A GENERALIZED MACRO FOR SURVIVAL ANALYSIS

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Abstract

The use of SAS macro facility in writing a user-friendly generalized application to perform survival analysis on clinical data is illustrated here. The example shows a SAS program with the macro invocation and the SAS outputs generated by the macro, for a CHF study of total mortality with active and control treatment groups. The time interval used in the study was month and the event considered was death.

Introduction

‘MACSURV’ is an enhancement of an original macro by I. Hwang and J. Bolognese (1981). The present version of the macro was developed at HMR Bridgewater and is a part of our in-house system library which houses many such user-friendly macros, designed primarily to reduce programming time and effort in producing accurate, readable and understandable tabular and graphical outputs for clinical/statistical reports. This macro was developed to run on both UNIX and PC-window platforms.

Statistical Methodology

In many clinical trials, the outcome of interest is time to an event, such as time to death or time to first occurrence of morbidity. Other situations include time to reach a threshold such as duration of exercise until pain, or other specified endpoint. The outcomes are the event-free time periods for each patient. These are used to estimate the probability of surviving an interval of time without the occurrence of an event. The probabilities are displayed as Kaplan-Meier survival curves for each treatment group. Various methodologies for comparing survival curves have been developed and are listed on the reference page of the output. These procedures can be divided into two groups: 1) The modified Mantel-Haenszel procedure and Peto’s Logrank test, which provide greater weight to later events, 2) The various Wilcoxon tests, which are more sensitive to differences in the rates of early events.

MACSURV Macro

User Inputs are described to MACSURV by use of Keyword Parameters, some of which have variable names and values as defaults. The important parameters with their defaults and a brief summary of options used are listed here.

The Data (_LAST_) Parameter is the name of the survival analysis dataset. By default, the macro picks up the last dataset created in the program before macro invocation.

A typical dataset to be analyzed would contain patient or subject number, treatment variable, start date of treatment, event variable and event date as variables of interest. A partial dataset and the program with the macro call submitted on the UNIX platform are shown here:

TYPICAL INPUT DATA FOR SURVIVAL ANALYSIS

<table>
<thead>
<tr>
<th>OBS</th>
<th>AN</th>
<th>TRT</th>
<th>DEATH</th>
<th>SDATE</th>
<th>DDATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>04/07/89</td>
<td>06/05/90</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>04/19/89</td>
<td>11/13/90</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>04/29/89</td>
<td>02/23/93</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>05/23/89</td>
<td>02/23/93</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>1</td>
<td>0</td>
<td>05/15/89</td>
<td>02/23/93</td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td>2</td>
<td>1</td>
<td>06/17/89</td>
<td>12/04/90</td>
</tr>
<tr>
<td>7</td>
<td>7</td>
<td>1</td>
<td>0</td>
<td>08/23/89</td>
<td>02/23/93</td>
</tr>
<tr>
<td>8</td>
<td>8</td>
<td>2</td>
<td>1</td>
<td>08/26/89</td>
<td>05/24/90</td>
</tr>
<tr>
<td>9</td>
<td>9</td>
<td>1</td>
<td>0</td>
<td>08/26/89</td>
<td>02/23/93</td>
</tr>
<tr>
<td>10</td>
<td>10</td>
<td>2</td>
<td>0</td>
<td>08/29/89</td>
<td>02/28/93</td>
</tr>
</tbody>
</table>

Program:

```sas
%let progname=progsug;
filename F1 '/users/somml051/survmac/aire.dat';
filename F2 '/users/somml051/survmac/temp.dat';
filename survrnac '/users/somml051/survmac/survmac';
filename pmtout '/users/somml051/survmac/&progname.lst' new;
filename grafout '/users/somml051/survmac/surv.ps' new;
%include survrnac(macsurv.sas);
```

```sas
/* PROC PRINT ;TITLE 'INPUT DATA FOR SURVIVAL ANALYSIS'; */
%MACSURV(data=A,event=death,edate=ddate,sdate=sdate,etime=month,patno=an,
title1=study xxx - CHF study for total mortality, title2=final analysis - as of 02-28-93,
title3=analyses performed by I. K. Hwang, HMR, USA on 10-10-93 retrospectively,
title4=end-point: total mortality (intention-to-treat approach),*/
```

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The macro accommodates up to 6 titles along with footnotes. The Parameter PLNSIZE is the print line size with a default of 132 characters, and could be wider depending on the printers available. TRTLBL_A and TRTLBL_C refer to treatment labels for active and control groups.

