

SAS/STAT[®] 15.1 User's Guide The LIFETEST Procedure

This document is an individual chapter from SAS/STAT® 15.1 User's Guide.

The correct bibliographic citation for this manual is as follows: SAS Institute Inc. 2018. SAS/STAT® 15.1 User's Guide. Cary, NC: SAS Institute Inc.

SAS/STAT® 15.1 User's Guide

Copyright © 2018, SAS Institute Inc., Cary, NC, USA

All Rights Reserved. Produced in the United States of America.

For a hard-copy book: No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without the prior written permission of the publisher, SAS Institute Inc.

For a web download or e-book: Your use of this publication shall be governed by the terms established by the vendor at the time you acquire this publication.

The scanning, uploading, and distribution of this book via the Internet or any other means without the permission of the publisher is illegal and punishable by law. Please purchase only authorized electronic editions and do not participate in or encourage electronic piracy of copyrighted materials. Your support of others' rights is appreciated.

U.S. Government License Rights; Restricted Rights: The Software and its documentation is commercial computer software developed at private expense and is provided with RESTRICTED RIGHTS to the United States Government. Use, duplication, or disclosure of the Software by the United States Government is subject to the license terms of this Agreement pursuant to, as applicable, FAR 12.212, DFAR 227.7202-1(a), DFAR 227.7202-3(a), and DFAR 227.7202-4, and, to the extent required under U.S. federal law, the minimum restricted rights as set out in FAR 52.227-19 (DEC 2007). If FAR 52.227-19 is applicable, this provision serves as notice under clause (c) thereof and no other notice is required to be affixed to the Software or documentation. The Government's rights in Software and documentation shall be only those set forth in this Agreement.

SAS Institute Inc., SAS Campus Drive, Cary, NC 27513-2414

November 2018

 $SAS^{@}$ 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.

Other brand and product names are trademarks of their respective companies.

SAS software may be provided with certain third-party software, including but not limited to open-source software, which is licensed under its applicable third-party software license agreement. For license information about third-party software distributed with SAS software, refer to http://support.sas.com/thirdpartylicenses.

Chapter 74

The LIFETEST Procedure

$\boldsymbol{\alpha}$	4	4
Co	nte	ntc
w		

Overview: LIFETEST Procedure	5566
Getting Started: LIFETEST Procedure	5567
Syntax: LIFETEST Procedure	5576
PROC LIFETEST Statement	5576
BY Statement	5588
FREQ Statement	5588
ID Statement	5589
STRATA Statement	5589
TEST Statement	5594
TIME Statement	5594
WEIGHT Statement	5595
Details: LIFETEST Procedure	5596
Missing Values	5596
Computational Formulas	5596
Breslow, Fleming-Harrington, and Kaplan-Meier Methods	5596
Life-Table Method	5600
Pointwise Confidence Limits in the OUTSURV= Data Set	5601
Simultaneous Confidence Intervals for Kaplan-Meier Curves	5603
Kernel-Smoothed Hazard Estimate	5605
Comparison of Two or More Groups of Survival Data	5607
Rank Tests for the Association of Survival Time with Covariates	5611
Analysis of Competing-Risks Data	5613
Restricted Mean Analysis	5616
Output Data Sets	5618
OUTCIF= Data Set	5618
OUTSURV= Data Set	5619
OUTTEST= Data Set	5621
Displayed Output	5621
Plot Options Superseded by ODS Graphics	5631
ODS Table Names	5635
ODS Graphics	5637
Modifying the Survival Plots	5639
Examples: LIFETEST Procedure	5640
Example 74.1: Product-Limit Estimates and Tests of Association	5640
Example 74.2: Enhanced Survival Plot and Multiple-Comparison Adjustments	5654
Example 74.3: Life-Table Estimates for Males with Angina Pectoris	5659

Example 74.4: Nonparametric Analysis of Competing-Risks Data	5666
Example 74.5: Restricted Mean Analysis	5673
References	5678

Overview: LIFETEST Procedure

A common feature of lifetime or survival data is the presence of right-censored observations due either to withdrawal of experimental units or to termination of the experiment. For such observations, you know only that the lifetime exceeded a given value; the exact lifetime remains unknown. Such data cannot be analyzed by ignoring the censored observations because, among other considerations, the longer-lived units are generally more likely to be censored. The analysis methodology must correctly use the censored observations in addition to the uncensored observations.

Texts that discuss the survival analysis methodology include Collett (1994), Cox and Oakes (1984); Kalbfleisch and Prentice (1980); Klein and Moeschberger (1997); Lawless (1982); Lee (1992). Users interested in the theory should consult Fleming and Harrington (1991); Andersen et al. (1992).

Usually, a first step in the analysis of survival data is the estimation of the distribution of the survival times. Survival times are often called *failure* times, and *event* times are uncensored survival times. The survival distribution function (SDF), also known as the survivor function, is used to describe the lifetimes of the population of interest. The SDF evaluated at *t* is the probability that an experimental unit from the population will have a lifetime that exceeds *t*—that is,

$$S(t) = \Pr(T > t)$$

where S(t) denotes the survivor function and T is the lifetime of a randomly selected experimental unit. The LIFETEST procedure can be used to compute nonparametric estimates of the survivor function either by the product-limit method (also called the Kaplan-Meier method) or by the life-table method (also called the actuarial method). The life-table estimator is a grouped-data analog of the Kaplan-Meier estimator. The procedure can also compute the Breslow estimator or the Fleming-Harrington estimator, which are asymptotic equivalent alternatives to the Kaplan-Meier estimator.

Some functions closely related to the SDF are the cumulative distribution function (CDF), the probability density function (PDF), and the hazard function. The CDF, denoted F(t), is defined as 1 - S(t) and is the probability that a lifetime does not exceed t. The PDF, denoted f(t), is defined as the derivative of F(t), and the hazard function, denoted h(t), is defined as f(t)/S(t). If the life-table method is chosen, the estimates of the probability density function can also be computed. Plots of these estimates can be produced with ODS Graphics.

An important task in the analysis of survival data is the comparison of survival curves. It is of interest to determine whether the underlying populations of k ($k \ge 2$) samples have identical survivor functions. PROC LIFETEST provides nonparametric k-sample tests based on weighted comparisons of the estimated hazard rate of the individual population under the null and alternative hypotheses. Corresponding to various weight functions, a variety of tests can be specified, which include the log-rank test, Wilcoxon test, Tarone-Ware test, Peto-Peto test, modified Peto-Peto test, and Fleming-Harrington G_{ρ} family of tests. PROC LIFETEST also provides corresponding trend tests to detect ordered alternatives. Stratified tests can be specified to adjust for prognostic factors that affect the events rates in the various populations. A likelihood ratio test, based on an underlying exponential model, is also included to compare the survival curves of the samples.

There are other prognostic variables, called covariates, that are thought to be related to the failure time. These covariates can also be used to construct statistics to test for association between the covariates and the lifetime variable. PROC LIFETEST can compute two such test statistics: censored data linear rank statistics based on the exponential scores and the Wilcoxon scores. The corresponding tests are known as the log-rank test and the Wilcoxon test, respectively. These tests are computed by pooling over any defined strata, thus adjusting for the stratum variables.

One change in SAS 9.2 and later is that the calculation of confidence limits for the quartiles of survival time is based on the transformation specified by the CONFTYPE= option. Another change is that the SURVIVAL statement in SAS 9.1 is folded into the PROC LIFETEST statement; that is, options that were in the SURVIVAL statement can now be specified in the PROC LIFETEST statement. The SURVIVAL statement is no longer needed and it is not documented.

Starting in SAS/STAT 14.1, you can use PROC LIFETEST to carry out nonparametric analysis of competingrisks data. Competing risks arise in studies in which individuals are subject to a number of potential failure events and the occurrence of one event might impede the occurrence of other events. You can use PROC LIFETEST to estimate the cumulative incidence function (CIF), which is the probability subdistribution of failure of a specific cause. If you have more than one sample of competing-risks data, you can use PROC LIFETEST to perform Gray's test (Gray 1988) to compare the CIFs of the samples.

Getting Started: LIFETEST Procedure

You can use the LIFETEST procedure to compute nonparametric estimates of the survivor functions, to compare survival curves, and to compute rank tests for association of the failure time variable with covariates.

For simple analyses, only the PROC LIFETEST and TIME statements are required. Consider a sample of survival data. Suppose that the time variable is T and the censoring variable is C with value 1 indicating censored observations. The following statements compute the product-limit estimate for the sample:

```
proc lifetest;
   time t*c(1);
```

You can use the STRATA statement to divide the data into various strata. A separate survivor function is then estimated for each stratum, and tests of the homogeneity of strata are performed. However, if the GROUP= option is also specified in the STRATA statement, the GROUP= variable is used to identify the samples whose survivor functions are to be compared, and the STRATA variables are used to define the strata for the stratified tests. You can specify covariates (prognostic variables) in the TEST statement, and PROC LIFETEST computes linear rank statistics to test the effects of these covariates on survival.

For example, consider the results of a small randomized trial on rats. Suppose you randomize 40 rats that have been exposed to a carcinogen into two treatment groups (Drug X and Placebo). The event of interest is death from cancer induced by the carcinogen. The response is the time from randomization to death. Four rats died of other causes; their survival times are regarded as censored observations. Interest lies in whether the survival distributions differ between the two treatments.

The following DATA step creates the data set Exposed, which contains four variables: Days (survival time in days from treatment to death), Status (censoring indicator variable: 0 if censored and 1 if not censored), Treatment (treatment indicator), and Sex (gender: F if female and M if male).

```
proc format;
   value Rx 1='Drug X' 0='Placebo';
run;
data exposed;
   input Days Status Treatment Sex $ @@;
   format Treatment Rx.;
   datalines;
179
      1
           1
               F
                    378
                          0
                               1
                                   М
      1
               F
                    355
                          1
256
           1
                               1
                                   М
                                   М
262
      1
           1
                   319
               М
                          1
                               1
               F
256
      1
           1
                   256
                          1
                              1
                                   М
255
      1
           1
               М
                   171
                          1
                               1
                                   F
224
      0
           1
               F
                    325
                          1
                               1
                                   М
225
      1
           1
               F
                    325
                          1
                               1
                                   М
287
      1
           1
               М
                   217
                          1
                               1
                                   F
                                   F
319
      1
           1
               M
                   255
                          1
                               1
264
           1
                   256
                          1
                               1
                                   F
      1
               M
237
      0
           0
               F
                   291
                          1
                               0
                                   М
156
      1
           0
               F
                    323
                          1
                               0
                                   М
270
      1
           0
               М
                   253
                          1
                               0
                                   М
257
           0
                   206
                               0
                                   F
      1
               М
                          1
242
      1
           0
               М
                   206
                          1
                               0
                                   F
157
      1
           0
               F
                   237
                          1
                               0
                                  М
249
      1
           0
               М
                   211
                          1
                                  F
180
               F
                   229
                               0
                                  F
      1
           0
                          1
226
               F
                   234
                               0
                                   F
      1
           0
                          1
                               0
                                   F
268
      0
           0
                   209
                          1
               М
```

PROC LIFETEST is invoked as follows to compute the product-limit estimate of the survivor function for each treatment and to compare the survivor functions between the two treatments:

```
ods graphics on;
proc lifetest data=Exposed plots=(survival(atrisk) logsurv);
   time Days*Status(0);
   strata Treatment;
run;
ods graphics off;
```

In the TIME statement, the survival time variable, Days, is crossed with the censoring variable, Status, with the value 0 indicating censoring. That is, the values of Days are considered censored if the corresponding values of Status are 0; otherwise, they are considered as event times. In the STRATA statement, the variable Treatment is specified, which indicates that the data are to be divided into strata based on the values of Treatment. ODS Graphics must be enabled before producing graphs. Two plots are requested through the PLOTS= option—a plot of the survival curves with at risk numbers and a plot of the negative log of the survival curves.

The results of the analysis are displayed in the following figures.

Figure 74.1 Survivor Function Estimate for the Drug X-Treated Rats

The LIFETEST Procedure

Stratum 1: Treatment = Drug X

	Product-Limit Survival Estimates						
Survival Standard Number Numb							
Days	Survival	Failure	Error	Failed	Left		
0.000	1.0000	0	0	0	20		
171.000	0.9500	0.0500	0.0487	1	19		
179.000	0.9000	0.1000	0.0671	2	18		
217.000	0.8500	0.1500	0.0798	3	17		
224.000	* .			3	16		
225.000	0.7969	0.2031	0.0908	4	15		
255.000				5	14		
255.000	0.6906	0.3094	0.1053	6	13		
256.000				7	12		
256.000				8	11		
256.000	•			9	10		
256.000	0.4781	0.5219	0.1146	10	9		
262.000	0.4250	0.5750	0.1135	11	8		
264.000	0.3719	0.6281	0.1111	12	7		
287.000	0.3187	0.6813	0.1071	13	6		
319.000				14	5		
319.000	0.2125	0.7875	0.0942	15	4		
325.000				16	3		
325.000	0.1062	0.8938	0.0710	17	2		
355.000	0.0531	0.9469	0.0517	18	1		
378.000	* .			18	0		

Note: The marked survival times are censored observations.

Figure 74.2 displays summary statistics of survival times for the Drug X group. It contains estimates of the 25th, 50th, and 75th percentiles and the corresponding 95% confidence limits. The median survival time for rats in this treatment is 256 days. The mean and standard error are also displayed; however, these values are underestimated because the largest observed time is censored and the estimation is restricted to the largest event time.

Figure 74.2 Summary Statistics of Survival Times for Drug X-Treated Rats

	Quartile Estimates					
	95% Confidence Interval					
	Point					
Percent	Estimate	Transform	[Lower	Upper)		
75	319.000	LOGLOG	256.000	355.000		
50	256.000	LOGLOG	255.000	319.000		
25	255.000	LOGLOG	171.000	256.000		

Figure 74.2 continued

	Standard		
Mean	Error		
271.131	11.877		

Note: The mean survival time and its standard error were underestimated because the largest observation was censored and the estimation was restricted to the largest event time.

Figure 74.3 and Figure 74.4 display the survival estimates and the summary statistics of the survival times for Placebo (Treatment=0). The median survival time for rats in this treatment is 235 days.

Figure 74.3 Survivor Function Estimate for Placebo-Treated Rats

The LIFETEST Procedure

Stratum 2: Treatment = Placebo

	Product-Limit Survival Estimates							
	Survival							
_				Standard				
Days		Survival	Failure	Error	Failed	Left		
0.000		1.0000	0	0	0	20		
156.000		0.9500	0.0500	0.0487	1	19		
157.000		0.9000	0.1000	0.0671	2	18		
180.000		0.8500	0.1500	0.0798	3	17		
206.000					4	16		
206.000		0.7500	0.2500	0.0968	5	15		
209.000		0.7000	0.3000	0.1025	6	14		
211.000		0.6500	0.3500	0.1067	7	13		
226.000		0.6000	0.4000	0.1095	8	12		
229.000		0.5500	0.4500	0.1112	9	11		
234.000		0.5000	0.5000	0.1118	10	10		
237.000		0.4500	0.5500	0.1112	11	9		
237.000	*				11	8		
242.000		0.3938	0.6063	0.1106	12	7		
249.000		0.3375	0.6625	0.1082	13	6		
253.000		0.2813	0.7188	0.1038	14	5		
257.000		0.2250	0.7750	0.0971	15	4		
268.000	*				15	3		
270.000		0.1500	0.8500	0.0891	16	2		
291.000		0.0750	0.9250	0.0693	17	1		
323.000		0	1.0000		18	0		

Note: The marked survival times are censored observations.

Figure 74.4 Summary Statistics of Survival Times for Placebo-Treated Rats

Quartile Estimates						
		95%	Con	fidence	Interval	
	Point					
Percent	Estimate	Trans	form	[Lowe	r Upper)	
75	257.000	LOGL	.OG	237.000	323.000	
50	235.500	LOGL	.OG	206.000	253.000	
25	207.500	LOGL	.OG	156.000	229.000	
		S	tanda	ırd		
	M	lean	Err	or		
	235.	.156	10.2	11		

A summary of the number of censored and event observations is shown in Figure 74.5. The figure lists, for each stratum, the number of event and censored observations, and the percentage of censored observations.

Figure 74.5 Number of Event and Censored Observations

Summary of the Number of Censored and Uncensored Values							
Stratum	Treatment	Total	Failed	Censored	Percent Censored		
1	Drug X	20	18	2	10.00		
2	Placebo	20	18	2	10.00		
Total		40	36	4	10.00		

Figure 74.6 displays the graph of the product-limit survivor function estimates versus survival time. The two treatments differ primarily at larger survival times. Note the number of subjects at risk in the plot. You can display the number of subjects at risk at specific time points by using the ATRISK= option.

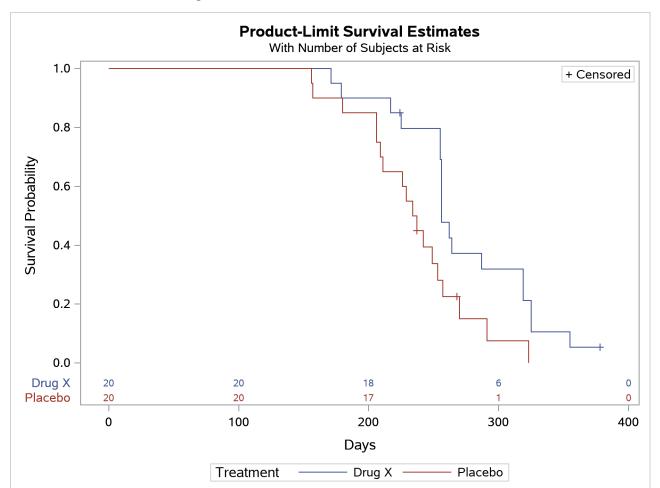


Figure 74.6 Plot of Estimated Survivor Functions

Figure 74.7 displays the graph of the log survivor function estimates versus survival time. Neither curve approximates a straight line through the origin—the exponential model is not appropriate for the survival data.

Note that these graphical displays are generated through ODS. For general information about ODS Graphics, see Chapter 21, "Statistical Graphics Using ODS."

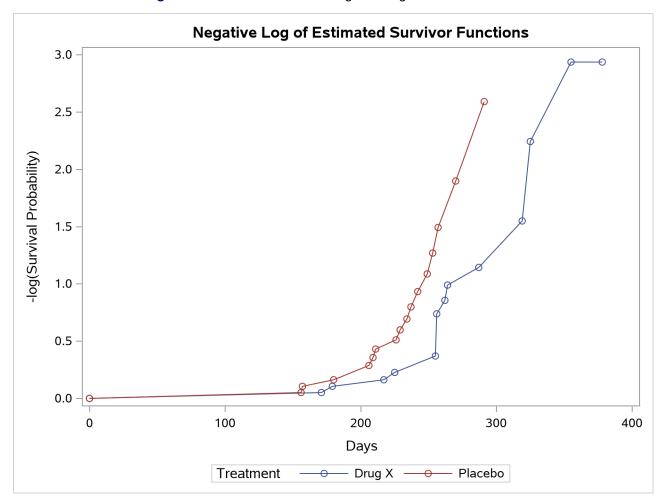


Figure 74.7 Plot of Estimated Negative Log Survivor Functions

Results of the comparison of survival curves between the two treatments are shown in Figure 74.8. The rank tests for homogeneity indicate a significant difference between the treatments (p = 0.0175 for the log-rank test and p = 0.0249 for the Wilcoxon test). Rats treated with Drug X live significantly longer than those treated with Placebo. Since the survival curves for the two treatments differ primarily at longer survival times, the Wilcoxon test, which places more weight on shorter survival times, becomes less significant than the log-rank test. As noted earlier, the exponential model is not appropriate for the given survival data; consequently, the result of the likelihood ratio test should be ignored.

Figure 74.8 Results of the Two-Sample Tests

Test of Equality over Strata							
Pr							
Test	Chi-Square	DF	Chi-Square				
Log-Rank	5.6485	1	0.0175				
Wilcoxon	5.0312	1	0.0249				
-2Log(LR)	0.1983	1	0.6561				

Next, suppose male rats and female rats are thought to have different survival rates, and you want to assess the treatment effect while adjusting for the gender differences. By specifying the variable Sex in the STRATA statement as a stratifying variable and by specifying the variable Treatment in the GROUP= option, you can carry out a stratified test to test Treatment while adjusting for Sex. The test statistics are computed by pooling over the strata defined by the values of Sex, thus controlling for the effect of Sex. The NOTABLE option is added to the PROC LIFETEST statement as follows to avoid estimating a survival curve for each gender:

```
proc lifetest data=Exposed notable;
   time Days*Status(0);
   strata Sex / group=Treatment;
run;
```

Results of the stratified tests are shown in Figure 74.9. The treatment effect is statistically significant for both the log-rank test (p = 0.0071) and the Wilcoxon test (p = 0.0150). As compared to the results of the unstratified tests in Figure 74.8, the significance of the treatment effect has been sharpened by controlling for the effect of the gender of the subjects.

Figure 74.9 Results of the Stratified Two-Sample Tests

The LIFETEST Procedure

Stratified Test of Equality over Group						
Pr >						
Test	Chi-Square	DF	Chi-Square			
Log-Rank	7.2466	1	0.0071			
Wilcoxon	5.9179	1	0.0150			

Since Treatment is a binary variable, another way to study the effect of Treatment is to carry out a censored linear rank test with Treatment as an independent variable. This test is less popular than the two-sample test; nevertheless, in situations where the independent variables are continuous and are difficult to discretize, it might be infeasible to perform a *k*-sample test. To compute the censored linear rank statistics to test the Treatment effect, Treatment is specified in the TEST statement as follows:

```
proc lifetest data=Exposed notable;
  time Days*Status(0);
  test Treatment;
run;
```

Results of the linear rank tests are shown Figure 74.10. The *p*-values are very similar to those of the two-sample tests in Figure 74.8.

Figure 74.10 Results of Linear Rank Tests of Treatment

The LIFETEST Procedure

Univariate Chi-Squares for the Wilcoxon Test								
Test Standard Pr > Variable Statistic Error Chi-Square Chi-Square								
Treatment	3.9525	1.7524	5.0875	0.0241				
Univa	riate Chi-S	Squares for	the Log-Ran	ık Test				
	Test	Standard		Pr >				
Variable	Statistic	Error	Chi-Square	Chi-Square				
Treatment	6.2708	2.6793	5.4779	0.0193				

With Sex as a prognostic factor that you want to control, you can compute a stratified linear rank statistic to test the effect of Treatment by specifying Sex in the STRATA statement and Treatment in the TEST statement as in the following program. The TEST=NONE option is specified in the STRATA statement to suppress the two-sample tests for Sex.

```
proc lifetest data=Exposed notable;
   time Days*Status(0);
   strata Sex / test=none;
   test Treatment;
run;
```

Results of the stratified linear rank tests are shown in Figure 74.11. The *p*-values are very similar to those of the stratified tests in Figure 74.9.

Figure 74.11 Results of Stratified Linear Rank Tests of Treatment

The LIFETEST Procedure

Univariate Chi-Squares for the Wilcoxon Test						
Variable		Standard Error	Chi-Square	Pr > Chi-Square		
Treatment	4.2372	1.7371	5.9503	0.0147		
Univariate Chi-Squares for the Log-Rank Test						
Univa	riate Chi-S	Squares for	the Log-Ran	ık Test		
Univa		Squares for Standard	the Log-Ran	ık Test Pr >		
		Standard	the Log-Ran	Pr>		

Syntax: LIFETEST Procedure

The following statements are available in the LIFETEST procedure:

```
PROC LIFETEST < options > ;
BY variables;
FREQ variable < / option > ;
ID variables;
STRATA variable < (list) > < ... variable < (list) >> < / options > ;
TEST variables;
TIME variable < * censor(list) > < / option > ;
WEIGHT variable;
```

The simplest use of PROC LIFETEST is to request the nonparametric estimates of the survivor function for a sample of survival times. In such a case, only the PROC LIFETEST statement and the TIME statement are required. You can use the STRATA statement to divide the data into various strata. A separate survivor function is then estimated for each stratum, and tests of the homogeneity of strata are performed. However, if the GROUP= option is also specified in the STRATA statement, stratified tests are carried out to test the k samples that are defined by the GROUP= variable while controlling for the effect of the STRATA variables. You can specify covariates in the TEST statement. PROC LIFETEST computes linear rank statistics to test the effects of these covariates on survival.

The PROC LIFETEST statement invokes the procedure. All statements except the TIME statement are optional, and there is no required order for the statements that follow the PROC LIFETEST statement. The TIME statement specifies the variables that define the survival time and censoring indicator. The STRATA statement specifies a variable or set of variables that define the strata for the analysis. The TEST statement specifies a list of numeric covariates to be tested for their association with the response survival time. Each variable is tested individually, and a joint test statistic is also computed. The ID statement provides a list of variables whose values identify observations in the product-limit, Breslow, or Fleming-Harrington estimates. When only the TIME statement appears, no strata are defined and no tests of homogeneity are performed.

PROC LIFETEST Statement

```
PROC LIFETEST < options > ;
```

The PROC LIFETEST statement invokes the LIFETEST procedure. Optionally, this statement identifies an input data set and an output data set, and specifies the computation details of the survivor function estimation. Table 74.1 summarizes the *options* available in the PROC LIFETEST statement. These *options* are described in alphabetic order.

ODS Graphics is the preferred method of creating graphs. Many new features have been added to the ODS Graphics plots. For example, you can display the number of subjects at risk in a survival plot. For information about ODS Graphics options, see the PLOTS= option.

If no plotting options are specified, PROC LIFETEST displays a table that shows the product-limit estimate of the survivor function. If ODS Graphics is enabled, PROC LIFETEST also displays a plot of the estimated survivor function. Other *options* for displaying the estimated survivor function are documented in the section "Plot Options Superseded by ODS Graphics" on page 5631.

 Table 74.1
 Options Available in the PROC LIFETEST Statement

	<u>'</u>	
Option	Description	
Input and Output Da	ata Sets	
DATA=	Specifies the input SAS data set	
OUTCIF=	Names an output data set to contain cumulative incidence function	
OLUMULIDA	(CIF) estimates	
OUTSURV=	Names an output data set to contain survivor function estimates	
OUTTEST=	Names an output data set to contain rank test statistics for association of survival time with covariates	
Nonparametric Estin	nation	
ERROR=	Specifies the variance method of the CIF estimator	
INTERVALS=	Specifies interval endpoints for life-table estimates	
NELSON	Adds the Nelson-Aalen estimates	
METHOD=	Specifies the method to compute survivor function	
NINTERVAL=	Specifies the number of intervals for life-table estimates	
RMST	Performs the restricted mean survival time (RMST) analysis	
RMTL	Performs the restricted mean time lost (RMTL) analysis	
WIDTH=	Specifies the width of intervals for life-table estimates	
Confidence Limits fo	or Survivorship	
ALPHA=	Sets the confidence level for interval estimation estimates	
BANDMAXTIME=	Specifies the maximum time for confidence band	
BANDMINTIME=	Specifies the minimum time for confidence band	
CONFBAND=	Specifies the type of confidence band in the OUTSURV= data set	
CONFTYPE=	Specifies the transformation applied to the survivor function to	
	obtain confidence limits	
ODS Graphics		
MAXTIME=	Specifies the maximum time value for plotting	
PLOTS=	Specifies plots to display	
Control Output		
ATRISK	Adds the number of subjects at risk to the survival estimate table	
INTERVALS=	Displays only the estimate for the smallest time in each interval	
NOLEFT	Suppresses the Number Left and Number Event columns in the	
	survival estimate table	
NOPRINT	Suppresses the display of printed output	
NOTABLE	Suppresses the display of survival function estimates	
REDUCEOUT	Lists only INTERVALS= or TIMELIST= observations in the OUT-	
	SURV= data set	
TIMELIST=	Lists the time points at which to display the survival estimate	
Miscellaneous		
ALPHAQT=	Sets the confidence level for survival time quartiles	
CIFVAR	Displays the variance of the CIF estimator	
MISSING	Allows missing values to be a stratum level	

Table 74.1 continued

Option	Description
SINGULAR=	Sets the tolerance for testing singularity of covariance matrix of rank statistics
STDERR	Outputs the standard error for the survival estimators to the OUT-SURV= data set
TIMELIM=	Specifies the time limit used to estimate the mean survival time and its standard error

$ALPHA=\alpha$

specifies the level of significance α for the $100(1-\alpha)\%$ confidence intervals for the survivor, hazard, and density functions. For example, the option ALPHA=0.05 requests the 95% confidence limits for the survivor function. The default value is 0.05.

ALPHAQT= α

specifies the significance level α for the 100(1 – α)% confidence intervals for the quartiles of the survival time. For example, the option ALPHAQT=0.05 requests a 95% confidence interval for the quartiles of the survival time. The default value is 0.05.

ATRISK

adds a column that represents the number of subjects at risk to the survival estimate table. Also added is a column that represents the number of events at each observed time. This option has no effect for the life-table method.

BANDMAXTIME=value

BANDMAX=value

specifies the maximum time for the confidence bands. The default is the largest observed event time. If the specified BANDMAX= time exceeds the largest observed event time, it is truncated to the largest observed event time.

BANDMINTIME=value

BANDMIN=value

specifies the minimum time for the confidence bands. The default is the smallest observed event time. For the equal-precision band, if the BANDMIN= value is less than the smallest observed event time, it is defaulted to the smallest observed event time.

CIFVAR

displays the variance of the cumulative incidence function (CIF) estimator for competing-risks data. By default, PROC LIFETEST displays the standard error of the CIF estimator.

CONFBAND=keyword

specifies the confidence bands to be output to the OUTSURV= data set. Confidence bands are available for METHOD=KM, METHOD=BRESLOW, or METHOD=FH. You can use the following keywords:

ALL outputs both the Hall-Wellner and the equal-precision confidence bands.

EP outputs the equal-precision confidence bands.

HW outputs the Hall-Wellner confidence bands.

CONFTYPE=*keyword*

specifies the transformation applied to S(t) to obtain the pointwise confidence intervals and the confidence bands for the survivor function in addition to the confidence intervals for the quartiles of the survival times. The following *keywords* can be used; the default is CONFTYPE=LOGLOG.

ASINSQRT the arcsine-square root transformation,

$$g(x) = \sin^{-1}(\sqrt{x})$$

LOGLOG the log-log transformation,

$$g(x) = \log(-\log(x))$$

This is also referred to as the log cumulative hazard transformation since it applies the logarithmic function to the cumulative hazard function. Collett (1994) and Lachin (2000) refer to it as the complementary log-log transformation.

LINEAR the identity transformation,

$$g(x) = x$$

LOG the logarithmic transformation,

$$g(x) = \log(x)$$

LOGIT the logit transformation,

$$g(x) = \log\left(\frac{x}{1-x}\right)$$

DATA=SAS-data-set

names the SAS data set used by PROC LIFETEST. By default, the most recently created SAS data set is used.

ERROR=AALEN | DELTA

specifies the method of calculating the variance of the CIF estimator. When ERROR=AALEN, the variance estimator is based on the theory of counting process (Aalen 1978). When ERROR=DELTA, the delta method is used to compute the variance. By default, ERROR=AALEN. For more information, see the section "Estimation of the CIF" on page 5614.

INTERVALS=values

specifies a list of interval endpoints for the life-table method. These endpoints must all be nonnegative numbers. The initial interval is assumed to start at zero whether or not zero is specified in the list. Each interval contains its lower endpoint but does not contain its upper endpoint. When this option is used with METHOD=KM, METHOD=BRESLOW, or METHOD=FH, it reduces the number of survival estimates displayed by showing only the estimates for the smallest time within each specified interval. The INTERVALS= option can be specified in any of the following ways:

• a list separated by blanks INTERVALS=1 3 5 7

• a list separated by commas INTERVALS=1, 3, 5, 7

• x to y INTERVALS=1 to 7

• x to y BY z INTERVALS=1 to 7 by 1

• a combination of the above INTERVALS=1,3 to 5,7

For example, the specification

produces the set of intervals

$$\{[0,5), [5,10), [10,20), [20,30), [30,\infty)\}$$

MAXTIME=value

specifies the maximum value of the time variable allowed on the plots so that outlying points do not determine the scale of the time axis of the plots. This option affects only the displayed plots and has no effect on any calculations.

