

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

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Dermatology
beyond the skin

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Who are we

Claus Stenberg
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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?

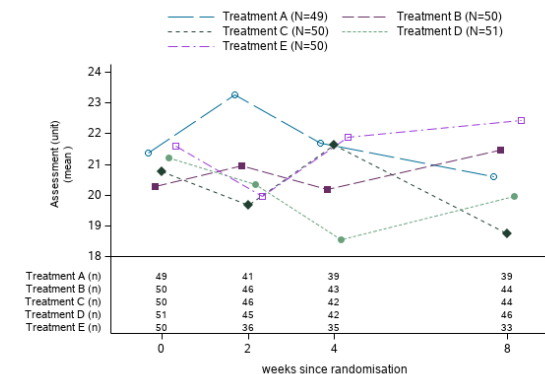
ADaMs



Single program



Single program



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

09MAY21:13:44:50-f_meanplot_pos_sasexample2.png

	Treat A 1 mg/g (N=49)	Treat B 3 mg/g (N=50)	Treat C 8 mg/g (N=50)	Treat D 20 mg/g (N=52)	Treat E Vehicle (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	10.30
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	43.800	41.470	44.500	40.000
Q1;Q3	(35.900;56.350)	(32.400;52.400)	(32.040;49.000)	(38.000;58.940)	(31.300;50.900)

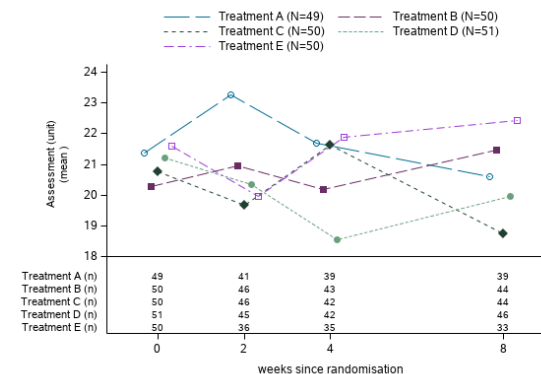
Same data -two outputs!

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

ADaMs



Modular programming



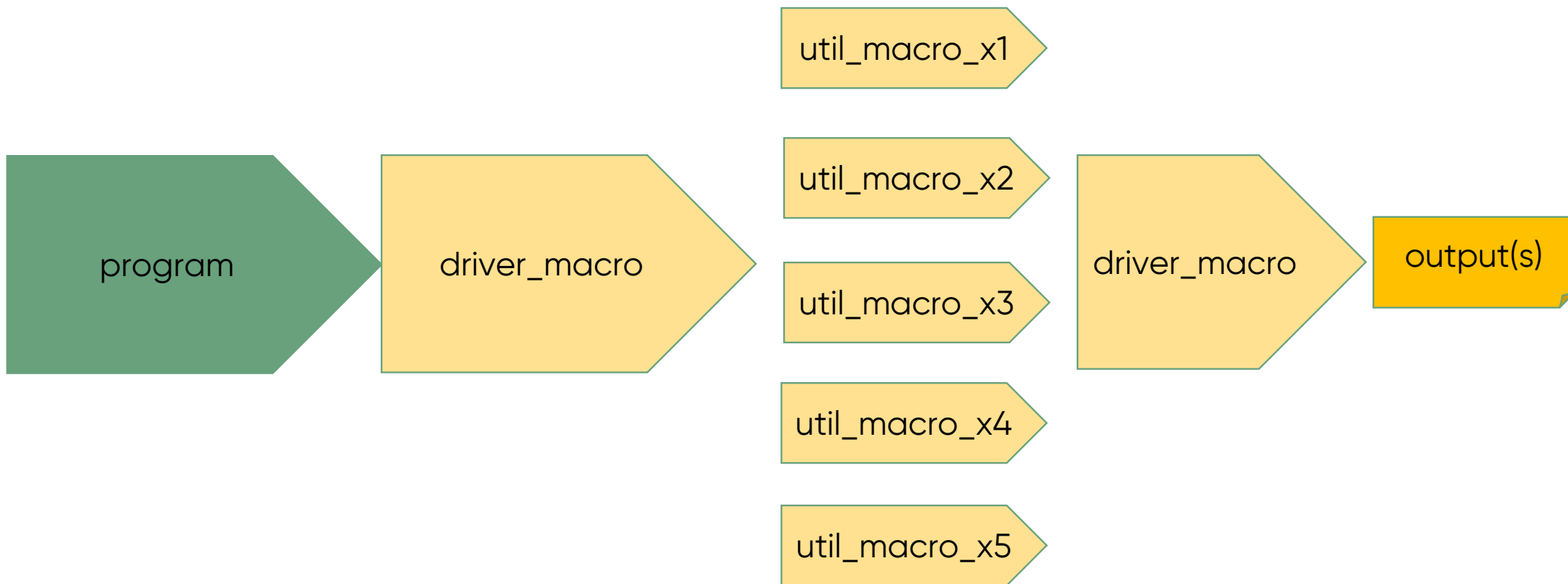
Abbreviation: This is abbreviation1. This is abbreviation2. This is abbreviation3.
Note: This is note1. This is note2. This is note3.

09MAY21:13:44:50-f_meanplot_pos_sasexample2.png

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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	43.800	41.470	44.500	40.000
Q1;Q3	(35.900;56.350)	(32.400;52.400)	(32.040;49.000)	(38.000;58.940)	(31.300;50.900)



