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Know Your AREA!
Creating Professional SAS® Graphics in Clinical Safety Data by Using the AREAS Option in PROC GPLOT.

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ABSTRACT

In monitoring safety data in clinical trials, visual displays of individual patient data over time (i.e. vitals and lab data) are indispensable. This paper will introduce examples of these displays for a Data Safety Monitoring Committee, using the GPLOT procedure in SAS/GRAPH. Specifically, the AREAS option in GPLOT will be used to show how SAS/GRAPH can be employed to produce complex and professional graphics. Examples from safety monitoring data in the clinical trial environment will be drawn.

INTRODUCTION

This paper will introduce how the AREAS option in PROC GPLOT can be utilized to create shaded areas of treatment intervals, and display clinical measures relative to the baseline in clinical data.

Example 1: Shaded therapy intervals

To let our Data Monitoring committee to have a better grasp of the safety data in terms of the onset and end of the therapy, we can add shaded areas to our blood pressure graphical display.

Here is a sample of the blood pressure data with the YYY (from **29MAR2004:11:13:00 to 03APR2004:06:25:00**) and XXX therapy (from **30MAR2004:10:25:00 to 02APR2004:10:25:00**) intervals. Note that both the onset and the end of the therapies are denoted by the maximum value of the blood pressure data, **135 mm Hg** in this case.

SITE	RANDNO__	ASDT	yyy	XXX	SBP__	DBP__
3	2203	29MAR2004:00:00:00	.	.	115	73
3	2203	***29MAR2004:11:13:00***	***135***	.	.	.
3	2203	29MAR2004:17:15:00	.	.	115	75
3	2203	29MAR2004:21:15:00	.	.	101	67
3	2203	30MAR2004:01:15:00	.	.	121	74
3	2203	30MAR2004:05:15:00	.	.	***135***	80
3	2203	30MAR2004:09:15:00	.	.	116	69
3	2203	***30MAR2004:10:25:00***	.	***135***	.	.
3	2203	30MAR2004:10:40:00	.	.	93	56
3	2203	30MAR2004:10:55:00	.	.	76	47
3	2203	30MAR2004:11:10:00	.	.	102	61
3	2203	30MAR2004:11:25:00	.	.	107	63
3	2203	30MAR2004:12:25:00	.	.	103	60
3	2203	30MAR2004:14:25:00	.	.	131	79
3	2203	30MAR2004:16:25:00	.	.	126	78
3	2203	30MAR2004:18:25:00	.	.	127	78
3	2203	30MAR2004:20:25:00	.	.	117	53
3	2203	31MAR2004:22:25:00	.	.	90	53
3	2203	01APR2004:02:25:00	.	.	103	61
3	2203	01APR2004:06:25:00	.	.	98	55
3	2203	01APR2004:10:25:00	.	.	82	49
3	2203	01APR2004:14:25:00	.	.	108	54
3	2203	01APR2004:18:25:00	.	.	100	54
3	2203	01APR2004:22:25:00	.	.	110	56
3	2203	02APR2004:02:25:00	.	.	92	51
3	2203	02APR2004:06:25:00	.	.	116	56
3	2203	***02APR2004:10:25:00***	.	***135***	117	58
3	2203	02APR2004:14:25:00	.	.	99	48
3	2203	02APR2004:18:25:00	.	.	122	65
3	2203	02APR2004:22:25:00	.	.	91	49
3	2203	03APR2004:02:25:00	.	.	102	61
3	2203	***03APR2004:06:25:00***	***135***	.	108	64

Here is the PROC GPLOT code:

```
/**The first two symbol statements are for variables xxx and yyy
respectively**/
symbol1 v=none cv=black i=join l=1;
symbol2 v=none cv=black i=join l=1;
symbol3 v='S' color=blue cv=blue height=0.15 in cv=black i=join l=2;
symbol4 v='D' color=purple cv=purple height=0.15 in cv=black i=join l=3;


/**The color grayee denotes a lighter shade of gray for the xxx therapy**/
pattern1 value=solid color=grayee;
pattern2 value=solid color=grayaa;


/**Defining the axis statements**/
axis1 label=(h=0.17 in f=triplex "Assessment date and time") value=(h=0.135 in
f=triplex) offset=(1,1) ;
axis2 label=(h=0.17 in a=90 f=triplex "BP (mm Hg)") minor=none order=(0 to 160
by 10) offset=(1 pct) value=(h=0.135 in f=triplex);


/**The GPLOT procedure with the AREAS option**/
proc gplot data=d_vitals;
title1 j=c h=0.17 in "Using Proc Gplot with the Areas Option";
footnote1 j=c h=0.135 in "S = Systolic BP, D = Diastolic BP";
footnote3 j=c h=0.135 in "The light-grey shaded region indicates time on XXX
therapy.  The dark-grey shaded region indicates time on YYY therapy.";

 plot (xxx yyy sbp__ dbp__)*asdt / noframe overlay nolegend haxis=axis1
                                   vaxis=axis2 areas=2;
run;
quit;
```

