

A Modular Approach of Reporting Meta Analysis Statistics Using Forest Plots

Vikash Jain, eClinical Solutions, A Division of Eliassen Group, New London, CT

ABSTRACT

Forest plots are the favorites for reporting frequently with the popularity of Meta Analysis Statistics associated with systematic review in the clinical research. They are used to report array of statistics like estimates of treatment effects between multiple studies or ratios between subgroups for multiple studies in consideration or also occasionally by other comparative features based on the objective of hypothesis analysis under consideration. Our paper will concentrate on the various array of techniques and methodologies to be incorporated from a statistical programmers point of view to get these bit and pieces of valuable information in an modular presentation fashion which will be composite of both Text and Graphical displays or one of them, based on specification requirements set by the clinical team for regulatory submissions or abstract publications incorporating a very powerful PROC TEMPLATE introduced in SAS® 9.2 with versatility of options at users disposal using lattice layout presentation and SAS Annotate Facility from Graph Template Language (GTL) in SAS 9.2 to create sophisticated analytical displays.

INTRODUCTION

Meta-Analysis refers to the statistical analyses that are used to synthesize summary data from a series of studies. If the effect size (or treatment effect) is consistent across all the studies in the synthesis, then the meta-analysis yields a combined effect that is more precise than any of the separate estimates, and also allows us to conclude that the effect is robust across the kinds of studies sampled. One of the methods to graphically visualize this information is by using forest plots in modern statistical analysis methods. A forest plot is an arrangement of bars which represent clinical trials or other studies roughly addressing the same research question. The ends of the bars represent the 95% confidence limits associated with the estimated effect. At the point estimate a square is drawn. Its area represents the weight given to the respective study in the elicitation of a common effect estimate as part of a Meta analysis. The common effect estimate is represented by a diamond whose width corresponds to the confidence interval of the pooled estimate.

STEPS TO BE CONSIDERED WHILE PROGRAMMING

Components required getting the above information as a graphical presentation is outlined in steps, which will be elaborated in detail for the final production of the final output:

- 1) Develop the template as per the specification requirements using PROC TEMPLATE on the layout

- 2) Compute the statistics required to be displayed on the graphs in a structured format compliment as an input for the GTL template created
- 3) Develop the style template required for any cosmetics setup for fonts and background to be displayed on your graph
- 4) Incorporate the structured reporting dataset and templates developed in the PROC SG procedure to output the final output

SAMPLE DATA USED FOR REPORTING

Descriptive information of the studies considered for reporting

	Treatment		Control	
Study Name	Event in Study	Subjects Enrolled	Event in Study	Subjects Enrolled
Study1	101	12,991	130	12,209
Study2	39	7,076	41	7,006
Study3	37	7,764	80	7,755
Study4	152	12,541	210	12,264
Study5	138	3,786	167	3,411

Meta Analysis Results Computed from Statistical Procedure which computed the below Odds ratios and confidence intervals for the five studies under consideration for reporting

Study	Odds ratio	95% confidence interval
Study1	0.73	0.56, 0.95
Study2	0.94	0.61, 1.46
Study3	0.46	0.31, 0.68
Study4	0.70	0.57, 0.87
Study5	0.73	0.58, 0.93

