

# SAS/STAT® 13.2 User's Guide The LIFETEST Procedure



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# Chapter 58

# The LIFETEST Procedure

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

Organiana LIECTEST Decordure	4328
Getting Started: LIFETEST Procedure	4329
Syntax: LIFETEST Procedure	4337
PROC LIFETEST Statement	4337
BY Statement	4347
FREQ Statement	4348
ID Statement	4348
STRATA Statement	4348
TEST Statement	4353
TIME Statement	4354
WEIGHT Statement	4354
Details: LIFETEST Procedure	4354
Missing Values	4354
Computational Formulas	4355
Computer Resources	4371
Output Data Sets	4372
OUTSURV= Data Set	4372
OUTTEST= Data Set	4374
Displayed Output	4374
Plot Options Superseded by ODS Graphics	4381
ODS Table Names	4385
ODS Graphics	4387
Modifying the Survival Plots	4388
Examples: LIFETEST Procedure	4389
Example 58.1: Product-Limit Estimates and Tests of Association	4389
Example 58.2: Enhanced Survival Plot and Multiple-Comparison Adjustments	4402
Example 58.3: Life-Table Estimates for Males with Angina Pectoris	4408
References	4415

## **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  $G_{\rho}$  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.

# **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);
run;
```

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
                     355
256
       1
            1
                F
                            1
                                 1
                                     М
262
           1
                     319
       1
                М
                            1
                                 1
                                     М
256
       1
           1
                F
                     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
319
       1
            1
                М
                     255
                            1
                                 1
                                     F
                     256
                                     F
264
       1
            1
                М
                            1
                                 1
237
       0
            0
                F
                     291
                            1
                                 0
                                     М
156
       1
            0
                F
                     323
                            1
                                 0
                                     M
270
       1
            0
                М
                     253
                            1
                                     М
257
       1
            0
                М
                     206
                            1
                                 0
                                     F
       1
                     206
                            1
242
            0
                М
                                 0
                                     F
                                     М
157
       1
            0
                F
                     237
                            1
                                 0
249
       1
            0
                М
                     211
                            1
                                 0
                                     F
                                     F
180
            0
                F
                     229
                            1
                                 0
       1
                                 0
226
       1
            0
                F
                     234
                            1
                                     F
                                     F
268
       0
            0
                     209
                            1
                                 0
                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 58.1 displays the product-limit survival estimate for the Drug X group (Treatment=1). The figure lists, for each observed time, the survival estimate, failure rate, standard error of the estimate, cumulative number of failures, and number of subjects remaining in the study.

Figure 58.1 Survivor Function Estimate for the Drug X-Treated Rats

#### The LIFETEST Procedure

Stratum 1: Treatment = Drug X

Product-Limit Survival Estimates						
			Survival			
D	C	Fa!l	Standard		Number	
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	* 0.0531			18	0	

**Note:** The marked survival times are censored observations.

Figure 58.2 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 58.2 Summary Statistics of Survival Times for Drug X-Treated Rats

	Quartile Estimates							
		95% Con	fidence Ir	nterval				
	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				
		Sta	ndard					
	_	Mean	Error					
	5	771 131 1	1 877					

**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 58.3 and Figure 58.4 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 58.3 Survivor Function Estimate for Placebo-Treated Rats

#### The LIFETEST Procedure

#### Stratum 2: Treatment = Placebo

Product-Limit Survival Estimates						
Days	Survival	Failure	Survival Standard Error	Number Failed	Number 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 58.4 Summary Statistics of Survival Times for Placebo-Treated Rats

	Quartile Estimates						
	95% Confidence Interval						
	Point						
Percent	<b>Estimate</b>	Transform	[Lower	Upper)			
75	257.000	LOGLOG	237.000	323.000			
50	235.500	LOGLOG	206.000	253.000			
25	207.500	LOGLOG	156.000	229.000			

	Standard	
Mean	Error	
235.156	10.211	

A summary of the number of censored and event observations is shown in Figure 58.5. The figure lists, for each stratum, the number of event and censored observations, and the percentage of censored observations.

Figure 58.5 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 58.6 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 58.6 Plot of Estimated Survivor Functions

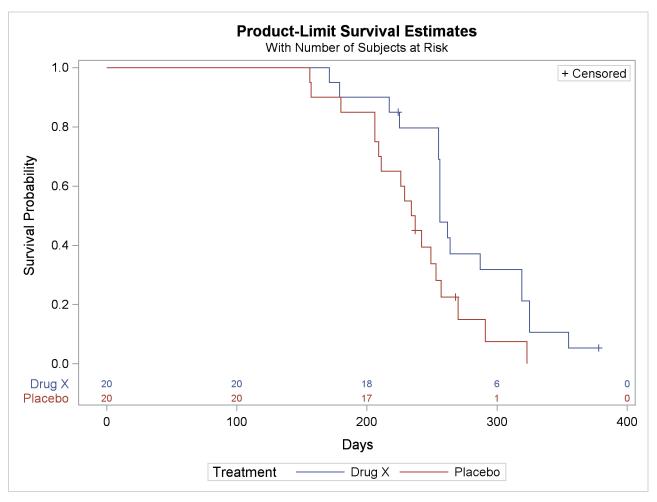


Figure 58.7 displays the graph of the log survivor function estimates versus survival time. Neither curve approximates a straight line through the origin—the exponential model is not appropriate for the survival data.

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

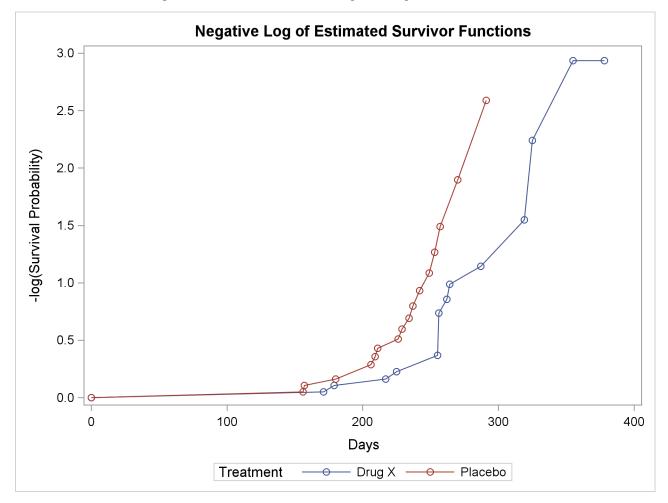


Figure 58.7 Plot of Estimated Negative Log Survivor Functions

Results of the comparison of survival curves between the two treatments are shown in Figure 58.8. 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 58.8 Results of the Two-Sample Tests

Test of Equality over Strata						
Test	Chi-Square	DE	Pr > 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 58.9. 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 58.8, the significance of the treatment effect has been sharpened by controlling for the effect of the gender of the subjects.

Figure 58.9 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 58.10. The *p*-values are very similar to those of the two-sample tests in Figure 58.8.

Figure 58.10 Results of Linear Rank Tests of Treatment

#### The LIFETEST Procedure

Univariate Chi-Squares for the Wilcoxon Test							
Variable	Test Statistic	Standard Error	Chi-Square	Pr > Chi-Square			
Treatment	3.9525	1.7524	5.0875	0.0241			
LIniva	Univariate Chi-Squares for the Log-Rank Test						
Omva	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 58.11. The p-values are very similar to those of the stratified tests in Figure 58.9.

Figure 58.11 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 Cni-S	squares for	tne Log-Rar	ik lest	
Univa		equares for Standard	tne Log-Rar	Pr >	
		Standard	Chi-Square	Pr >	

# **Syntax: LIFETEST Procedure**

The following statements are available in the LIFETEST procedure:

```
PROC LIFETEST < options > ;
BY variables;
FREQ variable;
ID variables;
STRATA variable < (list) > < ... variable < (list) >> < / options > ;
TEST variables;
TIME variable < * censor(list) > ;
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 58.1 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 4381.

