THE POWER TO KNOW®

Graphical Reporting of Clinical Trial Data with SAS ODS Graphics

Hans-Rainer Pauli
Solution Specialist Technology
SAS Switzerland

hans-rainer.pauli@sch.sas.com

David J Garbutt
Business & Decision Life Sciences
Switzerland

David.garbutt@businessdecsion.com

Why Graphics?

- Clinical trials generate a large amount of information
- A concise visual presentation of the results is essential for important information such as:
  - the patient population
  - drug dosages
  - clinical responses
  - adverse events
  - clinical laboratory results
- Graphics are a powerful way to display clinical trial data

This presentation...

- ...will show how graphs, common in the world of clinical data, can easily be created using the new capabilities of SAS ODS Graphics with examples from
  - Study Design
  - Pharmacology
  - Epidemiology
  - Demographics
  - Efficacy
  - Safety

This presentation...

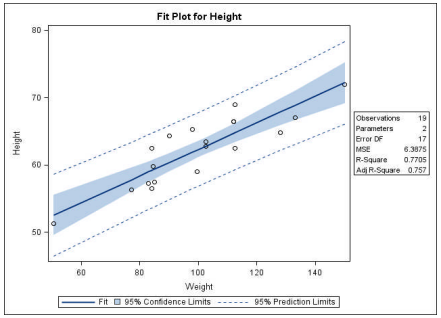
- ...will emphasize the following techniques:
  - Overlaying multiple plots in one graph
  - Construction a panel using classification variables
  - Presentation of a matrix of liver function tests for at-risk patients
  - Construction of a Forest-Plot for a Meta-Analysis using the graph template language (GTL)

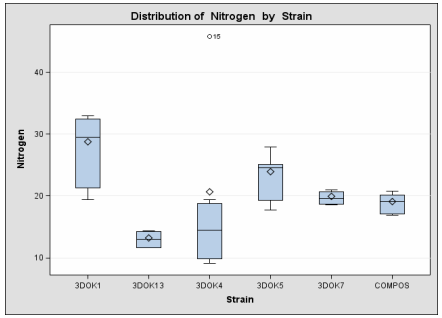
ODS Graphics

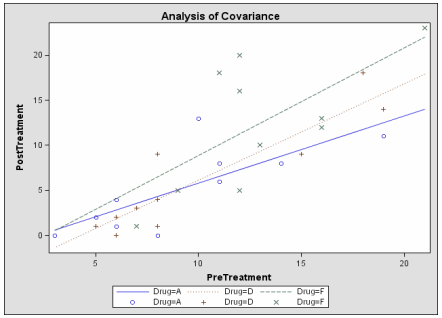
- ODS Statistical Graphics
- New ODS procedures (aka “SG” procedures)
- Graphics Template Language (GTL)
- ODS Graphics Editor
- ODS Graphics Designer (pre-production)

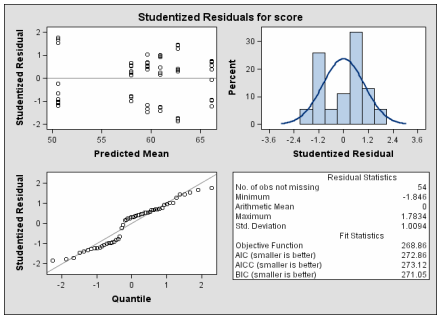
ODS Statistical Graphics

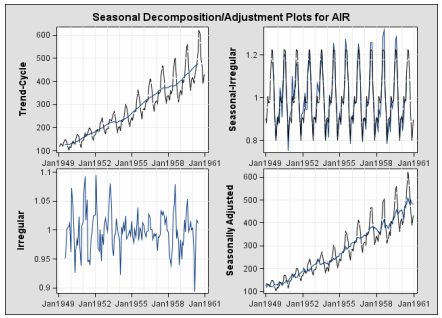
Single- and Multi-Cell Graphs



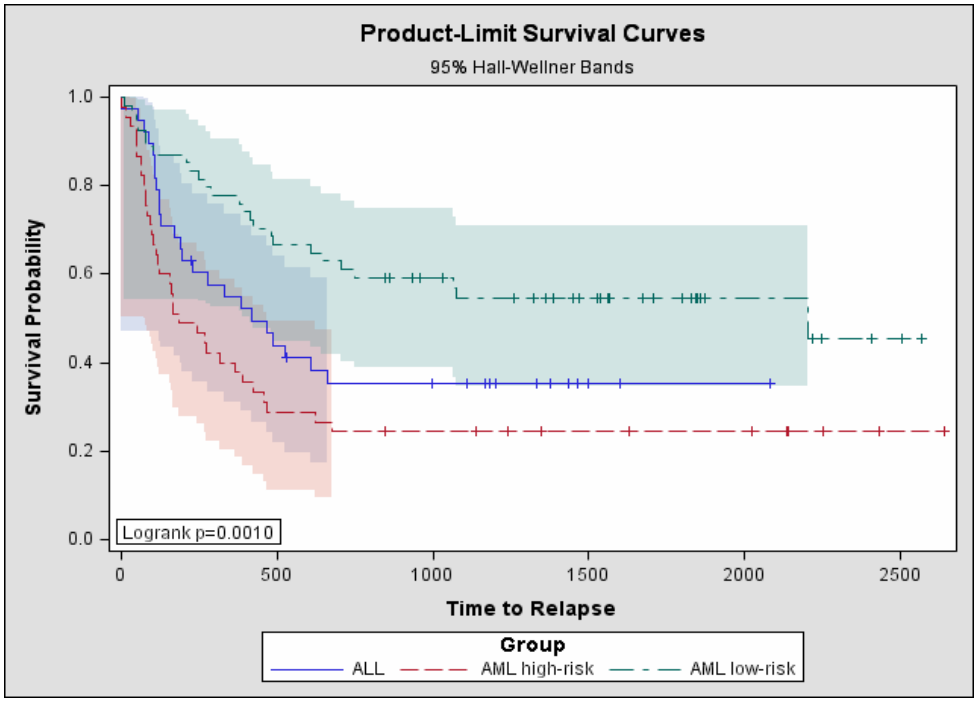








ODS Statistical Graphics



Survival Plot with LIFETEST

New ODS Procedures

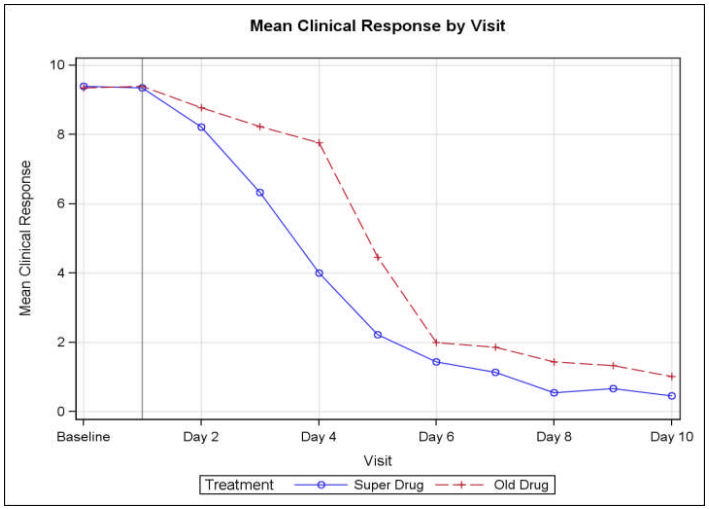
- SAS/GRAPH like syntax for analytical graphs
- Audience: SAS/GRAPH programmer using concise syntax to create commonly used analytical graphs
- New ODS procedures
  - PROC SGPLOT
  - PROC SGPANEL
  - PROC SGSCATTER
  - PROC SGRENDER