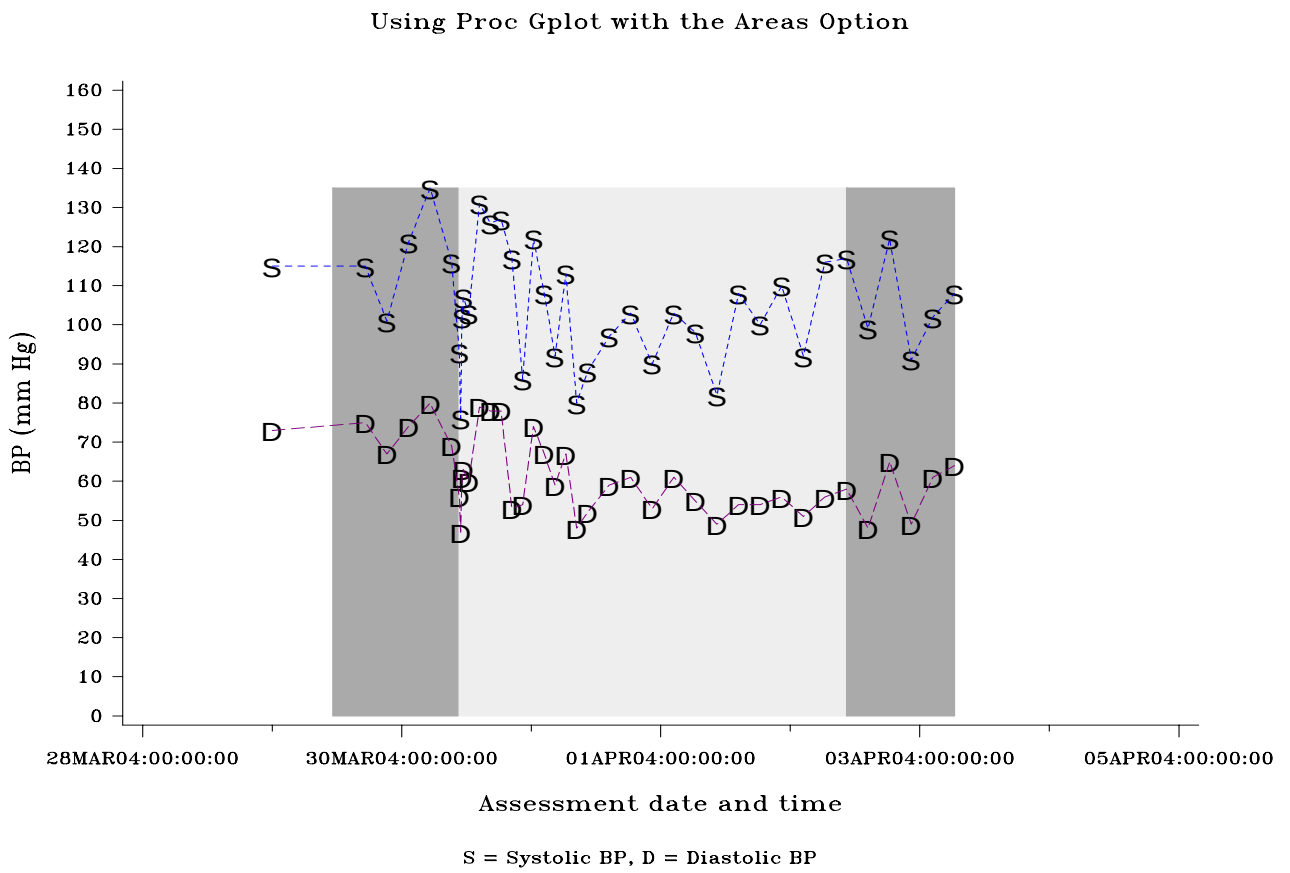
The **AREAS=2** option in the PLOT statement fills the areas under the first 2 plot lines on the graph, the plot lines generated by **XXX** and **YYY**. Before an area can be filled, the data points that border the area must be joined by a line. Therefore an interpolation method must be used in the SYMBOL statement to join the data points (i.e., **i=join** in the above **SYMBOL1** and **SYMBOL2** statements).

Pattern definitions are assigned to the areas below the plot lines in the order the plots are drawn. If the line that is drawn second lies below the line that is drawn first, the second area is hidden when the first is filled. The plots with the lower line values must be drawn first to prevent one area fill from overlaying another (SAS Institute, 2002).

In this case, when multiple plots are produced by submitting multiple plot requests using the OVERLAY option, the plot requests must be ordered in the PLOT statement so that the one that produces the lowest line values (i.e., XXX in the data) is plotted first.

The colors and/or the patterns of the area are defined by the **PATTERN** statements. In our data, the first plot request (XXX) uses a solid light gray to fill the area between the x-axis and y=135 within the x range of 30MAR2004:10:25:00 and 02APR2004:10:25:00. The second plot request (YYY) uses a solid dark gray to fill the area between the x-axis and y=135, and the area within the x range of 29MAR2004:11:13:00 and 03APR2004:06:25:00.

Here is the visual display of the blood pressure data with the shaded therapy intervals:



Example 2: Displaying Clinical Measures Relative to Baseline

We also want to generate graphical display of the different types of vasopressor use relative to their initial dose over the course of treatment. The types of vasopressors in this data are Dobutamine (mcg/kg/min), Dopamine (mcg/kg/min), Norepinephrine (mcg/min), Vasopressin (mcg/min), and the other category. The AREAS option in PROC GPLOT can be employed to accomplish this task.

Here is a sample display of the vasopressor data for Norepinephrine (mcg/min) in data set YDOSE. MN1 denotes the baseline value of vasopressor use, and YDOSE1 denotes the change in the vasopressor value relative to the first dose. MAXY1 represents the XXX therapy, and MAXYC1 represents the YYY therapy. Note that both the onset and the end of the therapies are denoted by the baseline vasopressor value 2 mcg/kg/min.

RANDNO__	ASDT	MAXY1	MAXYC1	MN1	YDOSE1
2203	***29MAR2004:11:13:00***	***.***	***2***	.	.
2203	29MAR2004:17:15:00	.	.	2	3.00000
2203	29MAR2004:21:15:00	.	.	2	2.60377
2203	30MAR2004:01:15:00	.	.	2	2.60377
2203	30MAR2004:05:15:00	.	.	2	2.60377
2203	30MAR2004:09:15:00	.	.	2	2.60377
2203	***30MAR2004:10:25:00***	***2***	.	.	.
2203	30MAR2004:10:40:00	.	.	2	3.20755
2203	30MAR2004:10:55:00	.	.	2	3.20755
2203	30MAR2004:11:10:00	.	.	2	3.20755
2203	30MAR2004:11:25:00	.	.	2	3.20755
2203	30MAR2004:12:25:00	.	.	2	3.81132
2203	30MAR2004:14:25:00	.	.	2	3.81132
2203	30MAR2004:22:25:00	.	.	2	2.60377
2203	01APR2004:06:25:00	.	.	2	5.20755
2203	01APR2004:10:25:00	.	.	2	5.96226
2203	01APR2004:14:25:00	.	.	2	5.39623
2203	01APR2004:18:25:00	.	.	2	5.20755
2203	01APR2004:22:25:00	.	.	2	5.81132
2203	02APR2004:02:25:00	.	.	2	7.47170
2203	02APR2004:06:25:00	.	.	2	6.62264
2203	***02APR2004:10:25:00***	***2***	.	2	6.43396
2203	02APR2004:14:25:00	.	.	2	5.96226
2203	02APR2004:18:25:00	.	.	2	5.01887
2203	02APR2004:22:25:00	.	.	2	5.39623
2203	03APR2004:02:25:00	.	.	2	5.20755
2203	***03APR2004:06:25:00***	***.***	***2***	2	5.20755

The following is a sample display of the vasopressor data for Vasopressin (mcg/min) in data set YDOSE. Similarly, MN2 denotes the baseline value of vasopressor use, and YDOSE2 denotes the change in the vasopressor value relative to the first dose. MAXY2 represents the XXX therapy, and MAXYC2 represents the YYY therapy. Both the onset and the end of the therapies are denoted by the baseline vasopressor value 9.4717 mcg/min.