Event time interval (ETIME=MONTH) parameter has month as its default. User options include year, week and quarter. Calculations are made for these values inside the macro, based on relative day, defined as (edate-sdate+1).

The macro generates a cover page with a list of references and a summary of results from various statistical tests and analyses. This is followed by life tables for each of the two treatments, i.e., active and control groups, followed by the probability plots (part of SAS print facility) as default set of outputs. In addition, the macro provides the user with an option to plot the survival curves, using the customizing features of the powerful SAS Graph facility, for finer graphs.

Users have a set of graph options to choose from: The HAXIS, VAXIS parameters have a default algorithm to calculate the H-axis and V-axis scales and step size which could be overridden by the user sending a character string as shown in the macro call. Graphs can be viewed on the screen and printed, or a graph-stream-file may be produced in UNIX batch mode to be routed to appropriate printers.

The survival curves were plotted using the powerful Proc Gplot procedure. With the array of options that SAS graph provides, we did not have to use the Annotate feature to draw these curves. Partial code from the macro that produced the graphs is provided in the Appendix to emphasize the versatility of Proc Gplot.

The example in the Appendix shows the outputs from the program above for a CHF study of total mortality with active and control treatment groups. The time interval used in the study was month, and the event considered was death.

Conclusion

The SAS macro facility offers a powerful tool for writing generalized applications like MACSURV, where complex SAS code and SAS procedures can be imbedded and made transparent to the user, thus saving time and programming effort. It facilitates standardization and validation of methods for efficient and global submission of reports.

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Appendix

Sample Code (Partial code from the macro):
Describes the Gplot procedure used to plot the survival curves.

%MACRO LTGRAPH;
%if %length(&ghaxis1) > 0 %then %do;
   PROC PLOT;
PLOT A &etime = T / HAXIS = &ghaxis1
   %if %length(&gvaxis1) > 0 %then %do;
      VAXIS = &gvaxis1
      %end;
   %* ends plotting *;
%end;
%else %do;
   PROC PLOT;
PLOT A &etime = T / HAXIS = &minhl to &maxhl by &stephl
   V AXIS = &minvl to &maxv1 by &stepv1;
%end;
footnote1 "TREATMENTS: A (ACTIVE) = &trtlbl_a; C (CONTROL) = &trtlbl_c;"
%if %length(&foot) > 0 %then %do;
   footnote2 ";&foot";
%end;
run;
%if %length(&ghaxis2) > 0 %then %do;
PLOT B &etime = T / HAXIS = &ghaxis2
   %if %length(&gvaxis2) > 0 %then %do;
      VAXIS = &gvaxis2
      %end;
   %* ends plotting *;
%end;
%else %do;
PLOT B &etime = T / HAXIS = &minh2 to &maxh2 by &steph2
   V AXIS = &minv2 to &maxv2 by &stepv2;
%end;
footnote1 "TREATMENTS: A (ACTIVE) = &trtlbl_a; C (CONTROL) = &trtlbl_c;"
%if %length(&foot) > 0 %then %do;
   footnote2 ";&foot";
%end;
%if %upcase(&grfplot) = YES %then %do;
   %let x1bl=%upcase(&etime);
   %if %length(&ghaxis1) > 0 %then %do;
      %let xorder1=%str(&ghaxis1);
      %end;
   %else %do;
      %let xorder1=%str(&minhl to &maxhl by &stephl);
      %end;
   %if %length(&gvaxis1) > 0 %then %do;
      %let yorder1=%str(&gvaxis1);
      %end;
   %else %do;
      %let yorder1=%str(&minv1 to &maxv1 by &stepv1);
      %end;
   %if %length(&ghaxis2) > 0 %then %do;
      %let xorder2=%str(&ghaxis2);
      %end;
   %else %do;
      %let xorder2=%str(&minh2 to &maxh2 by &steph2);
      %end;
   %if %length(&gvaxis2) > 0 %then %do;
      %let yorder2=%str(&gvaxis2);
      %end;
   %else %do;
      %let yorder2=%str(&minv2 to &maxv2 by &stepv2);
      %end;
%end;