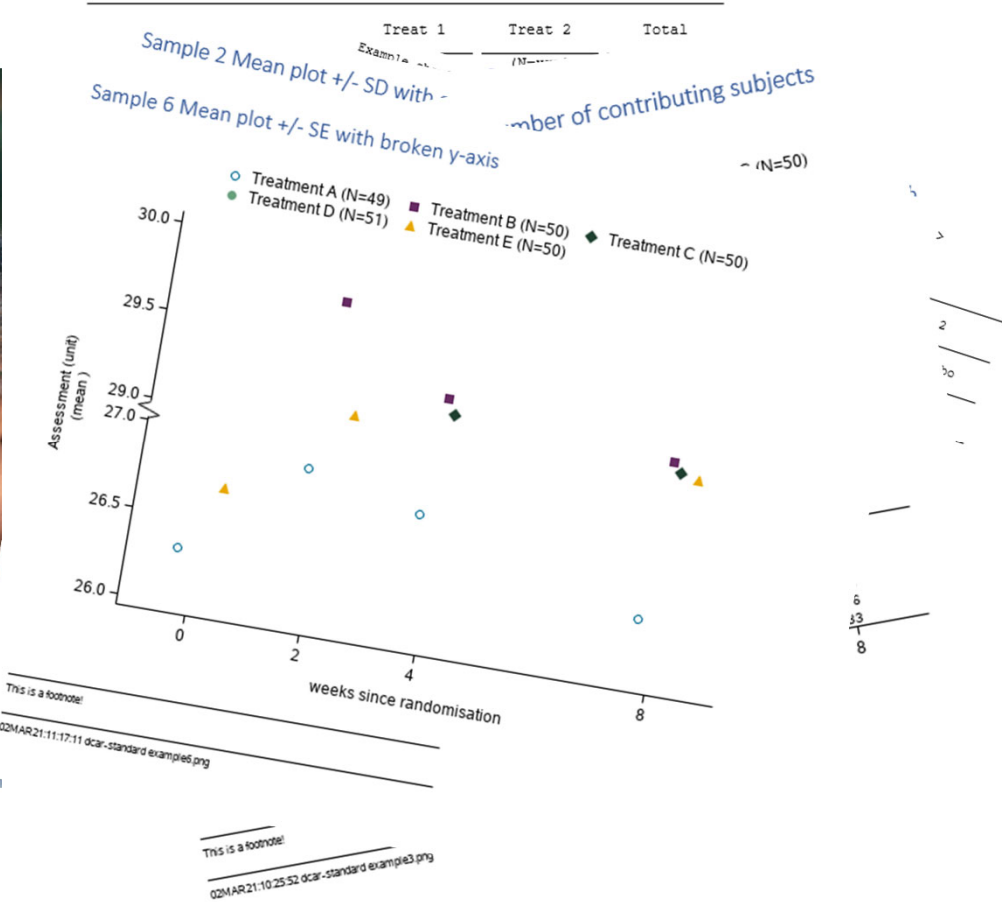
Modular programming at LEO Pharma



Development of new standard TFL programs and shells

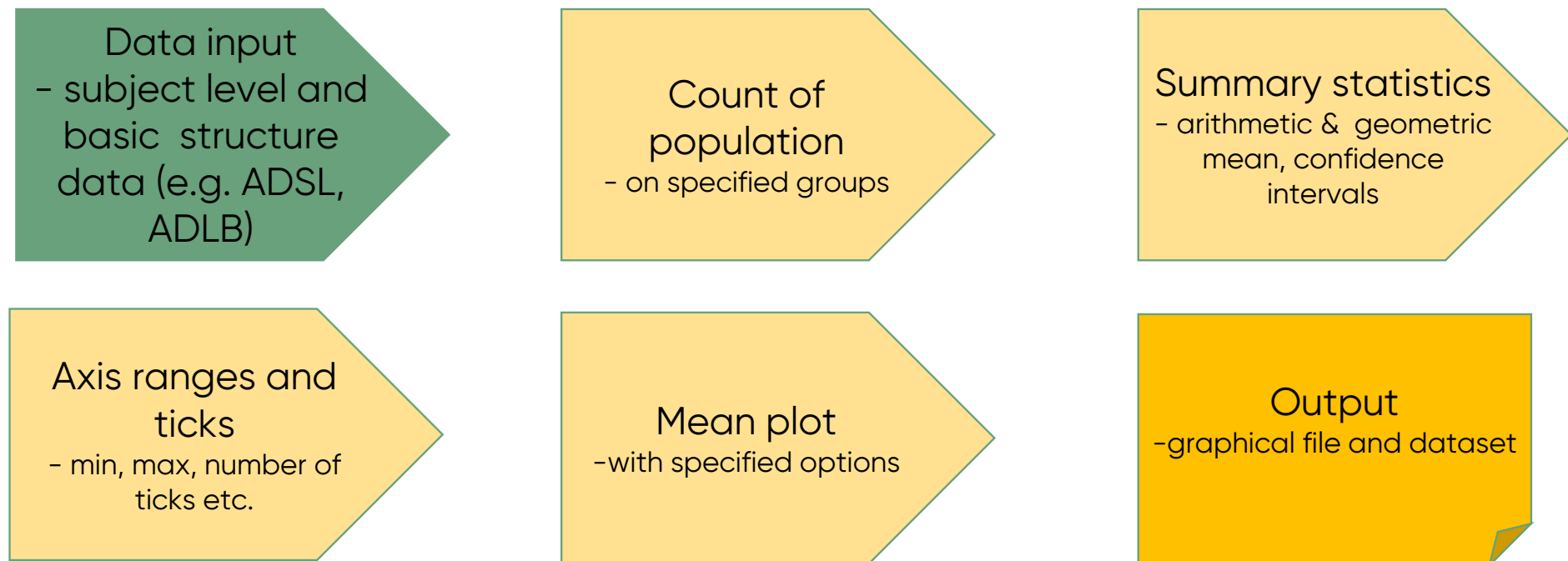


Template for summary statistics for categorical and continuous variables - <Analysis population set>