GTL TEMPLATE CODE WALKTHROUGH

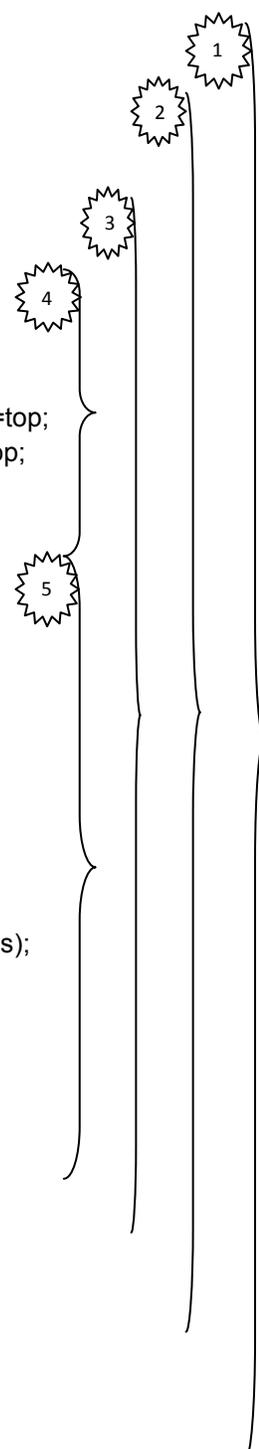
We will use the approach with SAS PROC TEMPLATE and utilize Graph Template Language in order to create foundation for the graphs to be created. One has to be aware of the fact that Graph Template Language and syntax used within SAS SG procedures are not identical. SAS PROC TEMPLATE is used jointly with PROC SGRENDER, which will invoke the graphic template created.

```

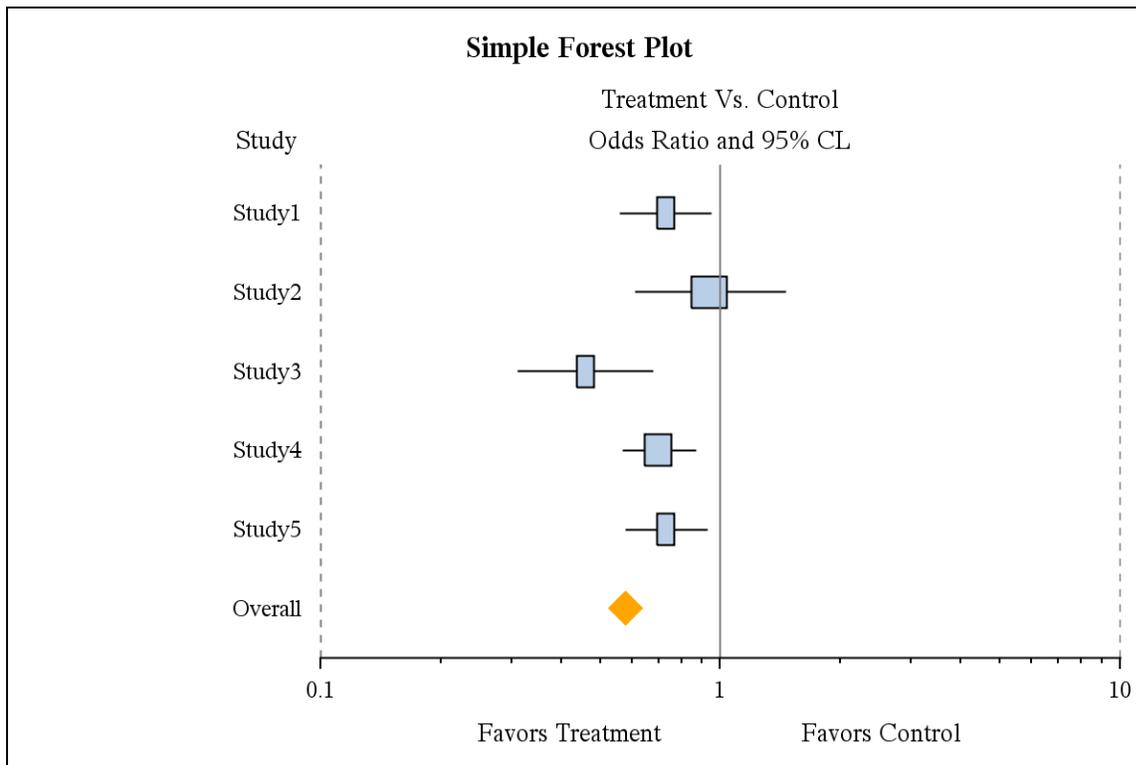
proc template;
/*****/
define statgraph ForestPlot;
/*****/
begingraph / designwidth=600px designheight=400px;
entrytitle "Simple Forest Plot" / pad=(bottom=5px);
/*****/
  layout lattice / columns=2 columngutter=0 columnweights=(.25 .75);
/*****/
  layout overlay / walldisplay=none border=false
    y2axisopts=(reverse=true type=discrete display=(tickvalues))
    xaxisopts=(display=none offsetmin=0 offsetmax=0);
  entry halign=Right "Study" / textattrs=GraphLabelText location=outside valign=top;
  entry halign=Right " " / textattrs=GraphLabelText location=outside valign=top;
  scatterplot y=Study2 x=constant / yaxis=y2 markerattrs=(size=0);
endlayout; /* End Overlay Layout */
/*****/
  layout overlay / walldisplay=(fill) yaxisopts=( display=none reverse=true
    offsetmin=.1 offsetmax=.1 linearopts=(integer=true))
    xaxisopts=(type=log offsetmin=0 offsetmax=0
    label="Favors Treatment Favors Control"
    logopts=(base=10 tickintervalstyle=logexpand
    minorticks=true viewmin=.1 viewmax=10 ));
  entry "Odds Ratio and 95% CL" / location=outside
    valign=top textattrs=GraphLabelText;
  entry "Treatment Vs. Control" / location=outside
    valign=top textattrs=GraphLabelText;
  boxplotparm x=Study y=value stat=stat / orient=horizontal display=(fill notches);
  scatterplot x=OverallValue y=overall / markerattrs=(color=orange
    symbol=diamondfilled size=4pct);
  referenceline x=1 / lineattrs=(pattern=solid);
  referenceline x=.1 / lineattrs=(pattern=shortdash);
  referenceline x=10 / lineattrs=(pattern=shortdash);
endlayout; /* End Overlay Layout */
/*****/
endlayout; /* End Lattice Layout */
/*****/
endgraph; /* End Graph */
/*****/
end; /* End Statgraph Template */
/*****/
run;

proc sgrender data=forest template=ForestPlot;
run;