RANDNO__	ASDT	MAXY2	MAXYC2	MN2	YDOSE2
2203	***29MAR2004:11:13:00***	***.***	***9.4717***	.	.
2203	29MAR2004:17:15:00	.	.	9.47170	10.4717
2203	29MAR2004:21:15:00	.	.	9.47170	10.4717
2203	30MAR2004:01:15:00	.	.	9.47170	10.2899
2203	30MAR2004:05:15:00	.	.	9.47170	10.2899
2203	30MAR2004:09:15:00	.	.	9.47170	9.6535
2203	***30MAR2004:10:25:00***	***9.4717***	.	.	.
2203	30MAR2004:10:40:00	.	.	9.47170	9.6535
2203	30MAR2004:10:55:00	.	.	9.47170	10.1990
2203	30MAR2004:11:10:00	.	.	9.47170	10.4717
2203	01APR2004:06:25:00	.	.	9.47170	10.1990
2203	01APR2004:10:25:00	.	.	9.47170	10.1990
2203	01APR2004:14:25:00	.	.	9.47170	10.1990
2203	01APR2004:18:25:00	.	.	9.47170	10.1990
2203	01APR2004:22:25:00	.	.	9.47170	10.1990
2203	02APR2004:02:25:00	.	.	9.47170	10.1990
2203	02APR2004:06:25:00	.	.	9.47170	10.1990
2203	02APR2004:10:25:00	.	.	9.47170	9.9262
2203	***02APR2004:10:25:00***	***9.4717***	.	.	.
2203	***03APR2004:06:25:00***	***.***	***9.4717***	.	.

The following is a sample display of the vasopressor data for the Other group in data set YDOSE. MN3 denotes the baseline value of vasopressor use, and YDOSE3 denotes the change in the vasopressor value relative to the first dose. MAXY3 represents the XXX therapy, and MAXYC3 represents the YYY therapy. Both the onset and the end of the therapies are denoted by the baseline vasopressor value 11.4717 mcg/min. MAXY7 and MAXY8, 18.9434 mcg/min, denote the maximum Y-value for the XXX therapy and YYY therapy respectively.

RANDNO__	ASDT	MAXY3	MAXYC3	MN3	YDOSE3	MAXY7	MAXY8
2203	***29MAR2004:11:13:00***	***.***	***11.4717***	.	.		***18.9434***
2203	29MAR2004:17:15:00	.	.	11.4717	12.4717		
2203	29MAR2004:21:15:00	.	.	11.4717	12.4717		
2203	30MAR2004:01:15:00	.	.	11.4717	12.4717		
2203	30MAR2004:05:15:00	.	.	11.4717	12.4717		
2203	30MAR2004:09:15:00	.	.	11.4717	12.4717		
2203	***30MAR2004:10:25:00***	***11.4717***	.	.	.	***18.9434***	
2203	30MAR2004:10:40:00	.	.	11.4717	12.4717		
2203	30MAR2004:10:55:00	.	.	11.4717	12.4717		
2203	30MAR2004:11:10:00	.	.	11.4717	12.4717		
2203	30MAR2004:11:25:00	.	.	11.4717	12.4513		
2203	30MAR2004:12:25:00	.	.	11.4717	12.4717		
2203	30MAR2004:14:25:00	.	.	11.4717	12.4717		
2203	30MAR2004:16:25:00	.	.	11.4717	12.4717		
2203	31MAR2004:08:25:00	.	.	11.4717	12.4717		
2203	31MAR2004:10:25:00	.	.	11.4717	12.4717		
2203	31MAR2004:14:25:00	.	.	11.4717	11.4717		
2203	31MAR2004:18:25:00	.	.	11.4717	12.1248		
2203	***02APR2004:10:25:00***	***11.4717***	.	.	.	***18.9434***	
2203	***03APR2004:06:25:00***	***.***	***11.4717***	.	.		***18.9434***

Here is the PROC GPLOT code:

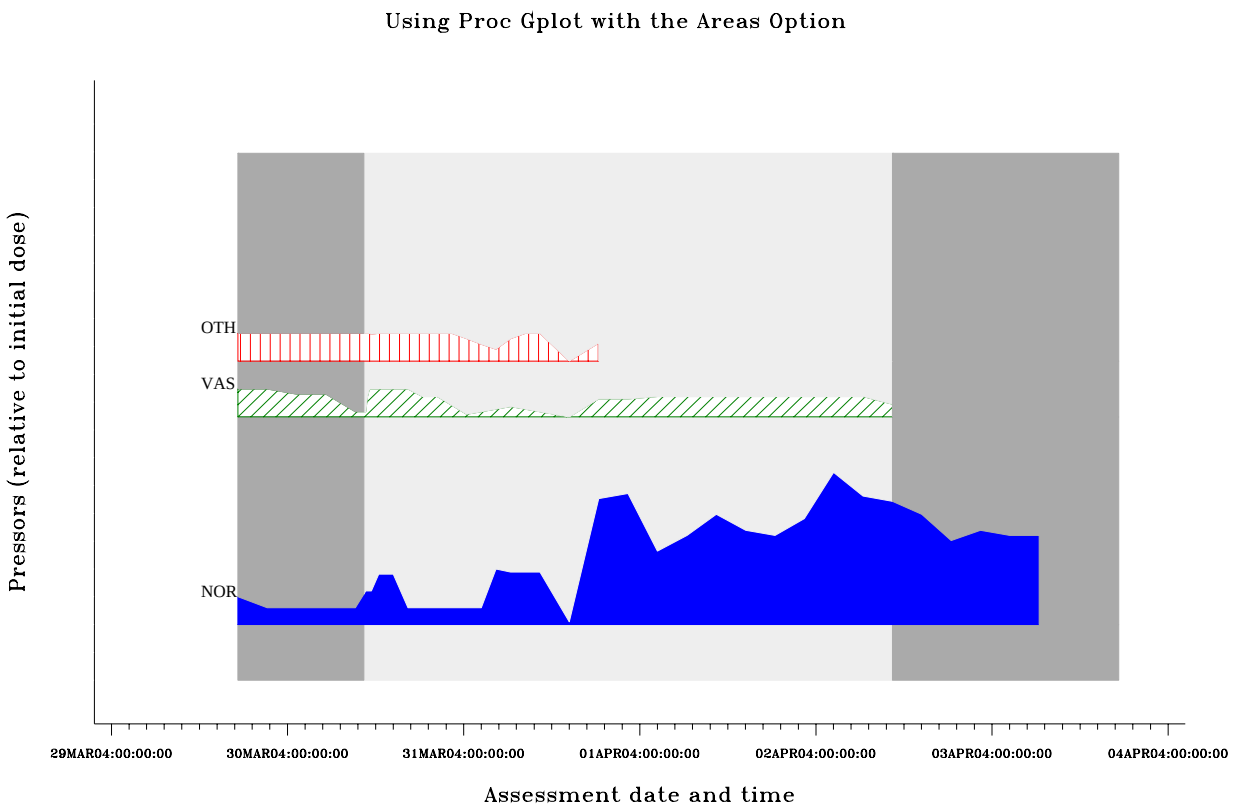
```
/**Defining the SYMBOL statements for the 11 plots**/
symbol1 v=none cv=black i=join l=1 repeat=11;

/**Defining the PATTERN statements for the 11 plots**/
pattern1 value=solid color=grayee;
pattern2 value=solid color=grayaa;
pattern3 value=solid color=blue;
pattern4 value=solid color=grayee;
pattern5 value=solid color=grayaa;
pattern6 value=m3n45 color=green;
pattern7 value=solid color=grayee;
pattern8 value=solid color=grayaa;
pattern9 value=m3n90 color=red;
pattern10 value=solid color=grayee;
pattern11 value=solid color=grayaa;

/**Defining the axis statements**/
axis1 label=(h=0.17 in f=triplex "Assessment date and time")
order=("29MAR04:00:00:00"dt to "04APR04:00:00:00"dt by dtday)
value=(h=0.1 in f=triplex)  offset=(1,1);
axis2  label=(h=0.17 in a=90 f=triplex "Pressors (relative to initial dose)")
value=(h=0.135 in f=triplex  color=white)
minor=none major=(color=white) order=(0 to 20 by 1) offset=(5 pct);
```

```
/**The GPLOT procedure with the AREAS option**/
       proc gplot data=ydose gout=temp.gphout1;
        format asdt datetime16. ;
          plot (maxy1 maxyc1 ydose1
                maxy2 maxyc2 ydose2
                 maxy3 maxyc3 ydose3 maxy7 maxy8)*asdt/
                overlay noframe nolegend haxis=axis1 vaxis=axis2 annotate=vasname
                areas=11;
        title1 j=c h=0.17 in "Using Proc Gplot with the Areas Option";
       footnote1 j=c h=0.135 in "DOB = Dobutamine, DOP = Dopamine, NOR =
       Norepinephrine, OTH = Other, VAS = Vasopressin";
       footnote2 j=c h=0.135 in "The light-grey shaded region indicates time on XXX
       therapy.  The dark-grey shaded region indicates time on YYY therapy.";
       run;
       quit;
```