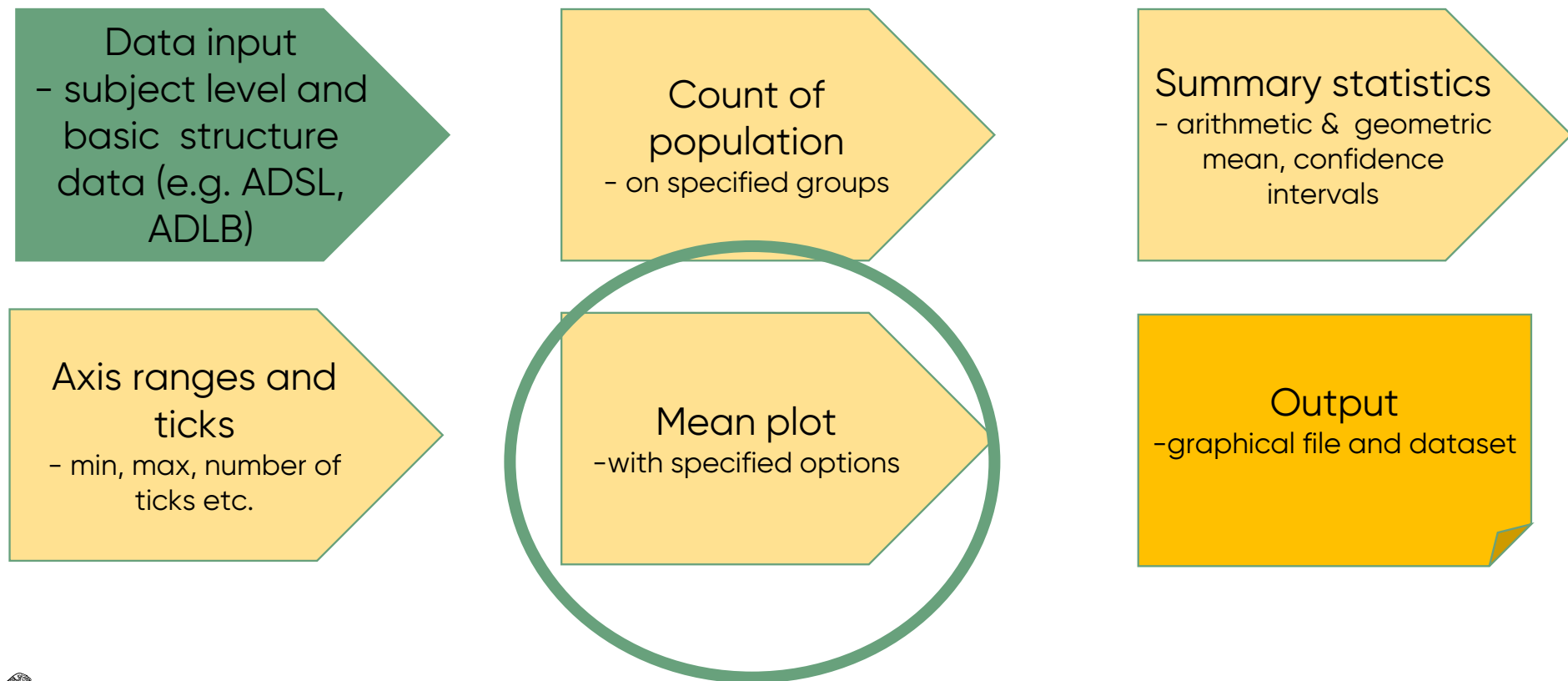
Driver for the mean plot macro

- the structure



Driver for the mean plot macro

- the structure

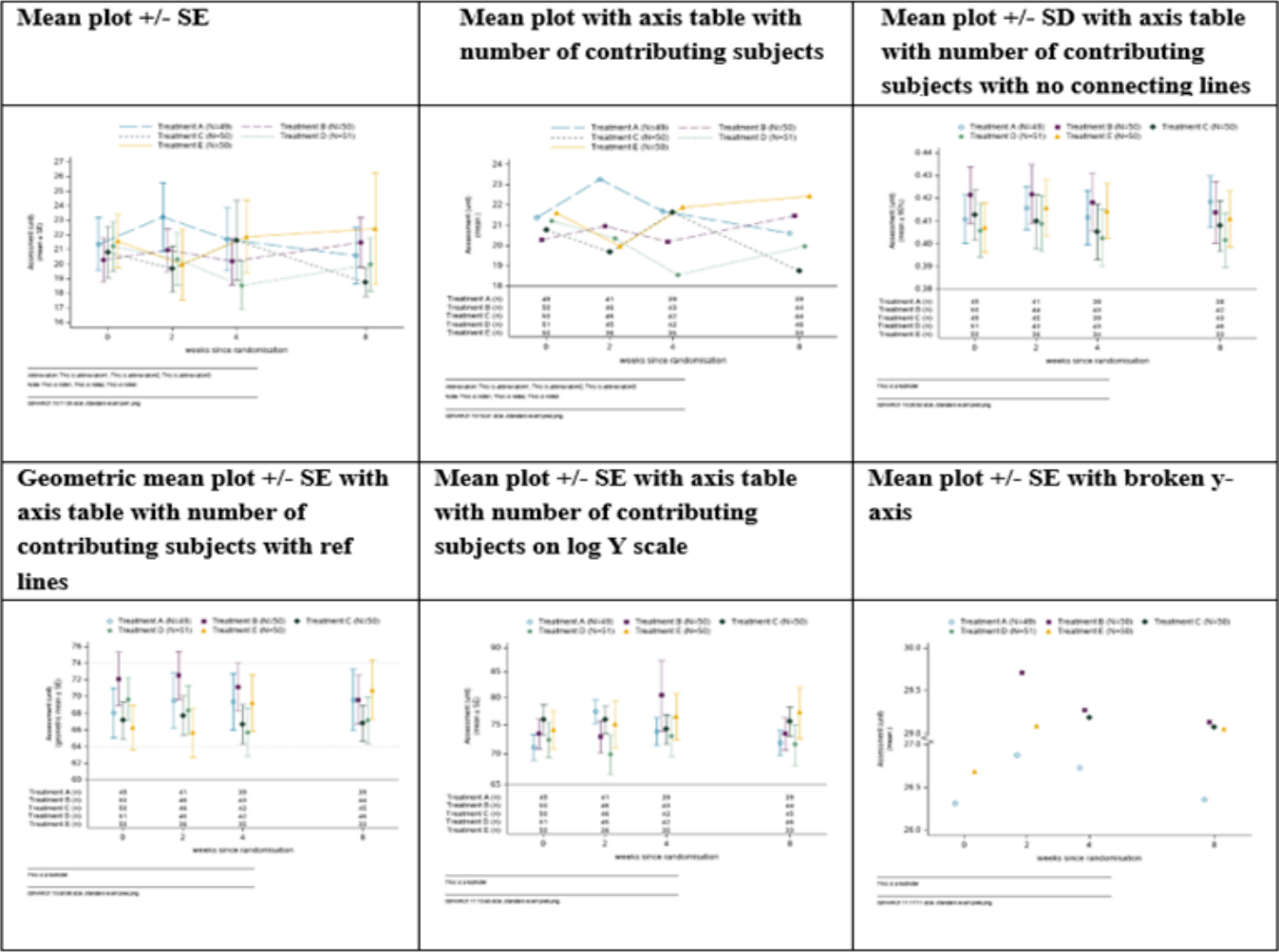


Full code and examples available at Github

- https://github.com/clausstenberg/phuse_2021_DV02

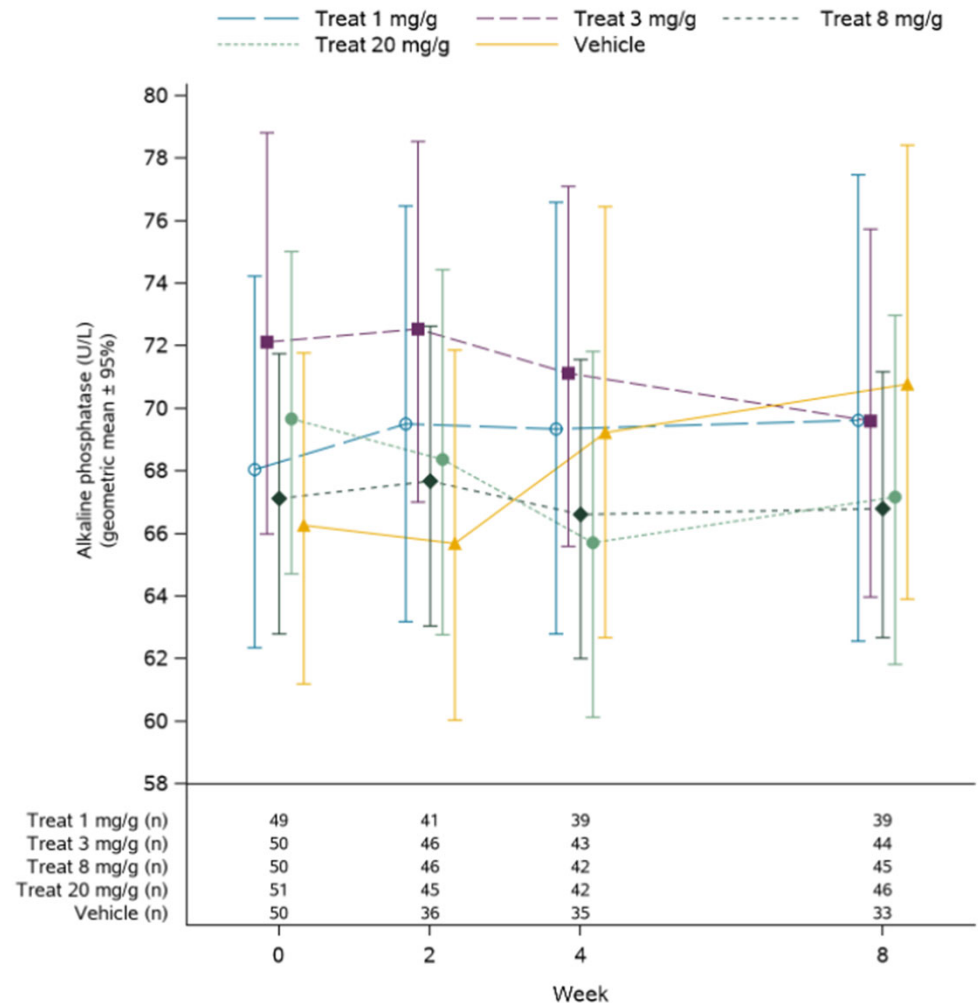


Mean plot



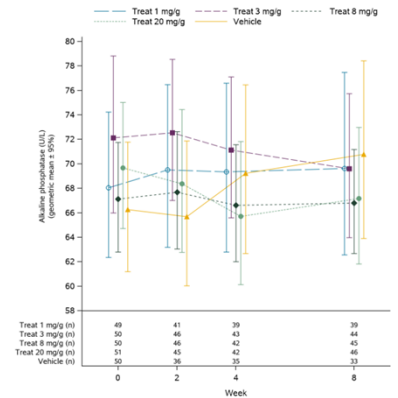
Mean plot

- 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	72.420261	78.8142618	65.0047244	50	50	Treat 2 mg/g	2	0	ALP	Alkaline phosphatase (U/L)		0-2