METHOD=*type*

specifies the method to be used to compute the survival function estimates. Valid values for *type* are as follows:

BRESLOW

specifies that the Breslow estimates be computed. The Breslow estimator is the exponentiation of the negative Nelson-Aalen estimator of the cumulative hazard function.

FΗ

specifies that the Fleming-Harrington (FH) estimates be computed. The FH estimator is a tiebreaking modification of the Breslow estimator. If there are no tied event times, this estimator is the same as the Breslow estimator.

KM

PL

specifies that Kaplan-Meier estimates (also known as the product-limit estimates) be computed.

ACT

LIFE

LT

specifies that life-table estimates (also known as actuarial estimates) be computed.

By default, METHOD=KM.

MISSING

treats missing values as valid values for the stratum variables. By default, PROC LIFETEST does not use observations that have a missing value in any stratum variables. For more information, see the section "Missing Values" on page 5596.

NELSON

AALEN

produces the Nelson-Aalen estimates of the cumulative hazards and the corresponding standard errors. This option is ignored if METHOD=LT is specified.

NINTERVAL=value

specifies the number of intervals used to compute the life-table estimates of the survivor function. This parameter is overridden by the WIDTH= option or the INTERVALS= option. When you specify the NINTERVAL= option, PROC LIFETEST tries to find an interval that results in round numbers for the endpoints. Consequently, the number of intervals can be different from the number requested. Use the INTERVALS= option to control the interval endpoints. The default is NINTERVAL=10.

NOLEFT

suppresses the Number Left and Number Event columns in the survival estimate table. This option has no effect for the life-table estimate.

NOPRINT

suppresses the display of output. This option is useful when only an output data set is needed. It temporarily disables the Output Delivery System (ODS); For more information about ODS, see Chapter 20, "Using the Output Delivery System."

NOTABLE

suppresses the display of survival function estimates. Only the number of censored and event times, plots, and test results is displayed.

OUTCIF=SAS-data-set

creates an output SAS data set to contain the point and interval estimates for the cumulative incidence function (CIF). The data set also contains the number of subjects at risk, the number of events of interest, and the number of events of all types. For more information about the contents of the OUTCIF= data set, see the section "OUTCIF= Data Set" on page 5618.

OUTSURV=SAS-data-set

OUTS=SAS-data-set

creates an output SAS data set to contain the estimates of the survival function and corresponding confidence limits for all strata. For more information about the contents of the OUTSURV= data set, see the section "OUTSURV= Data Set" on page 5619.

OUTTEST=SAS-data-set

OUTT=SAS-data-set

creates an output SAS data set to contain the overall chi-square test statistic for association with failure time for the variables in the TEST statement, the values of the univariate rank test statistics for each variable in the TEST statement, and the estimated covariance matrix of the univariate rank test statistics. For more information about the contents of the OUTTEST= data set, see the section "OUTTEST= Data Set" on page 5621.

RMST<(options)>

performs the analysis of the restricted mean survival time (RMST). You can specify the following *options*:

BC

applies bias correction to standard error estimation.

TAU=value

specifies the upper time limit of the RMST. The *value* must be positive. The default is the largest observed time.

RMTL<(options)>

performs the analysis of the restricted mean time lost (RMTL). You can specify the following options:

BC

applies bias correction to standard error estimation.

specifies the upper time limit of the RMTL. The *value* must be positive. The default is the largest observed time.

```
PLOTS<(global-plot-options)>=plot-request <(options)>
```

```
PLOTS<(global-plot-options)>=(plot-request < (options)> < ... plot-request < (options)>>)
```

controls the plots produced using ODS Graphics. When you specify only one *plot-request*, you can omit the parentheses around the *plot-request*. Here are some examples:

```
plots=none
plots=(survival(atrisk=100 to 350 by 50) logsurv)
plots(only)=hazard
```

ODS Graphics must be enabled before plots can be requested. For example:

```
ods graphics on;
proc lifetest plots=survival(atrisk);
   time T*Status(0);
run;
ods graphics off;
```

For more information about enabling and disabling ODS Graphics, see the section "Enabling and Disabling ODS Graphics" on page 623 in Chapter 21, "Statistical Graphics Using ODS."

If ODS Graphics is enabled but you do not specify the PLOTS= option, PROC LIFETEST produces a plot of the survivor function estimates, unless you use the FAILCODE option in the TIME statement to stipulate a competing-risks analysis. In such a case, PROC LIFETEST creates a plot of the cumulative incidence function (CIF) estimates.

You can specify the following *global-plot-option*:

ONLY

specifies that only the specified plots in the list be produced; otherwise, the default survivor function plot is also displayed. This option has no effect if you use the FAILCODE option in the TIME statement to stipulate a competing-risks analysis.

The *plot-requests* and *plot-request options* include the following.

ALL

produces all appropriate plots. For METHOD=KM, METHOD=BRESLOW, or METHOD=FH, specifying PLOTS=ALL is equivalent to specifying PLOTS=(SURVIVAL LOGSURV LOGLOGS); for the life-table method, specifying PLOTS=ALL is equivalent to specifying PLOTS=(SURVIVAL LOGSURV LOGLOGS DENSITY HAZARD). For a competing-risks analysis, specifying PLOTS=ALL is equivalent to specifying PLOTS=CIF.

CIF<(cif-options)>

plots the cumulative incidence function (CIF) estimates. If you specify a STRATA statement without the GROUP= option, PROC LIFETEST overlays the cumulative incidence curves of the strata in the same plot. If you specify a STRATA statement with the GROUP= option, PROC LIFETEST produces a panel plot, with one cell per stratum, and each cell contains the cumulative incidence curves for the groups within the given stratum.

You can specify the following *cif-options*:

CL

displays pointwise confidence limits for CIF.

TEST

displays the p-value of Gray's test (Gray 1988) for testing the homogeneity of CIFs.

HAZARD < (hazard-options) >

H < hazard-options >

plots the estimated hazard functions. Kernel-smoothed estimates are produced for METHOD=KM, METHOD=BRESLOW, or METHOD=FH. You can specify the following *hazard-options*, but only the CL option can be used for the life-table method:

BANDWIDTH=bandwidth-option

BW=bandwidth-option

specifies what bandwidth is chosen for the kernel-smoothing and how it is chosen. You can specify one of the following *bandwidth-options*.

value

sets the bandwidth to the given *value*.

numeric-list

selects the bandwidth from the given *numeric-list* that minimizes the mean integrated squared error.

RANGE(lower, upper)

selects the bandwidth from the interval (*lower, upper*) that minimizes the mean integrated squared error. PROC LIFETEST uses the golden section search algorithm to find the minimum. If there is more than one local minimum in the interval, there is no guarantee that the local minimum found is also the global minimum.

See the section "Optimal Bandwidth" on page 5606 for details about the mean integrated squared error. If the BANDWIDTH= option is not specified, the default is BANDWIDTH= RANGE(0.2b,20b), where $b = \frac{g_u - g_l}{8n \cdot 2}$, g_l and g_u are the values of the GRIDL= and GRIDU= options, respectively, and n is the total number of noncensored observations.

CL

displays the pointwise confidence limits for the smoothed hazard.

GRIDL=number

specifies the lower grid limit for the kernel-smoothed estimate. The default value is the time origin.

GRIDU=number

specifies the upper grid limit for the kernel-smoothed estimate. The default value equals the maximum event time.

KERNEL=*kernel*-option

specifies the kernel used. You can specify the following kernel-options:

BIWEIGHT

BW

$$K_{\text{BW}}(x) = \frac{15}{16}(1 - x^2)^2, \qquad -1 \le x \le 1$$

EPANECHNIKOV

Ε

$$K_{\rm E}(x) = \frac{3}{4}(1 - x^2), \qquad -1 \le x \le 1$$

UNIFORM

U

$$K_{\rm U}(x) = \frac{1}{2}, \qquad -1 \le x \le 1$$

By default, KERNEL=EPANECHNIKOV.

NGRID=number

specifies the number of grid points. By default, NGRID=101.

NMINGRID=*number*

specifies the number of grid points that are used in determining the mean integrated square error (MISE). By default, NMINGRID=51.

LOGLOGS

LLS

plots the log of negative log of estimated survivor functions versus the log of time.

LOGSURV

LS

plots the negative log of estimated survivor functions versus time.

NONE

suppresses all plots.

plots the estimated probability density functions (life-table method only). Pointwise confidence limits are displayed optionally by specifying the CL option.

RMST<CL>

plots the restricted mean survival time (RMST) versus τ values. If you specify a STRATA statement without the GROUP= option, PROC LIFETEST overlays the RMST curves of the strata in the same plot. If you specify a STRATA statement with the GROUP= option, the procedure produces a panel plot that has one cell per stratum, and each cell contains the RMST curves for the groups within the given stratum. The CL option displays pointwise confidence limits for the RMST.

RMTL<CL>

plots the restricted mean survival time (RMTL) versus τ values. If you specify a STRATA statement without the GROUP= option, PROC LIFETEST overlays the RMTL curves of the strata in the same plot. If you specify a STRATA statement with the GROUP= option, the procedure produces a panel plot that has one cell per stratum, and each cell contains the RMTL curves for the groups within the given stratum. The CL option displays pointwise confidence limits for the RMTL.

SURVIVAL < (survival-options) >

S < (survival-options) >

plots the estimated survivor functions. Censored times are plotted as a plus sign on the Kaplan-Meier, Breslow, or Fleming-Harrington survival curves unless the NOCENSOR option is specified. You can customize the display by using the following *survival-options*. If these options are not sufficient for your purposes, you can customize the survival plot by modifying its graph template. (For more information, see the section "Modifying the Survival Plots" on page 5639.)

ATRISK < (options) > < = number-list >

displays the numbers of subjects at risk at the given times. You can specify the following *options*:

ATRISKTICK

ATRISKLABEL

guarantees that tick values are shown on the time axis for those times when the numbers of subjects at risk are displayed. If this option is not specified, you might not be able to tell at exactly which times the number of subjects at risk are displayed. If the ATRISKTICKONLY option is also specified, it takes precedence over the ATRISKTICK option.

ATRISKTICKONLY

specifies that tick values on the time axis be shown only at the times that are given in the ATRISK= *list*. If the ATRISKTICK option is also specified, it is ignored; that is, ATRISKTICKONLY takes precedence over ATRISKTICK.

MAXLEN=n

specifies the number of characters n that are allowed for displaying the stratum labels. If n is greater than or equal to the maximum length of the stratum labels, the stratum labels are used in the at-risk display; otherwise, the stratum numbers are used. The default is MAXLEN=12.

OUTSIDE<(p)>

specifies that the at-risk table be drawn outside the plot area. PROC LIFETEST uses a graph template that has a two-row lattice layout. The upper cell displays the survival plot, and the bottom cell displays the at-risk table. You can specify an optional number p that represents the fractional proportion of the at-risk table height relative to the overall grid height, but that specification is not necessary. By default, p is the preferred row weight in the GTL layout lattice statement that ensures that the plot displays well. If you specify a value of p too small for the table to be properly displayed, some of the rows might get cut off.

The *number-list* identifies the times when the numbers at risk are displayed. If the *number*list is not specified, PROC LIFETEST displays the number of subjects at risk at each default tick value on the time axis of the survival plot.

CB <=keyword>

displays the confidence bands (that is, simultaneous confidence intervals) for the survivor functions. You can specify one of the following *keywords*. The default is CB=HW.

ALL

displays both the equal-precision and the Hall-Wellner bands.

EP

displays the equal-precision band.

HW

displays the Hall-Wellner confidence band.

CL

displays the pointwise confidence limits for the survivor functions.

FAILURE

F

changes all the displays for survivor functions to those for the failure functions. For example, if both the FAILURE and CL options are specified, the plot displays the failure curves in addition to the pointwise confidence limits for the failure functions.

NOCENSOR

suppresses the plotting of the censored times on a Kaplan-Meier, Breslow, or Fleming-Harrington survival curve.

STRATA=strata-option

specifies how to display the survival/failure curves for multiple strata. This option has no effect if there is only one stratum. You can choose one of the following strata options:

INDIVIDUAL

UNPACK

specifies that a separate plot be displayed for each stratum.

OVERLAY

specifies that the survival/failure curves for the strata be overlaid in one plot.

PANEL

specifies that separate plots for the strata be organized into panels of two or four plots, depending on the number of strata.

The default is STRATA=OVERLAY.

TEST

displays the p-value of a homogeneity test specified in the STRATA statement. If more than one test is produced, the test is chosen in the following order: LOGRANK, WILCOXON, TARONE, PETO, MODPETO, FLEMING, and LR.

REDUCEOUT

specifies that the OUTSURV= data set contain only those observations that are included in the INTERVALS= or TIMELIST= option. This option has no effect if the OUTSURV= option is not specified. It also has no effect if neither the INTERVALS= option nor the TIMELIST= option is specified.

SINGULAR=value

specifies the tolerance for testing singularity of the covariance matrix for the rank test statistics. The test requires that a pivot for sweeping a covariance matrix be at least this number times a norm of the matrix. The default value is 1E–12.

STDERR

specifies that the standard error of the survivor function (SDF_STDERR) be output to the OUTSURV= data set. If the life-table method is used, the standard error of the density function (PDF_STDERR) and the standard error of the hazard function (HAZ_STDERR) are also output.

TIMELIM=time-limit

specifies the time limit used in the estimation of the mean survival time and its standard error. The mean survival time can be shown to be the area under the Kaplan-Meier survival curve. However, if the largest observed time in the data is censored, the area under the survival curve is not a closed area. In such a situation, you can choose a time limit L and estimate the mean survival curve limited to a time L (Lee 1992, pp. 72–76). This option is ignored if the largest observed time is an event time. Valid *time-limit* values are as follows:

EVENT

LET

specifies that the time limit L be the largest event time in the data. TIMELIM=EVENT is the default.

OBSERVED

LOT

specifies that the time limit L be the largest observed time in the data.

number

specifies that the time limit L be the given *number*. The *number* must be positive and at least as large as the largest event time in the data.

TIMELIST=number-list

specifies a list of time points at which the Kaplan-Meier estimates are displayed. The time points are listed in the column labeled Timelist. Since the Kaplan-Meier survival curve is a decreasing step function, each given time point falls in an interval that has a constant survival estimate. The event time that corresponds to the beginning of the time interval is displayed along with its survival estimate.

WIDTH=value

sets the width of the intervals used in the life-table calculation of the survival function. This parameter is overridden by the INTERVALS= option.

BY Statement

BY variables:

You can specify a BY statement in PROC LIFETEST to obtain separate analyses of observations in groups that are defined by the BY variables. When a BY statement appears, the procedure expects the input data set to be sorted in order of the BY variables. If you specify more than one BY statement, only the last one specified is used.

If your input data set is not sorted in ascending order, use one of the following alternatives:

- Sort the data by using the SORT procedure with a similar BY statement.
- Specify the NOTSORTED or DESCENDING option in the BY statement in the LIFETEST procedure. The NOTSORTED option does not mean that the data are unsorted but rather that the data are arranged in groups (according to values of the BY variables) and that these groups are not necessarily in alphabetical or increasing numeric order.
- Create an index on the BY variables by using the DATASETS procedure (in Base SAS software).

The BY statement is more efficient than the STRATA statement for defining strata in large data sets. However, if you use the BY statement to define strata, PROC LIFETEST does not pool over strata for testing the association of survival time with covariates, nor does it test for homogeneity across the BY groups.

When the life-table method is used to estimate survivor functions, each BY group might have a different set of intervals. To make intervals the same across BY groups, use the INTERVALS= or WIDTH= option in the PROC LIFETEST statement.

For more information about BY-group processing, see the discussion in SAS Language Reference: Concepts. For more information about the DATASETS procedure, see the discussion in the Base SAS Procedures Guide.

FREQ Statement

FREQ variable </option>;

The FREQ statement identifies a variable that contains the frequency of occurrence of each observation. PROC LIFETEST treats each observation as if it appeared n times, where n is the value of the FREQ variable for the observation. The FREQ statement is useful for producing life tables when the data are already in the form of a summary data set. If it is not an integer, it is truncated to an integer unless the NOTRUNCATE option is specified. If it is missing or less than or equal zero, the observation is not used.

The following *option* can be specified in the FREQ statement after a slash (/):

NOTRUNCATE

NOTRUNC

specifies that the frequency values are not truncated to integers. This option does not apply to the Fleming-Harrington estimator (METHOD=FH).

ID Statement

ID variables:

The ID statement identifies *variables* whose values are used to label the observations of the Kaplan-Meier, Breslow, or Fleming-Harrington survivor function estimates. SAS format statements can be used to format the values of the ID variables.

STRATA Statement

```
STRATA variable < (list) > < . . . variable < (list) >> < / options > ;
```

The STRATA statement identifies the variables that determine the strata levels. Strata are formed according to the nonmissing values of these variables. The MISSING option can be used to allow missing values as a valid stratum level. Other options enable you to specify various *k*-sample tests, stratified tests, or trend tests and to make multiple-comparison adjustments for paired differences.

In the preceding syntax, *variable* is a variable whose values determine the stratum levels, and *list* is a list of endpoints for a numeric variable. The values for *variable* can be formatted or unformatted. If *variable* is a character variable, or if *variable* is numeric and no list appears, then the strata are defined by the unique values of the STRATA *variable*. More than one *variable* can be specified in the STRATA statement, and each numeric variable can be followed by a list. Each interval contains its lower endpoint but not its upper endpoint. The corresponding strata are formed by the combination of levels. If a variable is numeric and is followed by a list, then the levels for that variable correspond to the intervals defined by the list. The initial interval is assumed to start at $-\infty$, and the final interval is assumed to end at ∞ .

The specification of a STRATA *variable* can have any of the following forms:

```
    a list separated by blanks
    a list separated by commas
    x to y
    x to y
    x to y by z
    a combination of the above
    Age (5 to 10)
    Age (5 to 30 by 10)
    Age (5,10 to 50 by 10)
```

For example, the specification

```
strata Age(5,20 to 50 by 10) Sex;
```

indicates the following levels for the Age variable:

```
\{(-\infty, 5), [5, 20), [20, 30), [30, 40), [40, 50), [50, \infty)\}
```

This statement also specifies that the Age strata be further subdivided by values of the variable Sex. In this example, there are six age groups by two sex groups, forming a total of 12 strata.

The specification of several STRATA variables, such as

strata A B C;

is equivalent to the A*B*C syntax of the TABLES statement in the FREQ procedure. The number of strata levels usually grows very rapidly with the number of STRATA variables, so you must be cautious when specifying the list of STRATA variables.

When comparing more than two survival curves, a *k*-sample test tells you whether the curves are significantly different from each other, but it does not identify which pairs of curves are different. A multiple-comparison adjustment of the *p*-values for the paired comparisons retains the same overall false positives as the *k*-sample test. Two types of paired comparisons can be made: comparisons between all pairs of curves and comparisons between a control curve and all other curves. You use the DIFF= option to specify the comparison type, and you use the ADJUST= option to select a method of multiple-comparison adjustments.

Table 74.2 summarizes the *options* available in the STRATA statement.

Table 74.2 Options Available in the STRATA Statement

Option	Description		
Homogeneity	Tests		
GROUP=	Specifies the group variable for stratified tests		
NODETAIL	Suppresses printing the test statistic and covariance matrix		
NOTEST	Suppresses any tests		
TEST=	Specifies tests corresponding to various weight functions		
TREND	Requests a trend test		
Multiple Con	nparisons		
ADJUST=	Requests a multiple-comparison adjustment		
DIFF=	Specifies the type of differences to consider		
Missing Strata Value			
MISSING	Allows missing values as valid stratum values		
Display Option	on		
NOLABEL	Uses the names of the STRATA variables in the display		

You can specify the following *options* in the STRATA statement after a slash ("/").

ADJUST=method

ADJ=method

specifies the multiple-comparison method for adjusting the *p*-values of the paired tests. See the section "Multiple-Comparison Adjustments" on page 5610 for mathematical details; also see Westfall et al. (1999). The adjustment methods include the following:

BONFERRONI

BON

applies the Bonferroni correction to the raw p-values.

DUNNETT

performs Dunnett's two-tailed comparisons of the control group with all other groups. PROC LIFETEST uses the factor-analytic covariance approximation described in Hsu (1992) and

identifies the adjustment in the results as "Dunnett-Hsu." Note that ADJUST=DUNNETT is incompatible with DIFF=ALL.

SCHEFFE

performs Scheffé's multiple-comparison adjustment.

SIDAK

applies the Šidák correction to the raw p-values.

SMM

GTE

performs the paired comparisons based on the studentized maximum modulus test.

TUKEY

performs the paired comparisons based on Tukey's studentized range test. PROC LIFETEST uses the approximation described in Kramer (1956) and identifies the adjustment as "Tukey-Kramer" in the results. Note that ADJUST=TUKEY is incompatible with DIFF=CONTROL.

SIMULATE < (simulate-options) >

computes the adjusted p-values from the simulated distribution of the maximum or maximum absolute value of a multivariate normal random vector. The simulation estimates q, the true $(1 - \alpha)$ quantile, where α is the value of the ALPHA= *simulate-option*.

The number of samples for the SIMULATE adjustment is set so that the tail area for the simulated q is within a certain accuracy radius γ of $1 - \alpha$ with an accuracy confidence of $100(1 - \epsilon)\%$. In equation form,

$$\Pr(|F(\hat{q}) - (1 - \alpha)| \le \gamma) = 1 - \epsilon$$

where \hat{q} is the simulated q and F is the true distribution function of the maximum; see Edwards and Berry (1987) for details. By default, $\gamma = 0.005$ and $\epsilon = 0.01$ so that the tail area of \hat{q} is within 0.005 of 0.95 with 99% confidence.

The *simulate-options* include the following:

ACC=value

specifies the target accuracy radius γ of a $100(1 - \epsilon)\%$ confidence interval for the true probability content of the estimated $(1 - \alpha)$ quantile. The default value is ACC=0.005.

ALPHA=value

specifies the value α for estimating the $(1 - \alpha)$ quantile. The default value is the ALPHA= value in the PROC LIFETEST statement, or 0.05 if that option is not specified.

EPS=value

specifies the value ϵ for a $100(1-\epsilon)\%$ confidence interval for the true probability content of the estimated $(1-\alpha)$ quantile. The default value for the accuracy confidence is 99%, corresponding to EPS=0.01.

NSAMP=n

specifies the sample size for the simulation. By default, n is set based on the values of the target accuracy radius γ and accuracy confidence $100(1-\epsilon)\%$ for an interval for the true probability content of the estimated $(1-\alpha)$ quantile. With the default values for γ , ϵ , and α (0.005, 0.01, and 0.05, respectively), NSAMP=12604 by default.

REPORT

specifies that a report on the simulation should be displayed, including a listing of the parameters, such as γ , ϵ , and α , in addition to an analysis of various methods for estimating or approximating the quantile.

SEED=number

specifies an integer used to start the pseudorandom number generator for the simulation. If you do not specify a seed, or if you specify a value less than or equal to zero, the seed is generated by default from reading the time of day from the computer's clock.

DIFF=ALL | CONTROL< ('string' < . . . , 'string' >) >

specifies which pairs of survival curves are considered for the multiple comparisons.

DIFF=ALL

requests all paired comparisons

```
DIFF=CONTROL < ('string' < . . . 'string' >) >
```

requests comparisons of the control curve with all other curves. To specify the control curve, you specify the quotes strings of formatted values that represent the curve in parentheses. For example, if Cell='large' identifies the control group, you specify

```
DIFF=CONTROL('large')
```

If more than one variable is used to identify the curves (for example, if Cell='large' and Sex='F' represent the control), you specify

```
DIFF=CONTROL('large' 'F')
```

The order of the quoted strings should correspond to the order of the stratum variables. If no specific curve is specified as the control, the first stratum or group value is used.

By default, DIFF=ALL unless you specify ADJUST= DUNNETT, in which case DIFF=CONTROL.

GROUP=variable

stipulates a stratified test. You specify the *variable* to identify the groups whose survivor functions or cumulative incidence functions you want to compare. Tests are stratified on the levels of the STRATA variables. For example, in a multicenter trial in which two forms of therapy are to be compared, you specify the variable that identifies therapies as the GROUP= variable and the variable that identifies centers as the STRATA variable:

```
proc lifetest;
   time T*Status(0);
   strata Center / group=Therapy;
run;
```

With this specification, PROC LIFETEST performs a stratified test to compare the therapies while controlling the effect of the centers.

The GROUP= option has a side effect on the estimation of the survivor function or the cumulative incidence function (CIF). Instead of estimating a survivor function (or CIF) for each stratum, PROC LIFETEST estimates a survivor function (or CIF) for each group within a stratum. Suppose there are 10 centers and two therapies. The preceding PROC LIFETEST specification estimates 20 survivor functions: two for each center, and one for each therapy for each center.

If the GROUP= option is not specified, PROC LIFETEST performs a homogeneity test comparing the strata.

MISSING

allows missing values to be a stratum level or a valid value of the GROUP= variable.

NODETAIL

suppresses the display of the rank statistics and the corresponding covariance matrices for various strata. If you specified the TREND option, the display of the scores for computing the trend tests is suppressed.

NOLABEL

specifies that the names instead of the labels of the STRATA variables be used in the display of the survival estimate table and in the legend of the survival plot.

NOTEST

suppresses the *k*-sample tests, stratified tests, and trend tests.

ORDER=FORMATTED | INTERNAL

specifies the sorting order of the values of the STRATA variables. The strata are presented in the specified order in the analysis results. You can use this option, for example, to display the curve labels in your preferred order in the survival plot legend (see Example 74.2 for an illustration). The default is ORDER=FORMATTED, which sorts the strata according to their external formatted values, except for numeric variable with no explicit format, which are sorted by the unformatted (internal) values. ORDER=INTERNAL sorts the strata by their internal values. The ORDER= option has no effect on a stratum variable with cutpoints specified.

TREND

computes the trend tests for testing the null hypothesis that the k population hazards rate are the same versus an ordered alternatives. If there is only one STRATA variable and the variable is numeric, the unformatted values of the variable are used as the scores; otherwise, the scores are $1, 2, \ldots$, in the given order of the strata.

TEST=test-request | (test-request < . . . test-request >)

controls the tests produced. Each test corresponds to a different weight function (see the section "Nonparametric Tests" on page 5607 for the weight functions). The *test-requests* include the following:

ALL	specifies all the nonparametric tests with $\rho 1=1$ and $\rho 2=0$ for the Fleming and
	Harrington test—FLEMING(1,0).

FLEMING($\rho 1, \rho 2$) specifies the family of tests in Harrington and Fleming (1982), where $\rho 1$ and $\rho 2$

are nonnegative numbers. FLEMING(ρ 1, ρ 2) reduces to the Fleming-Harrington G^{ρ} family (Fleming and Harrington 1981) when ρ 2=0, which you can specify as FLEMING(ρ) with one argument. When ρ =0, the test becomes the log-rank

test. When ρ =1, the test should be very close to the Peto-Peto test.

LOGRANK specifies the log-rank test.

NONE suppresses all comparison tests. Specifying TEST=NONE is equivalent to

specify NOTEST.

LR specifies the likelihood ratio test based on the exponential model.

MODPETO specifies the modified Peto-Peto test.

PETO specifies the Peto-Peto test. The test is also referred to as the Peto-Peto-Prentice

test.

WILCOXON specifies the Wilcoxon test. The test is also referred to as the Gehan test or the

Breslow test.

TARONE specifies the Tarone-Ware test.

By default, TEST=(LOGRANK WILCOXON LR) for the *k*-sample tests, and TEST=(LOGRANK WILCOXON) for stratified and trend tests.

TEST Statement

TEST variables:

The TEST statement specifies a list of numeric covariates (prognostic variables) that you want tested for association with the failure time.

Two sets of rank statistics are computed. These rank statistics and their variances are pooled over all strata. Univariate (marginal) test statistics are displayed for each of the covariates.

Additionally, a sequence of test statistics for joint effects of covariates is displayed. The first element of the sequence is the largest univariate test statistic. Other variables are then added on the basis of the largest increase in the joint test statistic. The process continues until all the variables have been added or until the remaining variables are linearly dependent on the previously added variables.

For more information, see the section "Rank Tests for the Association of Survival Time with Covariates" on page 5611.

TIME Statement

```
TIME variable < * censor(list) > </ option > ;
```

The TIME statement is required. It is used to indicate the failure time variable, where *variable* is the name of the failure time variable that can be optionally followed by an asterisk, the name of the censoring variable, and a parenthetical list of values that correspond to right-censoring. The censoring values should be numeric, nonmissing values. For example, the following statement identifies the variable T as containing the observed failure times (event or censored):

```
time T*Status(0,2);
```

If the variable Status has the value 0 or 2, the corresponding value of T is a right-censored value.

You can specify the following *option* after a slash (/):

FAILCODE < = number-list >

EVENTCODE<=number-list>

stipulates a competing-risks analysis, which consists of estimating cumulative incidence functions and computing Gray's test (Gray 1988) for testing the homogeneity of two or more cumulative incidence functions. You specify a number that represents the event of interest after the equal sign. For example:

```
proc lifetest;
   time T*Status(0) / failcode=1;
run;
```

For this specification, PROC LIFETEST regards a Status value of 1 as the event of interest, a value of 0 as a censored observation indicator, and all other values as competing events.

You can specify a list of values after the equal sign. PROC LIFETEST performs a separate competing-risks analysis for each value, regarding it as representing the event of interest. For example:

```
proc lifetest;
   time T*Status(0) / failcode=1 2;
run;
```

This specification produces two analyses, one for FAILCODE=1 and the other for FAILCODE=2.

If you specify the FAILCODE option without the equal sign, PROC LIFETEST produces a separate analysis for each distinct event value. Consider a data set with an event indicator variable Status that assumes four distinct values, 0, 1, 2, and 3, where Status=0 represents observations that are censored and Status=1, Status=2, and Status=3 represent three different causes of failure. Consider the following statements:

```
proc lifetest;
   time T*Status(0) / failcode;
run;
```

PROC LIFETEST produces three separate competing-risks analyses: one uses Status=1 as the failure cause of interest, one uses Status=2 as the failure cause of interest, and one uses Status=3 as the failure cause of interest. This specification is convenient for an exploratory analysis when there is no predetermined failure cause of interest.

WEIGHT Statement

```
WEIGHT variable;
```

The *variable* in the WEIGHT statement identifies the variable in the input data set that contains the weights of the subjects. Values of the WEIGHT *variable* can be nonintegral and are not truncated. Observations with negative, zero, or missing values for the WEIGHT *variable* are not used in the computation.

The implementation of weights in PROC LIFETEST is based on Xie and Liu (2005, 2011), who use inverse probability of treatment weights to reduce confounding effects. A weight is assigned to each subject as the inverse probability of being in a certain group. If a subject has a higher probability of being in a group, it is considered as overrepresented and is therefore assigned a lower weight; on the other hand, if the subject has a smaller probability of being in a group, it is considered as underrepresented and is assigned a higher weight.

You can use the WEIGHT statement only for the Kaplan-Meier curves. Other methods of estimating the survival curves using weights are not available.

Details: LIFETEST Procedure

Missing Values

Observations with a missing value for either the failure time or the censoring variable are not used in the analysis. If a stratum variable value is missing, the observation is not used; however, the MISSING option can be used to request that missing values be treated as valid stratum values. If any variable specified in the TEST statement has a missing value, that observation is not used in the calculation of the rank statistics.

Computational Formulas

Breslow, Fleming-Harrington, and Kaplan-Meier Methods

Let $t_1 < t_2 < \cdots < t_D$ represent the distinct event times. For each $i = 1, \dots, D$, let Y_i be the number of surviving units (the size of the risk set) just prior to t_i and let d_i be the number of units that fail at t_i . If the NOTRUNCATE option is specified in the FREQ statement, Y_i and d_i can be nonintegers.

The Breslow estimate of the survivor function is

$$\hat{S}(t_i) = \exp\left(-\sum_{j=1}^i \frac{d_j}{Y_j}\right)$$

Note that the Breslow estimate is the exponentiation of the negative Nelson-Aalen estimate of the cumulative hazard function.