Single-Cell Graphs

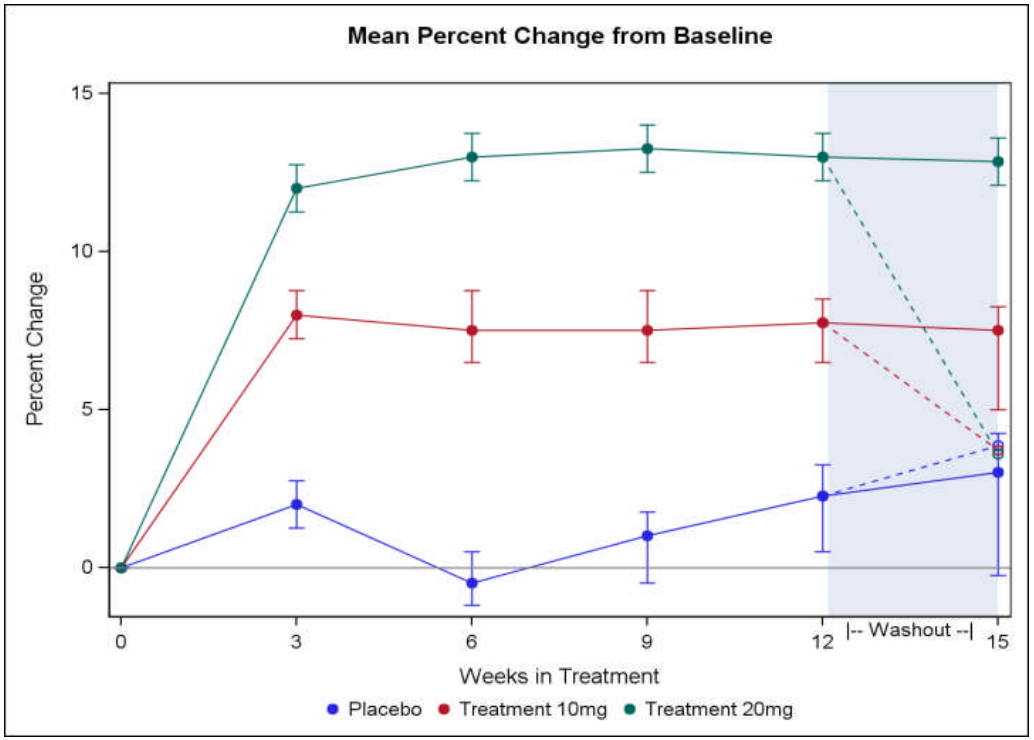
- Examples
  - Clinical Response by Visit
  - Clinical Response by Visit with Washout Period
    - Demonstration of Layering
  - Plasma Concentration Profile
  - Determination of Sample Size Requirements

Clinical Response By Visit

```
proc sgplot data=response;
format visit visitfmt. trt trtfmt.;
series x=visit y=response /
   group=trt markers;
refline 1 / axis=x;
xaxis grid;
yaxis grid;
run;
```

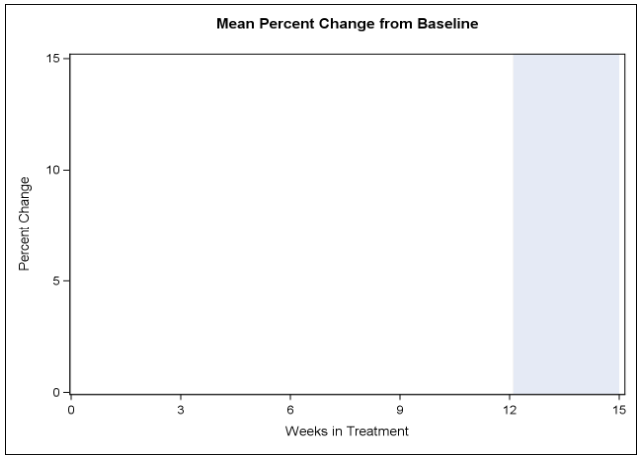


Clinical Response by Visit with Washout Period



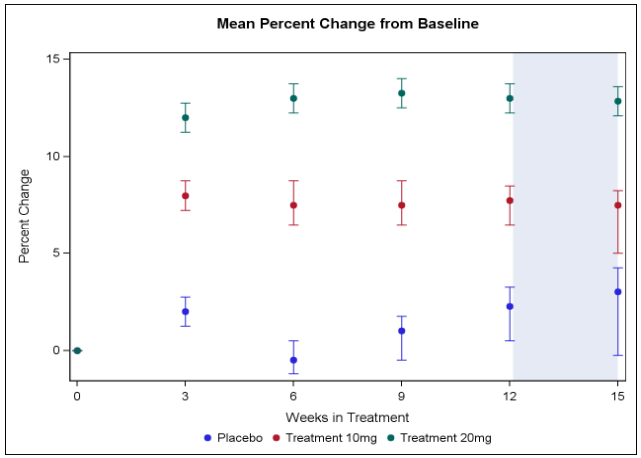
Clinical Response by Visit with Washout Period
Building a Graph in Six Layers (1)

```
proc sgplot data=response;
band y=ymax lower=12.1 upper=15 /
transparency=.8 fillattrs=graphdata1;
xaxis integer values=(0 to 15 by 3)
label="Weeks in Treatment";
yaxis label="Percent Change";
run;
```



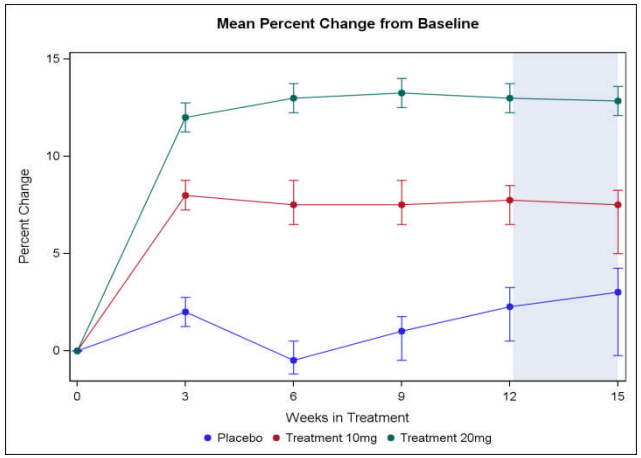
Clinical Response by Visit with Washout Period
Building a Graph in Six Layers (2)

```
proc sgplot data=response;
band y=ymax lower=12.1 upper=15 /
transparency=.8 fillattrs=graphdata1;
xaxis integer values=(0 to 15 by 3)
label="Weeks in Treatment";
yaxis label="Percent Change";
scatter x=week y=pct / group=trt
yerrorlower=lo yerrorupper=hi
markerattrs=(symbol=circlefilled)
name="scat";
keylegend "scat" / title="" noborder;
run;
```



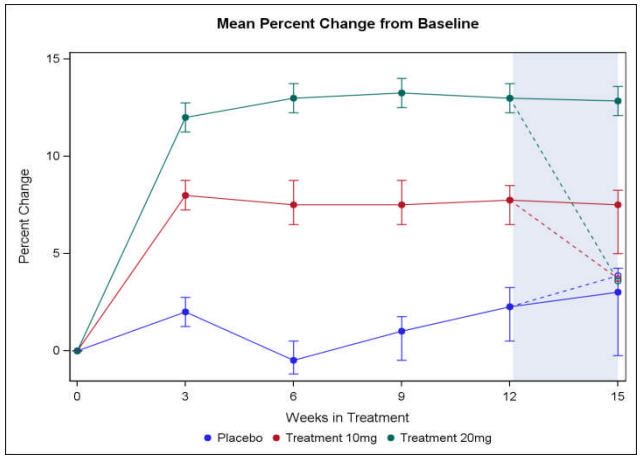
Clinical Response by Visit with Washout Period
Building a Graph in Six Layers (3)

```
proc sgplot data=response;
band y=ymax lower=12.1 upper=15 /
transparency=.8 fillattrs=graphdata1;
xaxis integer values=(0 to 15 by 3)
label="Weeks in Treatment";
yaxis label="Percent Change";
scatter x=week y=pct / group=trt
yerrorlower=lo yerrorupper=hi
markerattrs=(symbol=circlefilled)
name="scat";
keylegend "scat" / title="" noborder;
series x=week y=pct / group=trt
lineattrs=(pattern=solid);
run;
```