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goptions reset=goptions;
%if (%upcase(&grfpmt)=NOCOLOR or %length(&grfpmt)=0)
and (%upcase(&grfview)=SCREEN or %length(&grfview)=0)
%then
 %do;
 filename grafout pipe 'lp -dps 176bb';
 goptions device=XCOLOR gsfname=grafout
GOUTMODE=REPLACE
gaccess=sasgmed gprolog='252I 0dOd'
gunit=pct htitle=2.5 htext=2 ftext=DUPLEX
 targetdevice=pslmono display PROMPT ROTATE=LANDSCAPE
 PENMOUNTS=14 COLORS=(BL B SALMON G STEEL ROSE
 LIO LG MAGENTA BIB R
 LIL LG GOLD WHITE)
 CBACK=WHITE
 %end;
%else %if %upcase(&grfpmt)=COLOR and
%upcase(&grfview)=SCREEN %then
 %do;
 filename grafout pipe 'lp -dps118bb';
 goptions device=XCOLOR gsfname=grafout
GOUTMODE=REPLACE
gaccess=sasgmed gprolog='252I 0dOd'
gunit=pct htitle=2.5 htext=2 ftext=DUPLEX
 targetdevice=PS COLOR display PROMPT
 ROTATE=LANDSCAPE
 PENMOUNTS=14 COLORS=(BL B SALMON G STEEL ROSE
 LIO LG MAGENTA BIB R
 LIL LG GOLD WHITE)
 CBACK=WHITE
 %end;
%else %if %upcase(&grfpmt)=NOCOLOR or %length(&grfpmt)=0)
and %upcase(&grfview)=NO %then
 %do;
 goptions device=UIVPS rotate gsfname=&grffile
 gaccess=sasgmed gprolog='252I 0dOd'
gunit=pct htitle=2.5 htext=2
 targetdevice=UIVPS nodisplay
 CBACK=WHITE
 %end;
%else %if %upcase(&grfpmt)=COLOR and %upcase(&grfview)=NO
%then
 %do;
 goptions device=PS COLOR gsfname=&grffile
 gaccess=sasgmed gprolog='252I 0dOd'
gunit=pct htitle=2.5 htext=2
 targetdevice=PS COLOR display PROMPT
 ROTATE=LANDSCAPE
 PENMOUNTS=14 COLORS=(BL B SALMON G STEEL ROSE
 LIO LG MAGENTA BIB R
 LIL LG GOLD WHITE)
 CBACK=WHITE
 %end;
%end;

%do tcnt=1 %to 6;
 %if %length(&&gtitle&tcnt)>O %then %do;
 %if &tcnt=1 %then %do; title j=C Ispace=7 "&gtitle&tcnt";
 %end;
 %else %do; title j=C "&gtitle&tcnt"; %end;
 %end;
 %else %do; title &tcnt; %end;

%end;

LEGEND1 LABEL = (POSITION=LEFT J=L F=SIMPLEX
 C=BLACK 'TREATMENTS')
 MODE = RESERVE
 CBORDER=RED
 ACROSS=2
 SHAPE=LINE(1.5)
 VALUE=(F=SIMPLEX J=L C=BLUE "ACTIVE: &trtlbl_a"
 'CONTROL: &trtlbl_c')
 %if %length(&foot)>O %then %do; footnote j=1 "&foot"; %end;
 axis1 order=(&xorder1) minor=none
 label=j=c "&xlab1";
 axis2 label=(angle=90 "CUMULATIVE EVENT FREE
 PROBABILITY") minor=none
 order=(&yorder1);
 axis3 order=(&xorder2) minor=none
 label=j=c "&xlab2";
 axis4 label=(angle=90 "CUMULATIVE EVENT OCC
 PROBABILITY") minor=none
 order=(&yorder2);
 symbol1 color=green interpol=stepjs value=none width=3.0 LINE=1;
 symbol2 color=red interpol=stepjs value=none line=2 width=3.0;
 proc gpplot;
 plot A *&etime=T /
 haxis=axis1
 vaxis=axis2
 CAXIS=BLUE CTTEXT=MAGENTA
 legend=legend1
 run;
 plot B *&etime=T /
 haxis=axis3
 vaxis=axis4
 CAXIS=BLUE CTTEXT=MAGENTA
 legend=legend1
 run; quit;
 %end;
%MEND LTGRAPH;