The Fleming-Harrington estimate (Fleming and Harrington 1984) of the survivor function is

$$\hat{S}(t_i) = \exp\left(-\sum_{k=1}^{i} \sum_{j=0}^{d_k-1} \frac{1}{Y_k - j}\right)$$

If the frequency values are not integers, the Fleming-Harrington estimate cannot be computed.

The Kaplan-Meier (product-limit) estimate of the survivor function at t_i is the cumulative product

$$\hat{S}(t_i) = \prod_{i=1}^{i} \left(1 - \frac{d_j}{Y_j} \right)$$

Notice that all the estimators are defined to be right continuous; that is, the events at t_i are included in the estimate of $S(t_i)$. The corresponding estimate of the standard error is computed using Greenwood's formula (Kalbfleisch and Prentice 1980) as

$$\hat{\sigma}\left(\hat{S}(t_i)\right) = \hat{S}(t_i) \sqrt{\sum_{j=1}^{i} \frac{d_j}{Y_j(Y_j - d_j)}}$$

The first quartile (or the 25th percentile) of the survival time is the time beyond which 75% of the subjects in the population under study are expected to survive. It is estimated by

$$q_{.25} = \min\{t_i | \hat{S}(t_i) < 0.75\}$$

If $\hat{S}(t)$ is exactly equal to 0.75 from t_j to t_{j+1} , the first quartile is taken to be $(t_j + t_{j+1})/2$. If it happens that $\hat{S}(t)$ is greater than 0.75 for all values of t, the first quartile cannot be estimated and is represented by a missing value in the printed output.

The general formula for estimating the 100pth percentile point is

$$q_p = \min\{t_j | \hat{S}(t_j) < 1 - p\}$$

The second quartile (the median) and the third quartile of survival times correspond to p = 0.5 and p = 0.75, respectively.

Brookmeyer and Crowley (1982) have constructed the confidence interval for the median survival time based on the confidence interval for the S(t). The methodology is generalized to construct the confidence interval for the 100pth percentile based on a g-transformed confidence interval for S(t) (Klein and Moeschberger 1997). You can use the CONFTYPE= option to specify the g-transformation. The $100(1 - \alpha)\%$ confidence interval for the first quantile survival time is the set of all points t that satisfy

$$\left| \frac{g(\hat{S}(t)) - g(1 - 0.25)}{g'(\hat{S}(t))\hat{\sigma}(\hat{S}(t))} \right| \le z_{1 - \frac{\alpha}{2}}$$

where g'(x) is the first derivative of g(x) and $z_{1-\frac{\alpha}{2}}$ is the $(100(1-\frac{\alpha}{2}))$ th percentile of the standard normal distribution.

Consider the bone marrow transplant data described in Example 74.2. The following table illustrates the construction of the confidence limits for the first quartile in the ALL group. Values of $\frac{g(\hat{S}(t))-g(1-0.25)}{g'(\hat{S}(t))\hat{\sigma}(\hat{S}(t))}$ that lie between $\pm z_{1-\frac{0.05}{2}} = \pm 1.965$ are highlighted.

Constructing 95% Confidence Limits for the 25th Percentile							
			$\frac{g(\hat{S}(t)) - g(1 - 0.25)}{g'(\hat{S}(t))\hat{\sigma}(\hat{S}(t))}$				
t	$\hat{S}(t)$	$\hat{\sigma}(\hat{S}(t))$	LINEAR	LOGLOG	LOG	ASINSQRT	LOGIT
1	0.97368	0.025967	8.6141	2.37831	9.7871	4.44648	2.47903
55	0.94737	0.036224	5.4486	2.36375	6.1098	3.60151	2.46635
74	0.92105	0.043744	3.9103	2.16833	4.3257	2.94398	2.25757
86	0.89474	0.049784	2.9073	1.89961	3.1713	2.38164	1.97023
104	0.86842	0.054836	2.1595	1.59196	2.3217	1.87884	1.64297
107	0.84211	0.059153	1.5571	1.26050	1.6490	1.41733	1.29331
109	0.81579	0.062886	1.0462	0.91307	1.0908	0.98624	0.93069
110	0.78947	0.066135	0.5969	0.55415	0.6123	0.57846	0.56079
122	0.73684	0.071434	-0.1842	-0.18808	-0.1826	-0.18573	-0.18728
129	0.71053	0.073570	-0.5365	-0.56842	-0.5222	-0.54859	-0.56101
172	0.68421	0.075405	-0.8725	-0.95372	-0.8330	-0.90178	-0.93247
192	0.65789	0.076960	-1.1968	-1.34341	-1.1201	-1.24712	-1.30048
194	0.63158	0.078252	-1.5133	-1.73709	-1.3870	-1.58613	-1.66406
230	0.60412	0.079522	-1.8345	-2.14672	-1.6432	-1.92995	-2.03291
276	0.57666	0.080509	-2.1531	-2.55898	-1.8825	-2.26871	-2.39408
332	0.54920	0.081223	-2.4722	-2.97389	-2.1070	-2.60380	-2.74691
383	0.52174	0.081672	-2.7948	-3.39146	-2.3183	-2.93646	-3.09068
418	0.49428	0.081860	-3.1239	-3.81166	-2.5177	-3.26782	-3.42460
466	0.46682	0.081788	-3.4624	-4.23445	-2.7062	-3.59898	-3.74781
487	0.43936	0.081457	-3.8136	-4.65971	-2.8844	-3.93103	-4.05931
526	0.41190	0.080862	-4.1812	-5.08726	-3.0527	-4.26507	-4.35795
609	0.38248	0.080260	-4.5791	-5.52446	-3.2091	-4.60719	-4.64271
662	0.35306	0.079296	-5.0059	-5.96222	-3.3546	-4.95358	-4.90900

Consider the LINEAR transformation where g(x) = x. The event times that satisfy $\left| \frac{g(\hat{S}(t)) - g(1-p)}{g'(\hat{S}(t))\sqrt{\hat{V}(\hat{S}(t))}} \right|$ 1.9599 include 107, 109, 110, 122, 129, 172, 192, 194, and 230. The confidence of the interval [107, 230] is less than 95%. Brookmeyer and Crowley (1982) suggest extending the confidence interval to but not including the next event time. As such the 95% confidence interval for the first quartile based on the linear transform is [107, 276). The following table lists the confidence intervals for the various transforms.

95% CI's for the 25th Percentile				
CONFTYPE	[Lower	Upper)		
LINEAR	107	276		
LOGLOG	86	230		
LOG	107	332		
ASINSQRT	104	276		
LOGIT	104	230		

Sometimes, the confidence limits for the quartiles cannot be estimated. For convenience of explanation, consider the linear transform g(x) = x. If the curve that represents the upper confidence limits for the survivor function lies above 0.75, the upper confidence limit for first quartile cannot be estimated. On the other hand, if the curve that represents the lower confidence limits for the survivor function lies above 0.75, the lower confidence limit for the quartile cannot be estimated.

The estimated mean survival time is

$$\hat{\mu} = \sum_{i=1}^{D} \hat{S}(t_{i-1})(t_i - t_{i-1})$$

where t_0 is defined to be zero. When the largest observed time is censored, this sum underestimates the mean. The standard error of $\hat{\mu}$ is estimated as

$$\hat{\sigma}(\hat{\mu}) = \sqrt{\frac{m}{m-1} \sum_{i=1}^{D-1} \frac{d_i A_i^2}{Y_i (Y_i - d_i)}}$$

where

$$A_i = \sum_{j=i}^{D-1} \hat{S}(t_j)(t_{j+1} - t_j)$$

$$m = \sum_{j=1}^{D} d_j$$

If the largest observed time is not an event, you can use the TIMELIM= option to specify a time limit L and estimate the mean survival time limited to the time L and its standard error by replacing D by D+1 with $t_{D+1}=L$.

Nelson-Aalen Estimate of the Cumulative Hazard Function

The Nelson-Aalen cumulative hazard estimator, defined up to the largest observed time on study, is

$$\tilde{H}(t) = \sum_{t_i \le t} \frac{d_i}{Y_i}$$

and its estimated variance is

$$\hat{\sigma}^2 \left(\tilde{H}(t) \right) = \sum_{t_i \le t} \frac{d_i}{Y_i^2}$$

Adjusted Kaplan-Meier Estimate

PROC LIFETEST computes the adjusted Kaplan-Meier estimate (AKME) of the survivor function if you specify both METHOD=KM and the WEIGHT statement. Let $(T_i, \delta_i, w_i), i = 1, \ldots, n$, denote an independent sample of right-censored survival data, where T_i is the possibly right-censored time, δ_i is the censoring indicator ($\delta_i = 0$ if T_i is censored and $\delta_i = 1$ if T_i is an event time), and w_i is the weight (from the WEIGHT statement). Let $t_1 < t_2 < \cdots < t_D$ be the D distinct event times in the sample. At time $t_j, j = 1, \ldots, D$, there are $d_j = \sum_i \delta_i I(T_i = t_j)$ events out of $Y_j = \sum_i I(T_i \ge t_j)$ subjects. The weighted number of events and the weighted number at risk are $d_j^w = \sum_i w_i \delta_i I(T_i = t_j)$ and $Y_i^w = \sum_i w_i I(T_i \ge t_j)$, respectively. The AKME (Xie and Liu 2005) is

$$\hat{S}(t) = \begin{cases} 1 & \text{if } t < t_1 \\ \prod_{t_j \le t} \left[1 - \frac{d_j^w}{Y_j^w} \right] & \text{if } t \ge t_1 \end{cases}$$

The estimated variance of $\hat{S}(t)$ is

$$\hat{\sigma}^2 \left(\hat{S}(t) \right) = \left(\hat{S}(t) \right)^2 \sum_{j: t_j \le t} \frac{d_j^w / Y_j^w}{M_j (1 - d_j^w / Y_j^w)}$$

where

$$M_j = \frac{\left(\sum_{i:T_i \ge t_j} w_i\right)^2}{\sum_{i:T_i \ge t_j} w_i^2}$$

Life-Table Method

The life-table estimates are computed by counting the numbers of censored and uncensored observations that fall into each of the time intervals $[t_{i-1}, t_i)$, i = 1, 2, ..., k+1, where $t_0 = 0$ and $t_{k+1} = \infty$. Let n_i be the number of units that enter the interval $[t_{i-1}, t_i)$, and let d_i be the number of events that occur in the interval. Let $b_i = t_i - t_{i-1}$, and let $n'_i = n_i - w_i/2$, where w_i is the number of units censored in the interval. The effective sample size of the interval $[t_{i-1}, t_i)$ is denoted by n'_i . Let t_{mi} denote the midpoint of $[t_{i-1}, t_i)$.

The conditional probability of an event in $[t_{i-1}, t_i)$ is estimated by

$$\hat{q}_i = \frac{d_i}{n_i'}$$

and its estimated standard error is

$$\hat{\sigma}\left(\hat{q}_{i}\right) = \sqrt{\frac{\hat{q}_{i}\,\hat{p}_{i}}{n'_{i}}}$$

where $\hat{p}_i = 1 - \hat{q}_i$.

The estimate of the survival function at t_i is

$$\hat{S}(t_i) = \begin{cases} 1 & i = 0 \\ \hat{S}(t_{i-1})p_{i-1} & i > 0 \end{cases}$$

and its estimated standard error is

$$\hat{\sigma}\left(\hat{S}(t_i)\right) = \hat{S}(t_i) \sqrt{\sum_{j=1}^{i-1} \frac{\hat{q}_j}{n'_j \hat{p}_j}}$$

The density function at t_{mi} is estimated by

$$\hat{f}(t_{mi}) = \frac{\hat{S}(t_i)\hat{q}_i}{b_i}$$

and its estimated standard error is

$$\hat{\sigma}\left(\hat{f}(t_{mi})\right) = \hat{f}(t_{mi}) \sqrt{\sum_{j=1}^{i-1} \frac{\hat{q}_j}{n'_j \hat{p}_j} + \frac{\hat{p}_i}{n'_i \hat{q}_i}}$$

The estimated hazard function at t_{mi} is

$$\hat{h}(t_{mi}) = \frac{2\hat{q}_i}{b_i(1+\hat{p}_i)}$$

and its estimated standard error is

$$\hat{\sigma}\left(\hat{h}(t_{mi})\right) = \hat{h}(t_{mi})\sqrt{\frac{1 - (b_i\hat{h}(t_{mi})/2)^2}{n_i'\hat{q}_i}}$$

Let $[t_{j-1}, t_j)$ be the interval in which $\hat{S}(t_{j-1}) \geq \hat{S}(t_i)/2 > \hat{S}(t_j)$. The median residual lifetime at t_i is estimated by

$$\hat{M}_i = t_{j-1} - t_i + b_j \frac{\hat{S}(t_{j-1}) - \hat{S}(t_i)/2}{\hat{S}(t_{j-1}) - \hat{S}(t_j)}$$

and the corresponding standard error is estimated by

$$\hat{\sigma}(\hat{M}_i) = \frac{\hat{S}(t_i)}{2\hat{f}(t_{mj})\sqrt{n_i'}}$$

Interval Determination

If you want to determine the intervals exactly, use the INTERVALS= option in the PROC LIFETEST statement to specify the interval endpoints. Use the WIDTH= option to specify the width of the intervals, thus indirectly determining the number of intervals. If neither the INTERVALS= option nor the WIDTH= option is specified in the life-table estimation, the number of intervals is determined by the NINTERVAL= option. The width of the time intervals is 2, 5, or 10 times an integer (possibly a negative integer) power of 10. Let $c = \log_{10}(\text{maximum observed time/number of intervals})$, and let b be the largest integer not exceeding c. Let $d = 10^{c-b}$ and let

$$a = 2 \times I(d \le 2) + 5 \times I(2 < d \le 5) + 10 \times I(d > 5)$$

with I being the indicator function. The width is then given by

width =
$$a \times 10^b$$

By default, NINTERVAL=10.

Pointwise Confidence Limits in the OUTSURV= Data Set

Pointwise confidence limits are computed for the survivor function, and for the density function and hazard function when the life-table method is used. Let α be specified by the ALPHA= option. Let $z_{\alpha/2}$ be the critical value for the standard normal distribution. That is, $\Phi(-z_{\alpha/2}) = \alpha/2$, where Φ is the cumulative distribution function of the standard normal random variable.

Survivor Function

When the computation of confidence limits for the survivor function S(t) is based on the asymptotic normality of the survival estimator $\hat{S}(t)$, the approximate confidence interval might include impossible values outside the range [0,1] at extreme values of t. This problem can be avoided by applying the asymptotic normality to a transformation of S(t) for which the range is unrestricted. In addition, certain transformed confidence intervals for S(t) perform better than the usual linear confidence intervals (Borgan and Liestøl 1990). The CONFTYPE= option enables you to pick one of the following transformations: the log-log function (Kalbfleisch and Prentice 1980), the arcsine-square root function (Nair 1984), the logit function (Meeker and Escobar 1998), the log function, and the linear function.

Let g be the transformation that is being applied to the survivor function S(t). By the delta method, the standard error of $g(\hat{S}(t))$ is estimated by

$$\tau(t) = \hat{\sigma} \left[g(\hat{S}(t)) \right] = g' \left(\hat{S}(t) \right) \hat{\sigma} [\hat{S}(t)]$$

where g' is the first derivative of the function g. The $100(1-\alpha)\%$ confidence interval for S(t) is given by

$$g^{-1}\left\{g[\hat{S}(t)] \pm z_{\frac{\alpha}{2}}g'[\hat{S}(t)]\hat{\sigma}[\hat{S}(t)]\right\}$$

where g^{-1} is the inverse function of g. That choices of the transformation g are as follows:

• arcsine-square root transformation: The estimated variance of $\sin^{-1}\left(\sqrt{\hat{S}(t)}\right)$ is $\hat{\tau}^2(t) = \frac{\hat{\sigma}^2[\hat{S}(t)]}{4\hat{S}(t)[1-\hat{S}(t)]}$. The $100(1-\alpha)\%$ confidence interval for S(t) is given by

$$\sin^2\left\{\max\left[0,\sin^{-1}(\sqrt{\hat{S}(t)})-z_{\frac{\alpha}{2}}\hat{\tau}(t)\right]\right\} \leq S(t) \leq \sin^2\left\{\min\left[\frac{\pi}{2},\sin^{-1}(\sqrt{\hat{S}(t)})+z_{\frac{\alpha}{2}}\hat{\tau}(t)\right]\right\}$$

• linear transformation: This is the same as having no transformation in which g is the identity. The $100(1-\alpha)\%$ confidence interval for S(t) is given by

$$\hat{S}(t) - z_{\frac{\alpha}{2}}\hat{\sigma}\left[\hat{S}(t)\right] \le S(t) \le \hat{S}(t) + z_{\frac{\alpha}{2}}\hat{\sigma}\left[\hat{S}(t)\right]$$

• log transformation: The estimated variance of $\log(\hat{S}(t))$ is $\hat{\tau}^2(t) = \frac{\hat{\sigma}^2(\hat{S}(t))}{\hat{S}^2(t)}$. The 100(1- α)% confidence interval for S(t) is given by

$$\hat{S}(t) \exp\left(-z_{\frac{\alpha}{2}}\hat{\tau}(t)\right) \le S(t) \le \hat{S}(t) \exp\left(z_{\frac{\alpha}{2}}\hat{\tau}(t)\right)$$

• log-log transformation: The estimated variance of $\log(-\log(\hat{S}(t)))$ is $\hat{\tau}^2(t) = \frac{\hat{\sigma}^2[\hat{S}(t)]}{[\hat{S}(t)\log(\hat{S}(t))]^2}$. The $100(1-\alpha)\%$ confidence interval for S(t) is given by

$$\left[\hat{S}(t)\right]^{\exp\left(z_{\frac{\alpha}{2}}\hat{\tau}(t)\right)} \leq S(t) \leq \left[\hat{S}(t)\right]^{\exp\left(-z_{\frac{\alpha}{2}}\hat{\tau}(t)\right)}$$

• logit transformation: The estimated variance of $\log \left(\frac{\hat{S}(t)}{1 - \hat{S}(t)} \right)$ is

$$\hat{\tau}^2(t) = \frac{\hat{\sigma}^2(\hat{S}(t))}{\hat{S}^2(t)[1 - \hat{S}(t)]^2}.$$

The $100(1-\alpha)\%$ confidence limits for S(t) are given by

$$\frac{\hat{S}(t)}{\hat{S}(t) + \left[1 - \hat{S}(t)\right] \exp\left(z_{\frac{\alpha}{2}}\hat{\tau}(t)\right)} \le S(t) \le \frac{\hat{S}(t)}{\hat{S}(t) + \left[1 - \hat{S}(t)\right] \exp\left(-z_{\frac{\alpha}{2}}\hat{\tau}(t)\right)}$$

Density and Hazard Functions

For the life-table method, a $100(1-\alpha)\%$ confidence interval for hazard function or density function at time t is computed as

$$\hat{g}(t) \pm z_{\alpha/2} \hat{\sigma}[\hat{g}(t)]$$

where $\hat{g}(t)$ is the estimate of either the hazard function or the density function at time t, and $\hat{\sigma}[\hat{g}(t)]$ is the corresponding standard error estimate.

Simultaneous Confidence Intervals for Kaplan-Meier Curves

The pointwise confidence interval for the survivor function S(t) is valid for a single fixed time at which the inference is to be made. In some applications, it is of interest to find the upper and lower confidence bands that guarantee, with a given confidence level, that the survivor function falls within the band for all t in some interval. Hall and Wellner (1980) and Nair (1984) provide two different approaches for deriving the confidence bands. An excellent review can be found in Klein and Moeschberger (1997). You can use the CONFBAND= option in the PROC LIFETEST statement to select the confidence bands. The EP confidence band provides confidence bounds that are proportional to the pointwise confidence interval, while those of the HW band are not proportional to the pointwise confidence bounds. The maximum time, t_U , for the bands can be specified by the BANDMAX= option; the minimum time, t_L , can be specified by the BANDMIN= option. Transformations that are used to improve the pointwise confidence intervals can be applied to improve the confidence bands. It might turn out that the upper and lower bounds of the confidence bands are not decreasing in $t_L < t < t_U$, which is contrary to the nonincreasing characteristic of survivor function. Meeker and Escobar (1998) suggest making an adjustment so that the bounds do not increase: if the upper bound is increasing on the right, it is made flat from the minimum to t_{U} ; if the lower bound is increasing from the right, it is made flat from t_L to the maximum. PROC LIFETEST does not make any adjustment for the nondecreasing behavior of the confidence bands in the OUTSURV= data set. However, the adjustment was made in the display of the confidence bands by using ODS Graphics.

For Kaplan-Meier estimation, let $t_1 < t_2 < \cdots < t_D$ be the D distinct events times, and at time t_i , there are d_i events. Let Y_i be the number of individuals who are at risk at time t_i . The variance of $\hat{S}(t)$, given by the Greenwood formula, is $\hat{\sigma}^2[\hat{S}(t)] = \sigma_S^2(t)\hat{S}^2(t)$, where

$$\sigma_S^2(t) = \sum_{t_i \le t} \frac{d_i}{Y_i(Y_i - d_i)}$$

Let $t_L < t_U$ be the time range for the confidence band so that t_U is less than or equal to the largest event time. For the Hall-Wellner band, t_L can be zero, but for the equal-precision band, t_L is greater than or equal to the smallest event time. Let

$$a_L = \frac{n\sigma_S^2(t_L)}{1 + n\sigma_S^2(t_L)}$$
 and $a_U = \frac{n\sigma_S^2(t_U)}{1 + n\sigma_S^2(t_U)}$

Let $\{W^0(u), 0 \le u \le 1\}$ be a Brownian bridge.

Hall-Wellner Band

The $100(1-\alpha)\%$ HW band of Hall and Wellner (1980) is

$$\hat{S}(t) - h_{\alpha}(a_L, a_U)n^{-\frac{1}{2}}[1 + n\sigma_S^2(t)]\hat{S}(t) \le S(t) \le \hat{S}(t) + h_{\alpha}(a_L, a_U)n^{-\frac{1}{2}}[1 + n\sigma_S^2(t)]\hat{S}(t)$$

for all $t_L \le t \le t_U$, where the critical value $h_{\alpha}(a_L, a_U)$ is given by

$$\alpha = \Pr\{ \sup_{a_L \le u \le a_U} |W^0(u)| > h_\alpha(a_L, a_U) \}$$

The critical values are computed from the results in Chung (1986).

Note that the given confidence band has a formula similar to that of the (linear) pointwise confidence interval, where $h_{\alpha}(a_L, a_U)$ and $n^{-\frac{1}{2}}[1 + n\sigma_S^2(t)]\hat{S}(t)$ in the former correspond to $z_{\frac{\alpha}{2}}$ and $\hat{\sigma}(\hat{S}(t))$ in the latter, respectively. You can obtain the other transformations (arcsine-square root, log-log, log, and logit) for the confidence bands by replacing $z_{\frac{\alpha}{2}}$ and $\hat{\tau}(t)$ in the corresponding pointwise confidence interval formula by $h_{\alpha}(a_L, a_U)$ and the following $\hat{\tau}(t)$, respectively:

• arcsine-square root transformation:

$$\hat{\tau}(t) = \frac{1 + n\sigma_S^2(t)}{2} \sqrt{\frac{S(t)}{n[1 - S(t)]}}$$

• log transformation:

$$\hat{\tau}(t) = \frac{1 + n\sigma_S^2(t)}{\sqrt{n}}$$

• log-log transformation:

$$\hat{\tau}(t) = \frac{1 + n\sigma_S^2(t)}{\sqrt{n}|\log[\hat{S}(t)]|}$$

• logit transformation:

$$\hat{\tau}(t) = \frac{1 + n\sigma_S^2(t)}{\sqrt{n}[1 - \hat{S}(t)]}$$

Equal-Precision Band

The $100(1-\alpha)\%$ EP band of Nair (1984) is

$$\hat{S}(t) - e_{\alpha}(a_L, a_U)\hat{S}(t)\sigma_S(t) \le S(t) \le \hat{S}(t) + e_{\alpha}(a_L, a_U)\hat{S}(t)\sigma_S(t)$$

for all $t_L \le t \le t_U$, where $e_{\alpha}(a_L, a_U)$ is given by

$$\alpha = \Pr\{\sup_{a_L \leq u \leq a_U} \frac{|W^0(u)|}{[u(1-u)]^{\frac{1}{2}}} > e_\alpha(a_L, a_U)\}$$

PROC LIFETEST uses the approximation of Miller and Siegmund (1982, Equation 8) to approximate the tail probability in which $e_{\alpha}(a_L, a_U)$ is obtained by solving x in

$$\frac{4x\phi(x)}{x} + \phi(x)\left(x - \frac{1}{x}\right)\log\left[\frac{a_U(1-a_L)}{a_L(1-a_U)}\right] = \alpha$$

where $\phi(x)$ is the standard normal density function evaluated at x. Note that the confidence bounds given are proportional to the pointwise confidence intervals. As a matter of fact, this confidence band and the (linear) pointwise confidence interval have the same formula except for the critical values ($z_{\frac{\alpha}{2}}$ for the pointwise confidence interval and $e_{\alpha}(a_L, a_U)$ for the band). You can obtain the other transformations (arcsine-square root, log-log, log, and logit) for the confidence bands by replacing $z_{\frac{\alpha}{2}}$ by $e_{\alpha}(a_L, a_U)$ in the formula of the pointwise confidence intervals.

Kernel-Smoothed Hazard Estimate

Kernel-smoothed estimators of the hazard function h(t) are based on the Nelson-Aalen estimator $\tilde{H}(t)$ and its variance $\hat{V}(\tilde{H}(t))$. Consider the jumps of $\tilde{H}(t)$ and $\hat{V}(\tilde{H}(t))$ at the event times $t_1 < t_2 < \cdots < t_D$ as follows:

$$\Delta \tilde{H}(t_i) = \tilde{H}(t_i) - \tilde{H}(t_{i-1})$$

$$\hat{V}(\tilde{H}(t_i)) = \hat{V}(\tilde{H}(t_i)) - \hat{V}(\tilde{H}(t_{i-1}))$$

where $t_0=0$.

The kernel-smoothed estimator of h(t) is a weighted average of $\Delta \tilde{H}(t)$ over event times that are within a bandwidth distance b of t. The weights are controlled by the choice of kernel function, K(), defined on the interval [-1,1]. The choices are as follows:

• uniform kernel:

$$K_U(x) = \frac{1}{2}, -1 \le x \le 1$$

• Epanechnikov kernel:

$$K_E(x) = \frac{3}{4}(1 - x^2), -1 \le x \le 1$$

• biweight kernel:

$$K_{BW}(x) = \frac{15}{16}(1 - x^2)^2, -1 \le x \le 1$$

The kernel-smoothed hazard rate estimator is defined for all time points on $(0, t_D)$. For time points t for which $b \le t \le t_D - b$, the kernel-smoothed estimated of h(t) based on the kernel K(t) is given by

$$\hat{h}(t) = \frac{1}{b} \sum_{i=1}^{D} K\left(\frac{t - t_i}{b}\right) \Delta \tilde{H}(t_i)$$

The variance of $\hat{h}(t)$ is estimated by

$$\hat{\sigma^2}(\hat{h}(t)) = \frac{1}{b^2} \sum_{i=1}^{D} K\left(\frac{t - t_i}{b}\right)^2 \Delta \hat{V}(\tilde{H}(t_i))$$

For t < b, the symmetric kernels K() are replaced by the corresponding asymmetric kernels of Gasser and Müller (1979). Let $q = \frac{t}{b}$. The modified kernels are as follows:

• uniform kernel:

$$K_{U,q}(x) = \frac{4(1+q^3)}{(1+q)^4} + \frac{6(1-q)}{(1+q)^3}x, -1 \le x \le q$$

• Epanechnikov kernel:

$$K_{E,q}(x) = K_E(x) \frac{64(2 - 4q + 6q^2 - 3q^3) + 240(1 - q)^2 x}{(1 + q)^4 (19 - 18q + 3q^2)}, -1 \le x \le q$$

• biweight kernel:

$$K_{BW,q}(x) = K_{BW}(x) \frac{64(8 - 24q + 48q^2 - 45q^3 + 15q^4) + 1120(1 - q)^3 x}{(1 + q)^5(81 - 168q + 126q^2 - 40q^3 + 5q^4)}, -1 \le x \le q$$

For $t_D - b \le t \le t_D$, let $q = \frac{t_D - t}{b}$. The asymmetric kernels for t < b are used with x replaced by -x.

Using the log transform on the smoothed hazard rate, the $100(1-\alpha)\%$ pointwise confidence interval for the smoothed hazard rate h(t) is given by

$$\hat{h}(t) = \hat{h}(t) \exp\left[\pm \frac{z_{1-\alpha/2}\hat{\sigma}(\hat{h}(t))}{\hat{h}(t)}\right]$$

where $z_{1-\frac{\alpha}{2}}$ is the $(100(1-\frac{\alpha}{2}))$ th percentile of the standard normal distribution.

Optimal Bandwidth

The following mean integrated squared error (MISE) over the range τ_L and τ_U is used as a measure of the global performance of the kernel function estimator:

MISE(b) =
$$E \int_{\tau_L}^{\tau_U} (\hat{h}(i) - h(u))^2 du$$

= $E \int_{\tau_L}^{\tau_U} \hat{h}^2(u) du - 2E \int_{\tau_L}^{\tau_U} \hat{h}(u) h(u) du + E \int_{\tau_L}^{\tau_U} h^2(u) du$

The last term is independent of the choice of the kernel and bandwidth and can be ignored when you are looking for the best value of b. The first integral can be approximated by using the trapezoid rule by evaluating $\hat{h}(t)$ at a grid of points $\tau_L = u_1 < \cdots < u_M = \tau_U$. You can specify τ_L, τ_R , and M by using the options GRIDL=, GRIDU=, and NMINGRID=, respectively, of the HAZARD plot. The second integral can be estimated by the Ramlau-Hansen (1983a, b) cross-validation estimate:

$$\frac{1}{b} \sum_{i \neq j} K\left(\frac{t_i - t_j}{b}\right) \Delta \hat{H}(t_i) \Delta \hat{H}(t_j)$$

Therefore, for a fixed kernel, the optimal bandwidth is the quantity b that minimizes

$$g(b) = \sum_{i=1}^{M-1} \left[\frac{u_{i+1} - u_k}{2} \left(\hat{h}^2(u_i) + \hat{h}^2(u_{i+1}) \right) \right] - \frac{2}{b} \sum_{i \neq j} K\left(\frac{t_i - t_j}{b} \right) \Delta \hat{H}(t_i) \Delta \hat{H}(t_j)$$

The minimization is carried out by the golden section search algorithm.

Comparison of Two or More Groups of Survival Data

Let K be the number of groups. Let $S_k(t)$ be the underlying survivor function of the kth group, k = 1, ..., K. The null and alternative hypotheses to be tested are

$$H_0: S_1(t) = S_2(t) = \dots = S_K(t)$$
 for all $t \le \tau$

versus

 H_1 : at least one of the $S_k(t)$'s is different for some $t \leq \tau$

respectively, where τ is the largest observed time.

Likelihood Ratio Test

The likelihood ratio test statistic (Lawless 1982) for test H_0 versus H_1 assumes that the data in the various samples are exponentially distributed and tests that the scale parameters are equal. The test statistic is computed as

$$\chi^2 = 2N \log \left(\frac{T}{N}\right) - 2 \sum_{k=1}^{K} N_k \log \left(\frac{T_k}{N_k}\right)$$

where N_k is the total number of events in the kth group, $N = \sum_{k=1}^{k} N_k$, T_k is the total time on test in the kth stratum, and $T = \sum_{k=1}^{K} T_k$. The approximate probability value is computed by treating χ^2 as having a chi-square distribution with K-1 degrees of freedom.