```



Scenario 1: Forest Plot in its simple form



For this output above we have adopted the code outlined in the above walk through section as is.

Module 1: Define the graph within the template which is name as "ForestPlot"

Module 2: Define the physical attributes of your Forest Plot template in means of its width, height and its template title

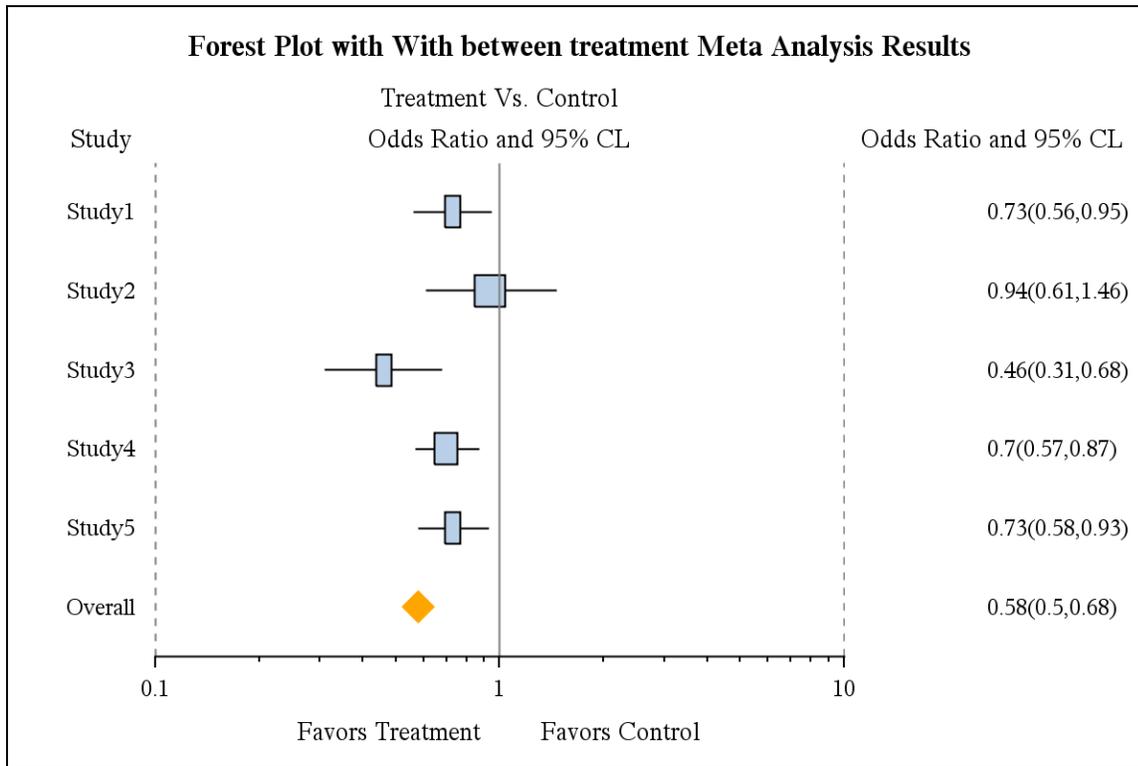
Module 3: Define the Lattice layout which will incorporate the 2 compartments for each of sections to be incorporated by respective overlay statement by column statement and its respective attributes of weight for its physical display