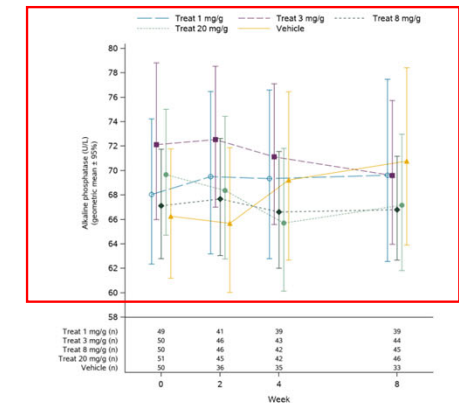
Mean plot

- proc SGPLOT
- Code for the plot

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

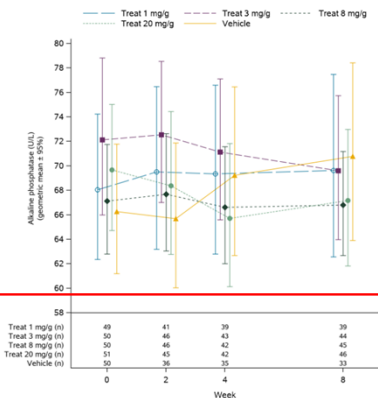
/* plot only with symbols */
%if %upcase(&only_symbols_meanplot.) = Y %then %do;
    scatter x=&x_var_meanplot y=&y_meanVar_meanplot. / group = _group_name groupdisplay=cluster clusterwidth=&clusterwidth. attrid=&attrid_meanplot. name="symbol"
/* adding confidence intervals if wanted*/
    %if %length(&up_civar_meanplot.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