Nonparametric Tests

Let (T_i, δ_i, X_i) , $i = 1, \ldots, n$, denote an independent sample of right-censored survival data, where T_i is the possibly right-censored time, δ_i is the censoring indicator $(\delta_i = 0 \text{ if } T_i \text{ is censored and } \delta_i = 1 \text{ if } T_i$ is an event time), and $X_i = 1, \ldots, K$ for K different groups. Let $t_1 < t_2 < \cdots < t_D$ be the distinct event times in the sample. At time t_j , $j = 1, \ldots, D$, let $W(t_j)$ be a positive weight function, and let $Y_{jk} = \sum_{i:T_i \geq t_j} I(X_i = k)$ and $d_{jk} = \sum_{i:T_i = t_j} \delta_i I(X_i = k)$ be the size of the risk set and the number of events in the kth group, respectively. Let $Y_j = \sum_{k=1}^K Y_{jk}$, $d_j = \sum_{k=1}^K d_{jk}$.

The choices of the weight function $W(t_i)$ are given in Table 74.3.

Test	$W(t_i)$
Log-rank	1.0
Wilcoxon	Y_{j}
Tarone-Ware	$\sqrt{Y_j}$
Peto-Peto	$ ilde{S}(t_j)$
Modified Peto-Peto	$\tilde{S}(t_j) \frac{Y_j}{Y_j+1}$
Harrington-Fleming (p,q)	$[\hat{S}(t_{j-1})]^p [1 - \hat{S}(t_{j-1})]^q, p \ge 0, q \ge 0$

Table 74.3 Weight Functions for Various Tests

In Table 74.3, $\hat{S}(t)$ is the product-limit estimate at t for the pooled sample, and $\tilde{S}(t)$ is a survivor function estimate close to $\hat{S}(t)$ given by

$$\tilde{S}(t) = \prod_{t_j \le t} \left(1 - \frac{d_j}{Y_j + 1} \right)$$

Unstratified Tests The rank statistics (Klein and Moeschberger 1997, Section 7.3) for testing H_0 versus H_1 have the form of a K-vector $\mathbf{v} = (v_1, v_2, \dots, v_K)'$ with

$$v_k = \sum_{j=1}^{D} \left[W(t_j) \left(d_{jk} - Y_{jk} \frac{d_j}{Y_j} \right) \right]$$

and the variance of v_k and the covariance of v_k and v_h are, respectively,

$$V_{kk} = \sum_{j=1}^{D} \left[W^{2}(t_{j}) \frac{d_{j}(Y_{j} - d_{j})Y_{jk}(Y_{j} - Y_{jk})}{Y_{j}^{2}(Y_{j} - 1)} \right], \quad 1 \leq k \leq K$$

$$V_{kh} = -\sum_{j=1}^{D} \left[W^{2}(t_{j}) \frac{d_{j}(Y_{j} - d_{j})Y_{jk}Y_{jh}}{Y_{j}^{2}(Y_{j} - 1)} \right], \quad 1 \leq k \neq h \leq K$$

The statistic v_k can be interpreted as a weighted sum of observed minus expected numbers of failure for the kth group under the null hypothesis of identical survival curves. Let $V = (V_{kh})$. The overall test statistic for homogeneity is $\mathbf{v}'\mathbf{V}^{-}\mathbf{v}$, where \mathbf{V}^{-} denotes a generalized inverse of \mathbf{V} . This statistic is treated as having a chi-square distribution with degrees of freedom equal to the rank of V for the purposes of computing an approximate probability level.

Adjusted Log-Rank Test PROC LIFETEST computes the weighted log-rank test (Xie and Liu 2005, 2011) if you specify the WEIGHT statement. Let $(T_i, \delta_i, X_i, w_i), i = 1, \dots, n$, denote an independent sample of right-censored survival data, where T_i is the possibly right-censored time, δ_i is the censoring indicator (δ_i =0 if T_i is censored and δ_i =1 if T_i is an event time), $X_i = 1, \dots, K$ for K different groups, and w_i is the weight from the WEIGHT statement. Let $t_1 < t_2 < \cdots < t_D$ be the distinct event times in the sample. At each

 t_j , j = 1, ..., D, and for each $1 \le k \le K$, let

$$\begin{aligned} d_{jk} &= \sum_{i:T_i = t_j} I(X_i = k) & d_{jk}^w &= \sum_{i:T_i = t_j} w_i I(X_i = k) \\ Y_{jk} &= \sum_{i:T_i \ge t_j} I(X_i = k) & Y_{jk}^w &= \sum_{i:T_i \ge t_j} w_i I(X_i = k) \end{aligned}$$

Let $d_j = \sum_{k=1}^K d_{jk}$ and $Y_j = \sum_{k=1}^K Y_{jk}$ denote the number of events and the number at risk, respectively, in the combined sample at time t_j . Similarly, let $d_j^w = \sum_{k=1}^K d_{jk}^w$ and $Y_j^w = \sum_{k=1}^K Y_{jk}^w$ denote the weighted number of events and the weighted number at risk, respectively, in the combined sample at time t_j . The test statistic is

$$v_k = \sum_{j=1}^{D} \left(d_{jk}^w - Y_{jk}^w \frac{d_j^w}{Y_j^w} \right), \quad k = 1, \dots, K$$

and the variance of v_k and the covariance of v_k and v_h are, respectively,

$$\begin{split} V_{kk} &= \sum_{j=1}^{D} \left\{ \frac{d_{j}(Y_{j} - d_{j})}{Y_{j}(Y_{j} - 1)} \sum_{i=1}^{Y_{j}} \left[\left(\frac{Y_{jk}^{w}}{Y_{j}^{w}} \right)^{2} w_{i}^{2} I\{X_{i} \neq k\} + \left(\frac{Y_{j}^{w} - Y_{jk}^{w}}{Y_{j}^{w}} \right)^{2} w_{i}^{2} I\{X_{i} = k\} \right] \right\}, \quad 1 \leq k \leq K \\ V_{kh} &= \sum_{j=1}^{D} \left\{ \frac{d_{j}(Y_{j} - d_{j})}{Y_{j}(Y_{j} - 1)} \sum_{i=1}^{Y_{j}} \left[\frac{Y_{jk}^{w} Y_{jh}^{w}}{(Y_{j}^{w})^{2}} w_{i}^{2} I\{X_{i} \neq k, h\} - \frac{(Y_{j}^{w} - Y_{jk}^{w}) Y_{jh}^{w}}{(Y_{j}^{w})^{2}} w_{i}^{2} I\{X_{i} = k\} \right. \\ &\left. - \frac{(Y_{j}^{w} - Y_{jh}^{w}) Y_{jk}^{w}}{(Y_{j}^{w})^{2}} w_{i}^{2} I\{X_{i} = h\} \right] \right\}, \quad 1 \leq k \neq h \leq K \end{split}$$

Let $V = (V_{kh})$. Under H_0 , the weighted K-sample test has a χ^2 statistic given by

$$\chi^2 = (v_1, \dots, v_K) \mathbf{V}^-(v_1, \dots, v_K)'$$

with K-1 degrees of freedom.

Stratified Tests Suppose the test is to be stratified on M levels of a set of STRATA variables. Based only on the data of the sth stratum (s = 1, ..., M), let \mathbf{v}_s be the test statistic (Klein and Moeschberger 1997, Section 7.5) for the sth stratum, and let \mathbf{V}_s be its covariance matrix. Let

$$\mathbf{v} = \sum_{s=1}^{M} \mathbf{v}_{s}$$

$$\mathbf{V} = \sum_{s=1}^{M} \mathbf{V}_{s}$$

A global test statistic is constructed as

$$\chi^2 = \mathbf{v}'\mathbf{V}^-\mathbf{v}$$

Under the null hypothesis, the test statistic has a χ^2 distribution with the same degrees of freedom as the individual test for each stratum.

Multiple-Comparison Adjustments Let χ_r^2 denote a chi-square random variable with r degrees of freedom. Denote ϕ and Φ as the density function and the cumulative distribution function of a standard normal distribution, respectively. Let m be the number of comparisons; that is,

$$m = \begin{cases} \frac{k(k-1)}{2} & \text{DIFF} = \text{ALL} \\ k-1 & \text{DIFF} = \text{CONTROL} \end{cases}$$

For a two-sided test that compares the survival of the jth group with that of lth group, $1 \le j \ne l \le r$, the test statistic is

$$z_{jl}^2 = \frac{(v_j - v_l)^2}{V_{ij} + V_{ll} - 2V_{il}}$$

and the raw p-value is

$$p = \Pr(\chi_1^2 > z_{il}^2)$$

Adjusted p-values for various multiple-comparison adjustments are computed as follows:

• Bonferroni adjustment:

$$p = \min\{1, m \Pr(\chi_1^2 > z_{jl}^2)\}$$

• Dunnett-Hsu adjustment: With the first group being the control, let $C = (c_{ij})$ be the $(r-1) \times r$ matrix of contrasts; that is,

$$c_{ij} = \begin{cases} 1 & i = 1, \dots, r - 1, j = 2, \dots, r \\ -1 & j = i + 1, i = 2, \dots, r \\ 0 & \text{otherwise} \end{cases}$$

Let $\Sigma \equiv (\sigma_{ij})$ and $\mathbf{R} \equiv (r_{ij})$ be covariance and correlation matrices of $\mathbf{C}\mathbf{v}$, respectively; that is,

$$\Sigma = CVC'$$

and

$$r_{ij} = \frac{\sigma_{ij}}{\sqrt{\sigma_{ii}\sigma_{jj}}}$$

The factor-analytic covariance approximation of Hsu (1992) is to find $\lambda_1, \ldots, \lambda_{r-1}$ such that

$$\mathbf{R} = \mathbf{D} + \lambda \lambda'$$

where **D** is a diagonal matrix with the *j*th diagonal element being $1 - \lambda_j$ and $\lambda = (\lambda_1, \dots, \lambda_{r-1})'$. The adjusted *p*-value is

$$p = 1 - \int_{-\infty}^{\infty} \phi(y) \prod_{i=1}^{r-1} \left[\Phi\left(\frac{\lambda_i y + z_{jl}}{\sqrt{1 - \lambda_i^2}}\right) - \Phi\left(\frac{\lambda_i y - z_{jl}}{\sqrt{1 - \lambda_i^2}}\right) \right] dy$$

which can be obtained in a DATA step as

$$p = \text{PROBMC}(\text{"DUNNETT2"}, z_{ij}, ..., r-1, \lambda_1, ..., \lambda_{r-1}).$$

• Scheffé adjustment:

$$p = \Pr(\chi^2_{r-1} > z^2_{il})$$

• Šidák adjustment:

$$p = 1 - \{1 - \Pr(\chi_1^2 > z_{jl}^2)\}^m$$

• SMM adjustment:

$$p = 1 - [2\Phi(z_{il}) - 1]^m$$

which can also be evaluated in a DATA step as

$$p = 1 - \text{PROBMC}(\text{"MAXMOD"}, z_{il}, ..., m).$$

• Tukey adjustment:

$$p = 1 - \int_{-\infty}^{\infty} r\phi(y) [\Phi(y) - \Phi(y - \sqrt{2}z_{jl})]^{r-1} dy$$

which can also be evaluated in a DATA step as

$$p = 1 - \text{PROBMC}(\text{"RANGE"}, \sqrt{2}z_{il}, ., ., r).$$

Trend Tests Trend tests (Klein and Moeschberger 1997, Section 7.4) have more power to detect ordered alternatives as

$$H_2: S_1(t) \geq S_2(t) \geq \cdots \geq S_k(t), t \leq \tau$$
, with at least one inequality

or

$$H_2: S_1(t) \leq S_2(t) \leq \cdots \leq S_k(t), t \leq \tau$$
, with at least one inequality

Let $a_1 < a_2 < \cdots < a_k$ be a sequence of scores associated with the k samples. The test statistic and its standard error are given by $\sum_{j=1}^k a_j v_j$ and $\sum_{j=1}^k \sum_{l=1}^k a_j a_l V_{jl}$, respectively. Under H_0 , the z-score

$$Z = \frac{\sum_{j=1}^{k} a_j v_j}{\sqrt{\{\sum_{j=1}^{k} \sum_{l=1}^{k} a_j a_l V_{jl}\}}}$$

has, asymptotically, a standard normal distribution. PROC LIFETEST provides both one-tail and two-tail *p*-values for the test.

Rank Tests for the Association of Survival Time with Covariates

The rank tests for the association of covariates (Kalbfleisch and Prentice 1980, Chapter 6) are more general cases of the rank tests for homogeneity. In this section, the index α is used to label all observations, $\alpha = 1, 2, ..., n$, and the indices i, j range only over the observations that correspond to events, i, j = 1, 2, ..., k. The ordered event times are denoted as $t_{(i)}$, the corresponding vectors of covariates are denoted as $\mathbf{z}_{(i)}$, and the ordered times, both censored and event times, are denoted as t_{α} .

The rank test statistics have the form

$$\mathbf{v} = \sum_{\alpha=1}^{n} c_{\alpha, \delta_{\alpha}} \mathbf{z}_{\alpha}$$

where n is the total number of observations, $c_{\alpha,\delta_{\alpha}}$ are rank scores, which can be either log-rank or Wilcoxon rank scores, δ_{α} is 1 if the observation is an event and 0 if the observation is censored, and \mathbf{z}_{α} is the vector of covariates in the TEST statement for the α th observation. Notice that the scores, $c_{\alpha,\delta_{\alpha}}$, depend on the censoring pattern and that the terms are summed up over all observations.

The log-rank scores are

$$c_{\alpha,\delta_{\alpha}} = \sum_{(j:t_{(j)} \le t_{\alpha})} \left(\frac{1}{n_{j}} - \delta_{\alpha}\right)$$

and the Wilcoxon scores are

$$c_{\alpha,\delta_{\alpha}} = 1 - (1 + \delta_{\alpha}) \prod_{(j:t_{(j)} \le t_{\alpha})} \frac{n_j}{n_j + 1}$$

where n_j is the number at risk just prior to $t_{(j)}$.

The estimates used for the covariance matrix of the log-rank statistics are

$$\mathbf{V} = \sum_{i=1}^{k} \frac{\mathbf{V}_i}{n_i}$$

where V_i is the corrected sum of squares and crossproducts matrix for the risk set at time $t_{(i)}$; that is,

$$\mathbf{V}_i = \sum_{(\alpha:t_{\alpha} > t_{(i)})} (\mathbf{z}_{\alpha} - \bar{\mathbf{z}}_i)' (\mathbf{z}_{\alpha} - \bar{\mathbf{z}}_i)$$

where

$$\bar{\mathbf{z}}_i = \sum_{(\alpha: t_{\alpha} \ge t_{(i)})} \frac{\mathbf{z}_{\alpha}}{n_i}$$

The estimate used for the covariance matrix of the Wilcoxon statistics is

$$\mathbf{V} = \sum_{i=1}^{k} \left[a_i (1 - a_i^*) (2\mathbf{z}_{(i)}\mathbf{z}'_{(i)} + \mathbf{S}_i) - (a_i^* - a_i) \left(a_i \mathbf{x}_i \mathbf{x}'_i + \sum_{j=i+1}^{k} a_j (\mathbf{x}_i \mathbf{x}'_j + \mathbf{x}_j \mathbf{x}'_i) \right) \right]$$

where

$$a_{i} = \prod_{j=1}^{i} \frac{n_{j}}{n_{j}+1}$$

$$a_{i}^{*} = \prod_{j=1}^{i} \frac{n_{j}+1}{n_{j}+2}$$

$$\mathbf{S}_{i} = \sum_{(\alpha:t_{(i+1)}>t_{\alpha}>t_{(i)})} \mathbf{z}_{\alpha}\mathbf{z}'_{\alpha}$$

$$\mathbf{x}_{i} = 2\mathbf{z}_{(i)} + \sum_{(\alpha:t_{(i+1)}>t_{\alpha}>t_{(i)})} \mathbf{z}_{\alpha}$$

In the case of tied failure times, the statistics **v** are averaged over the possible orderings of the tied failure times. The covariance matrices are also averaged over the tied failure times. Averaging the covariance matrices over the tied orderings produces functions with appropriate symmetries for the tied observations; however, the actual variances of the **v** statistics would be smaller than the preceding estimates. Unless the proportion of ties is large, it is unlikely that this will be a problem.

The univariate tests for each covariate are formed from each component of \mathbf{v} and the corresponding diagonal element of \mathbf{V} as v_i^2/V_{ii} . These statistics are treated as coming from a chi-square distribution for calculation of probability values.

The statistic $\mathbf{v'V^-v}$ is computed by sweeping each pivot of the V matrix in the order of greatest increase to the statistic. The corresponding sequence of partial statistics is tabulated. Sequential increments for including a given covariate and the corresponding probabilities are also included in the same table. These probabilities are calculated as the tail probabilities of a chi-square distribution with one degree of freedom. Because of the selection process, these probabilities should not be interpreted as p-values.

If desired for data screening purposes, the output data set requested by the OUTTEST= option can be treated as a sum of squares and crossproducts matrix and processed by the REG procedure by using the option METHOD=RSQUARE. Then the sets of variables of a given size can be found that give the largest test statistics. Output 74.1 illustrates this process.

Analysis of Competing-Risks Data

Competing risks arise in studies in which individuals are exposed to two or more mutually exclusive failure events, denoted by $\delta \in \{1, \ldots, J\}$. When a failure occurs, you observe the time T and the cause of failure δ . The cumulative incidence function (CIF), also known as the subdistribution function, for failures of cause j is the probability

$$F_j(t) = \Pr(T \le t, \delta = j)$$

The nonparametric analysis of competing-risks data consists of estimating the CIF and comparing the CIFs of two or more groups.

Estimation of the CIF

For a set of competing-risks data with $J \ge 2$ causes of failure, let $t_1 < t_2 < \cdots < t_L$ be the distinct uncensored times. For each $l = 1, \dots, L$, let Y_l be the number of subjects at risk at t_l , and let d_{jl} be the number of failures of cause j at t_l . Let $\hat{S}(t)$ be the Kaplan-Meier estimator that would have been obtained by assuming that all failure causes are of the same type. Denote $t_0 = 0$.

The nonparametric maximum likelihood estimator of the CIF of cause j is

$$\hat{F}_{j}(t) = \sum_{t_{l} < t} \frac{d_{ji}}{Y_{l}} \hat{S}(t_{l-1})$$

PROC LIFETEST provides two standard error estimators of the CIF estimator: one is based on the theory of counting processes (Aalen 1978), and the other is based on the delta method (Marubini and Valsecchi 1995). You use the ERROR= option in the PROC LIFETEST statement to choose the standard error estimator. The default is the Aalen estimator (ERROR=AALEN). Denote $d_{.l} = \sum_{j=1}^{J} d_{jl}$.

Aalen Estimator

$$\hat{\sigma}_{A}^{2}(\hat{F}_{j}(t)) = \sum_{t_{l} \leq t} \left[\hat{F}_{j}(t) - \hat{F}_{j}(t_{l}) \right]^{2} \frac{d_{.l}}{(Y_{l} - 1)(Y_{l} - d_{.l})}$$

$$+ \sum_{t_{l} \leq t} \hat{S}^{2}(t_{l-1}) \frac{d_{kj}(Y_{l} - d_{jl})}{Y_{l}^{2}(Y_{l} - 1)}$$

$$- 2 \sum_{t_{l} \leq t} \left[\hat{F}_{j}(t) - \hat{F}_{j}(t_{l}) \right] \hat{S}(t_{l-1}) \frac{d_{jl}(Y_{l} - d_{jl})}{Y_{l}(Y_{l} - d_{.l})(Y_{l} - 1)}$$

Delta Estimator

$$\hat{\sigma}_{D}^{2}(\hat{F}_{j}(t)) = \sum_{t_{l} \leq t} \left[\hat{F}_{j}(t) - \hat{F}_{j}(t_{l}) \right]^{2} \frac{d_{l}}{Y_{l}(Y_{l} - d_{l})}$$

$$+ \sum_{t_{l} \leq t} \hat{S}^{2}(t_{l-1}) \frac{d_{jl}(Y_{l} - d_{jl})}{Y_{l}^{3}}$$

$$- 2 \sum_{t_{l} \leq t} \left[\hat{F}_{j}(t) - \hat{F}_{j}(t_{l}) \right] \hat{S}(t_{l-1}) \frac{d_{jl}}{Y_{l}^{2}}$$

Comparison of the CIF of a Competing Risk for Two or More Groups

Let K be the number of groups. Consider failure of type 1 to be the failure type of interest. Let F_{1k} be the cumulative incidence function of type 1 in group k. The null hypothesis to be tested is

$$H_0: F_{11} = F_{12} = \cdots = F_{1K} \equiv F_1^0$$

Gray (1988, Section 2) gives the following K-sample test procedure for testing H_0 . Let $(T_{ik}, \delta_{ik}), i = 1, \ldots, n_k$ be the observed data in the kth group. Without loss of generality, assume that there are only two types of failure (J = 2). The number of failures of type j by t is

$$N_{jk}(t) = \sum_{i=1}^{n_k} I(T_{ik} \le t, \delta_{ik} = j), \quad j = 1, 2$$

and the number of subjects at risk just before t in group k is

$$Y_k(t) = \sum_{i=1}^{n_k} I(T_{ik} \ge t)$$

For group k, let $\hat{S}_k(t)$ be the Kaplan-Meier estimator of the survivor function that you obtain by assuming that all failure causes are of the same type. The cumulative incidence function $F_{jk}(t)$ of type j in the kth group is estimated by

$$\hat{F}_{jk}(t) = \int_0^t \hat{S}_k(u-)Y_k^{-1}(u)dN_{jk}(u)$$

Let τ_k be the largest uncensored time in group k. Define

$$\hat{G}_{jk}(t) = 1 - \hat{F}_{jk}(t)$$

$$R_k(t) = I(\tau_k \ge t)Y_k(t)\frac{\hat{G}_{1k}(t-)}{\hat{S}_k(t-)}$$

The cumulative hazard of the subdistribution for group k, Γ_{1k} , is estimated by

$$\hat{\Gamma}_{1k}(t) = \int_0^t \frac{d\hat{F}_{1k}(u)}{\hat{G}_{1k}(u-)} = \int_0^t \frac{dN_{1k}(u)}{R_k(u-)}, \quad t \le \tau_k$$

Under the null hypothesis H_0 , you can estimate the null value of $\Gamma_{1k}(t)$, denoted by $\Gamma_1^0(t)$, by

$$\hat{\Gamma}_{1}^{0}(t) = \int_{0}^{t} \frac{dN_{1.}(u)}{R_{.}(u)}$$

The *K*-sample test is based on $\mathbf{z} = (z_1, \dots, z_K)'$, where

$$z_k = \int_0^{\tau_k} R_k(t) \left[d\hat{\Gamma}_{1k}(t) - d\hat{\Gamma}_1^0(t) \right]$$

You can estimate the asymptotic covariance matrix $\Sigma = (\sigma_{kk'})$ as

$$\hat{\sigma}_{kk'}^2 = \sum_{r=1}^K \int_0^{\tau_k \wedge \tau_{k'}} \frac{a_{kr}(t)a_{k'r}(t)}{\hat{h}_r(t)} d\hat{F}_1^0(t) + \sum_{r=1}^K \int_0^{\tau_k \wedge \tau_{k'}} \frac{b_{2kr}(t)b_{2k'r}(t)}{\hat{h}_r(t)} d\hat{F}_{2r}(t)$$

where

$$\hat{h}_{r}(t) = \frac{I(t \leq \tau_{r})Y_{r}(t)}{\hat{S}_{r}(t-)}$$

$$\hat{F}_{1}^{0}(t) = \int_{0}^{t} \frac{dN_{1.}(u)}{\hat{h}_{.}(u)}$$

$$\hat{G}_{1}^{0}(t) = 1 - \hat{F}_{1}^{0}(t)$$

$$a_{kr}(t) = d_{1kr}(t) + b_{1kr}(t)$$

$$b_{jkr}(t) = \left[I(j=1) - \frac{\hat{G}_{1}^{0}(t)}{\hat{S}_{r}(t)}\right] [c_{kr}(\tau_{k}) - c_{kr}(t)]$$

$$c_{kr}(t) = \int_{0}^{t} d_{1kr}(u)d\hat{\Gamma}_{1}^{0}(u)$$

$$d_{jkr}(t) = I(j=1)R_{k}(t) \frac{I(k=r) - \frac{\hat{h}_{r}(t)}{\hat{h}_{.}(t)}}{\hat{G}_{1}^{0}(t)}$$

Because $\sum_{k=1}^{K} z_k = 0$, only K-1 scores are linearly independent. The K-sample test statistic is formed as a quadratic form of the first K-1 components of \mathbf{z} and the inverse of the estimated covariance matrix. Under the null hypothesis H_0 , this K-sample test statistic has approximately a chi-square distribution with K-1 degrees of freedom.

If you specify the GROUP= option in the STRATA statement, you can obtain a stratified version of the test by computing the contributions to z_k and $\sigma_{kk'}^2$ for each stratum, summing the contributions over the strata, and proceeding as before.

Restricted Mean Analysis

Let T be a nonnegative random variable that represents the failure time of an individual from a homogeneous population. The survivor function (also known as the survival function) of T is defined as

$$S(t) = \Pr(T > t)$$

Assume that τ is a prespecified time point of interest. Let R be the minimum of T and τ ,

$$R = T \wedge \tau = \min(T, \tau)$$

The restricted mean survival time (RMST) is defined as the expected value of R:

$$RMST(\tau) = E(R) = E[min(T, \tau)]$$

It can be evaluated by the area under the survivor function over $[0, \tau]$ as

$$RMST(\tau) = \int_0^{\tau} S(u) du$$

The restricted mean time lost (RMTL) is defined as the expected value of $\tau - R$:

$$RMTL(\tau) = E(\tau - R) = \tau - E[\min(T, \tau)] = \int_0^{\tau} [1 - S(u)] du$$

Let $t_1 < t_2 < \dots < t_D$ represent the distinct event times. For each $i = 1, \dots, D$, let Y_i be the number of surviving units (the size of the risk set) just prior to t_i , and let d_i be the number of units that fail at t_i .

The Kaplan-Meier (product-limit) estimate of the survivor function at t_i is the cumulative product

$$\hat{S}(t_i) = \prod_{j=1}^{i} \left(1 - \frac{d_j}{Y_j} \right)$$

If the largest observed time is uncensored, the estimated mean survival time is

$$\hat{\mu} = \sum_{i=1}^{D} \hat{S}(t_{i-1})(t_i - t_{i-1})$$

where t_0 is defined to be zero.

 $RMST(\tau)$ is estimated by

$$\widehat{\text{RMST}}(\tau) = \int_0^\tau \hat{S}(t) dt = \sum_{i=1}^{N^*} \hat{S}(t_{i-1})(t_i - t_{i-1}) + \hat{S}(t_{N^*})(\tau - t_{N^*})$$

where N^* is the number of t_i values that are less than τ .

 $RMTL(\tau)$ is estimated by $\widehat{RMTL}(\tau) = \tau - RMST(\tau)$.

The standard error of $\widehat{RMST}(\tau)$ or $\widehat{RMTL}(\tau)$ is estimated as

$$\hat{\sigma} = \sqrt{\frac{m}{m-1} \sum_{i=1}^{N^*} \frac{d_i A_i^2}{Y_i (Y_i - d_i)}}$$

where

$$A_{i} = \int_{t_{i}}^{\tau} \hat{S}(t)dt = \sum_{j=i}^{N^{*}} \hat{S}(t_{j})(t_{j+1} - t_{j}) + \hat{S}(t_{N^{*}})(\tau - t_{N^{*}})$$

$$\frac{N^{*}}{2}$$

$$m = \sum_{j=1}^{N^*} d_j$$

You can use the TAU= suboption in the RMST or RMTL option in the PROC LIFETEST statement to specify a τ value in the calculation. Note that the term $\frac{m}{m-1}$ is omitted unless you specify the BC suboption in the RMST or RMTL option in the PROC LIFETEST statement. The WEIGHT statement is not supported for the restricted mean analysis.

Comparing the Restricted Means of Two or More Groups

Let K be the number of groups. Let $S_k(t)$ be the underlying survivor function of the kth group, k = 1, ..., K.

Assume that τ is a prespecified time point of interest and $S_k(\tau) > 0$. The following methods are presented in terms of RMST(τ), but they also extend to the analysis of RMTL(τ).

The null and alternative hypotheses to be tested are

$$H_0: \text{RMST}_1(\tau) = \text{RMST}_2(\tau) = \dots = \text{RMST}_K(\tau)$$

versus

 H_1 : at least one of the RMST_k(τ)'s is different.

Let $\widehat{\mathrm{RMST}}(\tau) = [\widehat{\mathrm{RMST}}_1(\tau), \widehat{\mathrm{RMST}}_2(\tau), \dots, \widehat{\mathrm{RMST}}_K(\tau)]^T$ be the vector of estimated RMSTs for the K groups.

Let $\hat{\Sigma}$ be the estimated covariance matrix for $\widehat{RMST}(\tau)$. It is a diagonal matrix, and the *j*th diagonal element is $\hat{\sigma}_{j}^{2}$, which is the estimated variance of $\widehat{RMST}_{j}(\tau)$.

Let D be a $(K-1) \times K$ matrix whose jth row is $e_j - e_{j+1}$, where e_j is a K-dimensional vector whose jth element is 1 and whose other elements are 0. The test statistic is computed as

$$(\widehat{\mathrm{RMST}}(\tau))^T D^T (D\hat{\Sigma}D^T)^- D\widehat{\mathrm{RMST}}(\tau)$$

Under the null hypothesis H_0 , this K-sample test statistic has approximately a chi-square distribution with degrees of freedom equal to the rank of $D\hat{\Sigma}D^T$.

If you specify the GROUP= option in the STRATA statement, you can obtain a stratified version of the test by computing $\widehat{\mathrm{RMST}}(\tau)$ and $\widehat{\Sigma}$ for each stratum, summing them over the strata, and performing the chi-square test as before.

If you specify the DIFF= option in the STRATA statement, you can make inference with regard to paired differences of the RMST. If you also specify the GROUP= option, the RMST for a given group under comparison is computed as the sample mean of the stratum-specific RMSTs of the corresponding group, and the variance is obtained as the variance of the sample mean. You can use the ADJUST= option in the STRATA statement to make multiple-comparison adjustments to the *p*-values.

Output Data Sets

OUTCIF= Data Set

You can specify the OUTCIF= option in the PROC LIFETEST statement to create an output data set that contains the cumulative incidence estimates. The data set contains the following columns:

- any specified BY variables
- the censoring variable as given in the TIME statement to indicate the failure of interest
- a numeric variable named STRATUM that numbers the strata, if you specify the STRATA statement

- any specified STRATA variables, whose values come from either their original values or the midpoints of the stratum intervals if you use cutpoints to define strata (semi-infinite intervals are labeled by their finite endpoint)
- the GROUP= variable, if you specify the GROUP= option in the STRATA statement
- the Timelist variable, if you specify the TIMELIST= option and the REDUCEOUT option in the PROC LIFETEST statement
- the time variable as specified in the TIME statement
- AtRisk, a variable that contains the number of subjects at risk just before the specified time. This variable is omitted if you specify the REDUCEOUT option in the PROC LIFETEST statement.
- Event, a variable that contains the number of subjects that fail at the specified time from the cause of
 interest. This variable is omitted if you specify the REDUCEOUT option in the PROC LIFETEST
 statement.
- AllEventTypes, a variable that contains the number of subjects that fail at the specified time from any
 cause. This variable is omitted if you specify the REDUCEOUT option in the PROC LIFETEST
 statement.
- CIF, a variable that contains the point estimates of the cumulative incidence function
- CIF_STDERR, a variable that contains the standard errors of the CIF estimator
- ALPHA, a variable that contains the α -level of the confidence intervals
- CONFTYPE, a variable that contains the name of the transformation that is applied to the CIF to compute the confidence intervals for the CIF
- CIF LCL, a variable that contains the lower confidence limits of the CIF
- CIF_UCL, a variable that contains the upper confidence limits of the CIF

Each estimated CIF contains an initial observation whose value is 1 for the CIF and 0 for the time. The output data set contains an observation for each distinct failure time when an event occurs or an observation is censored.