Module 4a: Define the first overlay statement to outline each of the studies under consideration for which the Meta analysis results will be displayed against it

Module 4b: Define second overlay statement which will display the horizontal display of box plots as Forest Plot for each of the studies and its respective overall pooled estimate between treatment and control arms

Module 5: Define the input dataset name which is "forest" and the template on which the data will be displayed on "ForestPlot"

Scenario 2: Forest Plot outlined with between treatments Meta Analysis Results



For this output below following the modules adopted to display between treatments Meta analysis results

Module 1: Define the graph within the template which is name as “ForestPlot”

Module 2: Define the physical attributes of your Forest Plot template in means of its width, height and its template title

Module 3: Define the Lattice layout which will incorporate the 3 compartments for each of sections to be incorporated by respective overlay statement by column statement and its respective weight attributes for its display

```

/*****/
  layout lattice / columns=3  columngutter=0  columnweights=(.10 .65 .25);
/*****/

```

Module 4a: Define the first overlay statement to outline each of the studies under consideration for which the Meta analysis results will be displayed against it

Module 4b: Define second overlay statement which will display the horizontal display of box plots as Forest Plot for each of the studies and its respective overall pooled estimate between treatment and control arms

Module 4c: Define the third overlay statement to outline each of the studies within Meta analysis results of odd ratio and its respective 95% confidence interval

```

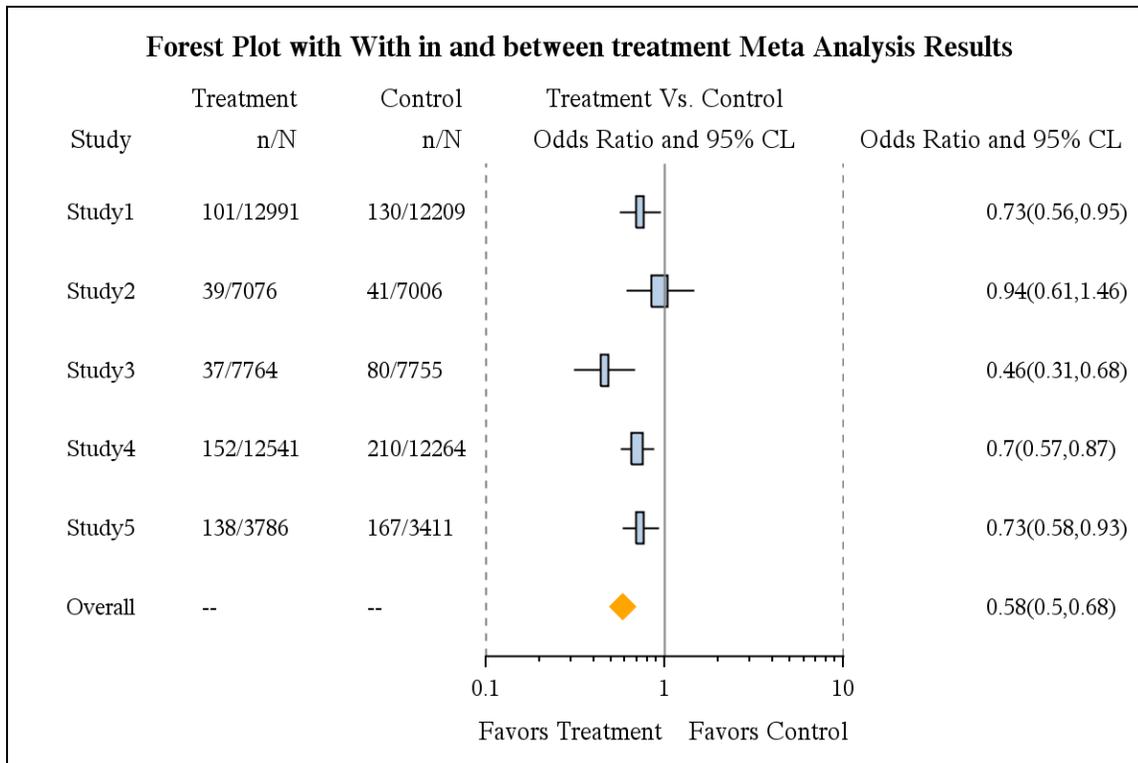
/*****/
layout overlay / walldisplay=none border=false
    y2axisopts=(reverse=true type=discrete display=(tickvalues))
    xaxisopts=(display=none offsetmin=0 offsetmax=0);
    entry halign=center "Odds Ratio and 95% CL" / textattrs=GraphLabelText location=outside
    valign=top;
    entry halign=center " " / textattrs=GraphLabelText location=outside valign=top;
    scatterplot y=mta_cmb x=constant / yaxis=y2 markerattrs=(size=0);
endlayout; /* End Overlay Layout */

endlayout; /* End Lattice Layout */
/*****/