 Table 58.1
 Options Available in the PROC LIFETEST Statement

Table 58.	Options Available in the PROC LIFETEST Statement		
Option	Description		
Input and Output Data Sets			
DATA=	Specifies the input SAS data set		
OUTSURV=	Names an output data set to contain survival estimates and confi-		
	dence limits		
OUTTEST=	Names an output data set to contain rank test statistics for associa-		
	tion of survival time with covariates		
Nonparametric Estin	mation		
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		
WIDTH=	Specifies the width of intervals for life-table estimates		
Cantilanaa I imita fa			
Confidence Limits for ALPHA=	Sets the confidence level for interval estimation estimates		
BANDMAXTIME=			
BANDMINTIME=	Specifies the maximum time for confidence band		
	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	obtain confidence films		
MAXTIME=	Specifies the maximum time value for plotting		
PLOTS=	Specifies plots to display		
	Special production of the prod		
Control Output	Add the month of Continue of the decided of the continue of the last		
ATRISK	Adds the number of subjects at risk to the survival estimate table		
NOPRINT	Suppresses the display of printed output		
NOTABLE	Suppresses the display of survival function estimates		
INTERVALS=	Displays only the estimate for the smallest time in each interval		
NOLEFT	Suppresses the Number Left column in the survival estimate table		
TIMELIST=	Specifies a list of time points to display the survival estimate		
REDUCEOUT	Specifies that only INTERVAL= or TIMELIST= observations be		
	listed in the OUTSURV= data set		
Miscellaneous			
ALPHAQT=	Sets the confidence level for survival time quartiles		
MISSING	Allows missing values to be a stratum level		
SINGULAR=	Sets the tolerance for testing singularity of covariance matrix of		
(MD ED D	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**=α

specifies the level of significance  $\alpha$  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= $\alpha$

specifies the significance level  $\alpha$  for the  $100(1-\alpha)\%$  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.

#### 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.

#### **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

intervals=5,10 to 30 by 10

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 tie-breaking 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

allows missing values for numeric variables and blank values for character variables as valid stratum levels. See the section "Missing Values" on page 4354 for details.

By default, PROC LIFETEST does not use observations with missing values for any stratum variables.

#### **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); see Chapter 20, "Using the Output Delivery System" for more information.

#### **NOTABLE**

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

#### **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. See the section "OUTSURV= Data Set" on page 4372 for more information about the contents of the OUTSURV= data set.

#### **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. See the section "OUTTEST= Data Set" on page 4374 for more information about the contents of the OUTTEST= data set.

```
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 606 in Chapter 21, "Statistical Graphics Using ODS."

If ODS Graphics is enabled but you do not specify the PLOTS= option, then PROC LIFETEST produces a plot of the estimated survivor functions by default.

The only *global-plot-option* follows:

#### **ONLY**

specifies that only the specified plots in the list be produced; otherwise, the default survivor function plot is also displayed.

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 LOGLOGLS HAZARD); for the life-table method, PLOTS=ALL is equivalent to specifying PLOTS=(SURVIVAL LOGSURV LOGLOGS DENSITY HAZARD).

#### 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 4365 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.

#### **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. The choices are as follows:

#### **BIWEIGHT**

BW

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

#### **EPANECHNIKOV**

Ε

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

#### **UNIFORM**

U

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

The default is KERNEL=EPANECHNIKOV.

#### **NMINGRID**=number

specifies the number of grid points in determining the mean integrated square error (MISE). The default value is 51.

#### **NGRID**=number

specifies the number of grid points. The default is 101.

CL

displays the pointwise confidence limits for the smoothed hazard.

#### 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.

#### PDF < (CL) >

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

#### 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 (see the section "Modifying the Survival Plots" on page 4388 for more information).

#### 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 with 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 for 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  $\infty$ .

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

<ul> <li>A list separated by blanks</li> </ul>	Age (5 10 20 30)
• A list separated by commas	Age (5, 10, 20, 30)
• <i>x</i> to <i>y</i>	Age(5 to 10)
• $x$ to $y$ by $z$	Age(5 to 30 by 10)
• A combination of the above	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 58.2 summarizes the *options* available in the STRATA statement.

Table 58.2	Options Available in the STRATA Statement
------------	---

Option	Description
Homogeneity	y Tests
GROUP=	Specifies the group variable for stratified tests
NODETAIL	Suppresses printing the test statistic and covariance matrix
NOTEST	Suppresses any tests

<b>Table 58.</b>	2 continued			
Option	Description			
TEST=	Specifies tests corresponding to various weight functions			
TREND	Requests a trend test			
Multiple Con	Multiple Comparisons			
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				
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

specifies the multiple-comparison method for adjusting the p-values of the paired tests. See the section "Multiple-Comparison Adjustments" on page 4368 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  $\alpha$  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  $\gamma$  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  $\gamma$  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  $\alpha$  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  $\epsilon$  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  $\gamma$  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  $\gamma$ ,  $\epsilon$ , and  $\alpha$  (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  $\gamma$ ,  $\epsilon$ , and  $\alpha$ , 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

specifies the variable whose formatted values identify the various samples whose underlying survival curves are to be compared. The 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, in order to perform a stratified test to compare the therapies while controlling the effect of the centers.

#### 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 58.2 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, ..., 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 4366 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( $\rho$ 1, $\rho$ 2) reduces to the Fleming-Harrington  $G^{\rho}$  family (Fleming and Harrington 1981) when  $\rho$ 2=0, which you can specify as FLEMING( $\rho$ ) with one argument. When  $\rho$ =0, the test becomes the log-rank

test. When  $\rho$ =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.

See the section "Rank Tests for the Association of Survival Time with Covariates" on page 4370 for more information.

#### **TIME Statement**

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

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 statement