OUTSURV= Data Set

You can specify the OUTSURV= option in the PROC LIFETEST statement to create an output data set that contains the survival estimates. The data set contains the following columns:

- any specified BY variables
- a numeric variable STRATUM that numbers the strata, if you specify the STRATA statement
- any specified STRATA variables, their values coming from either their original values or the midpoints
 of the stratum intervals if endpoints are used to define strata (semi-infinite intervals are labeled by their
 finite endpoint)
- the GROUP= variables, if you specify the GROUP= option in the STRATA statement

- the time variable as specified in the TIME statement. For METHOD=KM, METHOD=BRESLOW, or METHOD=FH, it contains the observed failure or censored times. For the life-table estimates, it contains the lower endpoints of the time intervals.
- SURVIVAL, a variable that contains the survivor function estimates
- CONFTYPE, a variable that contains the name of the transformation applied to the survival time in the computation of confidence intervals
- SDF_LCL, a variable that contains the lower limits of the pointwise confidence intervals for the survivor function
- SDF_UCL, a variable that contains the upper limits of the pointwise confidence intervals for the survivor function

If the estimation uses the product-limit, Breslow, or Fleming-Harrington method, then the data set also contains the following:

- _CENSOR_, an indicator variable that has a value 1 for a censored observation and a value 0 for an event observation
- SDF STDERR, a variable that contains the standard error of the survivor function estimator
- HW_LCL, a variable that contains the lower limits of the Hall-Wellner confidence bands (if you specify the CONFBAND=HW option or the CONFBAND=ALL option in the PROC LIFETEST statement)
- HW_UCL, a variable that contains the upper limits of the Hall-Wellner confidence bands (if you specify the CONFBAND=HW option or the CONFBAND=ALL option in the PROC LIFETEST statement)
- EP_LCL, a variable that contains the lower limits of the equal-precision confidence bands (if you specify the CONFBAND=EP option or the CONFBAND=ALL option in the PROC LIFETEST statement)
- EP_UCL, a variable that contains the upper limits of the equal-precision confidence bands (if you specify the CONFBAND=EP option or the CONFBAND=ALL option in the PROC LIFETEST statement)

If the estimation uses the life-table method, then the data set also contains the following:

- MIDPOINT, a variable that contains the value of the midpoint of the time interval
- PDF, a variable that contains the density function estimates
- PDF_LCL, a variable that contains the lower endpoints of the PDF confidence intervals
- PDF_UCL, a variable that contains the upper endpoints of the PDF confidence intervals
- HAZARD, a variable that contains the hazard estimates
- HAZ LCL, a variable that contains the lower endpoints of the hazard confidence intervals
- HAZ_UCL, a variable that contains the upper endpoints of the hazard confidence intervals

Each survival function contains an initial observation with the value 1 for the SDF and the value 0 for the time. The output data set contains an observation for each distinct failure time if the product-limit, Breslow, or Fleming-Harrington method is used, or it contains an observation for each time interval if the life-table method is used. The product-limit, Breslow, or Fleming-Harrington survival estimates are defined to be right continuous; that is, the estimates at a given time include the factor for the failure events that occur at that time.

OUTTEST= Data Set

The OUTTEST= option in the LIFETEST statement creates an output data set that contains the rank statistics for testing the association of failure time with covariates. It contains the following:

- any specified BY variables
- _TYPE_, a character variable of length 8 that labels the type of rank test, either "LOG-RANK" or "WILCOXON"
- _NAME_, a character variable of length 8 that labels the rows of the covariance matrix and the test statistics
- the TIME variable, containing the overall test statistic in the observation that has _NAME_ equal to the name of the time variable and the univariate test statistics under their respective covariates.
- all variables listed in the TEST statement

The output is in the form of a symmetric matrix formed by the covariance matrix of the rank statistics bordered by the rank statistics and the overall chi-square statistic. If the value of _NAME_ is the name of a variable in the TEST statement, the observation contains a row of the covariance matrix and the value of the rank statistic in the time variable. If the value of _NAME_ is the name of the TIME variable, the observation contains the values of the rank statistics in the variables from the TEST list and the value of the overall chi-square test statistic in the TIME variable.

Two complete sets of statistics labeled by the _TYPE_ variable are produced, one for the log-rank test and one for the Wilcoxon test.

Displayed Output

The following sections describe the output that PROC LIFETEST produces by default. The output is organized into various tables, which are discussed in their order of appearance. The set of tables that PROC LIFETEST produces for a survival analysis, specifically with one type of failure, is different from the set of tables that it produces for an analysis of competing-risks data, which have multiple types of failure.

Tables for Survival Analysis

Product-Limit Survival Estimates

The "Product-Limit Survival Estimates" table is displayed if you request the product-limit method of estimation. The table displays the following:

- the observed (event or censored) time
- the number of units at risk (if you specify the ATRISK option in the PROC LIFETEST statement)
- the number of events (if you specify the ATRISK option in the PROC LIFETEST statement)
- the product-limit estimate of the survivor function
- the corresponding estimate of the cumulative distribution function of the failure time
- the standard error estimate of the survivor function estimator
- the Nelson-Aalen cumulative hazard function estimate (if you specify the NELSON option in the PROC LIFETEST statement)
- the standard error of the Nelson-Aalen estimator (if you specify the NELSON option in the PROC LIFETEST statement)
- the number of event times that have been observed
- the number of event or censored times that remain to be observed
- the frequency of the observed times (if you specify the FREQ statement)
- values of the ID variables (if you specify the ID statement)

The ODS name of this table is ProductLimitEstimates.

Breslow Survival Estimates

The "Breslow Survival Estimates" table is displayed if you request the Breslow method of estimation. The table displays the following:

- the observed (event or censored) time
- the number of units at risk (if you specify the ATRISK option in the PROC LIFETEST statement)
- the number of events (if you specify the ATRISK option in the PROC LIFETEST statement)
- the Breslow estimate of the survivor function
- the corresponding estimate of the cumulative distribution function of the failure time
- the standard error estimate of the survivor function estimator
- the Nelson-Aalen cumulative hazard function estimate (if you specify the NELSON option in the PROC LIFETEST statement)
- the standard error of the Nelson-Aalen estimator (if you specify the NELSON option in the PROC LIFETEST statement)
- the number of event times that have been observed
- the number of event or censored times that remain to be observed
- the frequency of the observed times (if you specify the FREQ statement)

• values of the ID variables (if you specify the ID statement)

The ODS name of this table is BreslowEstimates.

Fleming-Harrington Survival Estimates

The "Fleming-Harrington Survival Estimates" table is displayed if you request the Fleming-Harrington method of estimation. The table displays the following:

- the observed (event or censored) time
- the number of units at risk (if you specify the ATRISK option in the PROC LIFETEST statement)
- the number of events (if you specify the ATRISK option in the PROC LIFETEST statement)
- the Fleming-Harrington estimate of the survivor function
- the corresponding estimate of the cumulative distribution function of the failure time
- the standard error estimate of the survivor function estimator
- the Nelson-Aalen cumulative hazard function estimate (if you specify the NELSON option in the PROC LIFETEST statement)
- the standard error of the Nelson-Aalen estimator (if you specify the NELSON option in the PROC LIFETEST statement)
- the number of event times that have been observed
- the number of event or censored times that remain to be observed
- the frequency of the observed times (if you specify the FREQ statement)
- values of the ID variables (if you specify the ID statement)

The ODS name of this table is FlemingEstimates.

Quartile Estimates

The "Quartiles Estimates" table is displayed if you request the product-limit, Breslow, or Fleming-Harrington method of estimation. The table displays the following:

- point estimates of the quartiles of the survival times
- the lower and upper confidence limits for the quartiles

The ODS name of this table is Quartiles.

Mean Estimate

The "Mean Estimate" table is displayed if you request the product-limit, Breslow, or Fleming-Harrington method of estimation. The table displays the following:

- the estimated mean survival time
- the estimated standard error of the mean estimator

The ODS name of this table is Means.

Life-Table Survival Estimates

The "Life-Table Survival Estimates" table is displayed if you request the life-table method of estimation. The table displays the following:

- the time intervals into which the failure and censored times are distributed. Each interval is from the lower limit, up to but not including the upper limit; if the upper limit is infinity, the missing value is printed.
- the number of events that occur in the interval
- the number of censored observations that fall into the interval
- the effective sample size for the interval
- the estimate of conditional probability of events (failures) in the interval
- the standard error of the conditional probability estimator
- the estimate of the survival function at the beginning of the interval
- the estimate of the cumulative distribution function of the failure time at the beginning of the interval
- the standard error estimate of the survivor function estimator
- the estimate of the median residual lifetime, which is the amount of time elapsed before reducing the number of at-risk units to one-half. This is also known as the *median future lifetime* in Elandt-Johnson and Johnson (1980)).
- the estimated standard error of the median residual lifetime estimator
- the density function estimated at the midpoint of the interval
- the standard error estimate of the density estimator
- the hazard rate estimated at the midpoint of the interval
- the standard error estimate of the hazard estimator

The ODS name of this table is LifetableEstimates.

Summary of the Number of Censored and Uncensored Values

The "Summary of the Number of Censored and Uncensored Values" table displays following:

- the stratum identification (if you specify the STRATA statement)
- the total number of observations
- the number of event observations
- the number of censored observations
- the percentage of censored observations

The ODS name of this table is CensoredSummary.

Rank Statistics

The "Rank Statistics" table contains the test statistics of the nonparametric *k*-sample tests. The ODS name of this table is HomStats.

Covariance Matrix for the Log-Rank Statistics

The "Covariance Matrix for the Log-Rank Statistics" table is displayed if the log-rank *k*-sample test is requested. The ODS name of this table is LogrankHomCov.

Covariance Matrix for the Wilcoxon Statistics

The "Covariance Matrix for the Wilcoxon Statistics" table is displayed if the Wilcoxon *k*-sample test is requested. The ODS name of this table is WilHomCov.

Covariance Matrix for the Tarone Statistics

The "Covariance Matrix for the Tarone Statistics" table is displayed if the Tarone-Ware *k*-sample test is requested. The ODS name of this table is TaroneHomCov.

Covariance Matrix for the Peto Statistics

The "Covariance Matrix for the Peto Statistics" table is displayed if the Peto-Peto *k*-sample test is requested. The ODS name of this table is PetoHomCov.

Covariance Matrix for the ModPeto Statistics

The "Covariance Matrix for the ModPeto Statistics" table is displayed if the modified Peto-Peto *k*-sample test is requested. The ODS name of this table is ModPetoHomCov.

Covariance Matrix for the Fleming Statistics

The "Covariance Matrix for the Fleming Statistics" table is displayed if the Fleming-Harrington *k*-sample test is requested. The ODS name of this table is FlemingHomCov.

Legend for Strata

The "Legend for Strata" table is displayed if two or more variables are specified in the STRATA statement. The ODS name of this table is Legend.

Test of Equality over Strata

The "Test of Equality over Strata" table is displayed if an unstratified *k*-sample test is carried out. The table contains the chi-square statistics, degrees of freedom, and *p*-values of the nonparametric tests and the likelihood ratio test (which is based on the exponential distribution). The ODS name of this table is HomTests.

Stratified Test of Equality over Group

The "Stratified Test of Equality over Group" table is displayed if a stratified test is carried out. The tables contains the chi-square statistics, degrees of freedom, and *p*-values of the stratified tests. The ODS name of this table is HomTests.

Scores for Trend Test

The "Scores for Trend Test" table is displayed if you specify the TREND option in the STRATA statement. The table contains the set of scores used to construct the trend tests. The ODS name of this table is TrendScores.

Trend Tests

The "Trend Tests" table is displayed if you specify the TREND option in the STRATA statement. The table contains the results of the trend tests. The ODS name of this table is TrendTests.

Adjustment for Multiple Comparisons for the Log-Rank Test

The "Adjustment for Multiple Comparisons for the Log-Rank Test" table is displayed if the log-rank test and a multiple-comparison adjustment method are specified. The table contains the chi-square statistics and the raw and adjusted *p*-values of the paired comparisons. The ODS name of this table is SurvDiff.

Adjustment for Multiple Comparisons for the Wilcoxon Test

The "Adjustment for Multiple Comparisons for the Wilcoxon Test" table is displayed if the Wilcoxon test and a multiple-comparison method are specified. The table contains the chi-square statistics and the raw and adjusted *p*-values of the paired comparisons. The ODS name of this table is SurvDiff.

Adjustment for Multiple Comparisons for the Tarone Test

The "Adjustment for Multiple Comparisons for the Tarone Test" table is displayed if the Tarone-Ware test and a multiple-comparison method are specified. The table contains the chi-square statistics and the raw and adjusted *p*-values of the paired comparisons. The ODS name of this table is SurvDiff.

Adjustment for Multiple Comparisons for the Peto Test

The "Adjustment for Multiple Comparisons for the Peto Test" table is displayed if the Peto-Peto test and a multiple-comparison method are specified. The table contains the chi-square statistics and the raw and adjusted *p*-values of the paired comparisons. The ODS name of this table is SurvDiff.

Adjustment for Multiple Comparisons for the ModPeto Test

The "Adjustment for Multiple Comparisons for the ModPeto Test" table is displayed if the modified Peto-Peto test and a multiple-comparison method are specified. The table contains the chi-square statistics and the raw and adjusted *p*-values of the paired comparisons. The ODS name of this table is SurvDiff.

Adjustment for Multiple Comparisons for the Fleming Test

The "Adjustment for Multiple Comparisons for the Fleming Test" table is displayed if the Fleming-Harrington test and a multiple-comparison method are specified. The table contains the chi-square statistics and the raw and adjusted *p*-values of the paired comparisons. The ODS name of this table is SurvDiff.

Univariate Chi-Squares for the Log-Rank Test

The "Univariate Chi-Squares for the Log-Rank Test" table is displayed if you specify the TEST statement. The table displays the log-rank test results for individual variables in the TEST statement. The ODS name of this table is LogUniChiSq.

Covariance Matrix of the Log-Rank Statistics

The "Covariance Matrix of the Log-Rank Statistics" table is displayed if you specify the TEST statement. The table displays the estimated covariance matrix of the log-rank statistics for association. The ODS name of this table is LogTestCov.

Forward Stepwise Sequence of Chi-Squares for the Log-Rank Test

The "Forward Stepwise Sequence of Chi-Squares for the Log-Rank Test" table is displayed if you specify the TEST statement. The table contains the sequence of partial chi-square statistics for the log-rank test in the order of the greatest increase to the overall test statistic, the degrees of freedom of the partial chi-square statistics, the approximate probability values of the partial chi-square statistics, the chi-square increments for including the given variables, and the probability values of the chi-square increments. The ODS name of this table is LogForStepSeq.

Univariate Chi-Squares for the Wilcoxon Test

The "Univariate Chi-Squares for the Wilcoxon Test" table displays the Wilcoxon test results for individual variables in the TEST statement. The ODS name of this table is WilUniChiSq.

Covariance Matrix of the Wilcoxon Statistics

The "Covariance Matrix of the Wilcoxon Statistics" table is displayed if you specify the TEST statement. The table displays the estimated covariance matrix of the Wilcoxon statistics for association. The ODS name of this table is WilTestCov.

Forward Stepwise Sequence of Chi-Squares for the Wilcoxon Test

The "Forward Stepwise Sequence of Chi-Squares for the Wilcoxon Test" table is displayed if you specify the TEST statement. The table contains the sequence of partial chi-square statistics for the Wilcoxon test in the order of the greatest increase to the overall test statistic, the degrees of freedom of the partial chi-square statistics, the approximate probability values of the partial chi-square statistics, the chi-square increments for including the given variables, and the probability values of the chi-square increments. The ODS name of this table is WilForStepSeq.

Tables for Competing-Risks Analysis

Summary of Failure Outcomes

The "Summary of Failure Outcomes" table displays the following:

- the stratum identification, if you specify the STRATA statement
- the group identification, if you specify the GROUP= option in the STRATA statement

- the number of failure events of interest
- the number of competing events
- the number of censored observations

The ODS name of this table is FailureSummary.

Cumulative Incidence Function Estimates

The "Cumulative Incidence Function Estimates" table is displayed if you use the FAILCODE= option in the TIME statement to stipulate a competing-risk analysis. The table displays the following:

- the group identification, if you specify the GROUP= option in the STRATA statement
- the failure time of the event of interest
- the estimated cumulative incidence function
- the standard error estimate of the cumulative incidence estimator
- the lower and upper confidence limits of the cumulative incidence function

The ODS name of this table is CIF.

Gray's Test for Equality of Cumulative Incidence Functions

The "Gray's Test for Equality of Cumulative Incidence Functions" table is displayed if you specify the STRATA statement. The table displays the following:

- the failure code, if you specify more than one FAILCODE= option value
- the chi-square statistic of Gray's test (Gray 1988)
- the degrees of freedom
- the *p*-value

The ODS name of this table is GrayTest.

Tables for Restricted Mean Analysis

RMST Analysis Information

The "RMST Analysis Information" table is displayed if you specify the RMST option in the PROC LIFETEST statement to perform an RMST analysis. The table displays the following:

• the τ value that is used in computing the RMST

The ODS name of this table is RMSTInfo.

RMST Estimates

The "RMST Estimates" table is displayed if you specify the RMST option in the PROC LIFETEST statement to perform an RMST analysis. The table displays the following:

- the stratum identification, if you specify the STRATA statement
- the group identification, if you specify the GROUP= option in the STRATA statement
- the estimated RMST
- the standard error estimate of the RMST

The ODS name of this table is RMST.

RMST Test for Equality

The "RMST Test for Equality" table is displayed if you specify the STRATA statement and the RMST option in the PROC LIFETEST statement. The table displays the following:

- the source of the groups under comparison
- the chi-square statistic of the test
- the degrees of freedom
- the *p*-value

The ODS name of this table is RMSTTest.

Stratified RMST Test for Equality

The "Stratified RMST Test for Equality" table is displayed if you specify the GROUP= option in the STRATA statement and the RMST option in the PROC LIFETEST statement. The table displays the following:

- the source of the groups under comparison
- the chi-square statistic of the test
- the degrees of freedom
- the *p*-value

The ODS name of this table is RMSTStratifiedTest.

Restricted Mean Survival Time Comparisons

The "Restricted Mean Survival Time Comparisons" table is displayed if you specify the DIFF= option in the STRATA statement and the RMST option in the PROC LIFETEST statement. The table contains the chi-square statistics and the unadjusted and adjusted *p*-values of the paired comparisons. The ODS name of this table is RMSTDiff.

RMTL Analysis Information

The "RMTL Analysis Information" table if you specify the RMTL option in the PROC LIFETEST statement to perform an RMST analysis. The table displays the following:

• the τ value that is used in computing the RMTL

The ODS name of this table is RMTLInfo.

RMTL Estimates

The "RMTL Estimates" table is displayed if you specify the RMTL option in the PROC LIFETEST statement to perform an RMTL analysis. The table displays the following:

- the stratum identification, if you specify the STRATA statement
- the group identification, if you specify the GROUP= option in the STRATA statement
- the estimated RMTL
- the standard error estimate of the RMTL

The ODS name of this table is RMTL.

RMTL Test for Equality

The "RMTL Test for Equality" table is displayed if you specify the STRATA statement and the RMTL option in the PROC LIFETEST statement. The table displays the following:

- the source of the groups under comparison
- the chi-square statistic of the test
- the degrees of freedom
- the *p*-value

The ODS name of this table is RMTLTest.

Stratified RMTL Test for Equality

The "Stratified RMTL Test for Equality" table is displayed if you specify the GROUP= option in the STRATA statement and the RMTL option in the PROC LIFETEST statement. The table displays the following:

- the source of the groups under comparison
- the chi-square statistic of the test
- the degrees of freedom
- the *p*-value

The ODS name of this table is RMTLStratifiedTest.

Restricted Mean Time Lost Comparisons

The "Restricted Mean Time Lost Comparisons" table is displayed if you specify the DIFF= option in the STRATA statement and the RMTL option in the PROC LIFETEST statement. The table contains the chisquare statistics and the unadjusted and adjusted p-values of the paired comparisons. The ODS name of this table is RMTLDiff.

Plot Options Superseded by ODS Graphics

You can select one of the following three types of graphics in PROC LIFETEST: ODS, traditional, and line printer. ODS Graphics is the preferred method of creating graphs, superseding the other two.

When ODS Graphics is enabled, you can use the PLOTS= option in the PROC LIFETEST statement to create plots by using ODS Graphics. For more information about ODS Graphics options, see the PLOTS= option in the section "PROC LIFETEST Statement" on page 5576.

If ODS Graphics is not enabled and you specify the LINEPRINTER option, line printer plots are produced; otherwise traditional graphics are produced.

Table 74.4 summarizes the ways in which you can request graphics.

		PLOTS=	LINEPRINTER
Graphics Result	ODS Graphics	Option Specified?	Option Specified?
ODS Graphics	Enabled	Yes	No
ODS Graphics survival plot	Enabled	No	No
Traditional graphics	Disabled	Yes	No
Line printer plot	Enabled	Yes	Yes
Line printer plot	Disabled	Yes	Yes
No graphics	Disabled	No	No
No graphics	Disabled	No	Yes
No graphics	Enabled	No	Yes

Table 74.4 Ways of Displaying Graphics

Table 74.5 summarizes the options available in the PROC LIFETEST statement for line printer and traditional graphics.

Table 74.5	Line Printer and Traditional Graphics Options
	Available in the PROC LIFETEST Statement

Option	Description
Line Printer Plots	
FORMCHAR(1,2,7,9)=	Defines the characters to be used for line printer plot axes
LINEPRINTER	Specifies that plots be produced by a line printer
MAXTIME=	Specifies the maximum time value for plotting
NOCENSPLOT	Suppresses the plot of censored observations
PLOTS=	Specifies the plots to display

Table 74.5 continued

Option	Description
Traditional Graphics	
ANNOTATE=	Specifies an Annotate data set that adds features to plots
CENSOREDSYMBOL=	Defines the symbol to be used for censored observations in plots
DESCRIPTION=	Specifies the string that appears in the description field of the PROC
	GREPLAY master menu for the plots
EVENTSYMBOL=	Specifies the symbol to be used for event observations in plots
GOUT=	Specifies the graphics catalog name for saving graphics output
LANNOTATE=	Specifies an input data set that contains variables for local annota-
	tion
MAXTIME=	Specifies the maximum time value for plotting
PLOTS=	Specifies the plots to display

The following *options* are used to produce line printer and traditional graphics:

ANNOTATE=SAS-data-set

ANNO=SAS-data-set

specifies an input data set that contains appropriate variables for annotation of the traditional graphics. The ANNOTATE= option enables you to add features (for example, labels that explain extreme observations) to plots produced on graphics devices. The ANNOTATE= option cannot be used if you specify LINEPRINTER option or if ODS Graphics is enabled. The data set specified must be an ANNOTATE= type data set, as described in SAS/GRAPH: Reference.

The data set specified with the ANNOTATE= option in the PROC LIFETEST statement is "global" in the sense that the information in this data set is displayed in every plot produced by a single invocation of PROC LIFETEST.

CENSOREDSYMBOL=name | 'string'

CS=name | 'string'

specifies the symbol value for the censored observations in traditional graphics. The value, *name* or 'string', is the symbol value specification allowed in SAS/GRAPH software. The default is CS=CIRCLE. If you want to omit plotting the censored observations, specify CS=NONE. The CENSOREDSYMBOL= option cannot be used if you specify LINEPRINTER option or if you enable ODS Graphics.

DESCRIPTION='string'

DES='string'

specifies a descriptive string of up to 256 characters that appears in the "Description" field of the traditional graphics catalog. The description does not appear in the plots. By default, PROC LIFETEST assigns a description of the form PLOT OF vname versus hname, where vname and hname are the names of the y variable and the x variable, respectively. The DESCRIPTION= option cannot be used if you specify the LINEPRINTER option or if you enable ODS Graphics.

EVENTSYMBOL=name | 'string'

ES=name | 'string'

specifies the symbol value for the event observations in traditional graphics. The value, *name* or 'string', is the symbol value specification allowed in SAS/GRAPH software. The default is ES=NONE. The EVENTSYMBOL= option cannot be used if you specify the LINEPRINTER option or if you enable ODS Graphics.

FORMCHAR(1,2,7,9)='string'

defines the characters to be used for constructing the vertical and horizontal axes of the line printer plots. The string should be four characters. The first and second characters define the vertical and horizontal bars, respectively, which are also used in drawing the steps of the Kaplan-Meier, Breslow, or Fleming-Harrington survival curve. The third character defines the tick mark for the axes, and the fourth character defines the lower left corner of the plot. The default is FORMCHAR(1,2,7,9)='l-+-'. Any character or hexadecimal string can be used to customize the plot appearance. If you use hexadecimals, you must put an x after the closing quote. For example, to send the plot output to a printer with the IBM graphics character set (1 or 2), specify the following:

formchar (1, 2, 7, 9) = 'B3C4C5C0'x

See the chapter titled "The PLOT Procedure" in the Base SAS Procedures Guide for further information.

GOUT=graphics-catalog

specifies the graphics catalog for saving traditional graphics output from PROC LIFETEST. The default is Work.Gseg. The GOUT= option cannot be used if you specify the LINEPRINTER option or if you enable ODS Graphics. For more information, see the chapter titled "The GREPLAY Procedure" in *SAS/GRAPH: Reference*.

LANNOTATE=SAS-data-set

LANN=SAS-data-set

specifies an input data set that contains variables for local annotation of traditional graphics. You can use the LANNOTATE= option to specify a different annotation for each BY group, in which case the BY variables must be included in the LANNOTATE= data set. The LANNOTATE= option cannot be used if you specify the LINEPRINTER option or if you enable ODS Graphics. The data set specified must be an ANNOTATE= type data set, as described in *SAS/GRAPH: Reference*.

If there is no BY-group processing, the ANNOTATE= and LANNOTATE= options have the same effects.

LINEPRINTER

LS

specifies that plots are produced by a line printer instead of by a graphical device.

MAXTIME=value

specifies the maximum value of the time variable allowed on the plots so that outlying points do not determine the scale of the time axis of the plots. This option affects only the displayed plots and has no effect on any calculations.

NOCENSPLOT

NOCENS

requests that the plot of censored observations be suppressed when the LINEPRINTER and PLOTS= options are specified. This option is not needed when the life-table method is used to compute the survival estimates, because the plot of censored observations is not produced.

Line Printer PLOTS= Option

PLOTS=plot-request

PLOTS=(plot-requests)

controls the line printer plots produced. You must also specify the LINEPRINTER option to obtain line printer plots. When you specify only one *plot-request*, you can omit the parentheses around the *plot-request*. Here are some examples:

```
plots=s
plots=(s ls lls)
```

The *plot-requests* include the following:

CENSORED

C

specifies a plot of censored observations. This option is available for METHOD=KM, METHOD=BRESLOW, or METHOD=FH only.

SURVIVAL

S

specifies a plot of the estimated SDF versus time.

LOGSURV

LS

specifies a plot of the negative log of the estimated SDF versus time.

LOGLOGS

LLS

specifies a plot of the log of the negative log of the estimated SDF versus the log of time.

HAZARD

Н

specifies a plot of the estimated hazard function versus time (life-table method only).

PDF

Р

specifies a plot of the estimated probability density function versus time (life-table method only).

Traditional Graphics PLOTS= Option

PLOTS=plot-request < (NAME=name | 'string') >

PLOTS=(plot-request < (NAME=name | 'string') > <, ..., plot-request < (NAME=name | 'string') > >) controls plots produced in traditional graphics. To obtain traditional graphics, you must neither enable ODS Graphics nor specify the LINEPRINTER option. For each plot-request, you can use the NAME= option to specify a name to identify the plot. The name can be specified as a SAS name or as a quoted string of up to 256 characters. Only the first eight characters are used as the entry name in the GOUT= catalog. The plot-requests include the following:

SURVIVAL

S

plots the estimated survivor functions versus time.

LOGSURV

LS

plots the negative log of estimated survivor functions versus time.

LOGLOGS

LLS

plots the log of negative log of estimated survivor functions versus the log of time.

HAZARD

Н

plots estimated hazard function versus time (life-table method only).

PDF

Р

plots the estimated probability density function versus time (life-table method only).

When you specify only one *plot-request*, you can omit the parentheses around the *plot-request*. Here are some examples:

```
plots=s
plots=(s(name=Surv2), h(name=Haz2))
```

The latter requests a plot of the estimated survivor function versus time and a plot of the estimated hazard function versus time, with Surv2 and Haz2 as their names in the GOUT= catalog, respectively.

ODS Table Names

PROC LIFETEST assigns a name to each table it creates. You can use these names to reference the table when using the Output Delivery System (ODS) to select tables and create output data sets. These names are listed in Table 74.6. For more information about ODS, see Chapter 20, "Using the Output Delivery System."

 Table 74.6
 ODS Tables Produced by PROC LIFETEST

ODS Table Name	Description	Statement	Option
BreslowEstimates	Breslow estimates	PROC	METHOD=BRESLOW
CensoredSummary	Number of event and censored observations	PROC	METHOD=BRESLOW FH PI
CIF	Cumulative incidence function estimates	TIME	EVENTCODE
FailureSummary	Summary of failure outcomes for competing-risks data	TIME	EVENTCODE
FlemingEstimates	Fleming-Harrington estimates	PROC	METHOD=FH
FlemingHomCov	Covariance matrix for <i>k</i> -sample FLEMING statistics	STRATA	TEST=FLEMING
GrayTest	Results of <i>k</i> -sample test of Gray (1988) comparing CIFs	TIME, STRATA	EVENTCODE
HomStats	Test statistics for <i>k</i> -sample tests	STRATA	Default
HomTests	Results of <i>k</i> -sample tests	STRATA	Default
Legend	Strata legend for two or more strata variables	STRATA	
LifetableEstimates	Life-table survival estimates	PROC	METHOD=LT
LogForStepSeq	Forward stepwise sequence for the log-rank statistics for association	TEST	Default
LogrankHomCov	Covariance matrix for <i>k</i> -sample log-rank statistics	STRATA	TEST=LOGRANK
LogTestCov	Covariance matrix for log-rank statistics for association	TEST	Default
LogUniChisq	Univariate chi-squares for log-rank statistics for association	TEST	Default
Means	Mean and standard error of survival times	PROC	METHOD=PL
ModPetoHomCov	Covariance matrix for <i>k</i> -sample MODPETO statistics	STRATA	TEST=MODPETO
PetoHomCov	Covariance matrix for <i>k</i> -sample PETO statistics	STRATA	TEST=PETO
ProductLimitEstimates	Product-limit survival estimates	PROC	METHOD=PL
Quartiles	Quartiles of the survival times	PROC	METHOD=BRESLOW FH PI
RMST	Restricted mean survival time estimates	PROC	RMST
RMSTDiff	Adjustments for multiple comparisons	STRATA	ADJUST=
RMSTInfo	RMST analysis information	PROC	RMST
RMSTStratifiedTest	Results of stratified <i>k</i> -sample	PROC,	RMST, GROUP=
RMSTTest	RMST test Results of <i>k</i> -sample RMST test	STRATA PROC, STRATA	RMST

Table 74.6 continued

ODS Table Name	Description	Statement	Option
RMTL	Restricted mean time lost estimates	PROC	RMTL
RMTLDiff	Adjustments for multiple comparisons	STRATA	ADJUST=
RMTLInfo	RMTL analysis information	PROC	RMTL
RMTLStratifiedTest	Results of stratified <i>k</i> -sample RMTL test	PROC, STRATA	RMTL, GROUP=
RMTLTest	Results of <i>k</i> -sample RMTL test	PROC, STRATA	RMTL
SimDetails	Details of quantile simulations	STRATA	ADJUST=SIMULATE(REPO
SimResults	Quantile simulation results	STRATA	ADJUST=SIMULATE(REPO
SurvDiff	Adjustments for multiple comparisons	STRATA	ADJUST=
TaroneHomCov	Covariance matrix for <i>k</i> -sample TARONE statistics	STRATA	TEST=TARONE
TrendScores	Scores used to construct trend tests	STRATA	TREND
TrendTests	Results of trend tests	STRATA	TREND
WilcoxonHomCov	Covariance matrix for <i>k</i> -sample WILCOXON statistics	STRATA	TEST=WILCOXON
WilForStepSeq	Forward stepwise sequence for the log-rank statistics for association	TEST	Default
WilTestCov	Covariance matrix for log-rank statistics for association	TEST	Default
WilUniChiSq	Univariate chi-squares for Wilcoxon statistics for association	TEST	Default

ODS Graphics

Statistical procedures use ODS Graphics to create graphs as part of their output. ODS Graphics is described in detail in Chapter 21, "Statistical Graphics Using ODS."