```

Module 5: Define the input dataset name which is “forest” and the template on which the data will be displayed on “ForestPlot”

Scenario 3: Forest Plot outlined with within and between treatments Meta Analysis Results



For this output below following the modules adopted to display within and between treatments
Meta analysis results

Module 1: Define the graph within the template which is name as "ForestPlot"

Module 2: Define the physical attributes of your Forest Plot template in means of its width,
height and its template title

Module 3: Define the Lattice layout which will incorporate the 5 compartments for each of
sections to be incorporated by respective overlay statement by column statement and its
respective weight attributes for its display

```
/******  
layout lattice / columns=5 columngutter=0 columnweights=(.10 .15 .15 .35 .25);  
/******
```

Module 4a: Define the first overlay statement to outline each of the studies under consideration
for which the Meta analysis results will be displayed against it

Module 4b: Define second overlay statement which will display the descriptive counts of each of
the studies for treatment arm

```
/******  
layout overlay / walldisplay=none border=false  
    y2axisopts=(reverse=true type=discrete display=(tickvalues))  
    xaxisopts=(display=none offsetmin=0 offsetmax=0);  
    entry halign=right "n/N" / textattrs=GraphLabelText location=outside valign=top;  
    entry halign=right "Treatment" / textattrs=GraphLabelText location=outside valign=top;  
    scatterplot y=trt_cmb x=constant / yaxis=y2 markerattrs=(size=0);  
endlayout; /* End Overlay Layout */  
/******
```

Module 4c: Define third overlay statement which will display the descriptive counts of each of
the studies for control arm

```
/******  
layout overlay / walldisplay=none border=false  
    y2axisopts=(reverse=true type=discrete display=(tickvalues))  
    xaxisopts=(display=none offsetmin=0 offsetmax=0);  
    entry halign=right "n/N" / textattrs=GraphLabelText location=outside valign=top;  
    entry halign=right "Control" / textattrs=GraphLabelText location=outside valign=top;  
    scatterplot y=con_cmb x=constant / yaxis=y2 markerattrs=(size=0);  
endlayout; /* End Overlay Layout */  
/******
```

Module 4d: Define fourth overlay statement which will display the horizontal display of box plots
as Forest Plot for each of the studies and its respective overall pooled estimate between
treatment and control arms

Module 4e: Define the fifth overlay statement to outline each of the studies within Meta analysis results of odd ratio and its respective 95% confidence interval

Module 5: Define the input dataset name which is “forest” and the template on which the data will be displayed on “ForestPlot”

CONCLUSION

With the various scenarios demonstrated during the course of this paper the user can incorporate the array of layouts within the template procedure using the lattice layout and outline its respective textual and graphical display with the layouts using various overlay statements, Graph Template Language allows users to create customized graphics, or flexible templates for anyone to use. In our examples we demonstrate both approaches in order to create forest plots. This paper has outlined a relatively simple and flexible alternative to produce forest plots displaying the meta-analysis as an example, which can be easily adopted to various other analytical displays. Finally the SAS SG procedure have the capability of producing high quality graphics with relatively little code, compared to exhaustive programming and annotation procedures adopted in past.

REFERENCES

SAS/GRAPH 9.2: Graph Template Language User's Guide, Second Edition

<http://support.sas.com/kb/35/143.html>

ACKNOWLEDGMENTS

I would like to acknowledge eClinical Solution for providing the opportunity to work on this paper.

SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc. in the USA and other countries. ® indicates USA registration.

CONTACT INFORMATION

Your comments and questions are valued and encouraged. Please contact me on,

vjain@eclinicalsol.com or jainvikash77@yahoo.com