Here is the visual display of the vasopressor data with the shaded therapy intervals and the types of vasopressor use relative to initial dose:

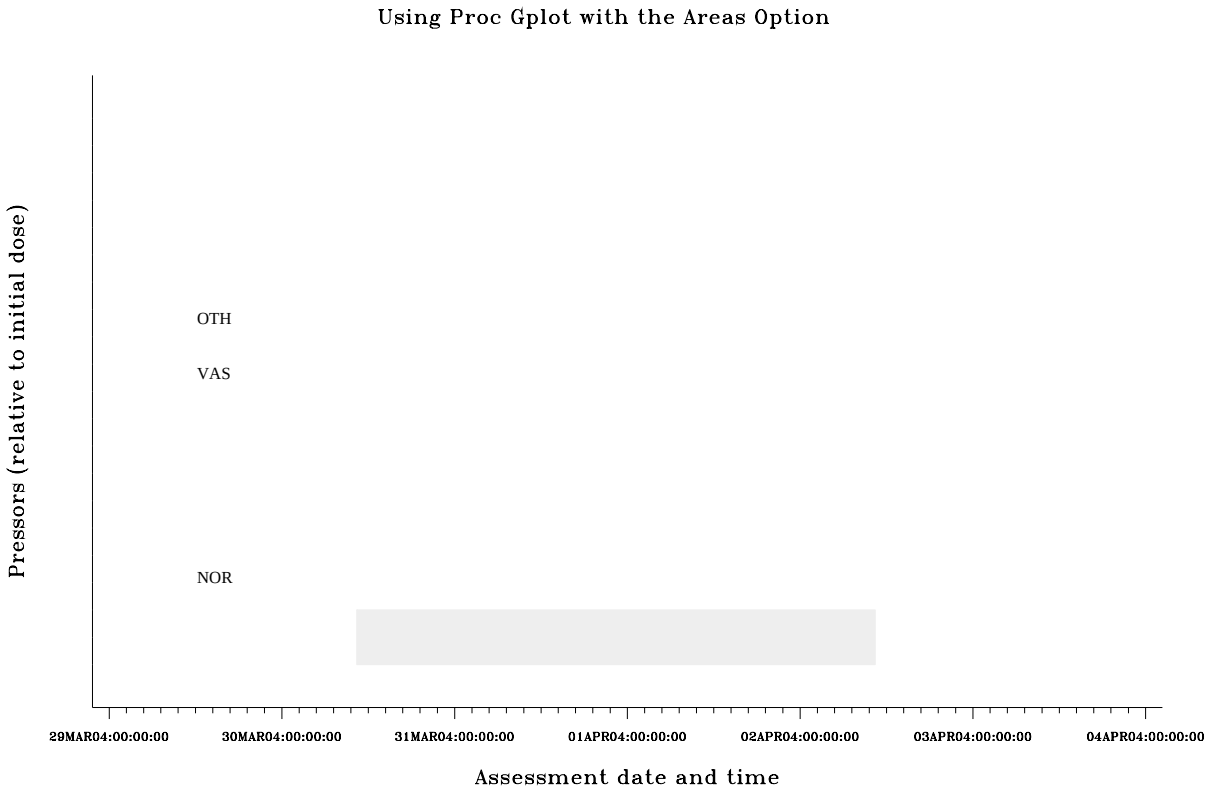


DOB = Dobutamine, DOP = Dopamine, NOR = Norepinephrine, OTH = Other, VAS = Vasopressin
The light-grey shaded region indicates time on XXX therapy. The dark-grey shaded region indicates time on YYY therapy.

To give you a better sense of how the AREAS option really works, here is a step-by-step approach.