Before you create graphs, ODS Graphics must be enabled (for example, by specifying the ODS GRAPH-ICS ON statement). For more information about enabling and disabling ODS Graphics, see the section "Enabling and Disabling ODS Graphics" on page 623 in Chapter 21, "Statistical Graphics Using ODS."

The overall appearance of graphs is controlled by ODS styles. Styles and other aspects of using ODS Graphics are discussed in the section "A Primer on ODS Statistical Graphics" on page 622 in Chapter 21, "Statistical Graphics Using ODS."

The survival plot is produced by default; other graphs are produced by using the PLOTS= option in the PROC LIFETEST statement. You can reference every graph produced through ODS Graphics with a name.

The names of the graphs that PROC LIFETEST generates are listed in Table 74.7, along with the required keywords for the PLOTS= option.

Table 74.7 Graphs Produced by PROC LIFETEST

ODS Graph Name	Plot Description	PLOTS= Option
cifPlot	Cumulative incidence function	CIF
cifPlot	Cumulative incidence function with pointwise confidence limits	CIF(CL)
cifPlot	Cumulative incidence function with Gray's test	CIF(TEST)
DensityPlot	Density function for life-table method	PDF
FailurePlot	Cumulative distribution function	survival(FAILURE)
HazardPlot	Hazard function for life-table method or smoothed hazard for product-limit,	HAZARD
	Breslow, or Fleming-Harrington method	
LogNegLogSurvivalPlot	Log(-log(survivor function))	LOGLOGS
NegLogSurvivalPlot	Log(survivor function)	LOGSURV
RMSTPlot	Restricted mean survival time curve	RMST
RMSTPlot	Restricted mean survival time curve with pointwise confidence limits	RMST(CL)
RMTLPlot	Restricted mean time lost curve	RMTL
RMTLPlot	Restricted mean time lost curve with pointwise confidence limits	RMTL(CL)
SurvivalPlot	Survivor function	SURVIVAL
SurvivalPlot	Survivor function with number of subjects at risk	SURVIVAL(ATRISK)
SurvivalPlot	Survivor function with pointwise confidence limits	SURVIVAL(CL)
SurvivalPlot	Survivor function with equal-precision band	SURVIVAL(CB=EP)
SurvivalPlot	Survivor function with Hall-Wellner band	SURVIVAL(CB=HW)
SurvivalPlot	Survivor function with homogeneity test	SURVIVAL(TEST)

Additional Dynamic Variables for Survival Plots Using ODS Graphics

PROC LIFETEST passes a number of summary statistics as dynamic variables to the ODS Graphics for survival plots. Table 74.8 and Table 74.9 list these additional dynamic variables for the Kaplan-Meier curves and the life-table curves, respectively. These dynamic variables are not declared in the templates for the survival curves, but you can declare them and use them to enhance the default plots. The names of the dynamic variables depend on the STRATA= suboption of the PLOTS=SURVIVAL option: STRATA=INDIVIDUAL produces a separate plot for each stratum, and STRATA=OVERALL produces one plot with overlaid curves.

STRATA= **Dynamic Description OVERLAY** StrVali Label for the *i*th stratum NObsi Number of observations in the *j*th stratum NEvent*i* Number of events in the *i*th stratum Median*j* Median survival time of the *j*th stratum LowerMedian*i* Lower median survival time of the *j*th stratum UpperMedian*i* Upper median survival time of the *j*th stratum PctMedianConfid Confidence of the median intervals in percent **INDIVIDUAL NObs** Number of observations **NEvent** Number of events Median Median survival time Lower median survival time LowerMedian UpperMedian Upper median survival time PctMedianConfid Confidence of the median interval in percent

Table 74.8 Additional Dynamic Variables for Stat.Graphics.ProductLimitSurvival

Table 74.9 Additional Dynamic Variables for Stat.Graphics.LifetableSurvival

STRATA=	Dynamic	Description
OVERLAY	StrVal <i>j</i>	Label for the <i>j</i> th stratum
	NObs <i>j</i>	Number of observations in the <i>j</i> th stratum
	NEvent <i>j</i>	Number of events in the <i>j</i> th stratum
INDIVIDUAL	NObs	Number of observations
	NEvent	Number of events

For information about all of the dynamic variables that are available for use in the ODS Graphics survival plot, see the section "Dynamic Variables" on page 936 in Chapter 23, "Customizing the Kaplan-Meier Survival Plot." For the use of the particular dynamic variables shown in this section, see the sections "Adding a Small Inset Table with Event Information" on page 915 and "Adding an External Table with Event Information" on page 917 in Chapter 23, "Customizing the Kaplan-Meier Survival Plot."

Modifying the Survival Plots

PROC LIFETEST, like other statistical procedures, provides a PLOTS= option and other options for modifying its graphical output without requiring template changes. Those options are sufficient for most purposes, and the following subsections of the section "Controlling the Survival Plot by Specifying Procedure Options" on page 873 in Chapter 23, "Customizing the Kaplan-Meier Survival Plot," provide examples:

- "Enabling ODS Graphics and the Default Kaplan-Meier Plot" on page 873
- "Individual Survival Plots" on page 875

- "Hall-Wellner Confidence Bands and Homogeneity Test" on page 877
- "Equal-Precision Bands" on page 878
- "Displaying the Patients-at-Risk Table inside the Plot" on page 880
- "Displaying the Patients-at-Risk Table outside the Plot" on page 882
- "Modifying At-Risk Table Times" on page 883
- "Reordering the Groups" on page 886
- "Suppressing the Censored Observations" on page 889
- "Failure Plots" on page 890

When those options are not sufficient, you can use a set of macros and macro variables to modify the graph templates. Using these macros and macro variables is easier than directly modifying the graph templates. The following subsections of the section "Controlling the Survival Plot by Modifying Graph Templates" on page 894 in Chapter 23, "Customizing the Kaplan-Meier Survival Plot," provide examples:

- "Changing the Plot Title" on page 897
- "Modifying the Y Axis" on page 899
- "Changing the Line Thickness" on page 901
- "Changing the Group Color" on page 902
- "Changing the Line Pattern" on page 903
- "Changing the Font" on page 904
- "Changing the Legend and Inset Position" on page 906
- "Changing How the Censored Points Are Displayed" on page 907
- "Adding a Y-Axis Reference Line" on page 908
- "Changing the Homogeneity Test Inset" on page 910
- "Changing the Second Title and Adding a Footnote" on page 912
- "Adding a Small Inset Table with Event Information" on page 915
- "Adding an External Table with Event Information" on page 917
- "Suppressing the Legend" on page 919
- "Kaplan-Meier Plot with Event Table and Other Customizations" on page 920

Examples: LIFETEST Procedure

Example 74.1: Product-Limit Estimates and Tests of Association

The data presented in Appendix I of Kalbfleisch and Prentice (1980) are coded in the following DATA step. The response variable, SurvTime, is the survival time in days of a lung cancer patient. Negative values of SurvTime are censored values. The covariates are Cell (type of cancer cell), Therapy (type of therapy: standard or test), Prior (prior therapy: 0=no, 10=yes), Age (age in years), DiagTime (time in months from diagnosis to entry into the trial), and Kps (performance status). A censoring indicator variable Censor is created from the data, with the value 1 indicating a censored time and the value 0 indicating an event time. Since there are only two types of therapy, an indicator variable, Treatment, is constructed for therapy type, with value 0 for standard therapy and value 1 for test therapy.

```
data VALung;
   drop check m;
  retain Therapy Cell;
   infile cards column=column;
   length Check $ 1;
   label SurvTime='Failure or Censoring Time'
     Kps='Karnofsky Index'
     DiagTime='Months till Randomization'
     Age='Age in Years'
     Prior='Prior Treatment?'
     Cell='Cell Type'
     Therapy='Type of Treatment'
     Treatment='Treatment Indicator';
  M=Column;
  input Check $ @@;
  if M>Column then M=1;
  if Check='s'|Check='t' then input @M Therapy $ Cell $ ;
   else input @M SurvTime Kps DiagTime Age Prior @@;
  if SurvTime > .;
   censor=(SurvTime<0);</pre>
  SurvTime=abs(SurvTime);
   Treatment=(Therapy='test');
   datalines;
standard squamous
 72 60 7 69 0
                 411 70 5 64 10
                                  228 60 3 38 0
                                                   126 60 9 63 10
118 70 11 65 10
                  10 20 5 49 0
                                   82 40 10 69 10
                                                   110 80 29 68 0
314 50 18 43 0
               -100 70 6 70 0
                                   42 60 4 81 0
                                                     8 40 58 63 10
                -25 80 9 52 10
                                   11 70 11 48 10
144 30 4 63 0
standard small
 30 60 3 61 0
                384 60 9 42
                              0
                                    4 40 2 35
                                                    54 80 4 63 10
 13 60 4 56 0
               -123 40 3 55 0
                                  -97 60 5 67 0
                                                   153 60 14 63 10
                117 80 3 46 0
 59 30 2 65 0
                                   16 30 4 53 10
                                                   151 50 12 69
                                                    18 20 15 42
 22 60 4 68 0
                 56 80 12 43 10
                                   21 40 2 55 10
                                                                 0
139 80 2 64 0
                  20 30 5 65
                              0
                                   31 75 3 65 0
                                                    52 70 2 55
                                                                 0
                  18 30 4 60 0
                                                   122 80 28 53 0
287 60 25 66 10
                                   51 60 1 67 0
27 60 8 62 0
                  54 70 1 67 0
                                    7 50 7 72 0
                                                     63 50 11 48 0
392 40 4 68 0
                  10 40 23 67 10
standard adeno
  8 20 19 61 10
                  92 70 10 60 0
                                   35 40 6 62
                                               0
                                                    117 80
                                                           2 38
132 80 5 50 0
                  12 50 4 63 10
                                  162 80 5 64 0
                                                     3 30 3 43 0
 95 80 4 34
standard large
177 50 16 66 10
                 162 80 5 62 0
                                  216 50 15 52
                                                    553 70 2 47 0
                                               0
                                                    200 80 12 41 10
278 60 12 63 0
                 12 40 12 68 10
                                  260 80 5 45
                                                0
156 70 2 66 0
                -182 90 2 62 0
                                  143 90 8 60 0
                                                    105 80 11 66 0
103 80 5 38 0
                 250 70 8 53 10
                                  100 60 13 37 10
test squamous
                                                  -231 50 8 52 10
                                  -87 80 3 48 0
999 90 12 54 10
                 112 80 6 60 0
242 50 1 70 0
                 991 70 7 50 10
                                  111 70 3 62 0
                                                     1 20 21 65 10
587 60 3 58 0
                389 90 2 62 0
                                   33 30 6 64 0
                                                     25 20 36 63 0
357 70 13 58 0
                 467 90 2 64 0
                                  201 80 28 52 10
                                                     1 50 7 35 0
 30 70 11 63 0
                 44 60 13 70 10
                                                     15 50 13 40 10
                                  283 90 2 51 0
test small
```

```
25 30
       2 69
             0
                -103 70 22 36 10
                                   21 20 4 71 0
                                                    13 30 2 62
                                                                 0
 87 60
       2 60 0
                   2 40 36 44 10
                                   20 30
                                          9 54 10
                                                     7 20 11 66
                                                                 0
       8 49 0
                  99 70
                        3 72
                                   8 80
                                          2 68
                                                    99 85
 24 60
                              0
                                              0
                                                           4 62
                                                                 0
 61 70 2 71 0
                  25 70
                        2 70
                              0
                                   95 70 1 61 0
                                                    80 50 17 71
                                                                 0
 51 30 87 59 10
                  29 40
                        8 67
test adeno
 24 40
       2 60 0
                  18 40 5 69 10
                                  -83 99
                                          3 57
                                               O
                                                    31 80
                                                           3 39
                                                                 0
 51 60
       5 62
                  90 60 22 50 10
                                   52 60
                                          3 43
                                               0
                                                    73 60
                                                           3 70
             0
                                                                 0
                                   48 10 4 81 0
  8 50
       5 66 0
                 36 70 8 61
                              0
                                                     7 40 4 58
                                                                 0
                 186 90
                              0
                                   84 80 4 62 10
                                                    19 50 10 42
140 70
       3 63 0
                        3 60
                                                                 0
       3 69 0
                 80 40
                        4 63
                              0
 45 40
test large
 52 60
       4 45 0
               164 70 15 68 10
                                   19 30 4 39 10
                                                    53 60 12 66
                                                                 0
 15 30 5 63 0
                 43 60 11 49 10
                                  340 80 10 64 10
                                                   133 75
                                                           1 65
                                                                 0
111 60 5 64 0
                 231 70 18 67 10
                                  378 80 4 65 0
                                                    49 30 3 37
;
```

In the following statements, PROC LIFETEST is invoked to compute the product-limit estimate of the survivor function for each type of cancer cell and to analyze the effects of the variables Age, Prior, DiagTime, Kps, and Treatment on the survival of the patients. These prognostic factors are specified in the TEST statement, and the variable Cell is specified in the STRATA statement. ODS Graphics must be enabled before producing graphs. Graphical displays of the product-limit estimates (S), the negative log estimates (LS), and the log of negative log estimates (LLS) are requested through the PLOTS= option in the PROC LIFETEST statement. Because of a few large survival times, a MAXTIME of 600 is used to set the scale of the time axis; that is, the time scale extends from 0 to a maximum of 600 days in the plots. The variable Therapy is specified in the ID statement to identify the type of therapy for each observation in the product-limit estimates. The OUTTEST option specifies the creation of an output data set named Test to contain the rank test matrices for the covariates.

```
ods graphics on;
proc lifetest data=VALung plots=(s,ls,lls) outtest=Test maxtime=600;
    time SurvTime*Censor(1);
    id Therapy;
    strata Cell;
    test Age Prior DiagTime Kps Treatment;
run;
ods graphics off;
```

Output 74.1.1 through Output 74.1.4 display the product-limit estimates of the survivor functions for the four cell types. Summary statistics of the survival times are also shown. The median survival times are 51 days, 156 days, 51 days, and 118 days for patients with adeno cells, large cells, small cells, and squamous cells, respectively.

Stratum 1: Cell Type = adeno

Product-Limit Survival Estimates							
			Survival				
C T	C	F - 11	Standard			T I	
SurvTime	Survival		Error	Failed	Left	Therapy	
0.000	1.0000	0	0	0	27		
3.000	0.9630	0.0370	0.0363	1		standard	
7.000	0.9259	0.0741	0.0504	2	25	test	
8.000	•		•	3	24	standard	
8.000	0.8519	0.1481	0.0684	4	23	test	
12.000	0.8148	0.1852	0.0748	5	22	standard	
18.000	0.7778	0.2222	0.0800	6	21	test	
19.000	0.7407	0.2593	0.0843	7	20	test	
24.000	0.7037	0.2963	0.0879	8	19	test	
31.000	0.6667	0.3333	0.0907	9	18	test	
35.000	0.6296	0.3704	0.0929	10	17	standard	
36.000	0.5926	0.4074	0.0946	11	16	test	
45.000	0.5556	0.4444	0.0956	12	15	test	
48.000	0.5185	0.4815	0.0962	13	14	test	
51.000	0.4815	0.5185	0.0962	14	13	test	
52.000	0.4444	0.5556	0.0956	15	12	test	
73.000	0.4074	0.5926	0.0946	16	11	test	
80.000	0.3704	0.6296	0.0929	17	10	test	
83.000	* .			17	9	test	
84.000	0.3292	0.6708	0.0913	18	8	test	
90.000	0.2881	0.7119	0.0887	19	7	test	
92.000	0.2469	0.7531	0.0850	20	6	standard	
95.000	0.2058	0.7942	0.0802	21	5	standard	
117.000	0.1646	0.8354	0.0740	22	4	standard	
132.000	0.1235	0.8765	0.0659	23	3	standard	
140.000	0.0823	0.9177	0.0553	24	2	test	
162.000	0.0412	0.9588	0.0401	25	1	standard	
186.000	0	1.0000		26	0	test	

Note: The marked survival times are censored observations.

Stratum 2: Cell Type = large

Product-Limit Survival Estimates							
			Survival Standard	Number	Number		
SurvTime	Survival	Failure	Error	Failed	Left	Therapy	
0.000	1.0000	0	0	0	27		
12.000	0.9630	0.0370	0.0363	1	26	standard	
15.000	0.9259	0.0741	0.0504	2	25	test	
19.000	0.8889	0.1111	0.0605	3	24	test	
43.000	0.8519	0.1481	0.0684	4	23	test	
49.000	0.8148	0.1852	0.0748	5	22	test	
52.000	0.7778	0.2222	0.0800	6	21	test	
53.000	0.7407	0.2593	0.0843	7	20	test	
100.000	0.7037	0.2963	0.0879	8	19	standard	
103.000	0.6667	0.3333	0.0907	9	18	standard	
105.000	0.6296	0.3704	0.0929	10	17	standard	
111.000	0.5926	0.4074	0.0946	11	16	test	
133.000	0.5556	0.4444	0.0956	12	15	test	
143.000	0.5185	0.4815	0.0962	13	14	standard	
156.000	0.4815	0.5185	0.0962	14	13	standard	
162.000	0.4444	0.5556	0.0956	15	12	standard	
164.000	0.4074	0.5926	0.0946	16	11	test	
177.000	0.3704	0.6296	0.0929	17	10	standard	
182.000	* .			17	9	standard	
200.000	0.3292	0.6708	0.0913	18	8	standard	
216.000	0.2881	0.7119	0.0887	19	7	standard	
231.000	0.2469	0.7531	0.0850	20	6	test	
250.000	0.2058	0.7942	0.0802	21	5	standard	
260.000	0.1646	0.8354	0.0740	22	4	standard	
278.000	0.1235	0.8765	0.0659	23	3	standard	
340.000	0.0823	0.9177	0.0553	24	2	test	
378.000	0.0412	0.9588	0.0401	25	1	test	
553.000	0	1.0000		26	0	standard	

Note: The marked survival times are censored observations.

Stratum 3: Cell Type = small

Product-Limit Survival Estimates								
	riou	uct-Liiiii	Survival	LStilliates	•			
			Standard					
SurvTime	Survival		Error	Failed	Left	Therapy		
0.000	1.0000	0	0	0	48			
2.000	0.9792	0.0208	0.0206	1		test		
4.000	0.9583	0.0417	0.0288	2		standard		
7.000				3		standard		
7.000	0.9167	0.0833	0.0399	4		test		
8.000	0.8958	0.1042	0.0441	5		test		
10.000	0.8750	0.1250	0.0477	6		standard		
13.000				7		standard		
13.000	0.8333	0.1667	0.0538	8		test		
16.000	0.8125	0.1875	0.0563	9		standard		
18.000				10		standard		
18.000	0.7708	0.2292	0.0607	11	-	standard		
20.000				12		standard		
20.000	0.7292	0.2708	0.0641	13		test		
21.000				14		standard		
21.000	0.6875	0.3125	0.0669	15		test		
22.000	0.6667	0.3333	0.0680	16		standard		
24.000	0.6458	0.3542	0.0690	17		test		
25.000	•	•	•	18		test		
25.000	0.6042	0.3958	0.0706	19		test		
27.000	0.5833	0.4167	0.0712	20	28	standard		
29.000	0.5625	0.4375	0.0716	21	27	test		
30.000	0.5417	0.4583	0.0719	22	26	standard		
31.000	0.5208	0.4792	0.0721	23	25	standard		
51.000	٠		•	24	24	standard		
51.000	0.4792	0.5208	0.0721	25	23	test		
52.000	0.4583	0.5417	0.0719	26	22	standard		
54.000				27	21	standard		
54.000	0.4167	0.5833	0.0712	28	20	standard		
56.000	0.3958	0.6042	0.0706	29		standard		
59.000	0.3750	0.6250	0.0699	30	18	standard		
61.000	0.3542	0.6458	0.0690	31	17	test		
63.000	0.3333	0.6667	0.0680	32	16	standard		
80.000	0.3125	0.6875	0.0669	33	15	test		
87.000	0.2917	0.7083	0.0656	34	14	test		
95.000	0.2708	0.7292	0.0641	35	13	test		
97.000	* .			35	12	standard		
99.000				36	11	test		
99.000	0.2257	0.7743	0.0609	37	10	test		
103.000	* .			37	9	test		
117.000	0.2006	0.7994	0.0591	38	8	standard		
122.000	0.1755	0.8245	0.0567	39	7	standard		
123.000	* .			39	6	standard		

Output 74.1.3 continued

The LIFETEST Procedure

Stratum 3: Cell Type = small

Product-Limit Survival Estimates							
SurvTime	Survival	Failure	Survival Standard Error	Number Failed	Number Left	Therapy	
139.000	0.1463	0.8537	0.0543	40	5	standard	
151.000	0.1170	0.8830	0.0507	41	4	standard	
153.000	0.0878	0.9122	0.0457	42	3	standard	
287.000	0.0585	0.9415	0.0387	43	2	standard	
384.000	0.0293	0.9707	0.0283	44	1	standard	
392.000	0	1.0000		45	0	standard	

Note: The marked survival times are censored observations.

Stratum 4: Cell Type = squamous

Product-Limit Survival Estimates							
				Survival Standard			
SurvTime		Survival		Error	Failed	Left	Therapy
0.000		1.0000	0	0	0	35	
1.000					1		test
1.000		0.9429	0.0571	0.0392	2		test
8.000		0.9143	0.0857	0.0473	3		standard
10.000		0.8857	0.1143	0.0538	4		standard
11.000		0.8571	0.1429	0.0591	5		standard
15.000		0.8286	0.1714	0.0637	6		test
25.000		0.8000	0.2000	0.0676	7		test
25.000	•				7		standard
30.000		0.7704	0.2296	0.0713	8		test
33.000		0.7407	0.2593	0.0745	9		test
42.000		0.7111	0.2889	0.0772	10		standard
44.000		0.6815	0.3185	0.0794	11		test
72.000		0.6519	0.3481	0.0813	12		standard
82.000		0.6222	0.3778	0.0828	13		standard
87.000	*		•	·	13		test
100.000	*			•	13	19	standard
110.000		0.5895	0.4105	0.0847	14	18	standard
111.000		0.5567	0.4433	0.0861	15	17	test
112.000		0.5240	0.4760	0.0870	16	16	test
118.000		0.4912	0.5088	0.0875	17	15	standard
126.000		0.4585	0.5415	0.0876	18	14	standard
144.000		0.4257	0.5743	0.0873	19	13	standard
201.000		0.3930	0.6070	0.0865	20	12	test
228.000		0.3602	0.6398	0.0852	21	11	standard
231.000	*				21	10	test
242.000		0.3242	0.6758	0.0840	22	9	test
283.000		0.2882	0.7118	0.0820	23	8	test
314.000		0.2522	0.7478	0.0793	24	7	standard
357.000		0.2161	0.7839	0.0757	25	6	test
389.000		0.1801	0.8199	0.0711	26	5	test
411.000		0.1441	0.8559	0.0654	27	4	standard
467.000		0.1081	0.8919	0.0581	28	3	test
587.000		0.0720	0.9280	0.0487	29	2	test
991.000		0.0360	0.9640	0.0352	30	1	test
999.000		0	1.0000		31	0	test

Note: The marked survival times are censored observations.

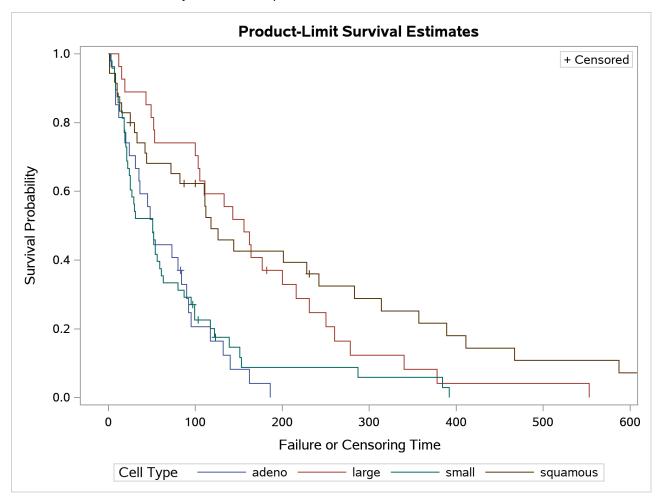
The distribution of event and censored observations among the four cell types is summarized in Output 74.1.5.

Output 74.1.5 Summary of Censored and Uncensored Values

Summary of the Number of Censored and Uncensored Values							
Stratum Cell Total Failed Censored Censored							
1	adeno	27	26	1	3.70		
2	large	27	26	1	3.70		
3	small	48	45	3	6.25		
4	squamous	35	31	4	11.43		
Total		137	128	9	6.57		

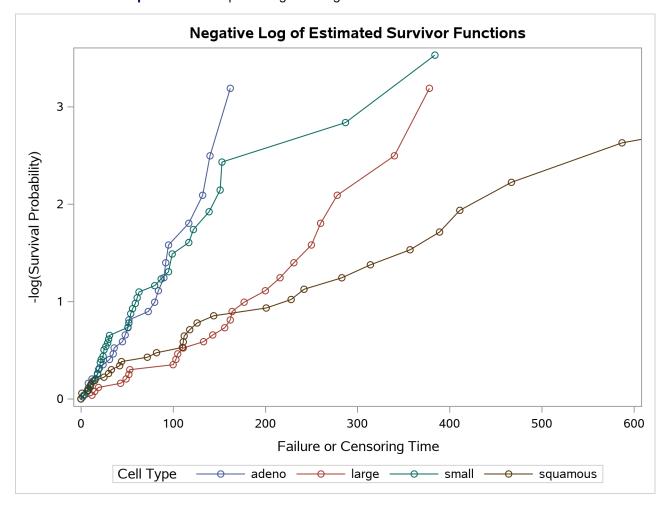
The graph of the estimated survivor functions is shown in Output 74.1.6. The adeno cell curve and the small cell curve are much closer to each other than they are to the large cell curve or the squamous cell curve. The survival rates of the adeno cell patients and the small cell patients decrease rapidly to approximately 29% in 90 days. Shapes of the large cell curve and the squamous cell curve are quite different, although both decrease less rapidly than those of the adeno and small cells. The squamous cell curve decreases more rapidly initially than the large cell curve, but the role is reversed in the later period.

Output 74.1.6 Graph of the Estimated Survivor Functions



The graph of the negative log of the estimated survivor functions is displayed in Output 74.1.7. Output 74.1.8 displays the log of the negative log of the estimated survivor functions against the log of time.

Output 74.1.7 Graph of Negative Log of the Estimated Survivor Functions



Log of Negative Log of Estimated Survivor Functions 1 0 log[-log(Survival Probability)] -1 -2 -3 2 0 6 log(Failure or Censoring Time) Cell Type adeno — large -— small

Output 74.1.8 Graph of Log of the Negative Log of the Estimated Survivor Functions

Results of the homogeneity tests across cell types are given in Output 74.1.9. The log-rank and Wilcoxon statistics and their corresponding covariance matrices are displayed. Also given is a table that consists of the approximate chi-square statistics, degrees of freedom, and p-values for the log-rank, Wilcoxon, and likelihood ratio tests. All three tests indicate strong evidence of a significant difference among the survival curves for the four types of cancer cells (p < 0.0001).

Output 74.1.9 Homogeneity Tests across Cell Types

Rank Statistics							
Cell Log-Rank Wilcox							
adeno	10.306	697.0					
large	-8.549	-1085.0					
small	14.898	1278.0					
squamous	-16.655	-890.0					

Output 74.1.9 continued

Covariance Matrix for the Log-Rank Statistics							
Cell	adeno	large	small	squamous			
adeno	12.9662	-4.0701	-4.4087	-4.4873			
large	-4.0701	24.1990	-7.8117	-12.3172			
small	-4.4087	-7.8117	21.7543	-9.5339			
squamous	-4.4873	-12.3172	-9.5339	26.3384			

Covariance Matrix for the Wilcoxon Statistics					
Cell	adeno	large	small	squamous	
adeno	121188	-34718	-46639	-39831	
large	-34718	151241	-59948	-56576	
small	-46639	-59948	175590	-69002	
squamous	-39831	-56576	-69002	165410	

Test of Equality over Strata						
Test	Chi-Square	DF	Pr > Chi-Square			
Log-Rank	25.4037	3	<.0001			
Wilcoxon	19.4331	3	0.0002			
-2Log(LR)	33.9343	3	<.0001			

Results of the log-rank test of the prognostic variables are shown in Output 74.1.10. The univariate test results correspond to testing each prognostic factor marginally. The joint covariance matrix of these univariate test statistics is also displayed. In computing the overall chi-square statistic, the partial chi-square statistics following a forward stepwise entry approach are tabulated.

Consider the log-rank test in Output 74.1.10. Since the univariate test for Kps has the largest chi-square (43.4747) among all the covariates, Kps is entered first. At this stage, the partial chi-square and the chisquare increment for Kps are the same as the univariate chi-square. Among all the covariates not in the model (Age, Prior, DiagTime, Treatment), Treatment has the largest approximate chi-square increment (1.7261) and is entered next. The approximate chi-square for the model that contains Kps and Treatment is 43.4747+1.7261=45.2008 with 2 degrees of freedom. The third covariate entered is Age. The fourth is Prior, and the fifth is DiagTime. The overall chi-square statistic in the last line of the output is the partial chi-square for including all the covariates. It has a value of 46.4200 with 5 degrees of freedom, which is highly significant (p < 0.0001).

Output 74.1.10 Log-Rank Test of the Prognostic Factors

	Univariate Chi-Squares for the Log-Rank Test						
Variable	Test Statistic	Standard Error	Chi-Square	Pr > Chi-Square	Label		
Age	-40.7383	105.7	0.1485	0.7000	Age in Years		
Prior	-19.9435	46.9836	0.1802	0.6712	Prior Treatment?		
DiagTime	-115.9	97.8708	1.4013	0.2365	Months till Randomization		
Kps	1123.1	170.3	43.4747	<.0001	Karnofsky Index		
Treatment	-4.2076	5.0407	0.6967	0.4039	Treatment Indicator		

Output 74.1.10 continued

Covariance Matrix for the Log-Rank Statistics						
Variable	Age	Prior	DiagTime	Kps	Treatment	
Age	11175.4	-301.2	-892.2	-2948.4	119.3	
Prior	-301.2	2207.5	2010.9	78.6	13.9	
DiagTime	-892.2	2010.9	9578.7	-2295.3	21.9	
Kps	-2948.4	78.6	-2295.3	29015.6	61.9	
Treatment	119.3	13.9	21.9	61.9	25.4	

I	Forward Stepwise Sequence of Chi-Squares for the Log-Rank Test							
	Pr > Chi-Square Pr >							
Variable	DF	Chi-Square	Chi-Square	Increment	Increment	Label		
Kps	1	43.4747	<.0001	43.4747	<.0001	Karnofsky Index		
Treatment	2	45.2008	<.0001	1.7261	0.1889	Treatment Indicator		
Age	3	46.3012	<.0001	1.1004	0.2942	Age in Years		
Prior	4	46.4134	<.0001	0.1122	0.7377	Prior Treatment?		
DiagTime	5	46.4200	<.0001	0.00665	0.9350	Months till Randomization		

You can establish this forward stepwise entry of prognostic factors by passing the matrix corresponding to the log-rank test to the RSQUARE method in the REG procedure, as follows. PROC REG finds the sets of variables that yield the largest chi-square statistics.

```
data RSq;
  set Test;
  if _type_='LOG RANK';
  _type_='cov';
run;
proc print data=RSq;
proc reg data=RSq(type=COV);
  model SurvTime=Age Prior DiagTime Kps Treatment
      / selection=rsquare;
  title 'All Possible Subsets of Covariates for the log-rank Test';
run;
```

Output 74.1.11 displays the univariate statistics and their covariance matrix for the log-rank test.