```
time T*Flag(1,2);
```

identifies the variable T as containing the observed failure times (event or censored). If the variable Flag has the value 1 or 2, the corresponding value of T is a right-censored value.

#### **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.

# **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

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

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 100p 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 100p 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  $100(1-\frac{\alpha}{2})$  percentile of the standard normal distribution.

Consider the bone marrow transplant data described in Example 58.2. 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							
			$g(\hat{S}(t)) - g(1 - 0.25)$				
	â	• • • • • • • • • • • • • • • • • • • •			$g'(\hat{S}(t))\hat{\sigma}(\hat{S}(t))$		
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  $\left| \frac{g(\hat{S}(t)) - g(1-p)}{g'(\hat{S}(t))} \sqrt{\hat{V}(\hat{S}(t))} \right| \le 1.9599$  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

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

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 k by k+1 with  $t_{k+1}=L$ .

#### 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  $(T_i, \delta_i, w_i), i = 1, \dots, n$ , denote an independent sample of right-censored survival data, where  $T_i$  is the possibly right-censored time,  $\delta_i$  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  $t_1 < t_2, \ldots < t_D$  be the D distinct event times in the sample. At time  $t_j, j = 1, ..., D$ , 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

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

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  $[t_{i-1}, t_i)$ ,  $i = 1, 2, \dots, k+1$ , 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  $c = \log_{10}$  (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  $\alpha$  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  $\Phi$  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  $100(1-\alpha)\%$  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  $t_1 < t_2 < ... < t_D$  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

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

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

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

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  $t_1 < t_2 < \ldots < t_D$  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:

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

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  $\tau_L$  and  $\tau_U$  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  $\tau_L = u_1 < ... < u_M = \tau_U$ . You can specify  $\tau_L, \tau_R$ , 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

$$H_0: S_1(t) = S_2(t) = \ldots = S_K(t)$$
 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  $\tau$  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  $\chi^2$  as having a chi-square distribution with K-1 degrees of freedom.

### Nonparametric Tests

Let  $(T_i, \delta_i, X_i)$ , i = 1, ..., n, denote an independent sample of right-censored survival data, where  $T_i$  is the possibly right-censored time,  $\delta_i$  is the censoring indicator ( $\delta_i$ =0 if  $T_i$  is censored and  $\delta_i$ =1 if  $T_i$  is an event time), and  $X_i = 1, ..., K$  for K different groups. Let  $t_1 < t_2 < ... < t_D$  be the distinct event times in the sample. At time  $t_j$ , j = 1, ..., D, let  $W(t_j)$  be a positive weight function, and let  $Y_{jk} = \sum_{i:T_i \ge t_j} I(X_i = k)$  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  $W(t_j)$  are given in Table 58.3.

Table Colo Troight and	
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 58.3** Weight Functions for Various Tests

In Table 58.3,  $\hat{S}(t)$  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

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

**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,

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

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

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  $\mathbf{V} = (V_{kh})$ . The overall test statistic for homogeneity is  $\mathbf{v'V^-v}$ , 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  $\mathbf{V}$  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  $(T_i, \delta_i, X_i, w_i)$ ,  $i = 1, \ldots, n$ , denote an independent sample of right-censored survival data, where  $T_i$  is the possibly right-censored time,  $\delta_i$  is the censoring indicator ( $\delta_i$ =0 if  $T_i$  is censored and  $\delta_i$ =1 if  $T_i$  is an event time),  $X_i = 1, \ldots, K$  for K different groups, and  $W_i$  is the weight from the WEIGHT statement. Let  $t_1 < t_2 < \ldots < t_D$  be the distinct event times in the sample. At each  $t_j$ ,  $j = 1, \ldots, D$ , and for each  $1 \le k \le K$ , let

$$d_{jk} = \sum_{i:T_i = t_j} I(X_i = k) \qquad d_{jk}^w = \sum_{i:T_i = t_j} w_i I(X_i = k)$$

$$Y_{jk} = \sum_{i:T_i \ge t_j} I(X_i = k) \qquad Y_{jk}^w = \sum_{i:T_i \ge t_j} w_i I(X_i = k)$$

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

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

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

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

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

Let  $V = (V_{kh})$ . Under  $H_0$ , the weighted K-sample test has a  $\chi^2$  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 ( $s = 1 \dots M$ ), 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  $\chi^2$  distribution with the same degrees of freedom as the individual test for each stratum.

**Multiple-Comparison Adjustments** Let  $\chi_r^2$  denote a chi-square random variable with r degrees of freedom. Denote  $\phi$  and  $\Phi$  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

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

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:

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

• 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 Cv, 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:

$$p = \Pr(\chi_{r-1}^2 > z_{il}^2)$$

• 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

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

or

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

Let  $a_1 < a_2 < \ldots < a_k$  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  $\alpha$  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  $t_{\alpha}$ .

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,  $\delta_{\alpha}$  is 1 if the observation is an event and 0 if the observation is censored, and  $\mathbf{z}_{\alpha}$  is the vector of covariates in the TEST statement for the  $\alpha$ 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  $n_i$  is the number at risk just prior to  $t_{(i)}$ .

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

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

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

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

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 58.1 illustrates this process.

# **Computer Resources**

The data are first read and sorted into strata. If the data are originally sorted by failure time and censoring state, with smaller failure times coming first and event values preceding censored values in cases of ties, the data can be processed by strata without additional sorting. Otherwise, the data are read into memory by strata and sorted.

## **Memory Requirements**

For a given BY group, define the following:

- N the total number of observations
- V the number of STRATA variables
- C the number of covariates listed in the TEST statement
- L total length of the ID variables in bytes
- S number of strata
- *n* maximum number of observations within strata
- b 12 + 8C + L
- $m1 (112 + 16V) \times S$
- $m2 50 \times b \times S$
- $m3 (50 + n) \times (b + 4)$
- $m4 8(C+4)^2$
- $m5 20N + 8S \times (S + 4)$

The memory, in bytes, required to process the BY group is at least

$$m1 + \max(m2, m3) + m4$$