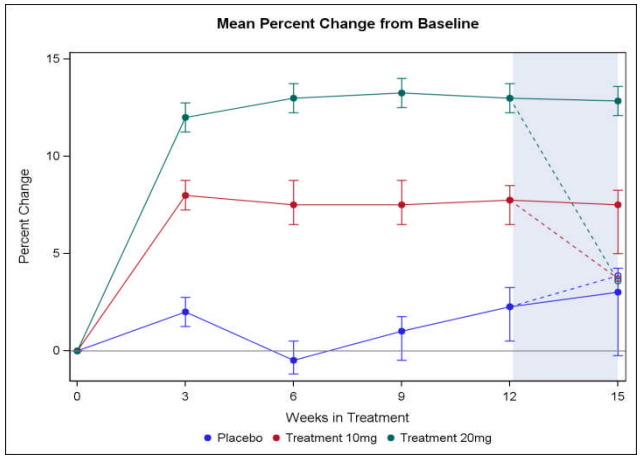
Clinical Response by Visit with Washout Period
Building a Graph in Six Layers (4)

```
proc sgplot data=response;
band y=ymax lower=12.1 upper=15 /
transparency=.8 fillattrs=graphdata1;
xaxis integer values=(0 to 15 by 3)
label="Weeks in Treatment";
yaxis label="Percent Change";
scatter x=week y=pct / group=trt
yerrorlower=lo yerrorupper=hi
markerattrs=(symbol=circlefilled)
name="scat";
keylegend "scat" / title="" noborder;
series x=week y=pct / group=trt
lineattrs=(pattern=solid);
                    /* placebo in washout */
series x=week y=end / group=trt
lineattrs=(pattern=shortdash) markers markerattrs=(symbol=circle);
run;
```



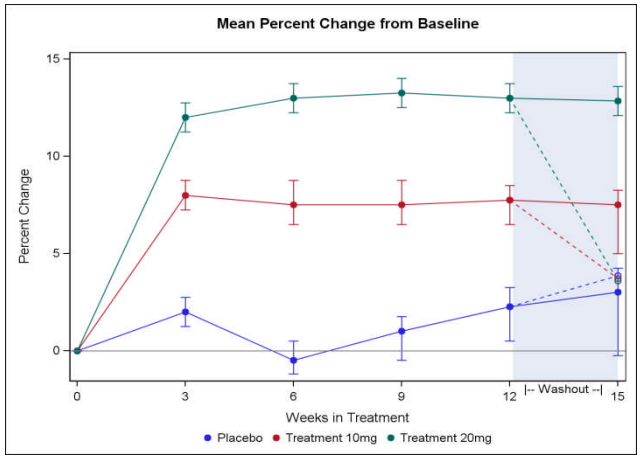
Clinical Response by Visit with Washout Period
Building a Graph in Six Layers (5)

```
proc sgplot data=response;
band y=ymax lower=12.1 upper=15 /
transparency=.8 fillattrs=graphdata1;
xaxis integer values=(0 to 15 by 3)
label="Weeks in Treatment";
yaxis label="Percent Change";
scatter x=week y=pct / group=trt
yerrorlower=lo yerrorupper=hi
markerattrs=(symbol=circlefilled)
name="scat";
keylegend "scat" / title="" noborder;
series x=week y=pct / group=trt
lineattrs=(pattern=solid);
                    /* placebo in washout */
series x=week y=end / group=trt
lineattrs=(pattern=shortdash)
markers markerattrs=(symbol=circle);
refline 0;
run;
```

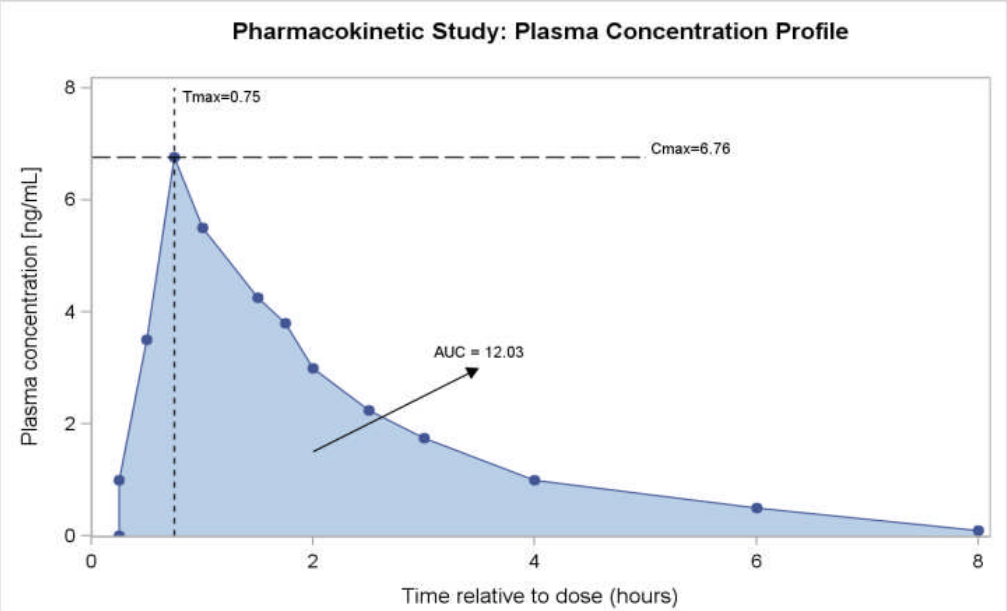


Clinical Response by Visit with Washout Period
Building a Graph in Six Layers (6)

```
proc sgplot data=response;
band y=ymax lower=12.1 upper=15 /
transparency=.8 fillattrs=graphdata1;
xaxis integer values=(0 to 15 by 3)
label="Weeks in Treatment";
yaxis label="Percent Change";
scatter x=week y=pct / group=trt
yerrorlower=lo yerrorupper=hi
markerattrs=(symbol=circlefilled)
name="scat";
keylegend "scat" / title="" noborder;
series x=week y=pct / group=trt
lineattrs=(pattern=solid);
                    /* placebo in washout */
series x=week y=end / group=trt
lineattrs=(pattern=shortdash)
markers markerattrs=(symbol=circle);
refline 0;
refline 13.5 / axis=x lineattrs=(thickness=0px)
label="|-- Washout --|" labelloc=outside labelpos=min;
run;
```

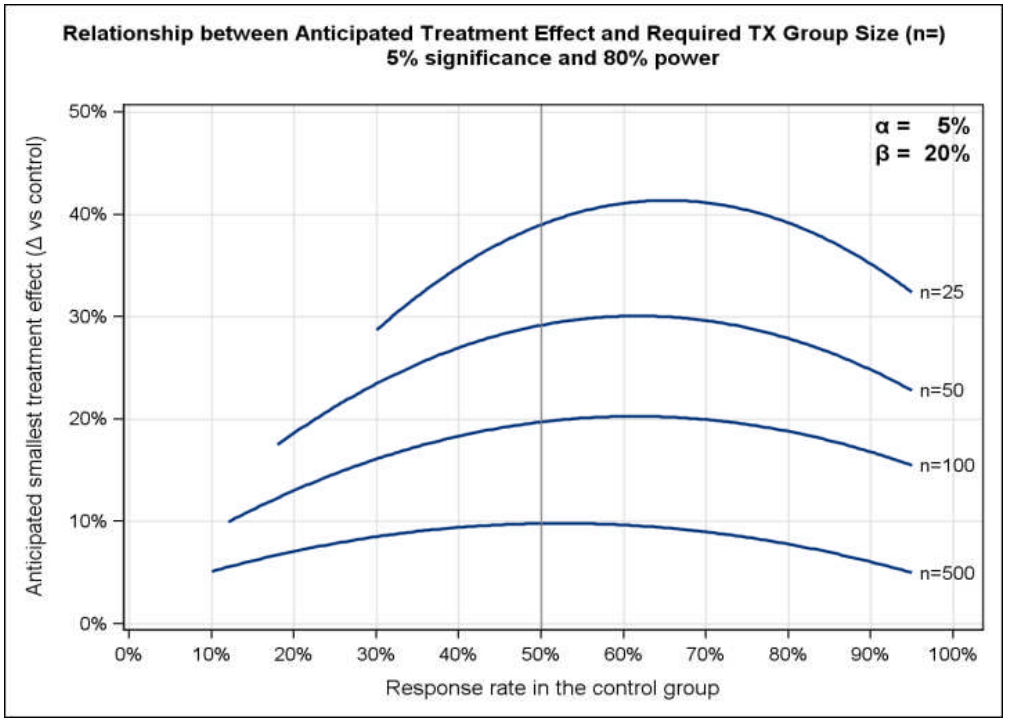


Plasma Concentration Profile



AUC = area under the concentration curve
Cmax = peak concentration of the drug in the body; Tmax = time to reach the peak concentration of the drug from dosing