Output 74.1.11 Log-Rank Statistics and Covariance Matrix

Obs	_TYPE_	_NAME_	SurvTime	Age	Prior	DiagTime	Kps	Treatment
1	cov	SurvTime	46.42	-40.74	-19.94	-115.86	1123.14	-4.208
2	cov	Age	-40.74	11175.44	-301.23	-892.24	-2948.45	119.297
3	cov	Prior	-19.94	-301.23	2207.46	2010.85	78.64	13.875
4	cov	DiagTime	-115.86	-892.24	2010.85	9578.69	-2295.32	21.859
5	cov	Kps	1123.14	-2948.45	78.64	-2295.32	29015.62	61.945
6	cov	Treatment	-4.21	119.30	13.87	21.86	61.95	25.409

Results of the best subset regression are shown in Output 74.1.12. The variable Kps generates the largest univariate test statistic among all the covariates, the pair Kps and Age generate the largest test statistic among any other pairs of covariates, and so on. The entry order of covariates is identical to that of PROC LIFETEST.

Output 74.1.12 Best Subset Regression from the REG Procedure

All Possible Subsets of Covariates for the log-rank Test

The REG Procedure Model: MODEL1 Dependent Variable: SurvTime

R-Square Selection Method

Number in Model	R-Square	Variables in Model
1	0.9366	
1		DiagTime
1		Treatment
1	0.0039	
1	0.0032	
2		Kps Treatment
2	0.9472	Age Kps
2		Prior Kps
2 0.9382		DiagTime Kps
		DiagTime Treatment
2	0.0353	Age DiagTime
2 0.03		Prior DiagTime
2	0.0181	Prior Treatment
2 0.0159		Age Treatment
2 0.0075		Age Prior
3	0.9974	Age Kps Treatment
3	0.9774	Prior Kps Treatment
3	0.9747	DiagTime Kps Treatment
3	0.9515	Age Prior Kps
3	0.9481	Age DiagTime Kps
3	0.9418	Prior DiagTime Kps
3	0.0456	Age DiagTime Treatment
3	0.0438	Prior DiagTime Treatment
3	0.0355	Age Prior DiagTime
3	0.0192	Age Prior Treatment
4	0.9999	Age Prior Kps Treatment
4		Age DiagTime Kps Treatment
4		Prior DiagTime Kps Treatment
4		Age Prior DiagTime Kps
4		Age Prior DiagTime Treatment
5	1.0000	Age Prior DiagTime Kps Treatmen

Example 74.2: Enhanced Survival Plot and Multiple-Comparison Adjustments

This example highlights a number of features in the survival plot that uses ODS Graphics. Also shown in this example are comparisons of survival curves based on multiple comparison adjustments. Data of 137 bone marrow transplant patients extracted from Klein and Moeschberger (1997) have been saved in the data set BMT in the Sashelp library. At the time of transplant, each patient is classified into one of three risk categories: ALL (acute lymphoblastic leukemia), AML (acute myelocytic leukemia)-Low Risk, and AML-High Risk. The endpoint of interest is the disease-free survival time, which is the time to death or relapse or to the end of the study in days. In this data set, the variable Group represents the patient's risk category, the variable T represents the disease-free survival time, and the variable Status is the censoring indicator, with the value 1 indicating an event time and the value 0 a censored time.

The following step displays the first 10 observations of the BMT data set in Output 74.2.1. The data set is available in the Sashelp library.

```
proc print data=Sashelp.BMT(obs=10);
run;
```

Obs	Group	Т	Status
1	ALL	2081	0
2	ALL	1602	0
3	ALL	1496	0
4	ALL	1462	0
5	ALL	1433	0
6	ALL	1377	0
7	ALL	1330	0
8	ALL	996	0
9	ALL	226	0
10	ALL	1199	0

In the following statements, PROC LIFETEST is invoked to compute the product-limit estimate of the survivor function for each risk category. Using ODS Graphics, you can display the number of subjects at risk in the survival plot. The PLOTS= option requests that the survival curves be plotted, and the ATRISK= suboption specifies the time points at which the at-risk numbers are displayed. In the STRATA statement, the ADJUST=SIDAK option requests the Šidák multiple-comparison adjustment, and by default, all paired comparisons are carried out.

```
ods graphics on;
proc lifetest data=sashelp.BMT plots=survival(atrisk=0 to 2500 by 500);
   time T * Status(0);
   strata Group / test=logrank adjust=sidak;
run;
```

Output 74.2.2 displays the estimated disease-free survival for the three leukemia groups with the number of subjects at risk at 0, 500, 1,000, 1,500, 2,000, and 2,500 days. Patients in the AML-Low Risk group experience a longer disease-free survival than those in the ALL group, who in turn fare better than those in the AML-High Risk group.

Product-Limit Survival Estimates With Number of Subjects at Risk 1.0 + Censored 8.0 Survival Probability 0.6 0.4 0.2 0.0 1 38 16 11 0 2 45 13 10 7 6 3 54 36 27 18 0 500 1000 1500 2000 2500 Disease-Free Survival Time Disease Group 1: ALL -— 2: AML-High Risk 3: AML-Low Risk

Output 74.2.2 Estimated Disease-Free Survival for 137 Bone Marrow Transplant Patients

The log-rank test (Output 74.2.3) shows that the disease-free survival times for these three risk groups are significantly different (p = 0.001).

Output 74.2.3 Log-Rank Test of Disease Group Homogeneity

Test of Equality over Strata				
Test	Chi-Square	DF	Pr > Chi-Square	
Log-Rank	13.8037	2	0.0010	

The Šidák multiple-comparison results are shown in Output 74.2.4. There is no significant difference in disease-free survivor functions between the ALL and AML-High Risk groups (p = 0.2779). The difference between the ALL and AML-Low Risk groups is marginal (p = 0.0685), but the AML-Low Risk and AML-High Risk groups have significantly different disease-free survivor functions (p = 0.0006).

Output 74.2.4 All Paired Comparisons

Adjustment for Multiple Comparisons for the Logrank Test					
Strata Comparison p-Values					
Group	Group	Chi-Square	Raw	Sidak	
ALL	AML-High Risk	2.6610	0.1028	0.2779	
ALL	AML-Low Risk	5.1400	0.0234	0.0685	
AML-High Risl	AML-Low Risk	13.8011	0.0002	0.0006	

Suppose you consider the AML-Low Risk group as the reference group. You can use the DIFF= option in the STRATA statement to designate this risk group as the control and apply a multiple-comparison adjustment to the p-values for the paired comparison between the AML-Low Risk group with each of the other groups. Consider the Sidák correction again. You specify the ADJUST= and DIFF= options as in the following statements:

```
proc lifetest data=sashelp.BMT notable plots=none;
   time T * Status(0);
   strata Group / test=logrank adjust=sidak diff=control('AML-Low Risk');
run;
```

Output 74.2.5 shows that although both the ALL and AML-High Risk groups differ from the AML-Low Risk group at the 0.05 level, the difference between the AML-High Risk and the AML-Low Risk group is highly significant (p = 0.0004).

Output 74.2.5 Comparisons with the Reference Group

The LIFETEST Procedure

Adjustment for Multiple Comparisons for the Logrank Test					
Strata Co	mparison		p-Va	lues	
Group	Group	Chi-Square	Raw	Sidak	
ALL	AML-Low Risk	5.1400	0.0234	0.0462	
AML-High Risk	AML-Low Risk	13.8011	0.0002	0.0004	

The survival plot that is displayed in Output 74.2.2 might be sufficient for many purposes, but you might have other preferences. Typical alternatives include displaying the number of subjects at risk outside the plot area, reordering the stratum labels in the survival plot legend, and displaying the strata in the at-risk table by using their full labels. PROC LIFETEST provides options that you can use to make these changes without requiring template changes. In the sashelp.BMT data set, the variable Group that represents the strata is a character variable with three values, namely (in alphabetical order), ALL, AML-High Risk, and AML-Low Risk. It might be desirable to present the strata in the order ALL, AML-Low Risk, and AML-High Risk. The ORDER=INTERNAL option in the STRATA statement enables you to order the strata by their internal values. In the following statements, the new data set Bmt2 is a copy of sashelp.BMT with the variable Group changed to a a numeric variable with values 1, 2, and 3 representing ALL, AML-Low Risk, and AML-High Risk, respectively. The original character values of Group are kept as the formatted values, which are used to label the strata in the printed output.

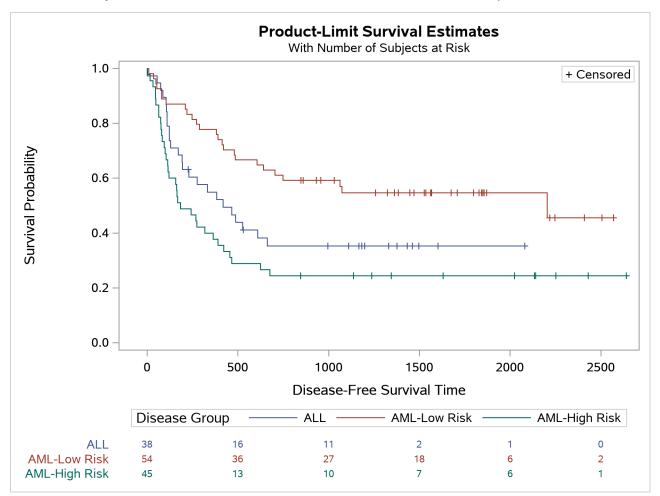
```
proc format;
  invalue $bmtifmt 'ALL' = 1 'AML-Low Risk' = 2 'AML-High Risk' = 3;
  value bmtfmt 1 = 'ALL' 2 = 'AML-Low Risk' 3 = 'AML-High Risk';
run;

data Bmt2;
  set sashelp.BMT(rename=(Group=G));
  Group = input(input(G, $bmtifmt.), 1.);
  label Group = 'Disease Group';
  format Group bmtfmt.;
  run:
```

The following statements produce a survival plot that has all the aforementioned modifications. The new data set Bmt2 is used as the input data. The OUTSIDE and MAXLEN= options are specified in the PLOTS= option. The OUTSIDE option draws the at-risk table outside the plot area. Because the longest label of the strata has 13 characters, specifying MAXLEN=13 is sufficient to display all the stratum labels in the at-risk table. The ORDER=INTERNAL option in the STRATA statement orders the strata by their numerical values 1, 2, and 3, which represent the order ALL, AML-Low Risk, and AML-High Risk, respectively.

```
proc LIFETEST data=Bmt2 plots=s(atrisk(outside maxlen=13)=0 to 2500 by 500);
  time T*Status(0);
  strata Group / order=internal;
run;
```

The modified survival plot is displayed in Output 74.2.6. The most noticeable change from Output 74.2.2 is that the number of subjects at risk is displayed below the time axis. Other changes include displaying the full labels of the strata in the at-risk table and presenting the strata in the order ALL, AML-Low Risk, and AML-High Risk.



Output 74.2.6 Modified Disease-Free Survival for Bone Marrow Transplant Patients

Klein and Moeschberger (1997, Section 4.4) describe in detail how to compute the Hall-Wellner (HW) and equal-precision (EP) confidence bands for the survivor function. You can output these simultaneous confidence intervals to a SAS data set by using the CONFBAND= and OUTSURV= options in the PROC LIFETEST statement. You can display survival curves with pointwise and simultaneous confidence limits through ODS Graphics. When the survival data are stratified, displaying all the survival curves and their confidence limits in the same plot can make the plot appear cluttered. In the following statements, the PLOTS= specification requests that the survivor functions be displayed along with their pointwise confidence limits (CL) and Hall-Wellner confidence bands (CB=HW). The STRATA=PANEL specification requests that the survival curves be displayed in a panel of three plots, one for each risk group.

```
proc lifetest data=Bmt2 plots=survival(cl cb=hw strata=panel);
   time T * Status(0);
   strata Group/order=internal;
run;
ods graphics off;
```

The panel plot is shown in Output 74.2.7.

0.2

0.0

0

500

1000

+ Censored

1500

Product-Limit Survival Curves Group = ALL 1.0 8.0 0.6 0.4 Survival Probability
SO 0 1 0 0 0 8 Group = AML-Low Risk Group = AML-High Risk 0.6 0.4

Output 74.2.7 Estimated Disease-Free Survivor Functions with Confidence Limits

Example 74.3: Life-Table Estimates for Males with Angina Pectoris

2000

The data in this example come from Lee (1992, p. 91) and represent the survival rates of males with angina pectoris. Survival time is measured as years from the time of diagnosis. In the following DATA step, the data are read as number of events and number of withdrawals in each one-year time interval for 16 intervals. Three variables are constructed from the data: Years (an artificial time variable with values that are the midpoints of the time intervals), Censored (a censoring indicator variable with the value 1 indicating censored observations and the value 0 indicating event observations), and Freq (the frequency variable). Two observations are created for each interval, one representing the event observations and the other representing the censored observations.

0

Disease-Free Survival Time

2500

500

95% Confidence Limits 95% Hall-Wellner Band

1000

1500

2000

2500

```
title 'Survival of Males with Angina Pectoris';
data Males;
  keep Freq Years Censored;
  retain Years -.5;
  input fail withdraw @@;
  Years + 1;
  Censored=0;
  Freq=fail;
  output;
  Censored=1;
  Freq=withdraw;
  output;
  datalines;
456 0 226 39 152 22 171 23 135 24 125 107
 83 133 74 102 51 68 42 64 43 45 34 53
 18 33 9 27 6 23 0 30
```

In the following statements, the ODS GRAPHICS ON specification enables ODS Graphics. PROC LIFETEST is invoked to compute the various life-table survival estimates, the median residual time, and their standard errors. The life-table method of computing estimates is requested by specifying METHOD=LT. The intervals are specified by the INTERVAL= option. Graphical displays of the life-table survivor function estimate, negative log of the estimate, log of negative log of the estimate, estimated density function, and estimated hazard function are requested by the PLOTS= option. No tests for homogeneity are carried out because the data are not stratified.

```
ods graphics on;
proc lifetest data=Males method=lt intervals=(0 to 15 by 1)
             plots=(s,ls,lls,h,p);
   time Years*Censored(1);
   freq Freq;
run;
ods graphics off;
```

Results of the life-table estimation are shown in Output 74.3.1. The five-year survival rate is 0.5193 with a standard error of 0.0103. The estimated median residual lifetime, which is 5.33 years initially, reaches a maximum of 6.34 years at the beginning of the second year and decreases gradually to a value lower than the initial 5.33 years at the beginning of the seventh year.

Output 74.3.1 Life-Table Survivor Function Estimate

Survival of Males with Angina Pectoris

The LIFETEST Procedure

	Life Table Survival Estimates										
Inte	rval										
[Lower,	Upper)	Number Failed	Number Censored		Conditional Probability of Failure	Conditional Probability Standard Error	Survival	Failure	Survival Standard Error	Median Residual Lifetime	Median Standard Error
0	1	456	0	2418.0	0.1886	0.00796	1.0000	0	0	5.3313	0.1749
1	2	226	39	1942.5	0.1163	0.00728	0.8114	0.1886	0.00796	6.2499	0.2001
2	3	152	22	1686.0	0.0902	0.00698	0.7170	0.2830	0.00918	6.3432	0.2361
3	4	171	23	1511.5	0.1131	0.00815	0.6524	0.3476	0.00973	6.2262	0.2361
4	5	135	24	1317.0	0.1025	0.00836	0.5786	0.4214	0.0101	6.2185	0.1853
5	6	125	107	1116.5	0.1120	0.00944	0.5193	0.4807	0.0103	5.9077	0.1806
6	7	83	133	871.5	0.0952	0.00994	0.4611	0.5389	0.0104	5.5962	0.1855
7	8	74	102	671.0	0.1103	0.0121	0.4172	0.5828	0.0105	5.1671	0.2713
8	9	51	68	512.0	0.0996	0.0132	0.3712	0.6288	0.0106	4.9421	0.2763
9	10	42	64	395.0	0.1063	0.0155	0.3342	0.6658	0.0107	4.8258	0.4141
10	11	43	45	298.5	0.1441	0.0203	0.2987	0.7013	0.0109	4.6888	0.4183
11	12	34	53	206.5	0.1646	0.0258	0.2557	0.7443	0.0111		
12	13	18	33	129.5	0.1390	0.0304	0.2136	0.7864	0.0114		
13	14	9	27	81.5	0.1104	0.0347	0.1839	0.8161	0.0118		
14	15	6	23	47.5	0.1263	0.0482	0.1636	0.8364	0.0123		
15		0	30	15.0	0	0	0.1429	0.8571	0.0133		

Interval		Evaluated at the Midpoint of the Interval					
[Lower,	Upper)	PDF	Hazard Standard Error				
0	1	0.1886	0.00796	0.208219	0.009698		
1	2	0.0944	0.00598	0.123531	0.008201		
2	3	0.0646	0.00507	0.09441	0.007649		
3	4	0.0738	0.00543	0.119916	0.009154		
4	5	0.0593	0.00495	0.108043	0.009285		
5	6	0.0581	0.00503	0.118596	0.010589		
6	7	0.0439	0.00469	0.1	0.010963		
7	8	0.0460	0.00518	0.116719	0.013545		
8	9	0.0370	0.00502	0.10483	0.014659		
9	10	0.0355	0.00531	0.112299	0.017301		
10	11	0.0430	0.00627	0.155235	0.023602		
11	12	0.0421	0.00685	0.17942	0.030646		
12	13	0.0297	0.00668	0.149378	0.03511		
13	14	0.0203	0.00651	0.116883	0.038894		
14	15	0.0207	0.00804	0.134831	0.054919		
15							

The breakdown of event and censored observations in the data is shown in Output 74.3.2. Note that 32.8% of the patients have withdrawn from the study.

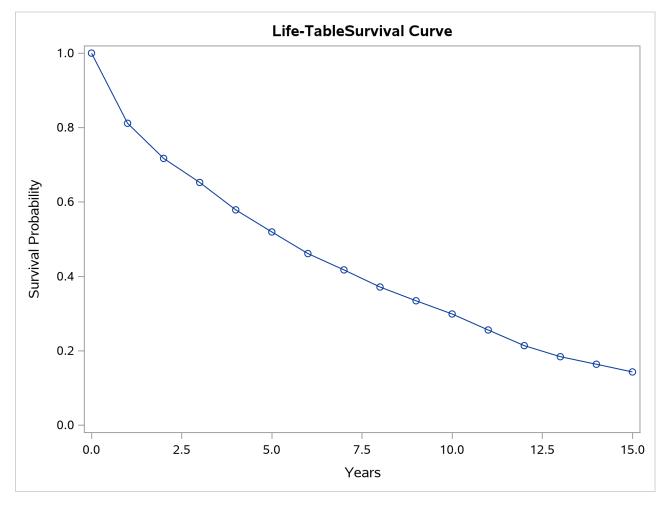
Output 74.3.2 Summary of Censored and Event Observations

Summary of the Number of							
Censored and Uncensored							
	Values						
			Percent				
Total	Failed	Censored	Censored				
2418		793	32.80				

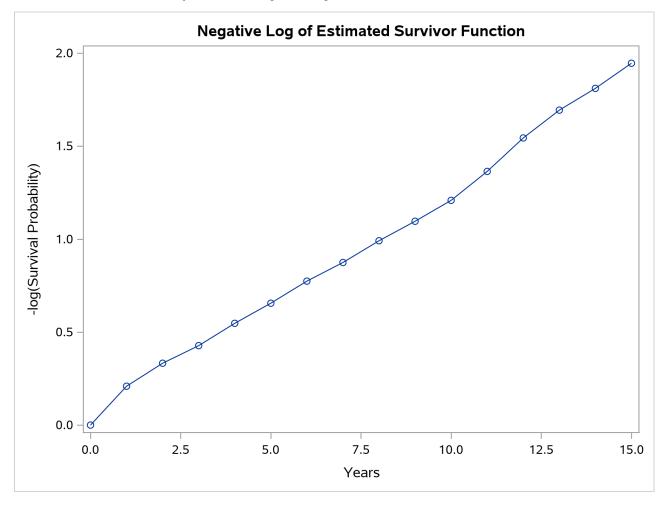
Note: 2 observations with invalid time, censoring, or frequency values were deleted.

Output 74.3.3 displays the graph of the life-table survivor function estimate. The median survival time, read from the survivor function curve, is 5.33 years, and the 25th and 75th percentiles are 1.04 and 11.13 years, respectively.

Output 74.3.3 Life-Table Survivor Function Estimate



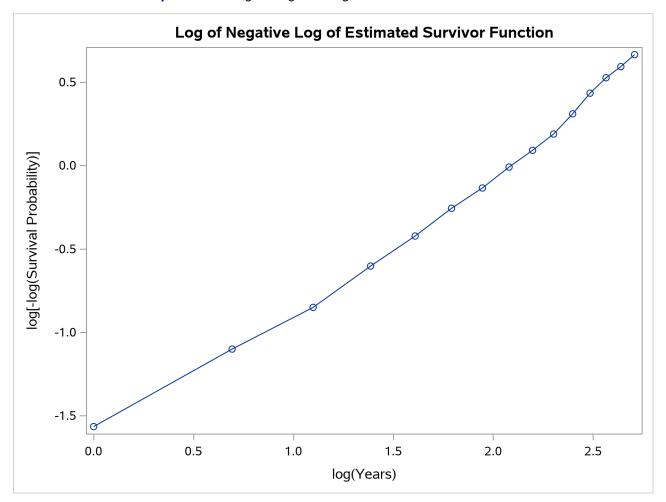
An exponential model might be appropriate for the survival of these male patients with angina pectoris since the curve of the negative log of the survivor function estimate versus the survival time (Output 74.3.4) approximates a straight line through the origin. Note that the graph of the log of the negative log of the survivor function estimate versus the log of time (Output 74.3.5) is practically a straight line.



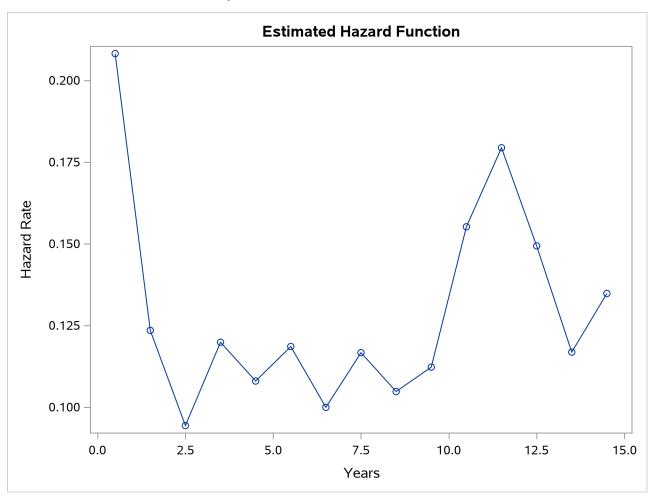
Output 74.3.4 Negative Log of Survivor Function Estimate

As discussed in Lee (1992), the graph of the estimated hazard function (Output 74.3.6) shows that the death rate is highest in the first year of diagnosis. From the end of the first year to the end of the tenth year, the death rate remains relatively constant, fluctuating between 0.09 and 0.12. The death rate is generally higher after the tenth year. This could indicate that a patient who has survived the first year has a better chance than a patient who has just been diagnosed. The profile of the median residual lifetimes also supports this interpretation.

Output 74.3.5 Log of Negative Log of Survivor Function Estimate



Output 74.3.6 Hazard Function Estimate



The density estimate is shown in (Output 74.3.7). Visually, it resembles the density function of an exponential distribution.

0.20 - 0.15 - 0.10 - 0.00 - 0.

Output 74.3.7 Density Function Estimate

Example 74.4: Nonparametric Analysis of Competing-Risks Data

Bone marrow transplant (BMT) is a standard treatment for acute leukemia. Klein and Moeschberger (1997) present a set of BMT data for 137 patients, grouped into three disease categories based on their status at the time of transplantation: acute lymphoblastic leukemia (ALL), acute myelocytic leukemia (AML) low-risk, and AML high-risk. During the follow-up period, some patients might relapse or some patients might die while in remission. Relapse and death in remission are competing events, and the disease-free survival time is the time from transplant to the occurrence of the earlier of these two events.

The following DATA step creates the data set Bmt. (This Bmt data set is not identical to the Sashelp.Bmt data set in Example 74.2, but both are derived from the same study.) The variable Disease denotes the disease group of a patient, which is either ALL, AML-low risk, or AML-high risk. The variable Dftime represents the disease-free survival time, which is the time to relapse, the time to death, or censored. The failure time is expressed in years by dividing the time in days by 356.25. The variable Status has three values: 0 for censored observations, 1 for relapsed patients, and 2 for patients who die before experiencing a relapse. The variable Gender, which indicates the gender of the BMT patients, is included to illustrate how to conduct a stratified test.

```
proc format;
   value diseaseLabel 1='ALL' 2='AML-Low Risk' 3='AML-High Risk';
   value genderLabel 0='Female' 1='Male';
run;
data Bmt;
   input Disease Dftime Status Gender@@;
   Dftime= Dftime / 365.25;
   label Dftime='Disease-Free Survival Time (Years)'
         Disease='Disease Group';
   datalines:
1
        2081
                   0
                                    1
                                            1602
                                                     0
                                                             1
1
        1496
                   0
                            1
                                    1
                                            1462
                                                     0
                                                             0
                   0
                                                             1
1
        1433
                            1
                                    1
                                             1377
                                                     0
                            1
                                    1
        1330
                                             996
                                                     0
                                                             1
   ... more lines ...
3
        625
                   1
                            0
                                    3
                                             48
                                                     1
                                                             0
3
        273
                   1
                            1
                                    3
                                             63
                                                     2
                                                             1
3
                                    3
                                                             0
        76
                   1
                            1
                                             113
                                                     1
3
        363
                    2
                            1
```

For competing-risks data, PROC LIFETEST estimates the cumulative incidence function (CIF). If you have multiple samples of data, it estimates the CIF for each sample and compares the CIFs between samples by using Gray's test (Gray 1988). The estimated CIF is a step function with a jump at each distinct time when the event of interest occurred. If there are a large number of such event times, the table of the estimated CIF could be quite lengthy. If you are interested in the cumulative incidence at specific time points, you can use the TIMELIST= option in the PROC LIFETEST statement to specify these time points, and PROC LIFETEST prints the CIF estimates only at these time points.

Consider relapse as the event of interest. The following statements use PROC LIFETEST to estimate the CIF for relapse. To designate relapse (Status=1) as the event of interest, you specify the option FAILCODE=1 in the TIME statement. The TIMELIST= option in the PROC LIFETEST statement specifies the time points to display the CIF estimate, at half a year, one year, one and a half years, two years, four years, and six years. The STRATA statement identifies the disease groups as different samples of data. The PLOTS= option requests a plot of the estimated CIF, with a inset that shows the *p*-value of Gray's test.

```
ods graphics on;
proc lifetest data=Bmt plots=cif(test) timelist=0.5 1.0 1.5 2.0 4.0 6.0;
   time Dftime*Status(0)/eventcode=1;
   strata Disease / order=internal;
   format Disease diseaseLabel. Gender genderLabel.;
run;
```

Output 74.4.1 tabulates the number of patients in each disease group who experience the event of interest (relapse) and those who experience the competing event (death in remission).

Failed Event: Status=1

Summary of Failure Outcomes								
	Failed Competing							
Stratum	Disease	Events	Events	Censored	Total			
1	ALL	12	12	14	38			
2	AML-Low Risk	9	16	29	54			
3	AML-High Risk	21	13	11	45			
Total		42	41	54	137			

Output 74.4.2 displays the CIF estimate of relapse for the ALL patients at the selected time points. The predicted CIF at half a year after transplant is 0.1842, with a 95% confidence interval of (0.0798, 0.3224). At two years after transplant, the estimated CIF is 0.3243, with a 95% confidence interval of (0.1778, 0.4787). It is not feasible to estimate the cumulative incidence at a time beyond the largest observed time, which is 5.6975 years in the ALL group. That is why the estimates are missing at six years.

Output 74.4.2 Estimated CIF for ALL Patients

Cumulative Incidence Function Estimates Stratum 1: Disease Group = ALL								
Timelist	Dftime	Cumulative Incidence	Standard Error	95% Confidence Interval				
0.5	0.353183	0.1842	0.0639	0.0798 0.3224				
1	0.629706	0.2380	0.0705	0.1164 0.3836				
1.5	1.048597	0.2654	0.0733	0.1360 0.4140				
2	1.812457	0.3243	0.0791	0.1788 0.4787				
4	1.812457	0.3243	0.0791	0.1788 0.4787				
6	•							

Output 74.4.3 and Output 74.4.4 display the CIF estimates at the selected times for AML-low risk and AML-high risk patients, respectively.

Output 74.4.3 Estimated CIF for AML-Low Risk Patients

Cumulative Incidence Function Estimates								
Stratum 2: Disease Group = AML-Low Risk								
	Cumulative Standard							
Timelist	Dftime	Incidence	Error	Interval				
0.5	0	0	0					
1	0.744695	0.0741	0.0360	0.0234 0.1646				
1.5	1.330595	0.1296	0.0463	0.0563 0.2344				
2	1.659138	0.1481	0.0489	0.0685 0.2565				
4	2.047912	0.1667	0.0514	0.0813 0.2783				
6	2.047912	0.1667	0.0514	0.0813 0.2783				

Output 74.4.4 Estimated CIF for AML-High Risk Patients

Cumulative Incidence Function Estimates Stratum 3: Disease Group = AML-High Risk Cumulative Standard Confidence Timelist Dftime Incidence Error Interval 0.5 0.429843 0.0686 0.1642 0.4259 0.2889 1 0.747433 0.3556 0.0726 0.2181 0.4955 1.5 1.278576 0.4444 0.0757 0.2940 0.5844 2 1.711157 0.4667 0.0761 0.3137 0.6059 0.0761 0.3137 0.6059 4 1.711157 0.4667 6 1.711157 0.4667 0.0761 0.3137 0.6059

Output 74.4.5 displays the homogeneity test of Gray (1988), which indicates strong evidence of a significant difference in the CIF for relapse among the three disease groups (p = 0.0028).

Output 74.4.5 Homogeneity Test of CIFs for Relapse

Gray's Test for Equality of
Cumulative Incidence
Functions

Pr >
Chi-Square
DF Chi-Square
11.9229 2 0.0026

The PLOTS= option produces a plot of the estimated CIFs (Output 74.4.5). Note that the range of each curve is from 0 to the largest observed time of the corresponding disease group, which is 5.6975 years for ALL patients, 7.0335 years for AML-low risk patients, and 7.2279 years for AML-high risk patients. With PLOTS=CIF(TEST) specified, that plot displays the *p*-value of the homogeneity test for the disease groups. The cumulative incidences of relapse are smallest for the AML-low risk patients and highest for the AML-high risk patients, with the ALL patients in between.

Cumulative Incidence Functions

1.0 - Gray's Test p=0.0026

0.8 - 0.4 - 0.2 - 0.0 -

Output 74.4.6 CIF Estimates of Relapse in Bone Marrow Transplant Study

When you specify the GROUP= option in the STRATA statement, PROC LIFETEST enables you to perform a stratified test to evaluate the homogeneity of the CIFs between groups. Consider Gender as the stratifying variable for the stratified test. You specify Gender in the STRATA statement with the GROUP=DISEASE option as follows:

ALL

Disease-Free Survival Time (Years)

- AML-Low Risk

AML-High Risk

```
proc lifetest data=bmt plots=cif(test);
    time Dftime*Status(0)/eventcode=1;
    strata Gender/group=Disease order=internal;
    format Disease diseaseLabel. Gender genderLabel.;
run;
ods graphics off;
```

Disease Group

PROC LIFETEST summarizes the number of events and censored observations in each disease group by gender (Output 74.4.7). PROC LIFETEST computes a separate CIF estimate for each disease category for the female patients (Output 74.4.8) and likewise for the male patients (not shown here).