With AREAS=1 in the PLOT statement, it'll give you the following graphical display:

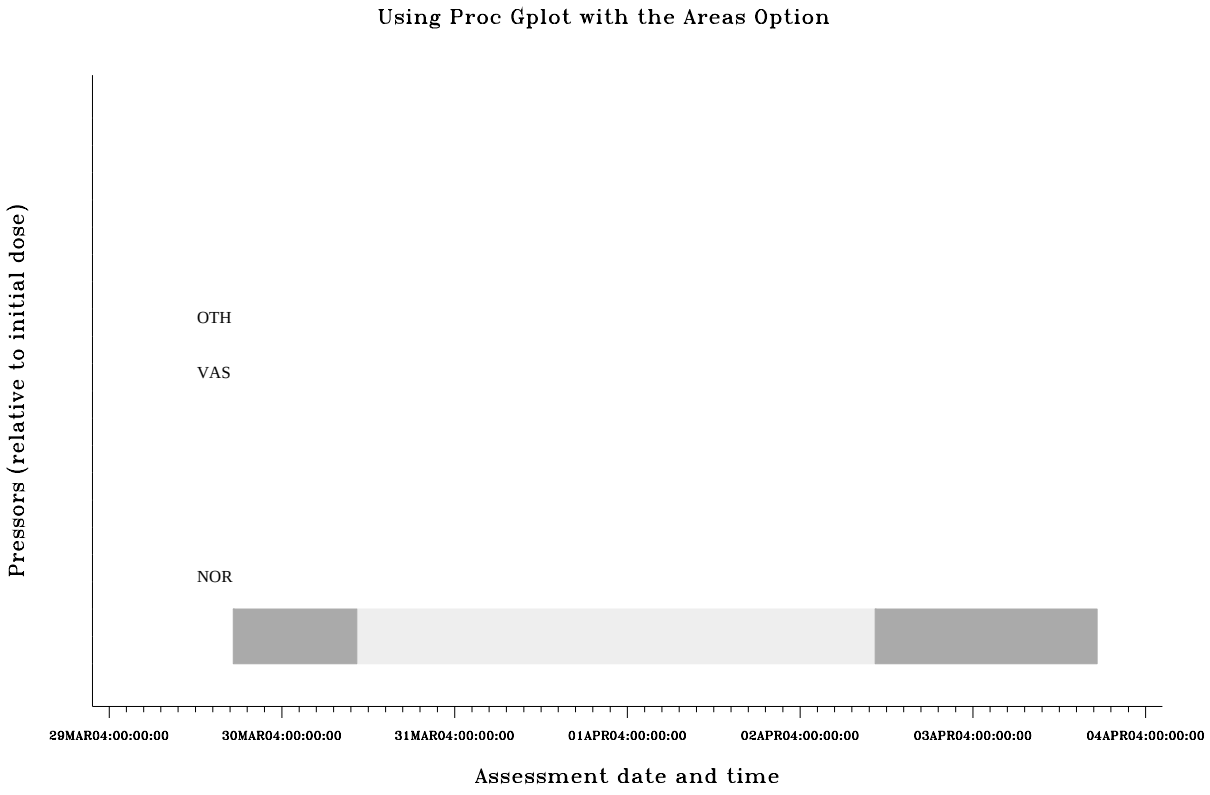
```
plot maxy1*asdt/
      noframe nolegend haxis=axis1 vaxis=axis2 annotate=vasname areas=1;
```



DOB = Dobutamine, DOP = Dopamine, NOR = Norepinephrine, OTH = Other, VAS = Vasopressin
The light-grey shaded region indicates time on XXX therapy. The dark-grey shaded region indicates time on YYY therapy.

With AREAS=2 in the PLOT statement, it'll give you the following graphical display:

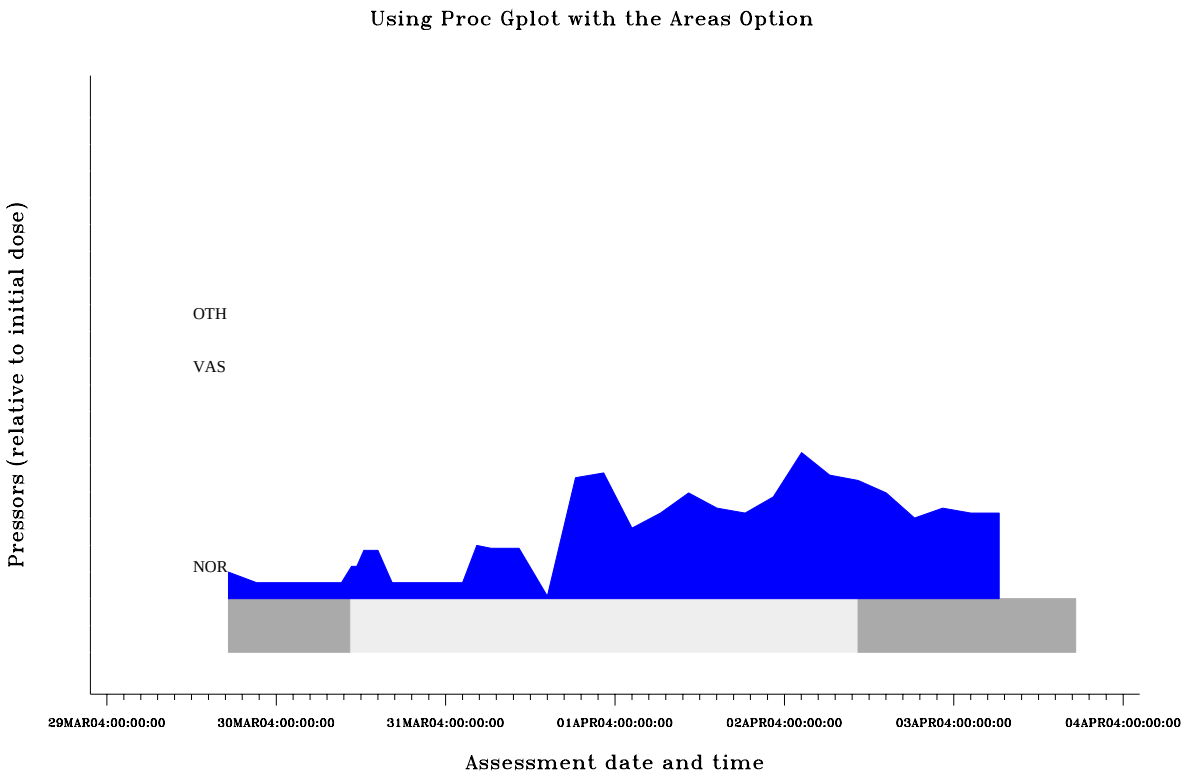
```
plot (maxy1 maxyc1)*asdt/
      overlay noframe nolegend haxis=axis1 vaxis=axis2 annotate=vasname
      areas=2;
```



DOB = Dobutamine, DOP = Dopamine, NOR = Norepinephrine, OTH = Other, VAS = Vasopressin
The light-grey shaded region indicates time on XXX therapy. The dark-grey shaded region indicates time on YYY therapy.