Sample Size Requirements



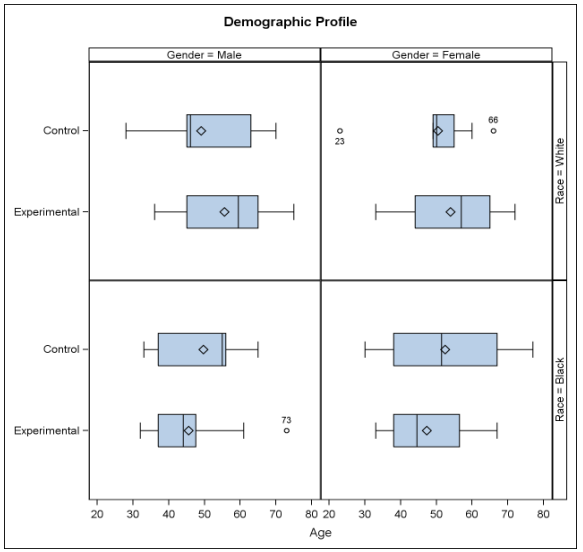
Multi-Cell Graphs

- Panels
  - Panel of Single-Cell Plots Within One or More Classification Variables
  - Arranged in a LATTICE, PANEL, COLUMNLATTICE, or ROWLATTICE
  - Common Axes and Legend
- Scatter Plots
  - Independend Scatter Plots
  - ScatterPlot Matrices
  - Axes can be Common or Independent, Legend Common

Panels: LATTICE Layout

Demographic Profile

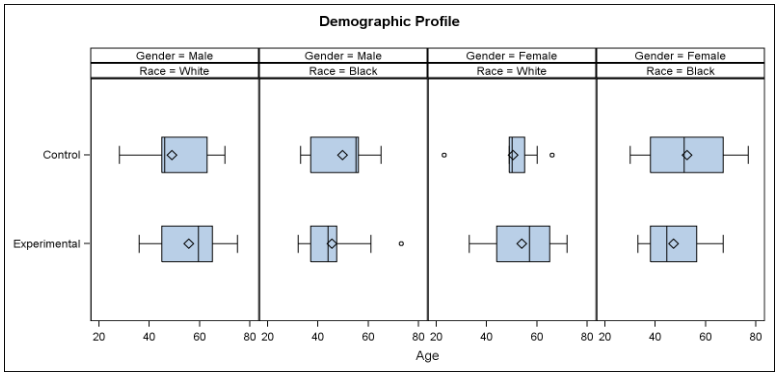
```
proc sgpanel data=demog;
 panelby gender race / layout=lattice;
 hbox age / category=trt datalabel;
 rowaxis display=(nolabel);
 run;
```



Panels: PANEL Layout

Demographic Profile

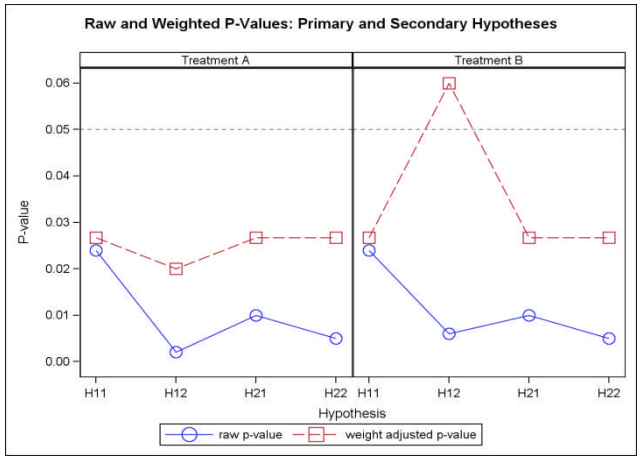
```
proc sgpanel data=demog;
 panelby gender race /
    layout=panel
    columns=4;
 hbox age / category=trt;
 rowaxis display=(nolabel);
 colaxis values=(20 40 60 80);
 run;
```



Panels: COLUMNLATTICE Layout

Primary and Secondary Hypothesis

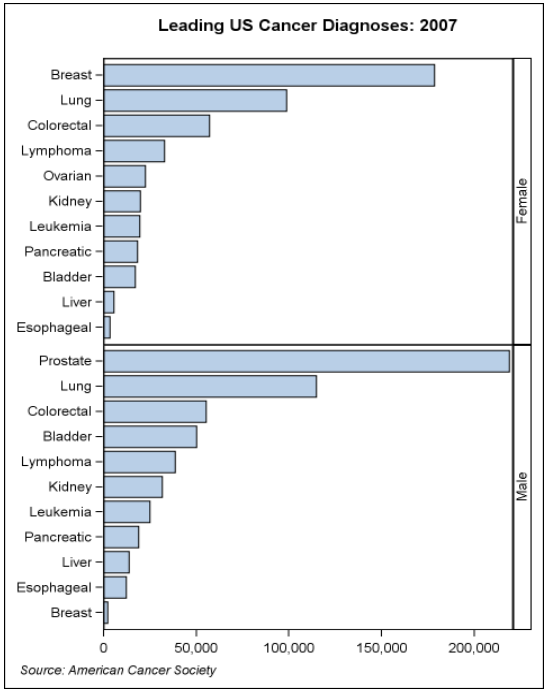
```
proc sgpanel data=hyp;
 panelby trt / novarname
    layout=columnlattice;
 series x=hyp y=rawp / markers
    markerattrs=(size=6pt);
 series x=hyp y=adjp / markers
    markerattrs=(size=6pt symbol=square);
 rowaxis label='P-value';
 colaxis label='Hypothesis';
 refline 0.05 /
    lineattrs=(pattern=shortdash);
 run;
```



Panels: ROWLATTICE Layout

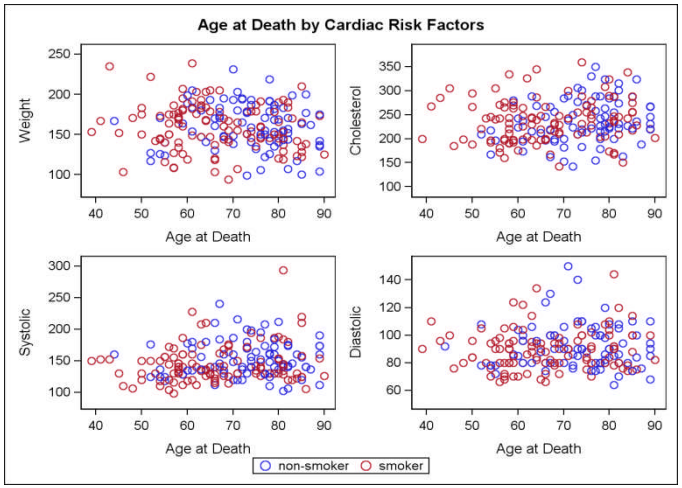
Cancer Diagnoses

```
proc sgpanel data=cancer;
panelby sex /
layout=rowlattice
novarname
uniscale=column;
hbar cause / response=cases stat=sum;
rowaxis display=(nolabel) discreteorder=data ;
colaxis display=(nolabel);
run;
```