Mean plot

- proc SGPLOT
- Code for the x-axis table



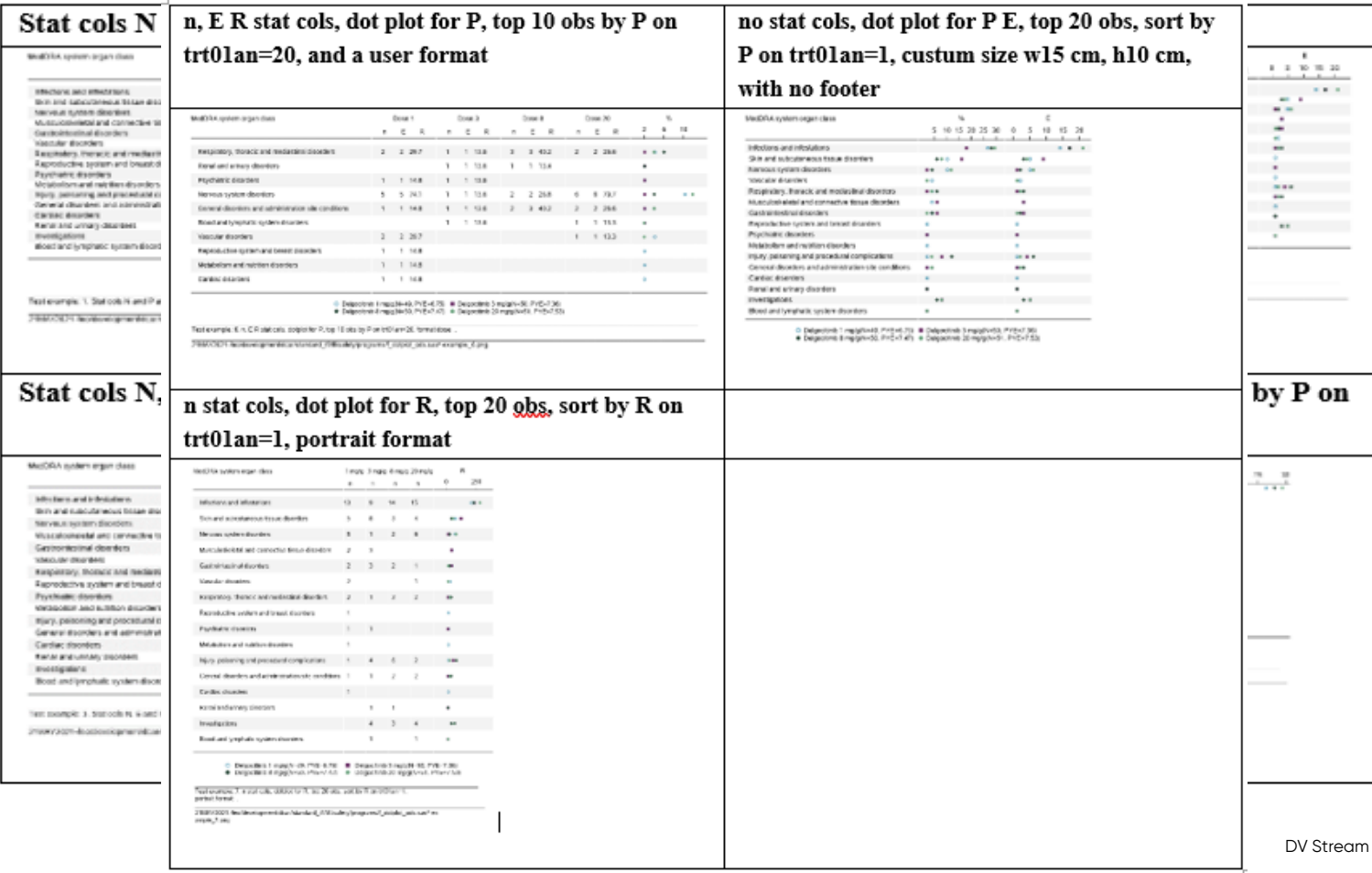
```

/* 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;

```

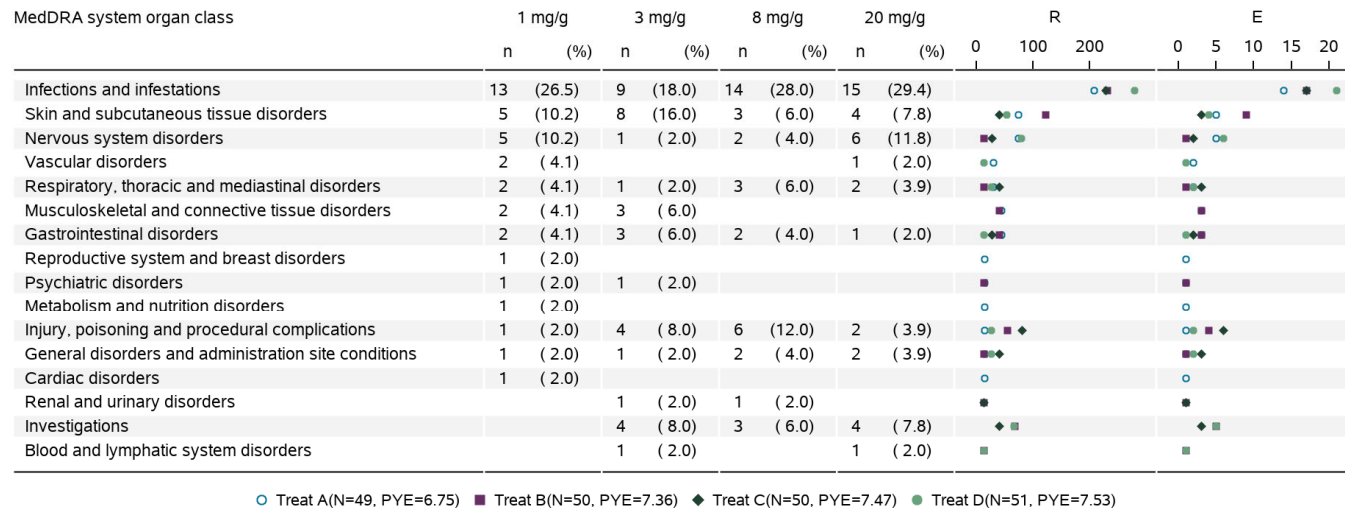


Most frequent adverse events plot



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.



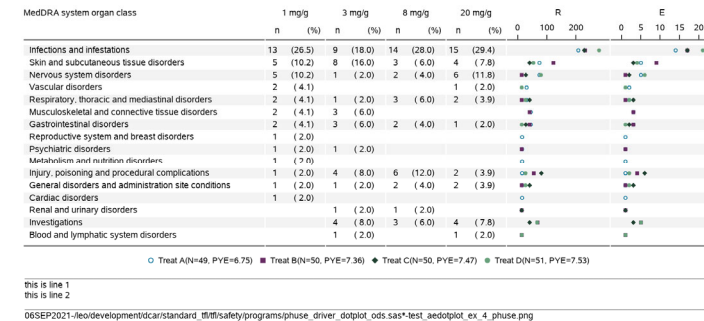
this is line 1
this is line 2

06SEP2021-/leo/development/dcar/standard_tf/tfl/safety/programs/phuse_driver_dotplot ods.sas*-test_aedotplot_ex_4_phuse.png