The test of equality of survival functions across strata requires additional memory (m5 bytes). However, if this additional memory is not available, PROC LIFETEST skips the test for equality of survival functions and finishes the other computations. Additional memory is required for the PLOTS= option. Temporary storage of 16n bytes is required to store the product-limit estimates for plotting.

# **Output Data Sets**

#### **OUTSURV= Data Set**

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

- any specified BY variables
- 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)
- STRATUM, a numeric variable that numbers the strata

- the time variable as given 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 (if the OUT= option is specified in the PROC LIFETEST statement)
- 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 (if the STDERR option is specified in the PROC LIFETEST statement)
- HW\_LCL, a variable that contains the lower limits of the Hall-Wellner confidence bands (if the CONFBAND=HW option or the CONFBAND=ALL option is specified in the PROC LIFETEST statement)
- HW\_UCL, a variable that contains the upper limits of the Hall-Wellner confidence bands (if the CONFBAND=HW option or the CONFBAND=ALL option is specified in the PROC LIFETEST statement)
- EP\_LCL, a variable that contains the lower limits of the equal-precision confidence bands (if the CONFBAND=EP option or the CONFBAND=ALL option is specified in the PROC LIFETEST statement)
- EP\_UCL, a variable that contains the upper limits of the equal-precision confidence bands (if the CONFBAND=EP option or the CONFBAND=ALL option is specified 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.

Labels are assigned to all the variables in the output data set except the BY variable and the STRATA variable.

#### **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 <code>NAME</code> 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 <code>NAME</code> 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**

If you use the NOPRINT option in the PROC LIFETEST statement, the procedure does not display any output.

#### **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 the NELSON option is specified in the PROC LIFETEST statement)
- the standard error of the Nelson-Aalen estimator (if the NELSON option is specified 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 the NELSON option is specified in the PROC LIFETEST statement)
- the standard error of the Nelson-Aalen estimator (if the NELSON option is specified 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 the NELSON option is specified in the PROC LIFETEST statement)
- the standard error of the Nelson-Aalen estimator (if the NELSON option is specified 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 the STRATA statement is specified)
- 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.

## **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 the TREND option is specified 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 the TREND option is specified 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 the TEST statement is specified. 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 the TEST statement is specified. 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 the TEST statement is specified. 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 the TEST statement is specified. 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 the TEST statement is specified. 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.

# **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 4337.

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

Table 58.4 summarizes the ways in which you can request graphics.

PLOTS= LINEPRINTER **ODS** Graphics **Option Specified? Graphics Result Option Specified? ODS** Graphics Enabled Yes No ODS Graphics survival plot Enabled No No Traditional graphics Disabled No Yes 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 58.4 Ways of Displaying Graphics

Table 58.5 summarizes the options available in the PROC LIFETEST statement for line printer and traditional graphics.

<b>Table 58.5</b>	Line Printer and Traditional Graphics Options
	Available in the PROCLIFFTEST Statement

Option	Description
<b>Line Printer Plots</b>	
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
<b>Traditional Graphics</b>	
ANNOTATE=	Specifies an Annotate data set that adds features to plots
CENSOREDSYMBOL=	Defines the symbol to be used for censored observations in plots

lable 58.5	continued
Option	Description
DESCRIPTION=	Specifies the string that appears in the description field of the PROC GREPLAY master menu for the plots
<b>EVENTSYMBOL=</b>	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 annotation
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 the LINEPRINTER option is specified 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 the LINEPRINTER option is specified or if ODS Graphics is enabled.

## **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 the LINEPRINTER option is specified or if ODS Graphics is enabled.

#### **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 the LINEPRINTER option is specified or if ODS Graphics is enabled.

### 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 the LINEPRINTER option is specified or if ODS Graphics is enabled. 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 the LINEPRINTER option is specified or if ODS Graphics is enabled. 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**

С

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**

Ρ

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**

D

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 58.6. For more information about ODS, see Chapter 20, "Using the Output Delivery System."

Table 30.	Table 30.0 Obo Tables Floudeed by Floor Ell Elles							
<b>ODS Table Name</b>	Description	Statement / Option						
BreslowEstimates	Breslow estimates	PROC LIFETEST METHOD=B						
CensoredSummary	Number of event and censored ob-	PROC LIFETEST						
	servations	METHOD=PL   B   FH						
FlemingEstimates	Fleming-Harrington estimates	PROC LIFETEST						
		METHOD=FH						
FlemingHomCov	Covariance matrix for <i>k</i> -sample	STRATA / TEST=FLEMING						
	FLEMING statistics							
HomStats	Test statistics for <i>k</i> -sample tests	STRATA / TEST=						

**Table 58.6** ODS Tables Produced by PROC LIFETEST

Table 58.6 continued

ODS Table Name	Description	Statement / Option
HomTests	Results of <i>k</i> -sample tests	STRATA / TEST=
LifetableEstimates	Life-table survival estimates	PROC LIFETEST
		METHOD=LT
LogForStepSeq	Forward stepwise sequence for the log-rank statistics for associa- tion	TEST
LogrankHomCov	Covariance matrix for <i>k</i> -sample LOGRANK statistics	STRATA / TEST=LOGRANK
LogTestCov	Covariance matrix for log-rank statistics for association	TEST
LogUniChisq	Univariate chi-squares for log- rank statistics for association	TEST
Means	Mean and standard error of survival times	PROC LIFETEST 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 LIFETEST METHOD=PL
Quartiles	Quartiles of the survival times	PROC LIFETEST METHOD=PL   B   FH
SimDetails	Details of quantile simulations	STRATA / ADJUST=SIMULATE
SimResults	Quantile simulation results	STRATA / ADJUST=SIMULATE
SurvDiff	Adjustments for multiple comparisons	STRATA / ADJUST= and DIFF=
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
WilForStepSeq	Forward stepwise sequence for the log-rank statistics for associa- tion	TEST
WilcoxonHomCov	Covariance matrix for <i>k</i> -sample WILCOXON statistics	STRATA / TEST=WILCOXON
WilTestCov	Covariance matrix for log-rank statistics for association	TEST
WilUniChiSq	Univariate chi-squares for Wilcoxon statistics for associa- tion	TEST

# **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 606 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 605 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 58.7, along with the required keywords for the PLOTS= option.

Table 58.7 Graphs Produced by PROC LIFETEST

ODS Graph Name	Plot Description	PLOTS=Option
DensityPlot	Estimated density for life-table method	PDF
FailurePlot	Estimated failure function	SURVIVAL(FAILURE)
HazardPlot	Estimated hazard function for life-table method or smoothed hazard for product-	HAZARD
	limit, Breslow, or Fleming-Harrington method	
LogNegLogSurvivalPlot	Log of negative log of the estimated survivor function	LOGLOGS
NegLogSurvivalPlot	Negative log of the estimated survivor function	LOGSURV
SurvivalPlot	Estimated survivor function	SURVIVAL