With AREAS=3 in the PLOT statement, it'll give you the following graphical display:

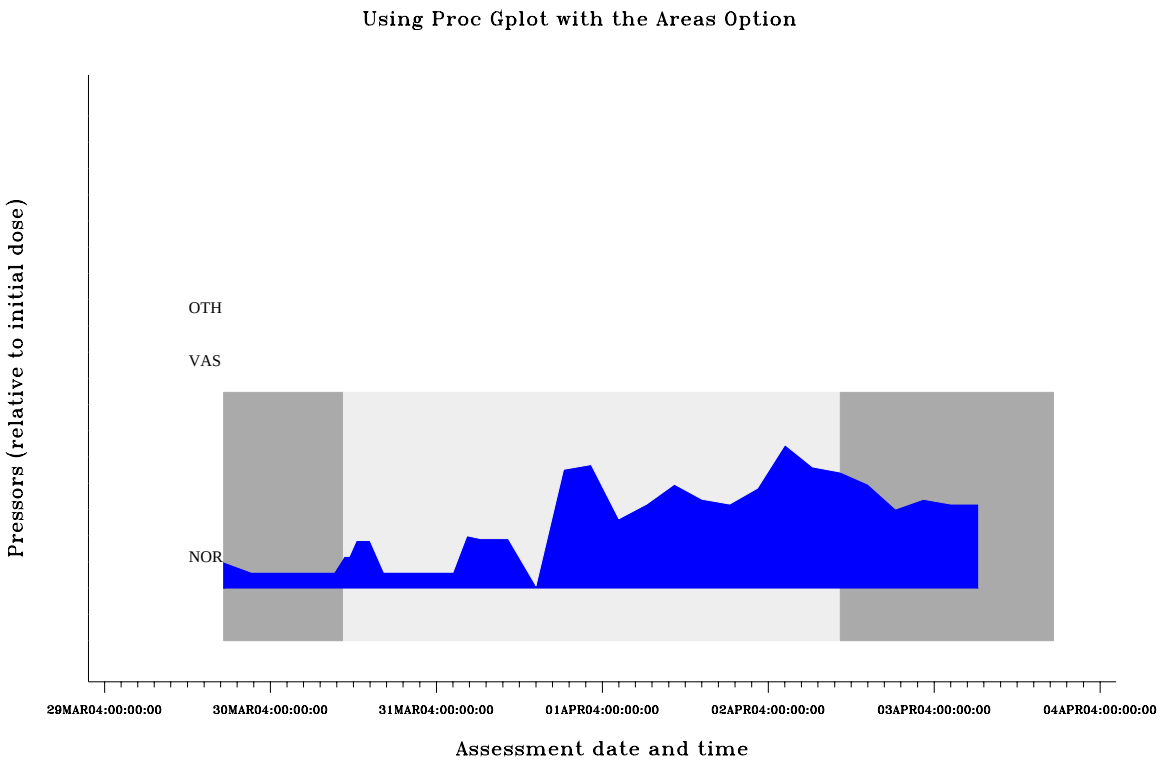
```
plot (maxy1 maxyc1 ydose1)*asdt/
      overlay noframe nolegend haxis=axis1 vaxis=axis2 annotate=vasname
      areas=3;
```



DOB = Dobutamine, DOP = Dopamine, NOR = Norepinephrine, OTH = Other, VAS = Vasopressin
The light-grey shaded region indicates time on XXX therapy. The dark-grey shaded region indicates time on YYY therapy.

With AREAS=5 in the PLOT statement, it'll give you the following graphical display:

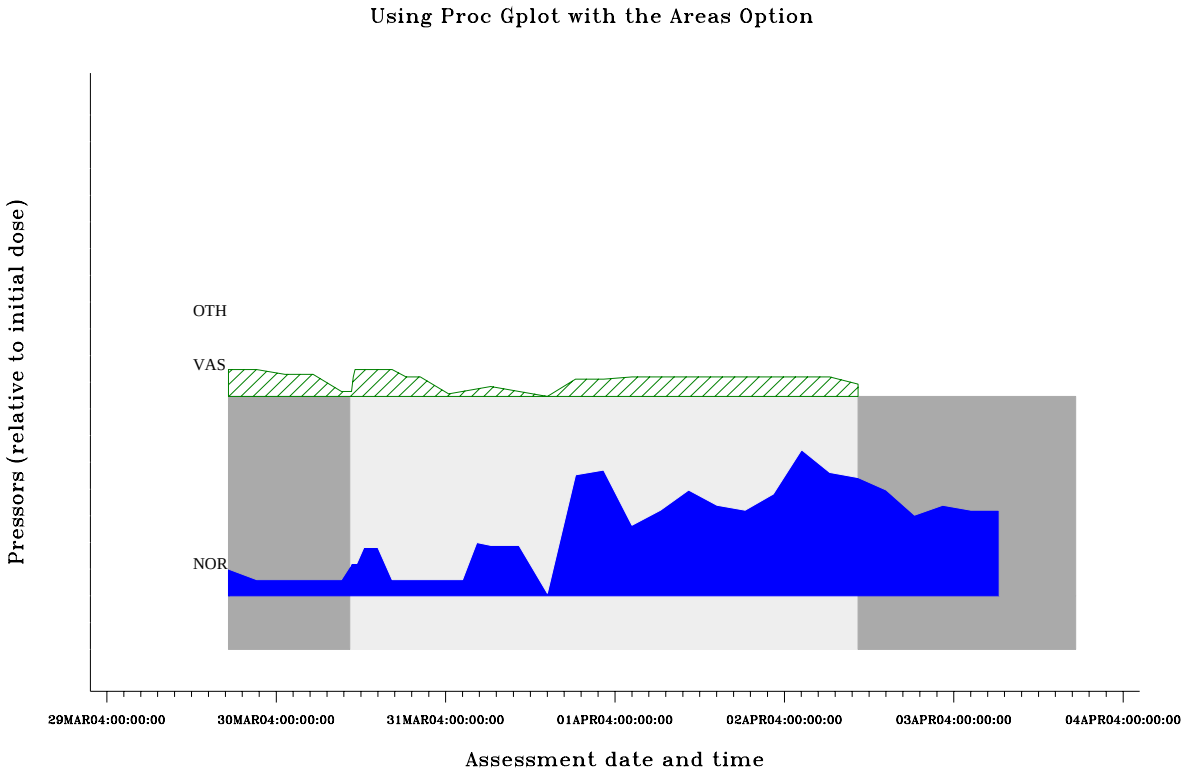
```
plot (maxy1 maxyc1 ydose1
      maxy2 maxyc2)*asdt/
     overlay noframe nolegend haxis=axis1 vaxis=axis2 annotate=vasname
     areas=5;
```



DOB = Dobutamine, DOP = Dopamine, NOR = Norepinephrine, OTH = Other, VAS = Vasopressin
The light-grey shaded region indicates time on XXX therapy. The dark-grey shaded region indicates time on YYY therapy.