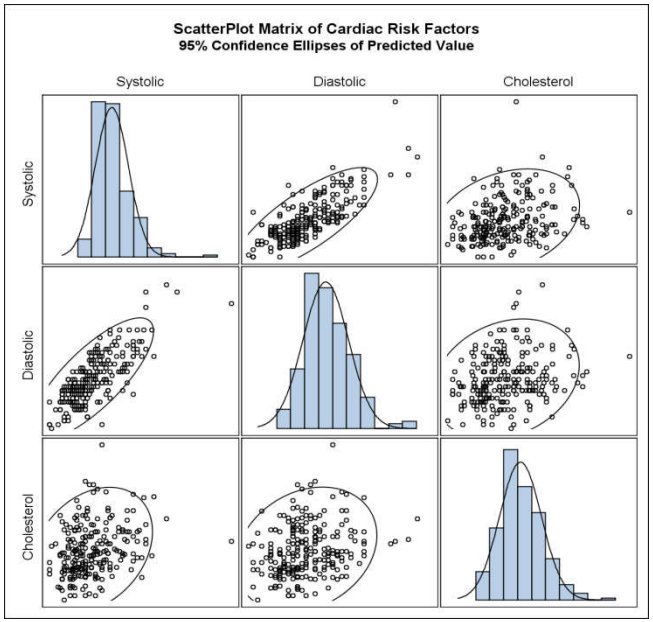
Independent Scatter Plots
Cardiac Risk Factors

```
proc sgscatter data=heart;
format smoking smoker.,
plot (weight cholesterol systolic diastolic)
* (ageatdeath) /
group=smoking
columns=2
markerattrs=(size=10 symbol=circle)
legend=(notitle);
run;
```



Scatter Plot Matrix
Cardiac Risk Factors

```
proc sgscatter data=heart;
 matrix systolic diastolic cholesterol /
    ellipse=(alpha=0.05 type=predicted)
    diagonal=(histogram normal);
 run;
```



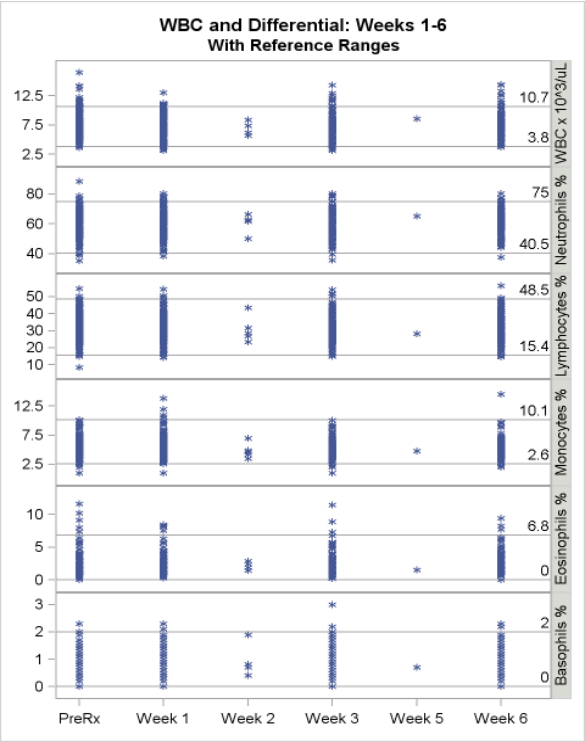
Laboratory Panels

- WBC Panel with Differential, Normal Ranges
- Liver Function Tests, Baseline vs. Study
- Liver Function Tests, At-Risk Patients

Laboratory Panel

WBC / Differential with Normal Ranges

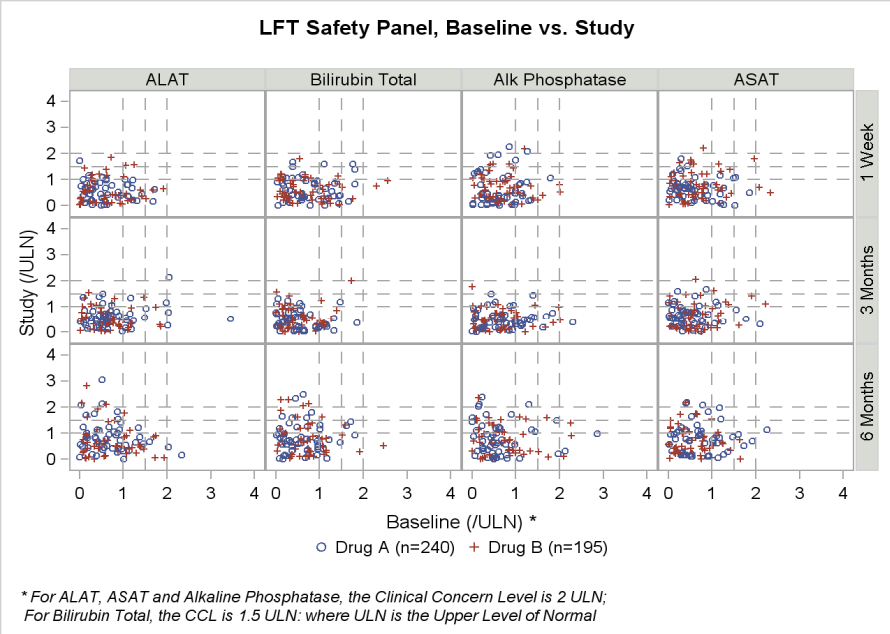
```
proc format;
  value visit
    .. formats for "PreRx" to "Week 6";
  value labname
    .. formats for "WBC x 10^3 /uL" ….;

proc sgpanel data=labs;
format visitnum visit. labtest labname.;
panelby labtest /
    layout=rowlattice
    onepanel
    novarname
    uniscale=column;
refline normlow / label noclip;
refline normhi / label noclip;
scatter x=visitnum y=result  /
   markerattrs=(symbol=asterisk size=10);
rowaxis display=(nolabel);
colaxis display=(nolabel) offsetmax=0.1;
run;
```



Laboratory Panel

Liver Function Tests, Baseline vs. Study

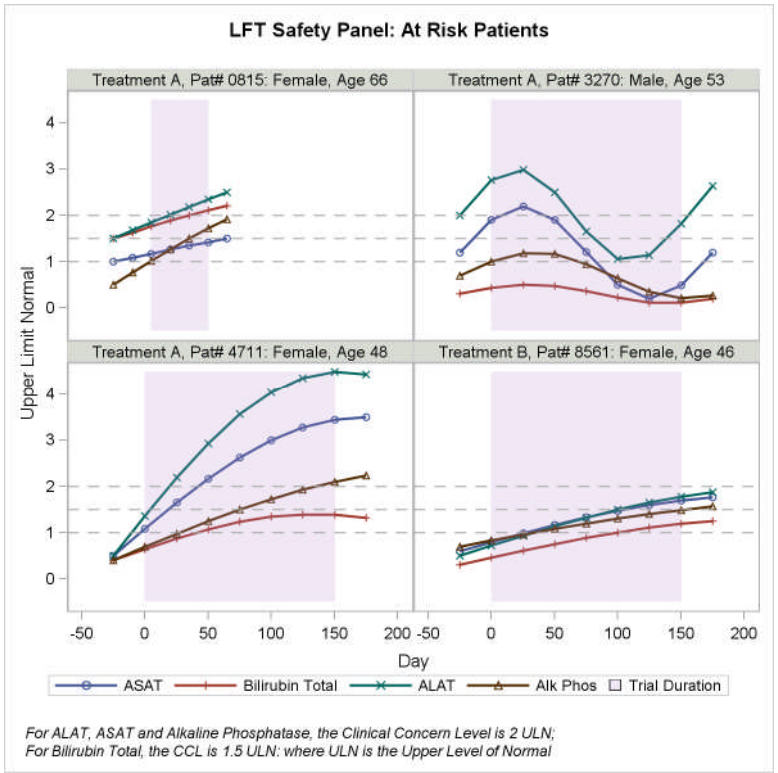
```
proc sgpanel data=labs;
format visitnum wk. labtest lab. drug $trt.;
panelby labtest visitnum /
    novarname
    layout=lattice
    onepanel;
scatter x=pre y=result /
    group=drug;
refline 1 1.5 2 / axis=X
    lineattrs=(pattern=dash);
refline 1 1.5 2 / axis=Y
    lineattrs=(pattern=dash);
rowaxis integer min=0 max=4
    label='Study (/ULN)';
colaxis integer min=0 max=4
    label='Baseline (/ULN) *';
keylegend / title=" " noborder;
run;
```