SurvivalPlot	Estimated survivor function with number of subjects at risk	SURVIVAL(ATRISK=)
SurvivalPlot	Estimated survivor function with pointwise confidence limits	SURVIVAL(CL)
SurvivalPlot	Estimated survivor function with equal- precision band	SURVIVAL(CB=EP)
SurvivalPlot	Estimated survivor function with Hall-Wellner band	SURVIVAL(CB=HW)
SurvivalPlot	Estimated survivor function with homogeneity test <i>p</i> -value	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 58.8 and Table 58.9 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.

Table 58.8 Additional Dynamic Variables for Stat.Graphics.ProductLimitSurvival

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
	Median <i>j</i>	Median survival time of the <i>j</i> th stratum
	LowerMedianj	Lower median survival time of the <i>j</i> th stratum
UpperMedian <i>j</i> PctMedianConfid		Upper median survival time of the <i>j</i> th stratum
		Confidence of the median intervals in percent
<b>INDIVIDUAL</b>	NObs	Number of observations
	NEvent	Number of events
	Median	Median survival time
	LowerMedian	Lower median survival time
	UpperMedian	Upper median survival time
	PctMedianConfid	Confidence of the median interval in percent

**Table 58.9** Additional Dynamic Variables for Stat.Graphics.LifetableSurvival

STRATA=	Dynamic	Description
OVERLAY StrValj Label for the jth stratum		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

See the section "Dynamic Variables" on page 839 in Chapter 23, "Customizing the Kaplan-Meier Survival Plot," for information about all of the dynamic variables that are available for use in the ODS Graphics 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 820 and "Adding an External Table with Event Information" on page 822 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 783 in Chapter 23, "Customizing the Kaplan-Meier Survival Plot" provide examples:

- "Enabling ODS Graphics and the Default Kaplan-Meier Plot" on page 783
- "Individual Survival Plots" on page 785
- "Hall-Wellner Confidence Bands and Homogeneity Test" on page 787
- "Equal-Precision Bands" on page 788
- "Displaying the Patients-at-Risk Table inside the Plot" on page 790
- "Displaying the Patients-at-Risk Table outside the Plot" on page 792
- "Modifying At-Risk Table Times" on page 793
- "Reordering the Groups" on page 796
- "Suppressing the Censored Observations" on page 799
- "Failure Plots" on page 800

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 801 in Chapter 23, "Customizing the Kaplan-Meier Survival Plot" provide examples:

- "Changing the Plot Title" on page 803
- "Modifying the Axis" on page 805
- "Changing the Line Thickness" on page 807
- "Changing the Group Color" on page 808
- "Changing the Line Pattern" on page 809
- "Changing the Font" on page 810
- "Changing the Legend and Inset Position" on page 812
- "Changing How the Censored Points Are Displayed" on page 814
- "Adding a Y-Axis Reference Line" on page 815
- "Changing the Homogeneity Test Inset" on page 817
- "Suppressing the Second Title and Adding a Footnote" on page 819
- "Adding a Small Inset Table with Event Information" on page 820
- "Adding an External Table with Event Information" on page 822
- "Suppressing the Legend" on page 824
- "Kaplan-Meier Plot with Event Table and Other Customizations" on page 825

# **Examples: LIFETEST Procedure**

# **Example 58.1: 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
                                228 60 3 38 0
72 60 7 69 0
               411 70 5 64 10
                                                 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
144 30 4 63 0 -25 80 9 52 10
                               11 70 11 48 10
standard small
30 60 3 61 0 384 60 9 42 0
                                 4 40 2 35 0
                                                 54 80 4 63 10
                                -97 60 5 67 0
13 60 4 56 0 -123 40 3 55 0
                                                153 60 14 63 10
59 30 2 65 0 117 80 3 46 0
                                 16 30 4 53 10
                                               151 50 12 69
22 60 4 68 0
                                 21 40 2 55 10
               56 80 12 43 10
                                                 18 20 15 42
              20 30 5 65 0
                                 31 75 3 65 0
139 80 2 64 0
                                                 52 70 2 55
51 60 1 67 0 122 80 28 53 0
                                 7 50 7 72 0
27 60 8 62 0 54 70 1 67 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 0
132 80 5 50 0
              12 50 4 63 10
                                162 80 5 64 0
                                                  3 30 3 43 0
95 80 4 34 0
standard large
177 50 16 66 10
              162 80 5 62 0
                                216 50 15 52 0
                                                 553 70 2 47 0
278 60 12 63 0 12 40 12 68 10
                                260 80 5 45 0
                                                 200 80 12 41 10
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
999 90 12 54 10 112 80 6 60 0
                                -87 80 3 48 0 -231 50 8 52 10
```

```
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
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
                                  283 90 2 51
                                              0
                                                    15 50 13 40 10
test small
 25 30
       2 69 0 -103 70 22 36 10
                                  21 20
                                         4 71 0
                                                    13 30 2 62
 87 60
       2 60 0
                  2 40 36 44 10
                                   20 30
                                         9 54 10
                                                    7 20 11 66
                                                                0
 24 60
       8 49 0
                  99 70
                        3 72
                              0
                                  8 80
                                         2 68
                                              0
                                                    99 85
                                                          4 62
                                                                0
                 25 70
 61 70 2 71 0
                       2 70
                              0
                                   95 70 1 61 0
                                                    80 50 17 71
 51 30 87 59 10
                 29 40
                        8 67
test adeno
                 18 40 5 69 10
                                  -83 99
                                         3 57
 24 40 2 60 0
                                               0
                                                    31 80
                                                          3 39
                                                                0
 51 60 5 62 0
                 90 60 22 50 10
                                   52 60 3 43 0
                                                    73 60
                                                          3 70
                                                                0
 8 50 5 66 0 36 70 8 61
                              0
                                   48 10 4 81 0
                                                    7 40 4 58
                                                                0
140 70
       3 63 0
                186 90
                        3 60
                                   84 80 4 62 10
                                                    19 50 10 42
                              0
                                                                0
 45 40 3 69 0
                 80 40
                        4 63
                              0
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 58.1.1 through Output 58.1.4 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.

Output 58.1.1 Estimation Results for Adeno Cells

# The LIFETEST Procedure

# Stratum 1: Cell Type = adeno

Product-Limit Survival Estimates						
			Survival			
SurvTime	Survival	Failure	Standard Error	Number Failed	Number Left	Therapy
0.000	1.0000	0	0	0	27	Петару
3.000	0.9630		0.0363	1		standard
7.000	0.9050		0.0503	2		test
8.000	0.9239	0.0741	0.0304	3		standard
8.000	0.8519	0.1481	0.0684	4		test