With AREAS=6 in the PLOT statement, it'll give you the following graphical display:

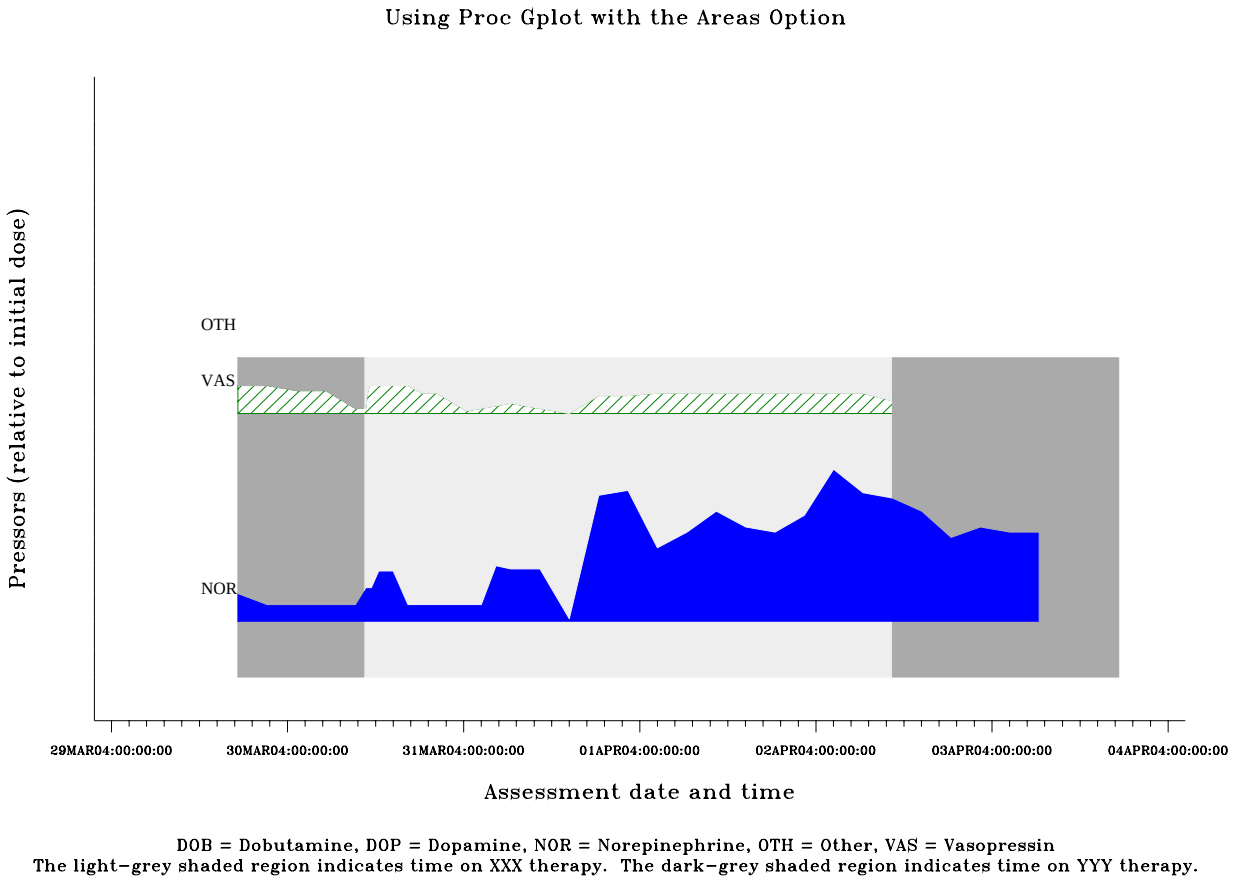
```
plot (maxy1 maxyc1 ydose1
      maxy2 maxyc2 ydose2)*asdt/
     overlay noframe nolegend haxis=axis1 vaxis=axis2 annotate=vasname
     areas=6;
```



DOB = Dobutamine, DOP = Dopamine, NOR = Norepinephrine, OTH = Other, VAS = Vasopressin
The light-grey shaded region indicates time on XXX therapy. The dark-grey shaded region indicates time on YYY therapy.

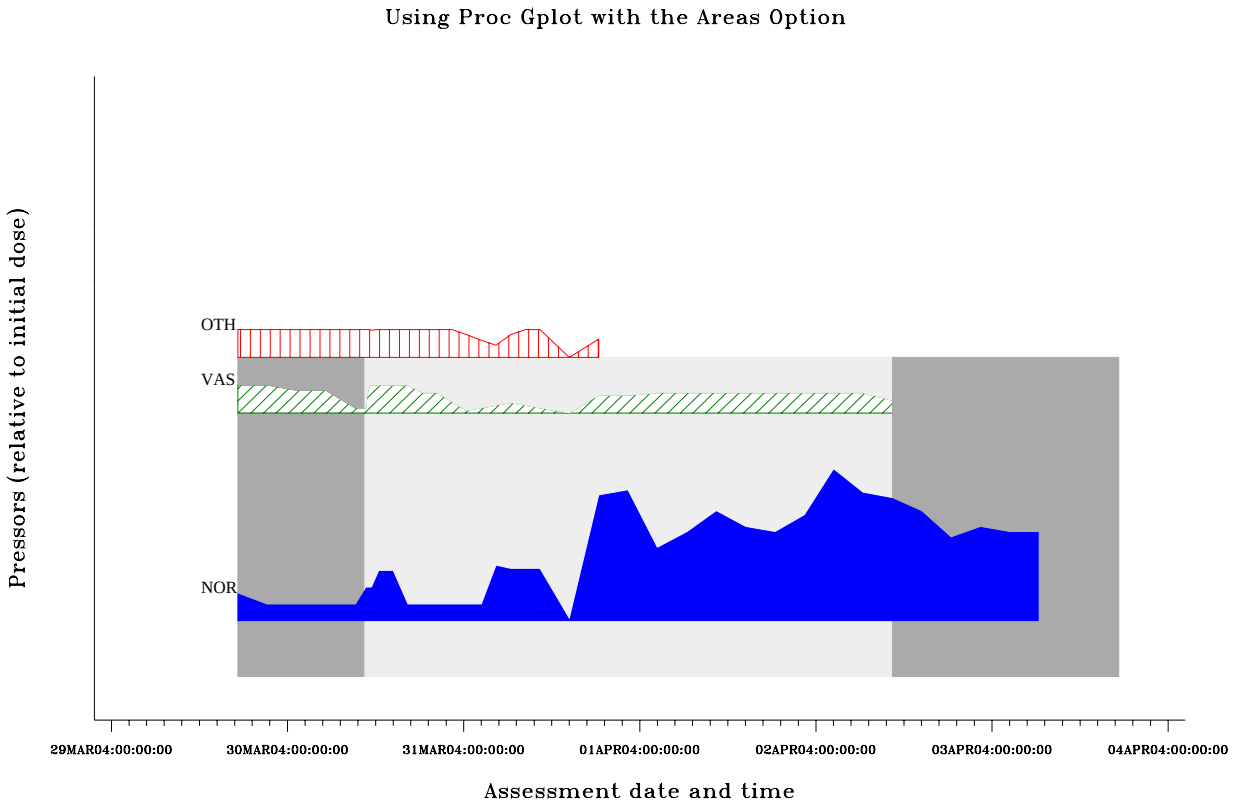
With AREAS=8 in the PLOT statement, it'll give you the following graphical display:

```
plot (maxy1 maxyc1 ydose1
      maxy2 maxyc2 ydose2
      maxy3 maxyc3)*asdt/
     overlay noframe nolegend haxis=axis1 vaxis=axis2 annotate=vasname
     areas=8;
```