Laboratory Panel

Liver Function Tests, At-Risk Patients

```
proc sgpanel data=labs cycleattrs;
panelby patient / novarname
layout=panel
columns=2;
series x=relday y=alat / markers
lineattrs=(thickness=2px pattern=solid);
series x=relday y=asat / markers
lineattrs=(thickness=2px pattern=solid);
series x=relday y=alkph / markers
lineattrs=(thickness=2px pattern=solid);
series x=relday y=biltot / markers
lineattrs=(thickness=2px pattern=solid);
band x=sday lower=miny upper=4.5 /
transparency=0.8
legendlabel='Trial Duration';
refline 1 1.5 2 / axis=Y
lineattrs=(pattern=dash);
colaxis min = -50 max = 200;
rowaxis label="Upper Limit Normal";
run;
```

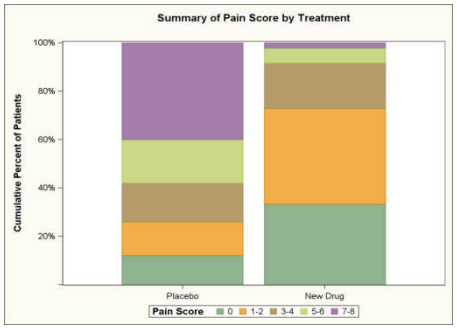


Grouped Bar Charts

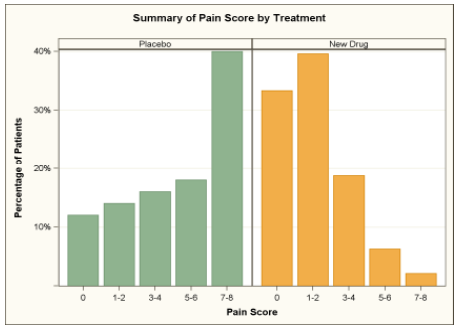
- Stacked Group Bar Chart
- Adjacent Group Bar Chart
- Latticed Group Bar Chart
- Butterfly Group Bar Chart

Grouped Bar Charts

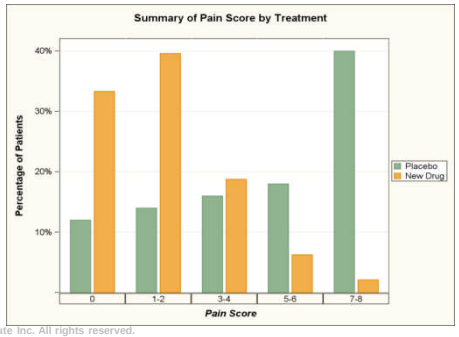
Stacked Groups

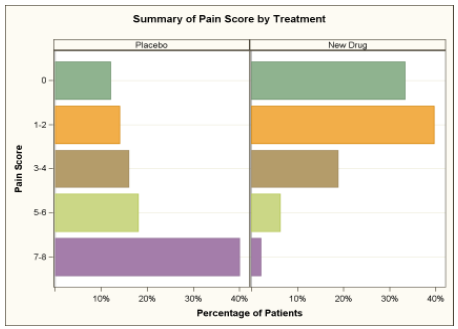


Latticed Groups



Adjacent Groups

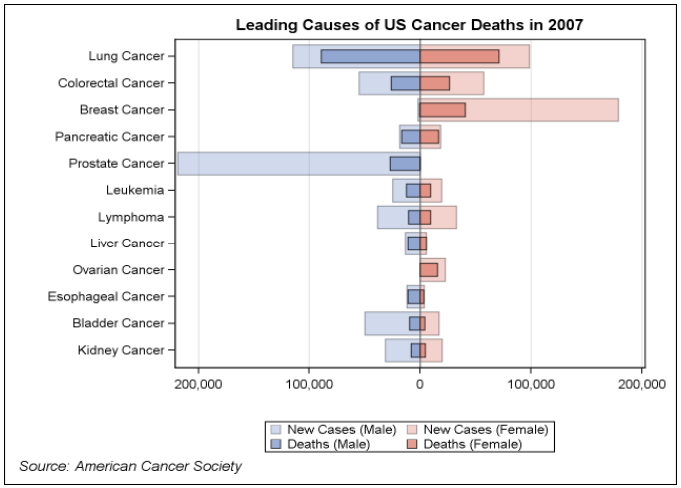




BUTTERFLY PLOT (Grouped Bar Charts)

Cancer Diagnoses

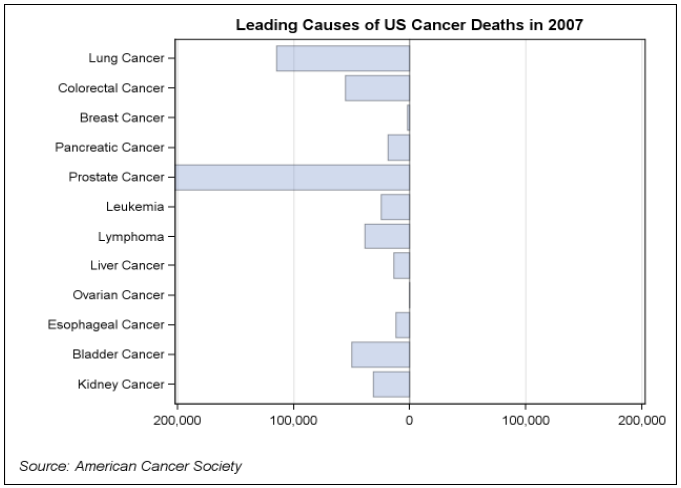
- Drawn across center axis
- To compare two halves of a whole
- Negative bars on left positive bars on right
- X axis formatted with Picture User-Defined Format
- Overlaid bar charts with different Barwidth



BUTTERFLY PLOT (Grouped Bar Charts)

Cancer Diagnoses

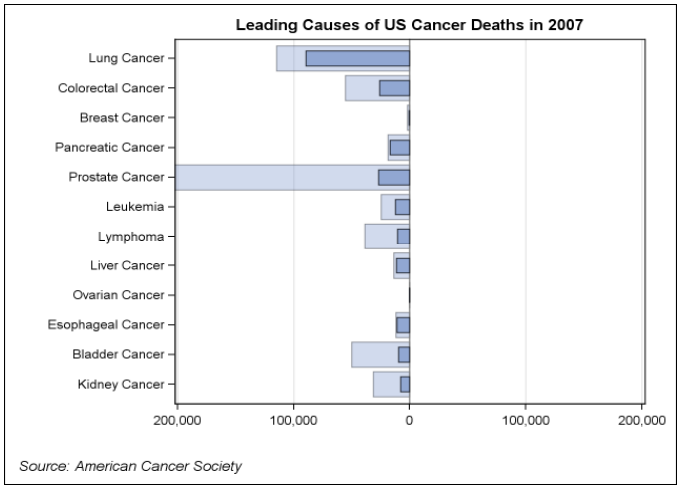
```
proc sgplot data=cancer;
format mcases mdeaths fcases fdeaths positive.;
hbar cause / response=mcases
fillattrs=graphdata1 transparency=.65
legendlabel="New Cases (Male)"
name="mcases" ;
```