- 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



Most frequent adverse events plot

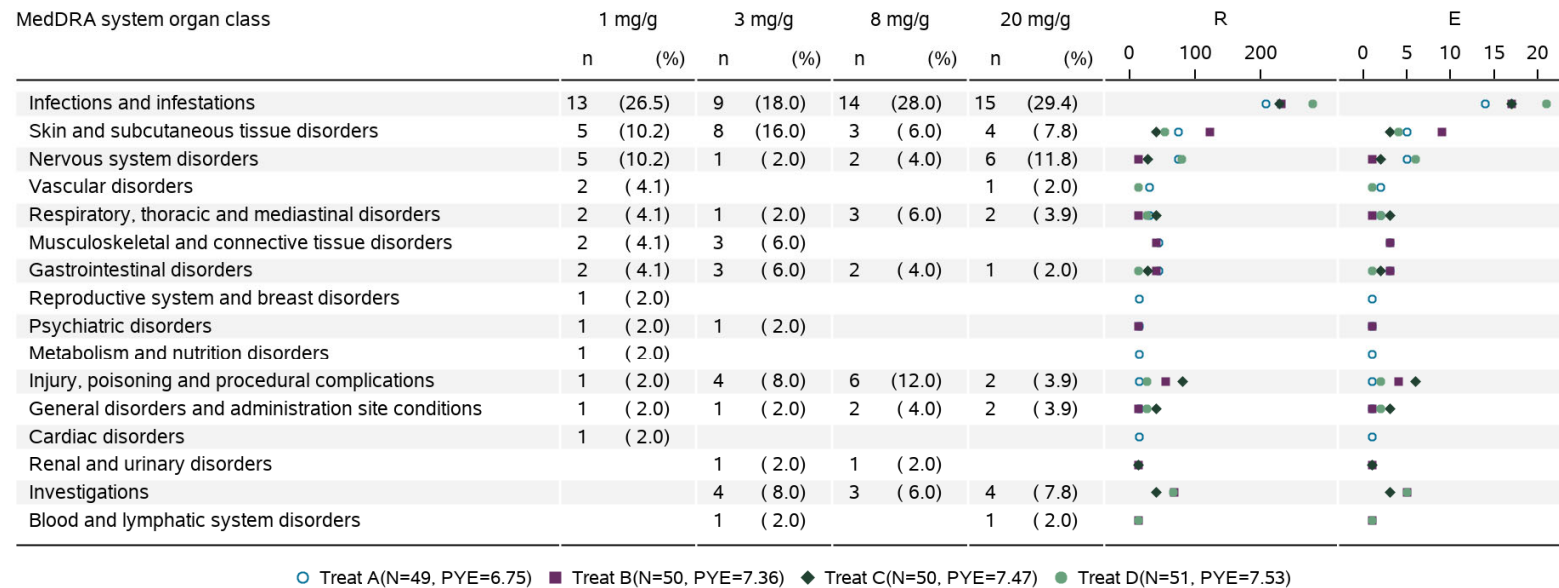


group	POPCOUNT	PY	AEBODSYS	VALN	VALE _r	LABEL	GROUPLABEL	VALP	VALR	shorttreat
3	50	7.3620807666	Respiratory, thoracic and mediastinal disor...	1	1	Treat B	Treat B (N=50, PYE=7.36)	2	13.58	3 mg/g
3	50	7.3620807666	Renal and urinary disorders	1	1	Treat B	Treat B (N=50, PYE=7.36)	2	13.58	3 mg/g
1	49	6.7460643395	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)



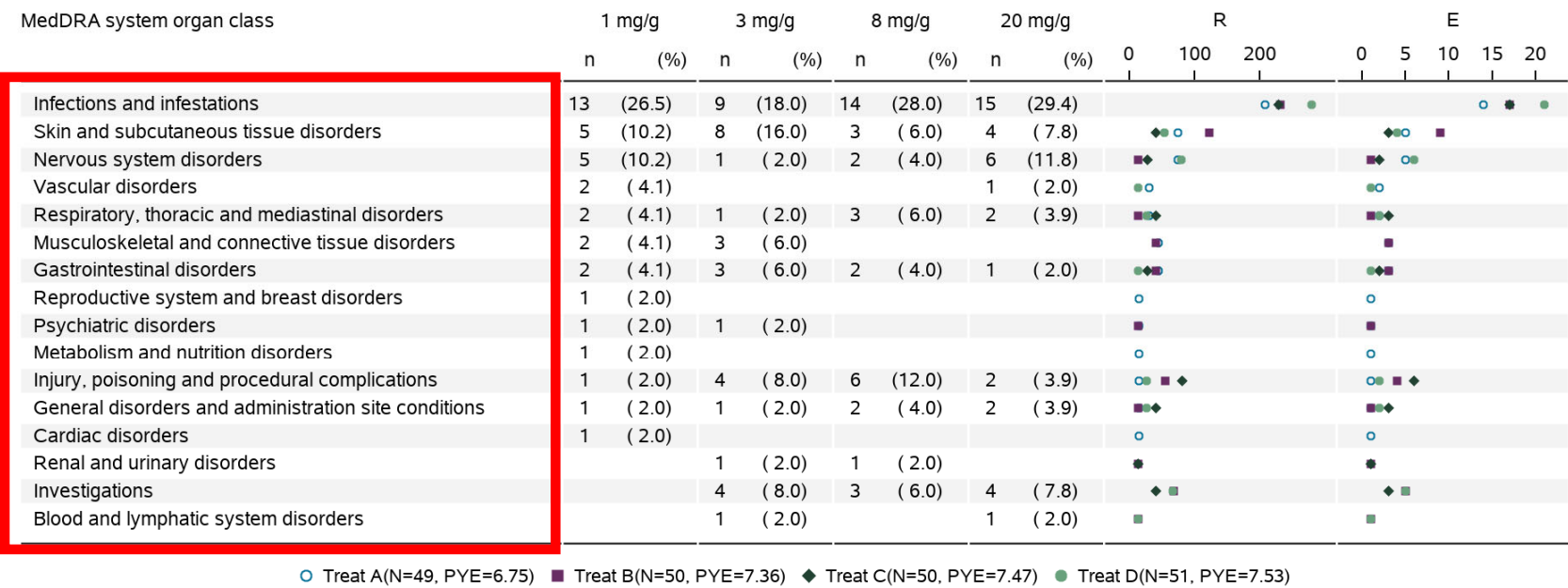
this is line 1
this is line 2

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)