12.000	0.8319		0.0034	5		standard
18.000	0.6146		0.0748	6		test
19.000	0.7778		0.0843	7		test
24.000	0.7407		0.0879	8		test
31.000	0.7037	0.2903	0.0907	9		test
35.000	0.6296		0.0907	10		standard
				10		test
36.000 45.000	0.5926		0.0946			
48.000	0.5556 0.5185		0.0956 0.0962	12 13		test
51.000	0.3163		0.0962			test test
52.000	0.4615		0.0962	14 15		test
73.000	0.4074		0.0946	16		test
80.000	0.3704	0.6296	0.0929	17		test
83.000				17		test
84.000	0.3292		0.0913	18		test
90.000	0.2881	0.7119	0.0887	19		test
92.000	0.2469		0.0850	20		standard
95.000	0.2058		0.0802	21		standard
117.000	0.1646		0.0740	22		standard
132.000	0.1235		0.0659	23		standard
140.000	0.0823		0.0553	24		test
162.000	0.0412		0.0401	25	1	standard
186.000	0	1.0000		26	0	test

**Note:** The marked survival times are censored observations.

# The LIFETEST Procedure

# Stratum 2: Cell Type = large

Product-Limit Survival Estimates						
			Survival			
			Standard			
SurvTime	Survival		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.

# The LIFETEST Procedure

# Stratum 3: Cell Type = small

	Product-Limit Survival Estimates						
SurvTime		Survival	Failure	Survival Standard Error	Number Failed	Number Left	Therapy
0.000		1.0000	0	0	0	48	
2.000		0.9792	0.0208	0.0206	1	47	test
4.000		0.9583	0.0417	0.0288	2	46	standard
7.000					3	45	standard
7.000		0.9167	0.0833	0.0399	4	44	test
8.000		0.8958	0.1042	0.0441	5	43	test
10.000		0.8750	0.1250	0.0477	6	42	standard
13.000					7	41	standard
13.000		0.8333	0.1667	0.0538	8	40	test
16.000		0.8125	0.1875	0.0563	9	39	standard
18.000					10	38	standard
18.000		0.7708	0.2292	0.0607	11	37	standard
20.000					12	36	standard
20.000		0.7292	0.2708	0.0641	13	35	test
21.000					14	34	standard
21.000		0.6875	0.3125	0.0669	15	33	test
22.000		0.6667	0.3333	0.0680	16	32	standard
24.000		0.6458	0.3542	0.0690	17	31	test
25.000					18	30	test
25.000		0.6042	0.3958	0.0706	19	29	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					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	19	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 58.1.3 continued

## The LIFETEST Procedure

## Stratum 3: Cell Type = small

	Prod	uct-Limi	it Survival	Estimates	<u> </u>	
			Survival			
SurvTime	Survival	Failure	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.

Output 58.1.4 Estimation Results for Squamous Cells

## The LIFETEST Procedure

## **Stratum 4: Cell Type = squamous**

		Prod	uct-Limi	t Survival	Estimates		
				Survival			
SurvTime		Survival	Failure	Standard Error	Number Failed	Number Left	Therapy
0.000		1.0000	0	0	0	35	
1.000					1		test
1.000		0.9429	0.0571	0.0392	2	33	test
8.000		0.9143	0.0857	0.0473	3		standard
10.000		0.8857	0.1143	0.0538	4	31	standard
11.000		0.8571	0.1429	0.0591	5	30	standard
15.000		0.8286	0.1714	0.0637	6	29	test
25.000		0.8000	0.2000	0.0676	7	28	test
25.000	*	•		•	7	27	standard
30.000		0.7704	0.2296	0.0713	8	26	test
33.000		0.7407	0.2593	0.0745	9	25	test
42.000		0.7111	0.2889	0.0772	10	24	standard
44.000		0.6815	0.3185	0.0794	11	23	test
72.000		0.6519	0.3481	0.0813	12	22	standard
82.000		0.6222	0.3778	0.0828	13	21	standard
87.000	*	ē		ē	13	20	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		test
389.000		0.1801	0.8199	0.0711	26	5	test
411.000		0.1441	0.8559	0.0654	27		standard
467.000		0.1081	0.8919	0.0581	28		test
587.000		0.0720	0.9280	0.0487	29		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.

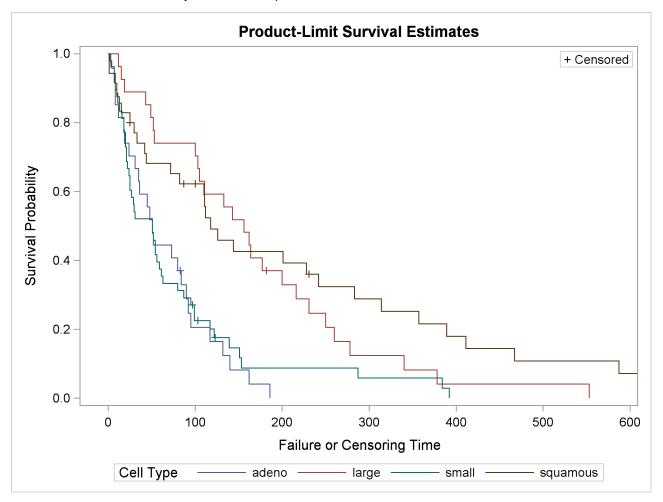
The distribution of event and censored observations among the four cell types is summarized in Output 58.1.5.

Output 58.1.5 Summary of Censored and Uncensored Values

Summary of the Number of Censored and Uncensored Values						
Stratum C	Cell	Total	Failed	Censored	Percent Censored	
<b>1</b> a	deno	27	26	1	3.70	
<b>2</b> la	arge	27	26	1	3.70	
<b>3</b> si	mall	48	45	3	6.25	
<b>4</b> se	quamous	35	31	4	11.43	
Total		137	128	9	6.57	

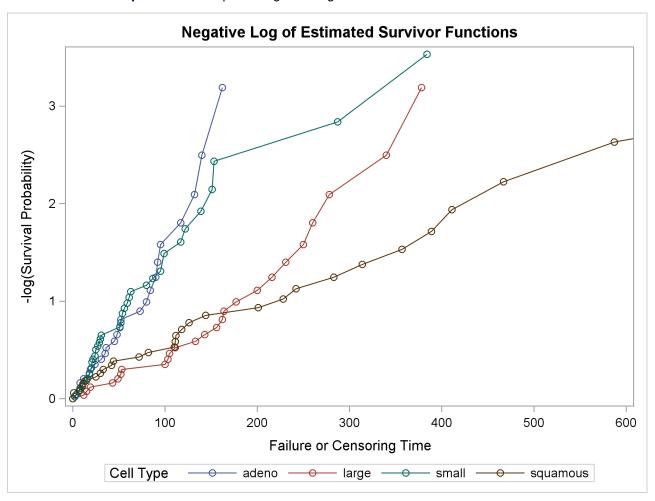
The graph of the estimated survivor functions is shown in Output 58.1.6. The adeno cell curve and the small cell curve are much closer to each other than they are to the large cell curve or the squamous cell curve. The survival rates of the adeno cell patients and the small cell patients decrease rapidly 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.

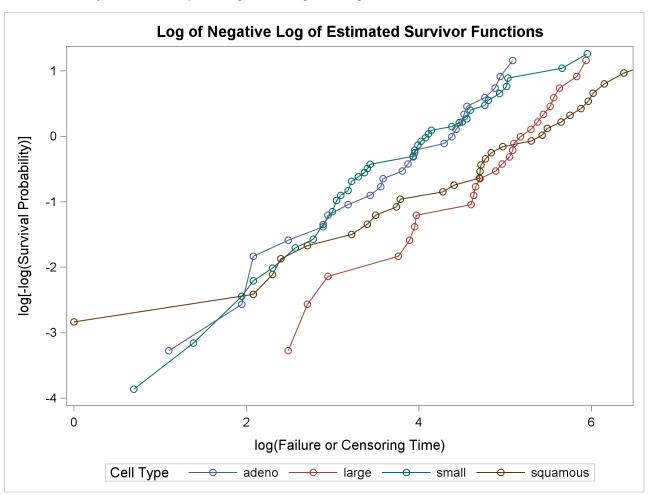
Output 58.1.6 Graph of the Estimated Survivor Functions



The graph of the negative log of the estimated survivor functions is displayed in Output 58.1.7. Output 58.1.8 displays the log of the negative log of the estimated survivor functions against the log of time.

Output 58.1.7 Graph of Negative Log of the Estimated Survivor Functions





Output 58.1.8 Graph of Log of the Negative Log of the Estimated Survivor Functions

Results of the homogeneity tests across cell types are given in Output 58.1.9. 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 58.1.9 Homogeneity Tests across Cell Types

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

Output 58.1.9 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 58.1.10. 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 58.1.10. 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 58.1.10 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 58.1.10 continued

Cova	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	

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;
run;
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 58.1.11 displays the univariate statistics and their covariance matrix for the log-rank test.

Output 58.1.11 Log-Rank Statistics and Covariance Matrix

Obs _TYP	PENAME_	SurvTime	Age	Prior	DiagTime	Kps	Treatment
1 cov	SurvTime	46.42	-40.74	-19.94	-115.86	1123.14	-4.208
<b>2</b> 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
<b>5</b> 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 58.1.12. 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.

## All Possible Subsets of Covariates for the log-rank Test

The REG Procedure
Model: MODEL1
Dependent Variable: SurvTime

## **R-Square Selection Method**

Number in		
		Variables in Model
1	0.9366	•
1		DiagTime
1		Treatment
1	0.0039	
1	0.0032	Age
2	0.9737	Kps Treatment
2	0.9472	Age Kps
2	0.9417	Prior Kps
2	0.9382	DiagTime Kps
2	0.0434	DiagTime Treatment
2	0.0353	Age DiagTime
2	0.0304	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	0.9976	Age DiagTime Kps Treatment
4	0.9774	Prior DiagTime Kps Treatment
4	0.9515	Age Prior DiagTime Kps
4	0.0459	Age Prior DiagTime Treatment
5	1.0000	Age Prior DiagTime Kps Treatmen

# **Example 58.2: 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 58.2.1. The data set is available in the Sashelp library.

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

Output 58.2.1	A Subset of the Bone Marro	w Transplant Data
---------------	----------------------------	-------------------

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 58.2.2 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 0.8 Survival Probability 0.6 0.4 0.2 0.0 38 16 11 1 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 58.2.2 Estimated Disease-Free Survival for 137 Bone Marrow Transplant Patients

The log-rank test (Output 58.2.3) shows that the disease-free survival times for these three risk groups are significantly different (p = 0.001).

Output 58.2.3 Log-Rank Test of Disease Group Homogeneity

Test of Equality over Strata				
Test	Chi Sauara	DE	Pr >	
rest	Cni-Square	DΓ	Chi-Square	
Log-Rank	13.8037	2	0.0010	

The Šidák multiple-comparison results are shown in Output 58.2.4. 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 58.2.4 All Paired Comparsions

Adjustment f	Adjustment for Multiple Comparisons for the Logrank Test				
Strata Co	mparison		p-Va	lues	
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 Risk	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 Šidák 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 58.2.5 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 58.2.5 Comparisons with the Reference Group

#### The LIFETEST Procedure

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

The survival plot that is displayed in Output 58.2.2 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 dataset 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.

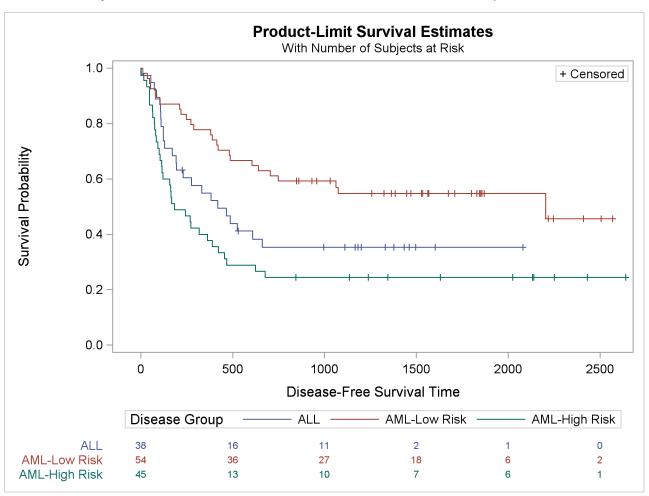
```
proc format;
  invalue $bmtifmt 'ALL' = 1 'AML-Low Risk' = 2 'AML-High Risk' = 3;
  value bmtfmt 1 = 'ALL' 2 = 'AML-Low Risk' 3 = 'AML-High Risk';
run;