The LIFETEST Procedure

Failed Event: Status=1

Summary of Failure Outcomes										
Failed Competing										
Stratum	Gender	Disease	Events	Events	Censored	Total				
1	Female	ALL	5	3	4	12				
1	Female	AML-Low Risk	3	7	14	24				
1	Female	AML-High Risk	12	6	3	21				
Subtotal			20	16	21	57				
2	Male	ALL	7	9	10	26				
2	Male	AML-Low Risk	6	9	15	30				
2	Male	AML-High Risk	9	7	8	24				
Subtotal			22	25	33	80				
Total			42	41	54	137				

Output 74.4.8 CIF Estimates for Female Patients

Cumulative Incidence Function Estimates Stratum 1: Gender = Female

	o a a a a	Genaei	· ciliale	
Disease	Dftime	Cumulative Incidence	Standard Error	95% Confidence Interval
				intervar
ALL	0	0	0	
ALL	0.150582	0.0833	0.0833	0.00422 0.3233
ALL	0.301164	0.1667	0.1126	0.0235 0.4250
ALL	0.334018	0.2500	0.1312	0.0544 0.5168
ALL	0.353183	0.3333	0.1433	0.0938 0.6004
ALL	0.629706	0.4333	0.1591	0.1384 0.7022
AML-Low Risk	0	0	0	
AML-Low Risk	0.744695	0.0417	0.0419	0.00271 0.1810
AML-Low Risk	1.043121	0.0833	0.0580	0.0135 0.2381
AML-Low Risk	1.330595	0.1250	0.0695	0.0299 0.2918
AML-High Risk	0	0	0	
AML-High Risk	0.131417	0.0476	0.0477	0.00303 0.2023
AML-High Risk	0.175222	0.0952	0.0658	0.0153 0.2665
AML-High Risk	0.229979	0.1429	0.0785	0.0339 0.3267
AML-High Risk	0.25462	0.1905	0.0882	0.0569 0.3832
AML-High Risk	0.309377	0.2381	0.0958	0.0832 0.4368
AML-High Risk	0.314853	0.2857	0.1018	0.1122 0.4879
AML-High Risk	0.328542	0.3333	0.1064	0.1435 0.5370
AML-High Risk	0.429843	0.3810	0.1098	0.1768 0.5841
AML-High Risk	0.733744	0.4286	0.1125	0.2113 0.6302
AML-High Risk	1.155373	0.4762	0.1144	0.2467 0.6748
AML-High Risk	1.278576	0.5238	0.1154	0.2834 0.7178
AML-High Risk	1.711157	0.5714	0.1155	0.3212 0.7590

Output 74.4.9 shows the results of the stratified test with a p-value of 0.0026, which is essentially the same as the p-value of the nonstratified test. The PLOTS= option creates a panel plot with two cells: one cell for female patients and the other cell for male patients. Each cell contains three CIF curves, one for each disease group (Output 74.4.10). Regardless of the gender of the patient, an AML-high risk patient is more likely to relapse than an ALL patient, and an ALL patient is more likely to relapse than an AML-low risk patient. This ordering of probabilities is revealed in the panel plots in Output 74.4.10.

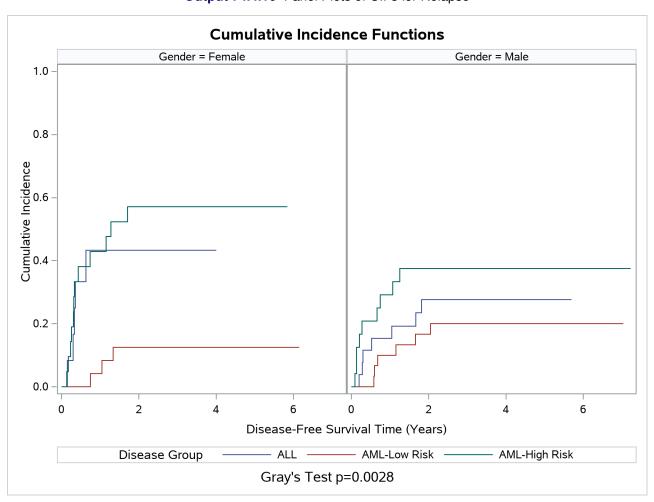
Output 74.4.9 Stratified Gray's Test

Gray's Test for Equality of Cumulative Incidence Functions

Pr > Chi-Square

11.7625 2 0.0028

Output 74.4.10 Panel Plots of CIFs for Relapse



Example 74.5: Restricted Mean Analysis

This example illustrates how to perform nonparametric analyses with respect to the restricted mean survival time (RMST) and the restricted mean time lost (RMTL). Consider the VALung data set in Example 74.1. The failure time variable is SurvTime. The censoring indicator variable is Censor, which has a value of 1 for a censored observation and a value of 0 for an uncensored observation. Each patient has one of the four types of cancer cells (adeno, large, small, and squamous) that are identified by the variable Cell.

The following statements use PROC LIFETEST to perform analyses of the restricted mean survival time (RMST) and restricted mean time lost (RMTL) in addition to the standard analyses:

```
ods graphics on;
proc lifetest data=VALung plots=(rmst rmt1) rmst rmt1(tau=90) maxtime=600;
    time SurvTime*Censor(1);
    strata Cell;
run;
ods graphics off;
```

The RMST and RMTL options estimate the restricted mean survival time and the restricted mean time lost, respectively. The variable Cell is specified in the STRATA statement to compute the RMST for each type of cancer cell. ODS Graphics must be enabled for graphs to be produced. Graphical displays of the RMST and RMTL curves are requested through the PLOTS= option in the PROC LIFETEST statement. Because of a few large survival times, a MAXTIME= option value of 600 is used to set the upper limit of the time axis; that is, the time horizon extends from 0 to a maximum of 600 days in the plots.

Output 74.5.1 displays the τ value that the RMST analysis uses. If you omit the TAU= option, PROC LIFETEST uses the smallest value among the largest observed times across the strata as the τ value.

Output 74.5.1 RMST Analysis Information

The LIFETEST Procedure

RMS	ST				
Analysis					
Information					
Tau	186				

Output 74.5.2 displays the RMST estimates for the four cell types.

Output 74.5.2 RMST Estimates

RMST Estimates							
Standard							
Stratum	Cell Type	Estimate	Error				
1	adeno	65.55556	9.9303				
2	large	128.0370	11.9858				
3	small	64.20647	8.2859				
4	squamous	113.8040	12.3703				

Output 74.5.3 displays information for the RMTL analysis. A τ value of 90 is shown; this is the value specified in the TAU= option.

Output 74.5.3 RMTL Analysis Information

RM	TL				
Analysis					
Information					
Tau	90				

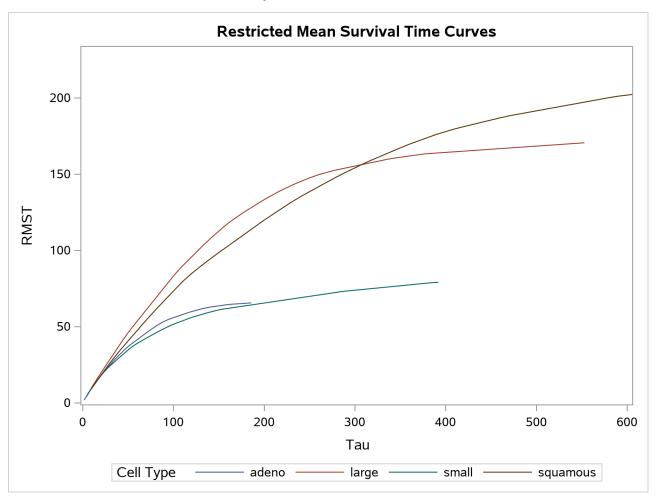
Output 74.5.4 displays the RMTL estimates for the four cell types at $\tau = 90$.

Output 74.5.4 RMTL Estimates at $\tau = 90$

RMTL Estimates								
Standard Stratum Cell Type Estimate Error								
	adeno	36.54321	6.3206					
2	large	14.33333	4.9560					
3	small	41.27083	4.6763					
4	squamous	22.99365	5.6430					

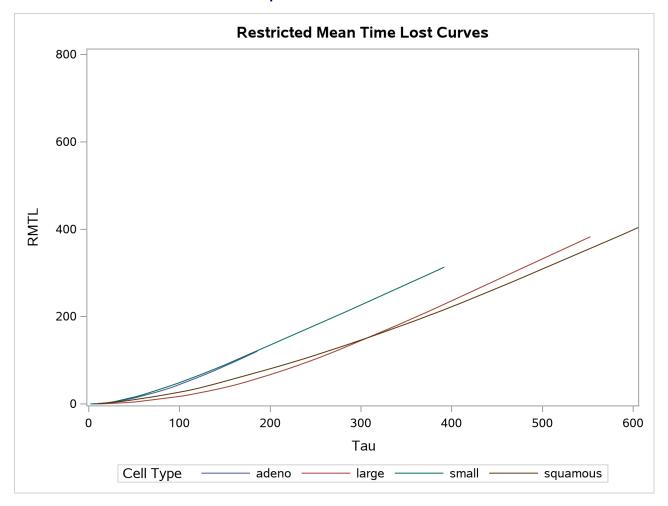
The graph of the estimated RMST curves is shown in Output 74.5.5. These curves exhibit a behavior similar to that of the survival curves in Example 74.1: the adeno cell curve and the small cell curve are much closer to each other than they are to the large cell curve or the squamous cell curve. The shapes of the large cell curve and the squamous cell curve are quite different, although both increase more rapidly than those of the adeno and small cells. The squamous cell curve initially increases less rapidly than the large cell curve, but the role is reversed in the later period.

Output 74.5.5 RMST Curves



The graph of the estimated RMTL curves is displayed in Output 74.5.6. Again, the adeno cell curve and the small cell curve are much closer to each other and farther away from the large cell and squamous cell curves.

Output 74.5.6 RMTL Curves



Results of the homogeneity test for the RMST across cell types are given in Output 74.5.7. The table displays the approximate chi-square statistic, degrees of freedom, and p-value. The test results indicate strong evidence that the RMSTs for the four types of cancer cells are not the same (p < 0.0001).

Output 74.5.7 Homogeneity Tests across Cell Types

RMST Test of Equality						
Source Chi-Square DF Pr > ChiSq						
Strata	28.4427	3	<.0001			

The homogeneity test does not identify which pairs of the RMSTs are different. In the following statements, you use the DIFF= option to compute the paired differences of the RMST among the groups. To protect yourself from falsely significant results, you use the ADJUST= option to make multiple-comparison adjustments to the resulting *p*-values.

```
proc lifetest data=VALung rmst;
   time SurvTime*Censor(1);
   strata Cell / diff=all adj=sidak;
run;
```

The Šidák multiple-comparison results are shown in Output 74.5.8.

Output 74.5.8 All Paired Comparisons

The LIFETEST Procedure

Restricted Mean Survival Time Comparisons Adjustment for Multiple Comparisons: Sidak

Pr > ChiSq

Stratum	Standard				
Comparison	Difference	Error	Chi-Square	Unadjusted	Adjusted
adeno large	-62.4815	15.5650	16.1141	<.0001	0.0004
adeno small	1.349087	12.9332	0.0109	0.9169	1.0000
adeno squamous	-48.2485	15.8630	9.2511	0.0024	0.0140
large small	63.83057	14.5710	19.1901	<.0001	<.0001
large squamous	14.23303	17.2245	0.6828	0.4086	0.9572
small squamous	-49.5975	14.8889	11.0967	0.0009	0.0052

The results suggest that you can divide the four risk groups into two classes. The first class consists of the small and adeno cell types, and there is no significant difference in the RMST between them (p = 1.0000). The second class consists of the large and squamous cell types, and the paired comparison is not significant (p = 0.9572). However, there is significant difference in any paired comparison between the two classes.

Suppose you consider the small cell type to be the reference group. You can use the DIFF= option in the STRATA statement to designate this risk group as the control and apply a multiple-comparison adjustment to the p-values for the paired comparison between the small cell type and the other cell types. Consider the Šidák correction again. You specify the ADJUST= and DIFF= options as in the following statements:

```
proc lifetest data=VALung rmst;
   time SurvTime*Censor(1);
   strata Cell / adj=sidak diff=control('small');
run;
```

Output 74.5.9 shows that both the large and squamous cell types differ from the small cell type at the 0.05 level, whereas the difference between the adeno and small cell types is not significant (p = 0.9994).

Output 74.5.9 Comparisons to the Reference Group

The LIFETEST Procedure

Restricted Mean Survival Time Comparisons Adjustment for Multiple Comparisons: Sidak

Pr > ChiSq

Stratum		Standard				
Comparison		Difference	Error	Chi-Square	Unadjusted	Adjusted
adeno	small	1.349087	12.9332	0.0109	0.9169	0.9994
large	small	63.83057	14.5710	19.1901	<.0001	<.0001
squamous	small	49.59754	14.8889	11.0967	0.0009	0.0026

- Aalen, O. (1978). "Nonparametric Estimation of Partial Transition Probabilities in Multiple Decrement Models." *Annals of Statistics* 6:534–545.
- Andersen, P. K., Borgan, Ø., Gill, R. D., and Keiding, N. (1992). *Statistical Models Based on Counting Processes*. New York: Springer-Verlag.
- Borgan, Ø., and Liestøl, K. (1990). "A Note on Confidence Interval and Bands for the Survival Curves Based on Transformations." *Scandinavian Journal of Statistics* 18:35–41.
- Brookmeyer, R., and Crowley, J. (1982). "A Confidence Interval for the Median Survival Time." *Biometrics* 38:29–41.
- Chung, C. F. (1986). Formulae for Probabilities Associated with Wiener and Brownian Bridge Processes. Technical Report 79, Laboratory for Research in Statistics and Probability, Carleton University, Ottawa.
- Collett, D. (1994). Modelling Survival Data in Medical Research. London: Chapman & Hall.
- Cox, D. R., and Oakes, D. (1984). Analysis of Survival Data. London: Chapman & Hall.
- Edwards, D., and Berry, J. J. (1987). "The Efficiency of Simulation-Based Multiple Comparisons." *Biometrics* 43:913–928.
- Elandt-Johnson, R. C., and Johnson, N. L. (1980). *Survival Models and Data Analysis*. New York: John Wiley & Sons.
- Fleming, T. R., and Harrington, D. P. (1981). "A Class of Hypothesis Tests for One and Two Samples of Censored Survival Data." *Communications in Statistics—Theory and Methods* 10:763–794.
- Fleming, T. R., and Harrington, D. P. (1984). "Nonparametric Estimation of the Survival Distribution in Censored Data." *Communications in Statistics—Theory and Methods* 13:2469–2486.
- Fleming, T. R., and Harrington, D. P. (1991). *Counting Processes and Survival Analysis*. New York: John Wiley & Sons.
- Gasser, T., and Müller, H. G. (1979). "Kernel Estimation of Regression Functions." In *Smoothing Techniques* for Curve Estimation: Proceedings of a Workshop Held in Heidelberg, April 2–4, 1979, edited by T. Gasser and M. Rosenblatt, 23–68. Vol. 757 of Lecture Notes in Mathematics. Berlin: Springer-Verlag.
- Gray, R. J. (1988). "A Class of K-Sample Tests for Comparing the Cumulative Incidence of a Competing Risk." *Annals of Statistics* 16:1141–1154.
- Hall, W. J., and Wellner, J. A. (1980). "Confidence Bands for a Survival Curve from Censored Data." *Biometrika* 67:133–143.
- Harrington, D. P., and Fleming, T. R. (1982). "A Class of Rank Test Procedures for Censored Survival Data." Biometrika 69:133–143.
- Hsu, J. C. (1992). "The Factor Analytic Approach to Simultaneous Inference in the General Linear Model." *Journal of Computational and Graphical Statistics* 1:151–168.

- Kalbfleisch, J. D., and Prentice, R. L. (1980). *The Statistical Analysis of Failure Time Data*. New York: John Wiley & Sons.
- Klein, J. P., and Moeschberger, M. L. (1997). *Survival Analysis: Techniques for Censored and Truncated Data*. New York: Springer-Verlag.
- Kramer, C. Y. (1956). "Extension of Multiple Range Tests to Group Means with Unequal Numbers of Replications." *Biometrics* 12:307–310.
- Lachin, J. M. (2000). *Biostatistical Methods: The Assessment of Relative Risks*. New York: John Wiley & Sons.
- Lawless, J. F. (1982). Statistical Methods and Methods for Lifetime Data. New York: John Wiley & Sons.
- Lee, E. T. (1992). Statistical Methods for Survival Data Analysis. 2nd ed. New York: John Wiley & Sons.
- Marubini, E., and Valsecchi, M. G. (1995). *Analysing Survival Data from Clinical Trials and Observational Studies*. Chichester, UK: John Wiley & Sons.
- Meeker, W. Q., and Escobar, L. A. (1998). *Statistical Methods for Reliability Data*. New York: John Wiley & Sons.
- Miller, R. G., Jr., and Siegmund, D. (1982). "Maximally Selected Chi-Square Statistics." *Biometrics* 1011–1016.
- Nair, V. N. (1984). "Confidence Bands for Survival Functions with Censored Data: A Comparative Study." *Technometrics* 26:265–275.
- Ramlau-Hansen, H. (1983a). "The Choice of a Kernel Function in the Graduation of Counting Process Intensities." *Scandinavian Actuarial Journal* 165–182.
- Ramlau-Hansen, H. (1983b). "Smoothing Counting Process Intensities by Means of Kernel Functions." *Annals of Statistics* 11:453–466.
- Westfall, P. H., Tobias, R. D., Rom, D., Wolfinger, R. D., and Hochberg, Y. (1999). *Multiple Comparisons and Multiple Tests Using the SAS System*. Cary, NC: SAS Institute Inc.
- Xie, J., and Liu, C. (2005). "Adjusted Kaplan-Meier Estimator and Log-Rank Test with Inverse Probability of Treatment Weighting for Survival Data." *Statistics in Medicine* 24:3089–3110.
- Xie, J., and Liu, C. (2011). "Adjusted Log-Rank Test for More Than Two Groups." Unpublished manuscript.

Subject Index

actuarial estimates, see life-table estimates	event symbol
alpha level	traditional graphics (LIFETEST), 5633
LIFETEST procedure, 5578	
annotate	Fleming-Harrington estimates
traditional graphics (LIFETEST), 5632	LIFETEST procedure, 5566, 5596
arcsine-square root transformation	Fleming-Harrington G_{ρ} test for homogeneity
confidence intervals (LIFETEST), 5579, 5602,	LIFETEST procedure, 5566, 5593
5604	Colon to the Wiles and the Colon was in
association tests	Gehan test, see Wilcoxon test for homogeneity
LIFETEST procedure, 5567, 5574, 5651	Hall-Wellner bands
at-risk	LIFETEST procedure, 5578, 5604, 5658
product-limit estimates (LIFETEST), 5578	hazard function
	LIFETEST procedure, 5566, 5665
Bonferroni adjustment	homogeneity tests
LIFETEST procedure, 5590	LIFETEST procedure, 5566, 5573, 5607, 5650
Breslow estimates	En E1E51 procedure, 5500, 5575, 5007, 5050
LIFETEST procedure, 5566, 5596	interval determination
Breslow test, see Wilcoxon test for homogeneity	LIFETEST procedure, 5601
	interval width
catalog	life-table method (LIFETEST), 5587
traditional graphics (LIFETEST), 5633	intervals
CDF, see cumulative distribution function	life-table estimates (LIFETEST), 5579
censored	
LIFETEST procedure, 5566, 5594	k-sample tests, see homogeneity tests
censored symbol	Kaplan-Meier estimates, see product-limit estimates
traditional graphics (LIFETEST), 5632	kernel-smoothed hazard
character set	LIFETEST procedure, 5583, 5605
line printer plots (LIFETEST), 5633	110 11
confidence bands	life-table estimates
LIFETEST procedure, 5578, 5603	LIFETEST procedure, 5566, 5624, 5662
confidence limits	LIFETEST procedure
LIFETEST procedure, 5601, 5620	alpha level, 5578
cumulative distribution function	association tests, 5567, 5574, 5611, 5640, 5651
LIFETEST procedure, 5566	Bonferroni adjustment, 5590
cumulative incidence function	Breslow estimates, 5566, 5580, 5596
LIFETEST procedure, 5619	censored, 5566, 5594
cumulative incidence function estimates	computational formulas, 5596
LIFETEST procedure, 5628	confidence bands, 5578, 5603
d	confidence limits, 5601, 5620
density function, see probability density function	cumulative distribution function, 5566
description	cumulative incidence estimate, 5666
traditional graphics (LIFETEST), 5632	cumulative incidence function estimates, 5628
Dunnett's adjustment	Dunnett's adjustment, 5590
LIFETEST procedure, 5590	effective sample size, 5600
effective sample size	equal-precision bands, 5605, 5658
LIFETEST procedure, 5600	estimation method, 5580
equal-precision bands	Fleming-Harrington estimates, 5566, 5580, 5596
LIFETEST procedure, 5578, 5605, 5658	Fleming-Harrington G_{ρ} test for homogeneity,
LITETEST PROCEDURE, 33/8, 3003, 3038	5566, 5593

Hall-Wellner bands, 5604, 5658	LIFETEST procedure, 5566
hazard function, 5566, 5665	line printer plots
homogeneity tests, 5566, 5573, 5607, 5650	LIFETEST procedure, 5631
input data set, 5579	linear rank tests, see association tests
interval determination, 5601	linear transformation
kernel-smoothed hazard, 5583, 5605	confidence intervals (LIFETEST), 5579, 5602
life-table estimates, 5566, 5580, 5600, 5624,	local annotate
5659, 5662	traditional graphics (LIFETEST), 5633
likelihood ratio test for homogeneity, 5566, 5607	log transformation
line printer plots, 5631	confidence intervals (LIFETEST), 5579, 5602,
log-rank test for association, 5567, 5612	5604
log-rank test for homogeneity, 5566, 5593, 5607	log-log transformation
maximum time, 5578, 5580	confidence intervals (LIFETEST), 5579, 5602,
median residual time, 5624	5604
minimum time, 5578	log-rank test for association
missing stratum values, 5580, 5589, 5593	LIFETEST procedure, 5567
missing values, 5596	log-rank test for homogeneity
modified Peto-Peto test for homogeneity, 5566,	LIFETEST procedure, 5566, 5593, 5607
5594	
	logit transformation
Nelson-Aalen estimates, 5580	confidence intervals (LIFETEST), 5579, 5603,
ODS graph names, 5638	5604
ODS Graphics, 5577	maximum time
ODS table names, 5635	confidence bands (LIFETEST), 5578
output data sets, 5618	plots (LIFETEST), 5580
partial listing, 5587	mean survival time
Peto-Peto test for homogeneity, 5566, 5594	time limit (LIFETEST), 5587
probability density function, 5566, 5666	median residual time
product-limit estimates, 5566, 5569, 5580, 5596,	LIFETEST procedure, 5624
5621–5623, 5640	minimum time
restricted mean survival time, 5616	
restricted mean time lost, 5617	confidence bands (LIFETEST), 5578
RMST analysis, 5581	missing stratum values
RMST estimates, 5629, 5673	LIFETEST procedure, 5580, 5589, 5593
RMST homogeneity tests, 5676	missing values
RMST tests, 5673	LIFETEST procedure, 5596
RMTL analysis, 5581	modified Peto-Peto test for homogeneity
RMTL estimates, 5630	LIFETEST procedure, 5566, 5594
Scheffe's adjustment, 5591	multiplicity adjustment
Sidak's adjustment, 5591	Bonferroni (LIFETEST), 5590
simulated adjustment, 5591	Dunnett (LIFETEST), 5590
stratified test, 5592	Scheffe (LIFETEST), 5591
stratified tests, 5566, 5567, 5574, 5576, 5609,	Sidak (LIFETEST), 5591
5626	simulated (LIFETEST), 5591
studentized maximum modulus adjustment, 5591	studentized maximum modulus (LIFETEST),
survival distribution function, 5566, 5596	5591
Tarone-Ware test for homogeneity, 5566, 5594	Tukey (LIFETEST), 5591
traditional graphics, 5632	Nelson-Aalen estimates
transformations for confidence intervals, 5579	
trend tests, 5566, 5593, 5611, 5626	LIFETEST procedure, 5580
Tukey's adjustment, 5591	number of intervals
variance estimator, 5579	life-table estimates (LIFETEST), 5580
Wilcoxon test for association, 5567, 5612	ODS graph names
Wilcoxon test for homogeneity, 5566, 5594, 5607	LIFETEST procedure, 5638
likelihood ratio test for homogeneity	ODS Graphics
<u> </u>	ODS Orupinos

LIFETEST procedure, 5577 output data sets LIFETEST procedure, 5618 partial listing product-limit estimate (LIFETEST), 5587 PDF, see probability density function Peto-Peto test for homogeneity LIFETEST procedure, 5566, 5594 Peto-Peto-Prentice, see Peto-Peto test for homogeneity probability density function LIFETEST procedure, 5566, 5666 product-limit estimates LIFETEST procedure, 5566, 5569, 5596, 5621-5623 restricted mean survival time definition (LIFETEST), 5616 restricted mean time lost definition (LIFETEST), 5617 RMST analysis LIFETEST procedure, 5581 **RMST** estimates LIFETEST procedure, 5629 RMST homogeneity tests LIFETEST procedure, 5676 RMTL analysis LIFETEST procedure, 5581 RMTL estimates LIFETEST procedure, 5630 Scheffe's adjustment LIFETEST procedure, 5591 SDF, see survival distribution function Sidak's adjustment LIFETEST procedure, 5591 simulated adjustment LIFETEST procedure, 5591 stratified test LIFETEST procedure, 5592 stratified tests LIFETEST procedure, 5566, 5567, 5574, 5576, 5609, 5626 studentized maximum modulus adjustment LIFETEST procedure, 5591 survival distribution function LIFETEST procedure, 5566, 5596, 5621 survivor function, see survival distribution function Tarone-Ware test for homogeneity LIFETEST procedure, 5566, 5594 traditional graphics LIFETEST procedure, 5632 transformations for confidence intervals LIFETEST procedure, 5579

trend tests
LIFETEST procedure, 5566, 5593, 5611, 5626
Tukey's adjustment
LIFETEST procedure, 5591

Wilcoxon test for association LIFETEST procedure, 5567 Wilcoxon test for homogeneity LIFETEST procedure, 5566, 5594, 5607

Syntax Index

ADJUST= option	STRATA statement (LIFETEST), 5592
STRATA statement (LIFETEST), 5590	
ALPHA= option	ID statement
PROC LIFETEST statement, 5578	LIFETEST procedure, 5589
ALPHAQT= option	INTERVALS= option
PROC LIFETEST statement, 5578	PROC LIFETEST statement, 5579
ANNOTATE= option	LANDIOTATE
PROC LIFETEST statement, 5632	LANNOTATE= option
ATRISK option	PROC LIFETEST statement, 5633
PROC LIFETEST statement, 5578	LIFETEST procedure, 5566
	BY statement, 5587
BANDMAX= option, see BANDMAXTIME= option	FREQ statement, 5588
BANDMAXTIME= option	ID statement, 5589
PROC LIFETEST statement, 5578	PROC LIFETEST statement, 5576
BANDMIN= option, see BANDMINTIME= option	STRATA statement, 5589
BANDMINTIME= option	syntax, 5576
PROC LIFETEST statement, 5578	TEST statement, 5594
BY statement	TIME statement, 5594, 5595
LIFETEST procedure, 5588	LIFETEST procedure, BY statement, 5588
ı	LIFETEST procedure, FREQ statement, 5588
CENSOREDSYMBOL= option	NOTRUNCATE option, 5588
PROC LIFETEST statement, 5632	LIFETEST procedure, ID statement, 5589
CIFVAR= option	LIFETEST procedure, PROC LIFETEST statement,
PROC LIFETEST statement, 5578	5576
CONFBAND= option	ALPHA= option, 5578
PROC LIFETEST statement, 5578	ALPHAQT= option, 5578
CONFTYPE= option	ANNOTATE= option, 5632
PROC LIFETEST statement, 5579	ATRISK option, 5578
	BANDMAXTIME= option, 5578
DATA= option	BANDMINTIME= option, 5578
PROC LIFETEST statement, 5579	CENSOREDSYMBOL= option, 5632
DESCRIPTION= option	CIFVAR= option, 5578
PROC LIFETEST statement, 5632	CONFBAND= option, 5578
DIFF= option	CONFTYPE= option, 5579
STRATA statement (LIFETEST), 5592	DATA= option, 5579
	DESCRIPTION= option, 5632
ERROR= option	ERROR= option, 5579
PROC LIFETEST statement, 5579	EVENTSYMBOL= option, 5633
EVENTSYMBOL= option	FORMCHAR= option, 5633
PROC LIFETEST statement, 5633	GOUT= option, 5633
	INTERVALS= option, 5579
FORMCHAR= option	LANNOTATE= option, 5633
PROC LIFETEST statement, 5633	LINEPRINTER option, 5633
FREQ statement	MAXTIME= option, 5580, 5633
LIFETEST procedure, 5588	METHOD= option, 5580
COLIT antique	MISSING option, 5580
GOUT= option	NELSON option, 5580
PROC LIFETEST statement, 5633	NINTERVAL= option, 5580
GROUP= option	NOCENSPLOT option, 5634

NOLEFT option, 5581	NOTABLE option
NOPRINT option, 5581	PROC LIFETEST statement, 5581
NOTABLE option, 5581	NOTEST option
OUTCIF= option, 5581	STRATA statement (LIFETEST), 5593
OUTSURV= option, 5581	NOTRUNCATE option
OUTTEST= option, 5581	FREQ statement, 5588
PLOTS= option, 5582, 5634, 5635	1124 0
REDUCEOUT option, 5587	ORDER= option
RMST option, 5581	STRATA statement (LIFETEST), 5593
RMTL option, 5581	OUTCIF= option
SINGULAR= option, 5587	PROC LIFETEST statement, 5581
STDERR option, 5587	OUTSURV= option
TIMELIM= option, 5587	PROC LIFETEST statement, 5581
TIMELIST= option, 5587	OUTTEST= option
<u> •</u>	PROC LIFETEST statement, 5581
WIDTH= option, 5587	TROCEMENTS statement, 3501
LIFETEST procedure, STRATA statement, 5589	PLOTS= option
ADJUST= option, 5590	PROC LIFETEST statement, 5582, 5634, 5635
DIFF= option, 5592	PROC LIFETEST statement
GROUP= option, 5592	LIFETEST procedure, 5576
MISSING option, 5593	En Elest procedure, 3370
NODETAIL option, 5593	REDUCEOUT option
NOLABEL option, 5593	PROC LIFETEST statement, 5587
NOTEST option, 5593	RMST option
ORDER= option, 5593	PROC LIFETEST statement, 5581
TEST= option, 5593	RMTL option
TREND option, 5593	PROC LIFETEST statement, 5581
LIFETEST procedure, TEST statement, 5594	1 ROC Ell ETEST statement, 5501
LIFETEST procedure, TIME statement, 5594	SINGULAR= option
LIFETEST procedure, WEIGHT statement, 5595	PROC LIFETEST statement, 5587
LINEPRINTER option	STDERR option
PROC LIFETEST statement, 5633	PROC LIFETEST statement, 5587
	STRATA statement
MAXTIME= option	LIFETEST procedure, 5589
PROC LIFETEST statement, 5580, 5633	En ETEST procedure, 3307
METHOD= option	TEST statement
PROC LIFETEST statement, 5580	LIFETEST procedure, 5594
MISSING option	TEST= option
PROC LIFETEST statement, 5580	STRATA statement (LIFETEST), 5593
STRATA statement (LIFETEST), 5593	TIME statement
	LIFETEST procedure, 5594, 5595
NELSON option	TIMELIM= option
PROC LIFETEST statement, 5580	PROC LIFETEST statement, 5587
NINTERVAL= option	
PROC LIFETEST statement, 5580	TIMELIST= option PROC LIFETEST statement, 5587
NOCENSPLOT option	
PROC LIFETEST statement, 5634	TREND option
NODETAIL option	STRATA statement (LIFETEST), 5593
STRATA statement (LIFETEST), 5593	WIDTH= option
NOLABEL option	PROC LIFETEST statement, 5587
STRATA statement (LIFETEST), 5593	TROC LITETEST Statement, 3307
NOLEFT option	
PROC LIFETEST statement, 5581	
NOPRINT ontion	

PROC LIFETEST statement, 5581