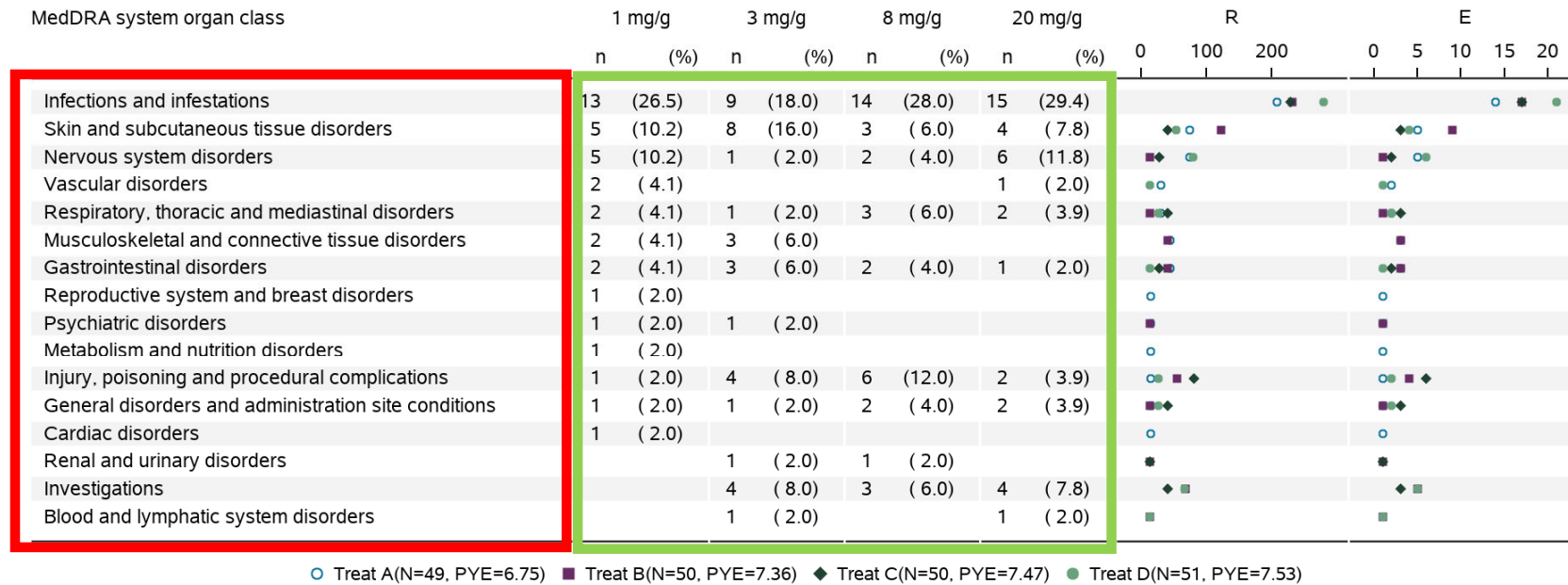
this is line 1
this is line 2

06SEP2021-/leo/development/dcar/standard_tfl/tfl/safety/programs/phuse_driver_dotplot ods.sas*-test_aedotplot_ex_4_phuse.png



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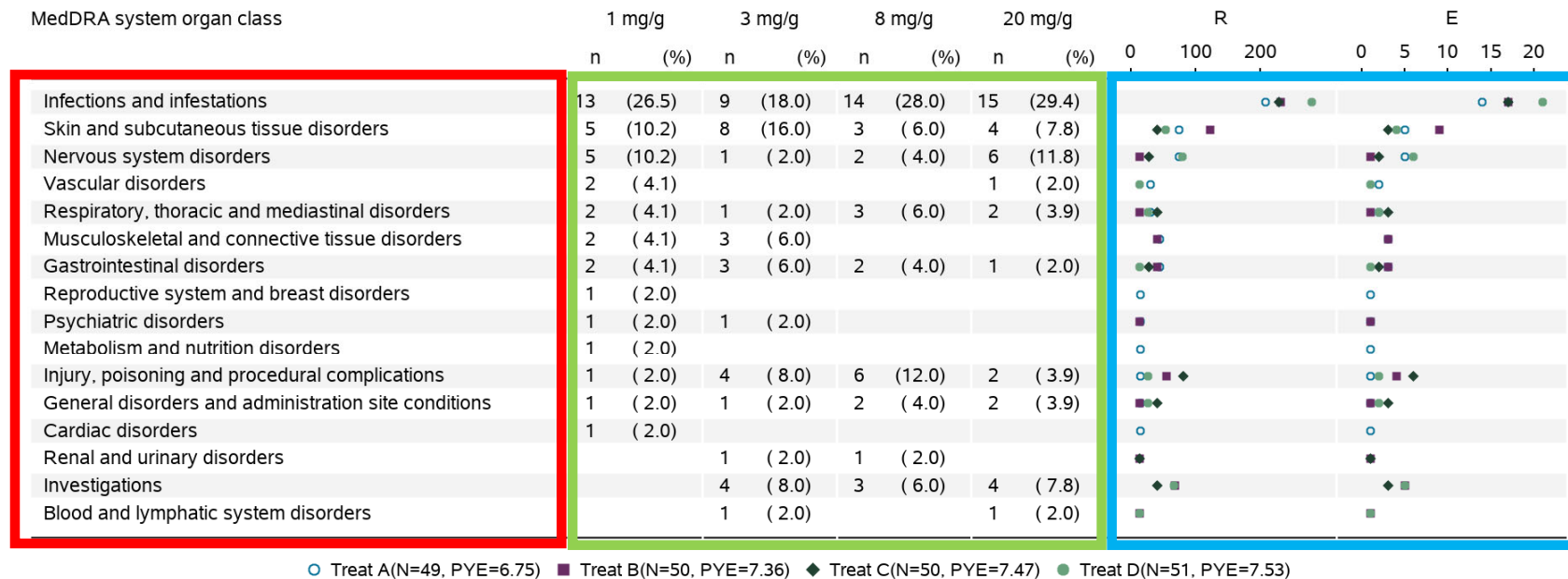
this is line 1
this is line 2

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)



