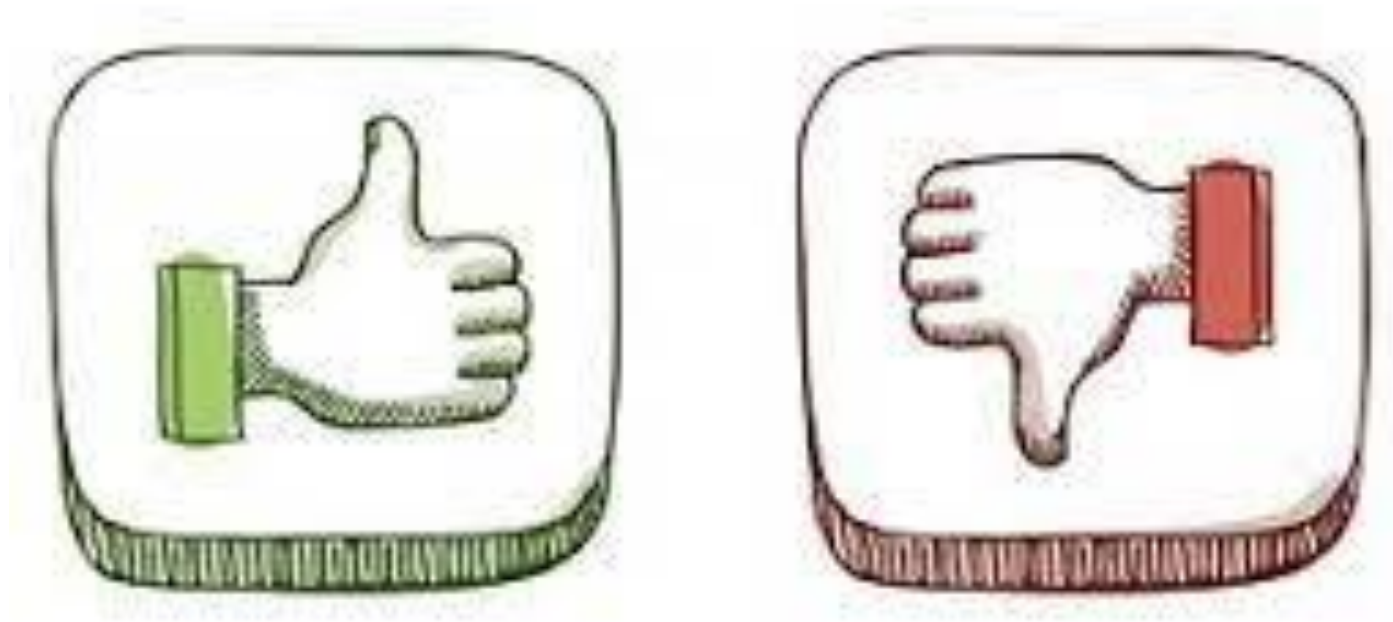
    %if &mk_dotplot_1.= Y %then %do;
        layout overlay / walldisplay=none
            border=false
            x2axisopts=(display=(label line ticks tickvalues)
                displaysecondary=(line)
                tickvalueattrs=(size=&fontsize_axisticks.)
                labelattrs=(size=&fontsize_axislabel.))
            yaxisopts=(linearopts=(tickvaluesequence=(start=1 end=&count. increment=1))
                display=none
                displaysecondary=none)
            ;
        /*--Draw alternating bands using referenceline--*/
        referenceline y = display_txt2nd/ lineattrs=(thickness=&band_thickness_dotplot.PCT) datatransparency=0.9;

        /*--Dot plots 1 - one overlay for each treatment group--*/
        %do i=1 %to &n_treatgrp.;
            scatterplot x = &&dotplot1_trt_&i. y=display_txt /xaxis=x2 markerattrs= (symbol=&&symbol&i. color=&&fillcolor&i.)
                legendlabel="&&treat&i.(N=&&popcount&i., PYE=&&pye&i.)" name="treat&i." ;
        %end;
    endlayout;
%end;

/* second dotplot */
%if &mk_dotplot_2.= Y %then %do;
```



# Pros and cons of the modular approach to output programming.





Thank you