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 58.2.6. The most noticeable change from Output 58.2.2 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.



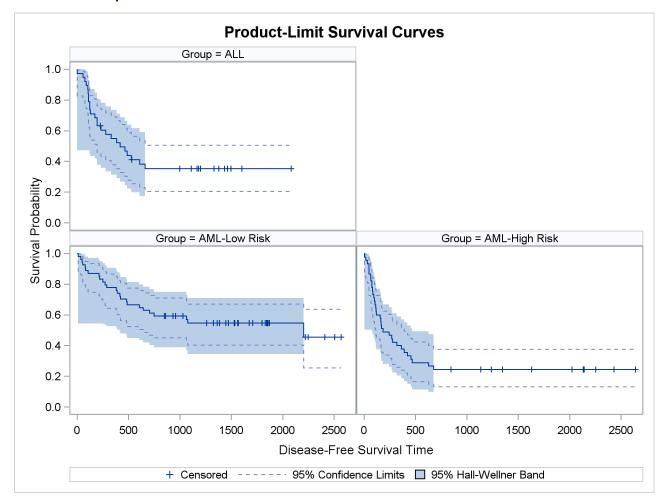
Output 58.2.6 Modified Disease-Free Survival for Bone Marrow Transplant Patients

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 58.2.7.

Output 58.2.7 Estimated Disease-Free Survivor Functions with Confidence Limits



# **Example 58.3: Life-Table Estimates for Males with Angina Pectoris**

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.

```
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.

Results of the life-table estimation are shown in Output 58.3.1. 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 58.3.1 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	Standard	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		

Eval Interval		uated at the Midpoint of the Interval			
[Lower,	Upper)	PDF	PDF Standard Error	Hazard	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 58.3.2. Note that 32.8% of the patients have withdrawn from the study.

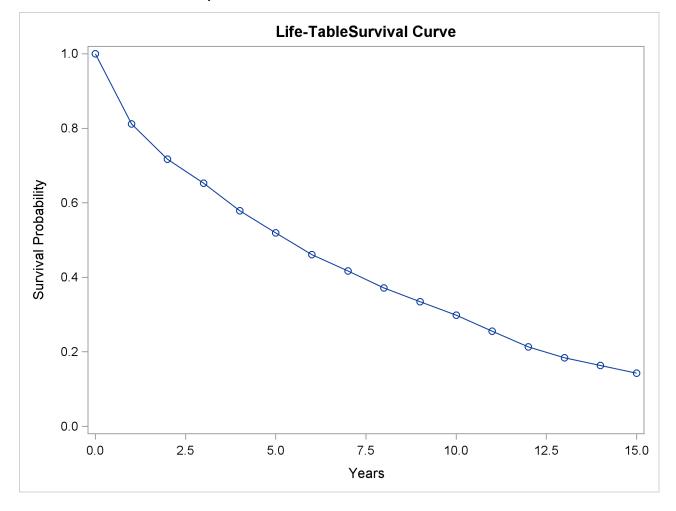
Output 58.3.2 Summary of Censored and Event Observations

Summary of the Number of				
C	ensored	d and Unce	nsored	
		Values		
			Percent	
Total	Failed	Censored	Censored	
2418	1625	793	32.80	

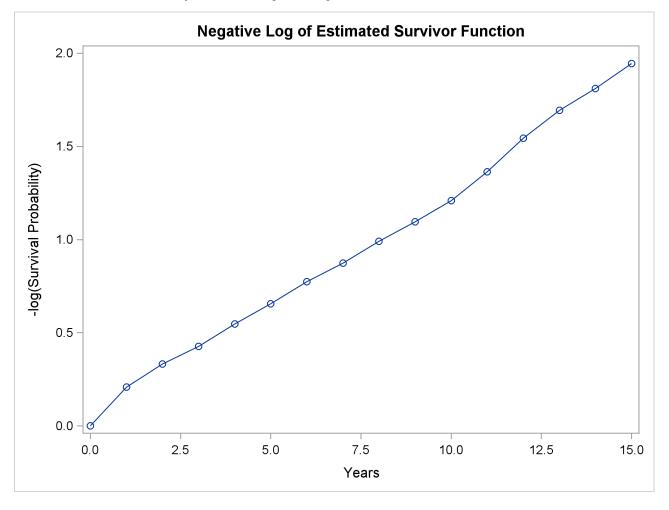
**Note:** 2 observations with invalid time, censoring, or frequency values were deleted.

Output 58.3.3 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 58.3.3 Life-Table Survivor Function Estimate



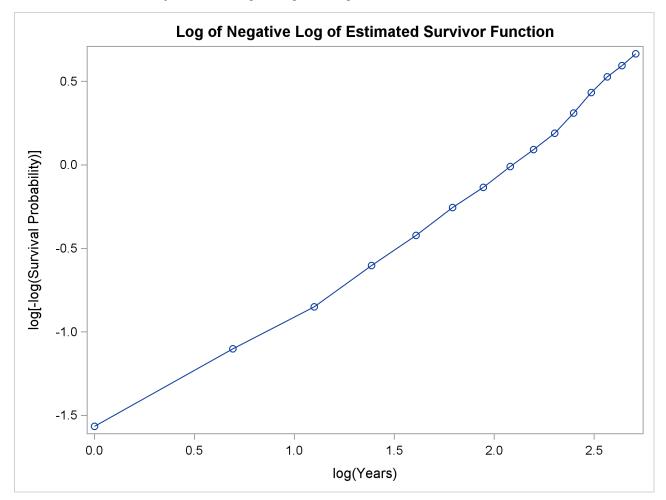
An exponential model might be appropriate for the survival of these male patients with angina pectoris since the curve of the negative log of the survivor function estimate versus the survival time (Output 58.3.4) approximates a straight line through the origin. Note that the graph of the log of the negative log of the survivor function estimate versus the log of time (Output 58.3.5) is practically a straight line.



Output 58.3.4 Negative Log of Survivor Function Estimate

As discussed in Lee (1992), the graph of the estimated hazard function (Output 58.3.6) 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 58.3.5 Log of Negative Log of Survivor Function Estimate

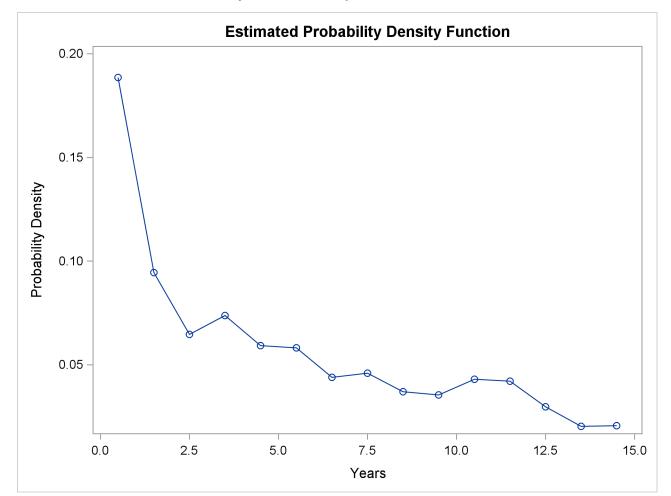


Estimated Hazard Function

0.200 - 0.175 - 0.150 - 0.125 - 0.100 - 0.0 2.5 5.0 7.5 10.0 12.5 15.0 Years

Output 58.3.6 Hazard Function Estimate

The density estimate is shown in (Output 58.3.7). Visually, it resembles the density function of an exponential distribution.



Output 58.3.7 Density Function Estimate

# References

Andersen, P. K., Borgan, O., Gill, R. D., and Keiding, N. (1992), *Statistical Models Based on Counting Processes*, New York: Springer-Verlag.

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# Subject Index

actuarial estimates, see life-table estimates	LIFETEST procedure, 4328, 4355
alpha level	Fleming-Harrington $G_{\rho}$ test for homogeneity
LIFETEST procedure, 4339	LIFETEST procedure, 4328, 4353
annotate	
traditional graphics (LIFETEST), 4382	Gehan test, see Wilcoxon test for homogeneity
arcsine-square root transformation	
confidence intervals (LIFETEST), 4339, 4360,	Hall-Wellner bands
4362	LIFETEST procedure, 4339, 4362, 4407
association tests	hazard function
LIFETEST procedure, 4329, 4335, 4400	LIFETEST procedure, 4328, 4414
-	homogeneity tests
at-risk	LIFETEST procedure, 4328, 4334, 4365, 4399
product-limit estimates (LIFETEST), 4339	
Bonferroni adjustment	interval determination
LIFETEST procedure, 4350	LIFETEST procedure, 4359
*	interval width
Breslow estimates	life-table method (LIFETEST), 4347
LIFETEST procedure, 4328, 4355	intervals
Breslow test, see Wilcoxon test for homogeneity	life-table estimates (LIFETEST), 4340
antala a	me table estimates (En ETEST), 1310
catalog	k-sample tests, see homogeneity tests
traditional graphics (LIFETEST), 4383	Kaplan-Meier estimates, <i>see</i> product-limit estimates
CDF, see cumulative distribution function	kernel-smoothed hazard
censored	LIFETEST procedure, 4343, 4363
LIFETEST procedure, 4328, 4354	En Bilbit procedure, 15 15, 1565
censored symbol	life-table estimates
traditional graphics (LIFETEST), 4382	LIFETEST procedure, 4328, 4377, 4411