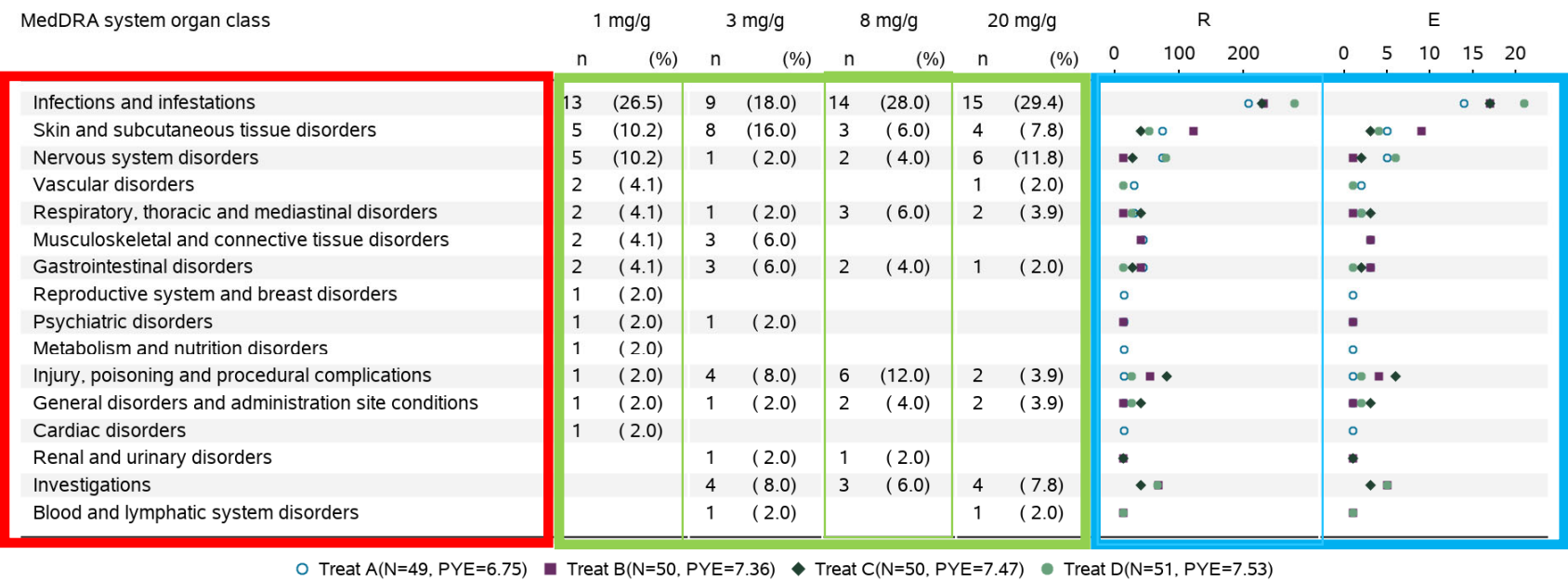
this is line 1
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06SEP2021-/leo/development/dcar/standard_tfl/tfl/safety/programs/phuse_driver_dotplot ods.sas*-test_aedotplot_ex_4_phuse.png



Most frequent adverse events plot

- proc TEMPLATE and SGRENDER (GTL)



this is line 1
this is line 2

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

Code for overall col N
and first col

```
proc template;
  define statgraph aedotplot;

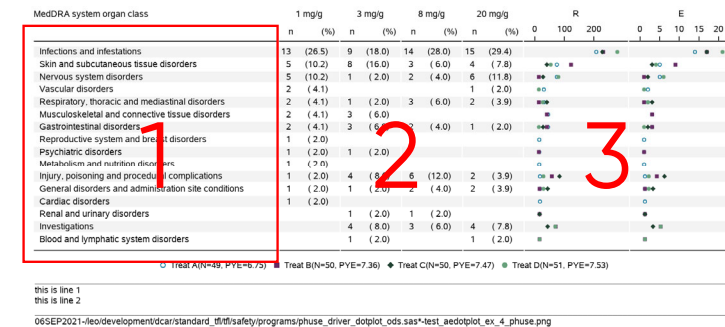
    begingraph ;

      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 = (tickvaluessequence=(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;
endtemplate;
```



Most frequent adverse events plot

proc TEMPLATE

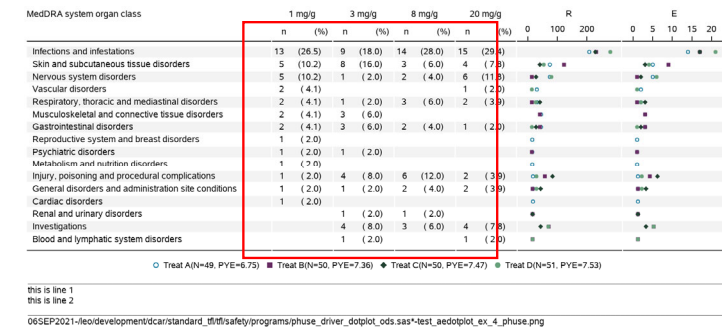
Code for col with stats

```
/* 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 reference line--*/
    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=(tickvaluessequence=(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;
    %end;
%end;

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

MedDRA system organ class	1 mg/g		3 mg/g		8 mg/g		20 mg/g		R				E			
	n	(%)	n	(%)	n	(%)	n	(%)	U	100	200	U	5	10	15	20
Infections and infestations	13	(26.5)	9	(18.0)	14	(28.0)	15	(29.4)	●	●	●	●	●	●	●	●
Skin and subcutaneous tissue disorders	5	(10.2)	8	(16.0)	3	(6.0)	4	(7.8)	●	●	●	●	●	●	●	●
Nervous system disorders	5	(10.2)	1	(2.0)	2	(4.0)	6	(11.8)	●	●	●	●	●	●	●	●
Vascular disorders	2	(4.1)					1	(2.0)	●	●	●	●	●	●	●	●
Respiratory, thoracic and mediastinal disorders	2	(4.1)	1	(2.0)	3	(6.0)	2	(3.9)	●	●	●	●	●	●	●	●
Musculoskeletal and connective tissue disorders	2	(4.1)	3	(6.0)					●	●	●	●	●	●	●	●
Gastrointestinal disorders	2	(4.1)	3	(6.0)	2	(4.0)	1	(2.0)	●	●	●	●	●	●	●	●
Reproductive system and breast disorders	1	(2.0)							●	●	●	●	●	●	●	●
Psychiatric disorders	1	(2.0)	1	(2.0)					●	●	●	●	●	●	●	●
Metabolism and nutrition disorders	1	(2.0)							●	●	●	●	●	●	●	●
Injury, poisoning and procedural complications	1	(2.0)	4	(8.0)	6	(12.0)	2	(3.9)	●	●	●	●	●	●	●	●
General disorders and administration site conditions	1	(2.0)	1	(2.0)	2	(4.0)	2	(3.9)	●	●	●	●	●	●	●	●
Cardiac disorders	1	(2.0)							●	●	●	●	●	●	●	●
Renal and urinary disorders			1	(2.0)	1	(2.0)			●	●	●	●	●	●	●	●
Investigations			4	(8.0)	3	(6.0)	4	(7.8)	●	●	●	●	●	●	●	●
Blood and lymphatic system disorders			1	(2.0)			1	(2.0)	●	●	●	●	●	●	●	●

● Treat A/N=49, PYE=6.75

● Treat B/N=50, PYE=7.36

● Treat C/N=50, PYE=7.47

● Treat D/N=51, PYE=7.53

● Treat A(N=48, PYE=6.75) ■ Treat B(N=50, PYE=7.36) ◆ Treat C(N=50, PYE=7.47) ● Treat D(N=51, PYE=7.53)

this is line 1

this is line 2

06SEP2021-leo\development\car\standard_06\trf\safety\programs\phuse_driver_dotplot ods.sas*test_aedotplot_ex_4_phuse.png



Pros and cons of the modular approach to output programming.



Thank you