BUTTERFLY PLOT (Grouped Bar Charts)

Cancer Diagnoses

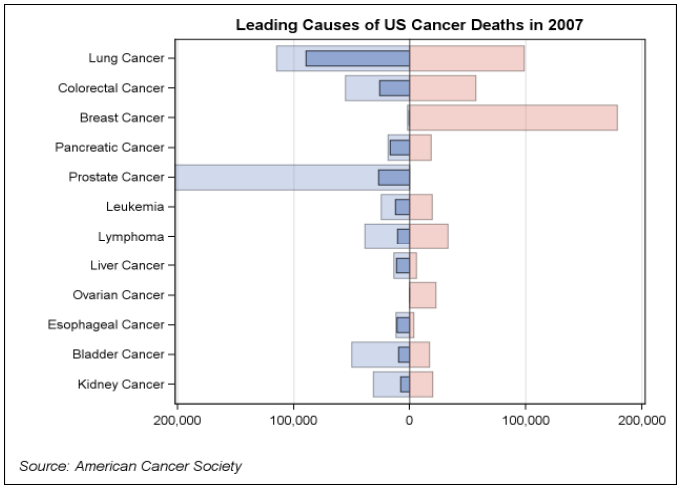
```
proc sgplot data=cancer;
format mcases mdeaths fcases fdeaths positive.;
hbar cause / response=mcases
fillattrs=graphdata1 transparency=.65
legendlabel="New Cases (Male)"
name="mcases" ;
hbar cause / response=mdeaths barwidth=.5
fillattrs=graphdata1 transparency=.25
legendlabel="Deaths (Male)"
name="mdeaths" ;
```



BUTTERFLY PLOT (Grouped Bar Charts)

Cancer Diagnoses

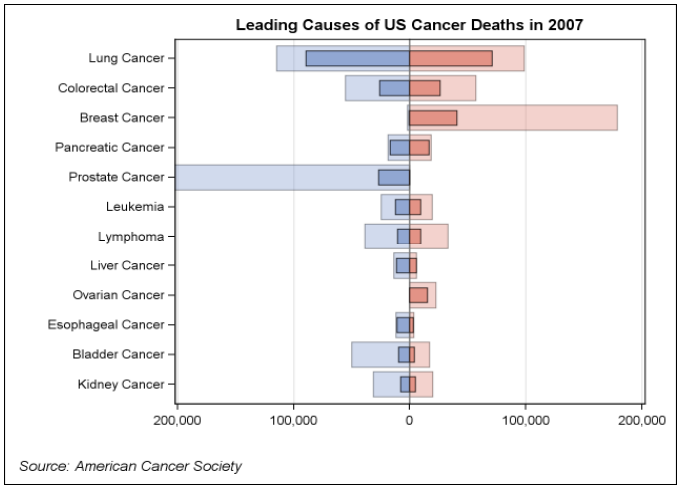
```
proc sgplot data=cancer;
format mcases mdeaths fcases fdeaths positive.;
hbar cause / response=mcases
fillattrs=graphdata1 transparency=.65
legendlabel="New Cases (Male)"
name="mcases" ;
hbar cause / response=mdeaths barwidth=.5
fillattrs=graphdata1 transparency=.25
legendlabel="Deaths (Male)"
name="mdeaths" ;
hbar cause / response=fcases
fillattrs=graphdata2 transparency=.65
legendlabel="New Cases (Female)"
name="fcases";
```



BUTTERFLY PLOT (Grouped Bar Charts)

Cancer Diagnoses

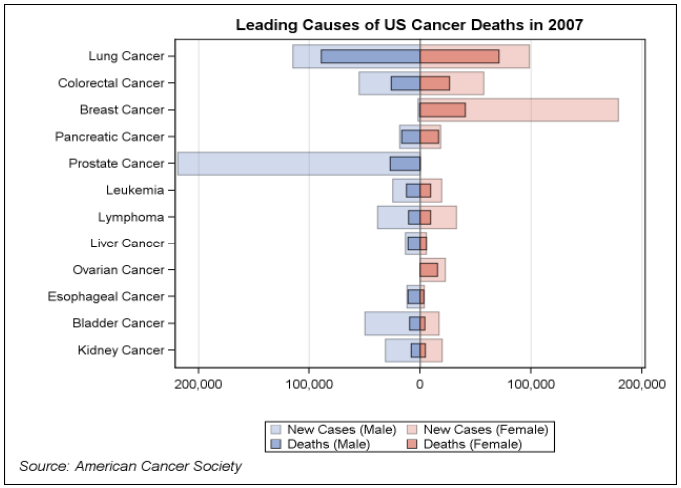
```
proc sgplot data=cancer;
format mcases mdeaths fcases fdeaths positive.;
hbar cause / response=mcases
fillattrs=graphdata1 transparency=.65
legendlabel="New Cases (Male)"
name="mcases" ;
hbar cause / response=mdeaths barwidth=.5
fillattrs=graphdata1 transparency=.25
legendlabel="Deaths (Male)"
name="mdeaths" ;
hbar cause / response=fcases
fillattrs=graphdata2 transparency=.65
legendlabel="New Cases (Female)"
name="fcases";
hbar cause / response=fdeaths barwidth=.5
fillattrs=graphdata2 transparency=.25 legendlabel="Deaths (Female)" name="fdeaths";
```



BUTTERFLY PLOT (Grouped Bar Charts)

Cancer Diagnoses

```
proc sgplot data=cancer;
format mcases mdeaths fcases fdeaths positive.;
hbar cause / response=mcases
fillattrs=graphdata1 transparency=.65
legendlabel="New Cases (Male)"
name="mcases" ;
hbar cause / response=mdeaths barwidth=.5
fillattrs=graphdata1 transparency=.25
legendlabel="Deaths (Male)"
name="mdeaths" ;
hbar cause / response=fcases
fillattrs=graphdata2 transparency=.65
legendlabel="New Cases (Female)"
name="fcases";
hbar cause / response=fdeaths barwidth=.5
fillattrs=graphdata2 transparency=.25 legendlabel="Deaths (Female)" name="fdeaths";
keylegend "mcases" "fcases" "mdeaths" "fdeaths" / across=2;
yaxis label=" " discreteorder=data;
xaxis label=" " grid;
run;
```

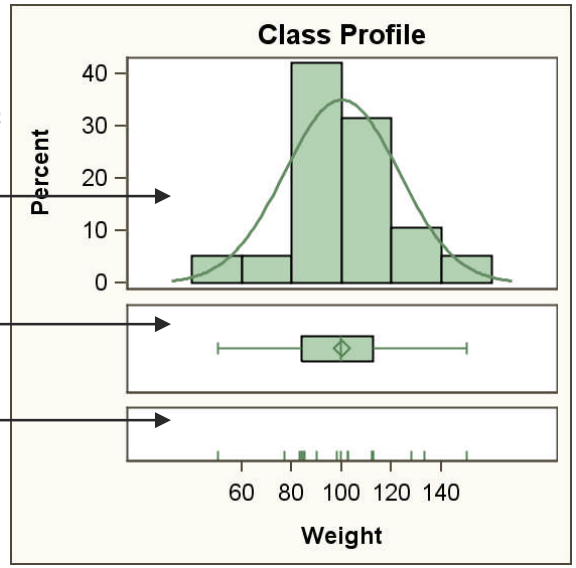


ODS Graphics
The Graph Template Language (GTL)

- A template is a program that describes individual graphs, written using the Graph Template Language
- The Graph Template Language
  - Is an extension to the TEMPLATE procedure
  - Combines Layouts and Plots in flexible ways
  - Supports statistical computations and plot types
  - Supports ODS Styles for a variety of usages
  - Power tool for creation of complex analytical graphs
  - Same tool is used to create the automatic graphics
- Most of the new features for analytical graphics in the future will be developed using GTL