With AREAS=9 in the PLOT statement, it'll give you the following graphical display:

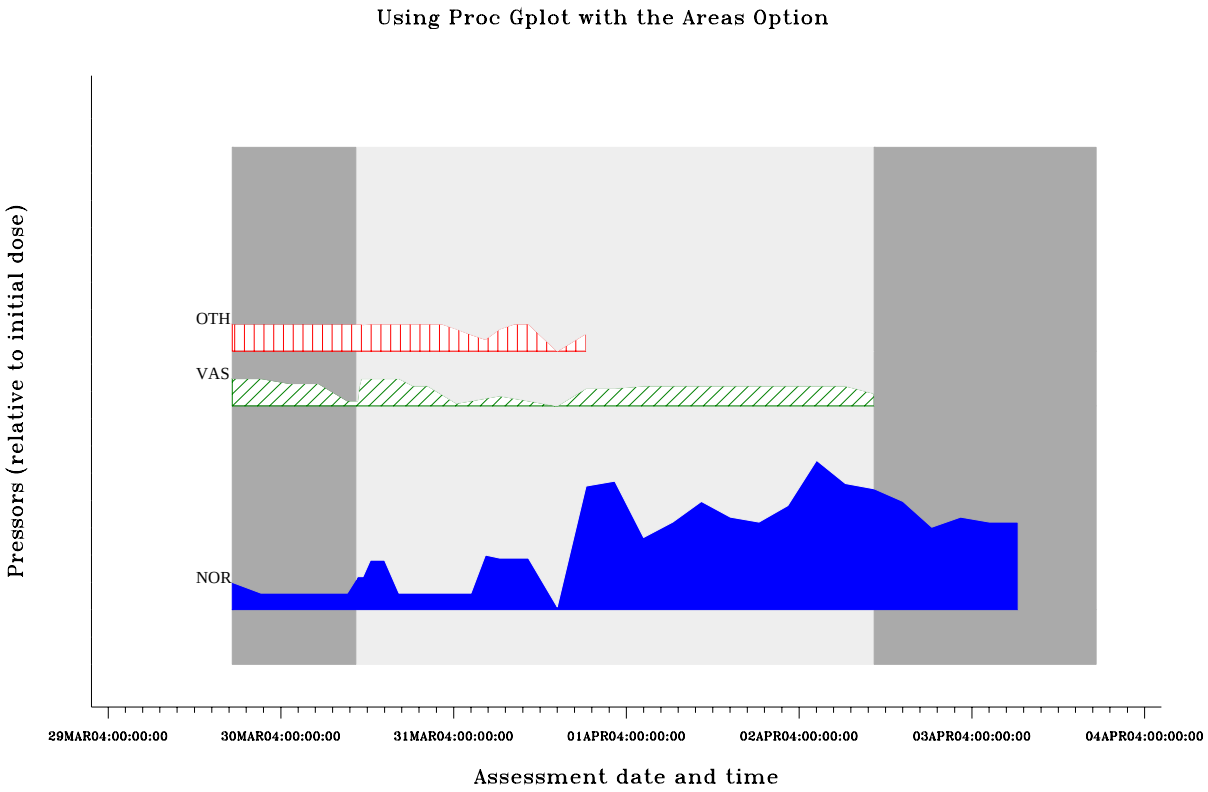
```
plot (maxy1 maxyc1 ydose1
      maxy2 maxyc2 ydose2
      maxy3 maxyc3 ydose3)*asdt/
     overlay noframe nolegend haxis=axis1 vaxis=axis2 annotate=vasname
     areas=9;
```



DOB = Dobutamine, DOP = Dopamine, NOR = Norepinephrine, OTH = Other, VAS = Vasopressin
The light-grey shaded region indicates time on XXX therapy. The dark-grey shaded region indicates time on YYY therapy.

With AREAS=11 in the PLOT statement, it'll give you the following graphical display:

```
plot (maxy1 maxyc1 ydose1
      maxy2 maxyc2 ydose2
      maxy3 maxyc3 ydose3
      maxy7 maxy8)*asdt/
     overlay noframe nolegend haxis=axis1 vaxis=axis2 annotate=vasname
     areas=11;
```



DOB = Dobutamine, DOP = Dopamine, NOR = Norepinephrine, OTH = Other, VAS = Vasopressin
The light-grey shaded region indicates time on XXX therapy. The dark-grey shaded region indicates time on YYY therapy.

CONCLUSION

The AREAS option in PROC GPLOT is a powerful tool to customize your graphical display professionally. This tool is particularly helpful in the clinical trials environment where graphical displays of patient data over time are frequently needed. More examples of these graphical displays for a Data Monitoring Committee for clinical safety are attached.

REFERENCES

SAS Institute (2002), SAS/GRAPH Software: Reference Volume 1, Version 8, Cary, NC: SAS Institute Inc.

SAS Institute (2002), SAS/GRAPH Software: Reference Volume 2 Version 8, Cary, NC: SAS Institute Inc.

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