ODS Graphics
Graph Template Language

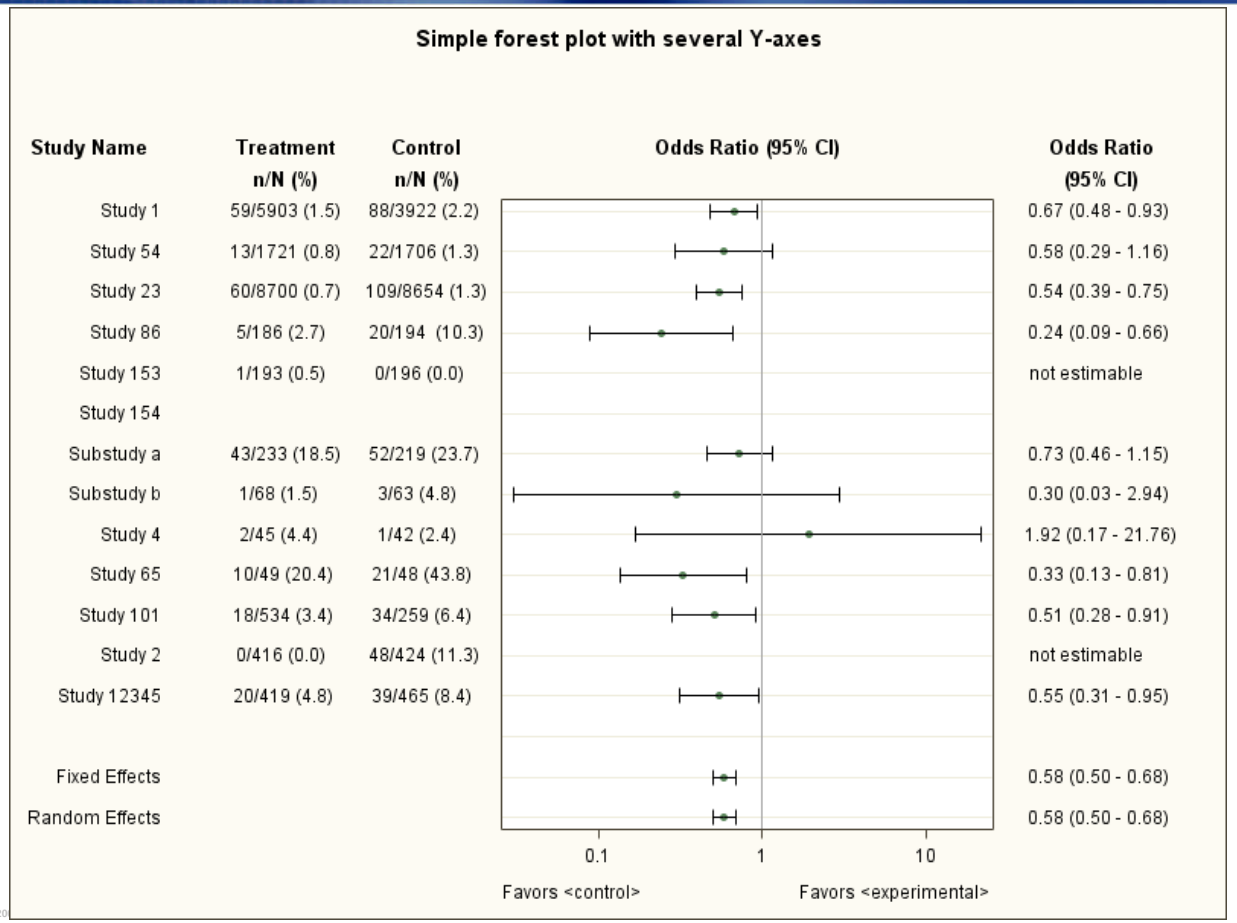
```
begingraph;
  entrytitle "Class Profile";
  layout lattice / rowweight=(0.5 0.2 0.3)
                   rowgutter=5 columndatarange=union;
    layout overlay / xaxisopts=(display=(line));
      histogram weight;
      densityplot weight / normal();
    endlayout;
    layout overlay / xaxisopts=(display=(line));
      boxplot y=weight / orient=horizontal;
    endlayout;
    layout overlay / xaxisopts=(label="Weight");
      fringeplot weight;
    endlayout;
  endlayout;
endgraph;
```



ODS Graphics
Graph Template Language

- Dynamic Elements in Templates
  - Templates can contain dynamic elements for more generalized use
- Dynamic references (DYNAMIC)
- Macro variables in templates
  - Macro Variables (MVAR)
  - Numeric Macro Variable values (NMVAR)
  - With & - Resolve at template compile time
  - Without & - Resolve at template execution
- Conditional logic to process DYNAMIC options

Simple forest plot with several Y-axes



Simple Forest Plot Example
Define Template (Code snippet)

```
proc template;
define statgraph tmplt;
  dynamic _X _Y _ERRORUPPER _ERRORLOWER _VSTART _VEND;
  begingraph / designwidth=800 designheight=600;
    entrytitle "Simple Forest Plot" /  textattrs=(size=14) ;
      layout lattice / columns=5 columngutter=0 columnweights=(.16 .12  .12 .42 .18 ) rowdatarange=data;
  …
        layout overlay / yaxisopts=(type=linear griddisplay=on reverse=true
                         linearopts=(tickvaluesequence=(start=1 end=16 increment=1)) display=none)
                         xaxisopts=(type=log display=(ticks tickvalues));
          entry halign=center "Odds Ratio (95% CI)" / location=outside valign=top textattrs=GraphLabelText;
          ScatterPlot Y=_Y X=_X / XErrorUpper=_ERRORUPPER XErrorLower=_ERRORLOWER
                                  Markerattrs=(symbol=CircleFilled size=13);
          ScatterPlot Y=_Y X=_X / Markerattrs=(symbol=CircleFilled size=10 color=white);
          entry halign=left "Favors <control>" halign=right "Favors <experimental>" / location=outside
                                                                                      valign=bottom;
         referenceline x=1 / lineattrs=(pattern=solid);
     endlayout;
  endlayout;
endgraph;
end;
run;
```

Simple Forest Plot Example
Use Template with Data

```
proc sgrender data=plotdata template=tmplt;
  dynamic
    _X="MEAN"
    _Y="STUDY"
    _VSTART="VSTART"
    _VEND="VEND"
    _ERRORUPPER="XHI"
    _ERRORLOWER="XLO"
    ;
run;
```

For More Information…

- Base focus area (with TS Samples and SAS Notes) (http://support.sas.com/rnd/base/ods/index.html)
- SAS/GRAPH 9.2 Manuals
  - SG Procedures Guide, GTL User's Guide, GTL Reference, ODS Graphics Editor User's Guide, SAS/STAT User's Guide
- SAS Global Forum, 2009
  - Secrets of the SG Procedures (http://support.sas.com/resources/papers/proceedings09/324-2009.pdf)
  - ODS Graphics Designer (http://support.sas.com/resources/papers/proceedings09/198-2009.pdf http://support.sas.com/resources/papers/proceedings09/331-2009.pdf)
  - Clinical Trial Reporting Using SAS/GRAPH® SG Procedures (http://support.sas.com/resources/papers/proceedings09/174-2009.pdf)

For More Information…

- SAS Global Forum, 2008
  - Effective Graphics Made Simple using SAS/GRAPH “SG” Procedures (http://www2.sas.com/proceedings/forum2008/255-2008.pdf)
  - ODS Graphics Editor (http://www2.sas.com/proceedings/forum2008/235-2008.pdf)
  - Butterflies, Heat Maps, and More (http://www2.sas.com/proceedings/forum2008/243-2008.pdf)
- SAS Global Forum, 2007
  - New SAS/GRAPH Procedures for Creating Statistical Graphics (http://www2.sas.com/proceedings/forum2007/193-2007.pdf)
- SUGI 31, 2006
  - Creating Statistical Graphics in SAS9.2: What Every Statistical User Should Know http://www2.sas.com/proceedings/sugi31/192-31.pdf