character set	LIFETEST procedure
line printer plots (LIFETEST), 4383	alpha level, 4339
confidence bands	association tests, 4329, 4335, 4370, 4389, 4400
LIFETEST procedure, 4339, 4361	Bonferroni adjustment, 4350
confidence limits	· · · · · · · · · · · · · · · · · · ·
LIFETEST procedure, 4360, 4373	Breslow estimates, 4328, 4341, 4355
cumulative distribution function	censored, 4328, 4354
LIFETEST procedure, 4328	computational formulas, 4355
,	confidence bands, 4339, 4361
density function, see probability density function	confidence limits, 4360, 4373
description	cumulative distribution function, 4328
traditional graphics (LIFETEST), 4382	Dunnett's adjustment, 4350
Dunnett's adjustment	effective sample size, 4358
LIFETEST procedure, 4350	equal-precision bands, 4363, 4407
En El Est procedure, 1880	estimation method, 4340
effective sample size	Fleming-Harrington estimates, 4328, 4341, 4355
LIFETEST procedure, 4358	Fleming-Harrington $G_{\rho}$ test for homogeneity,
equal-precision bands	4328, 4353
LIFETEST procedure, 4339, 4363, 4407	Hall-Wellner bands, 4362, 4407
*	hazard function, 4328, 4414
event symbol	homogeneity tests, 4328, 4334, 4365, 4399
traditional graphics (LIFETEST), 4382	input data set, 4340
Flaming Harrington actimates	interval determination, 4359
Fleming-Harrington estimates	interval determination, 4559

kernel-smoothed hazard, 4343, 4363	LIFETEST procedure, 4329
life-table estimates, 4328, 4341, 4358, 4377,	log-rank test for homogeneity
4408, 4411	LIFETEST procedure, 4328, 4353, 4365
likelihood ratio test for homogeneity, 4328, 4365	logit transformation
line printer plots, 4381	confidence intervals (LIFETEST), 4340, 4361,
log-rank test for association, 4329, 4370	4363
log-rank test for homogeneity, 4328, 4353, 4365	and the section
maximum time, 4339, 4340	maximum time
median residual time, 4377	confidence bands (LIFETEST), 4339
minimum time, 4339	plots (LIFETEST), 4340
missing stratum values, 4341, 4348, 4352	mean survival time
missing values, 4354	time limit (LIFETEST), 4347
modified Peto-Peto test for homogeneity, 4328,	median residual time
4353	LIFETEST procedure, 4377
Nelson-Aalen estimates, 4341	minimum time
ODS graph names, 4387	confidence bands (LIFETEST), 4339
ODS Graphics, 4338	missing stratum values
ODS table names, 4385	LIFETEST procedure, 4341, 4348, 4352
output data sets, 4372	missing values
partial listing, 4347	LIFETEST procedure, 4354
Peto-Peto test for homogeneity, 4328, 4353	modified Peto-Peto test for homogeneity
probability density function, 4328, 4415	LIFETEST procedure, 4328, 4353
product-limit estimates, 4328, 4330, 4341, 4355,	multiplicity adjustment
4375, 4376, 4389	Bonferroni (LIFETEST), 4350
Scheffe's adjustment, 4350	Dunnett (LIFETEST), 4350
Sidak's adjustment, 4350	Scheffe (LIFETEST), 4350
simulated adjustment, 4350	Sidak (LIFETEST), 4350
stratified tests, 4328, 4329, 4335, 4337, 4352,	simulated (LIFETEST), 4350
4367, 4379	studentized maximum modulus (LIFETEST),
studentized maximum modulus adjustment, 4350	4350
· ·	Tukey (LIFETEST), 4350
survival distribution function, 4328, 4355	Tukey (EH E1E51), 4330
Tarone-Ware test for homogeneity, 4328, 4353	Nelson-Aalen estimates
traditional graphics, 4381	LIFETEST procedure, 4341
transformations for confidence intervals, 4339	number of intervals
trend tests, 4328, 4352, 4353, 4369, 4379	life-table estimates (LIFETEST), 4341
Tukey's adjustment, 4350	me table estimates (En E1E61), 1311
Wilcoxon test for association, 4329, 4370	ODS graph names
Wilcoxon test for homogeneity, 4328, 4353, 4365	LIFETEST procedure, 4387
likelihood ratio test for homogeneity	ODS Graphics
LIFETEST procedure, 4328	LIFETEST procedure, 4338
line printer plots	output data sets
LIFETEST procedure, 4381	LIFETEST procedure, 4372
linear rank tests, see association tests	En ETEST procedure, 4372
linear transformation	partial listing
confidence intervals (LIFETEST), 4340, 4360	product-limit estimate (LIFETEST), 4347
local annotate	PDF, see probability density function
traditional graphics (LIFETEST), 4383	Peto-Peto test for homogeneity
log transformation	LIFETEST procedure, 4328, 4353
confidence intervals (LIFETEST), 4340, 4361,	Peto-Peto-Prentice, see Peto-Peto test for homogeneity
4362	
log-log transformation	probability density function
confidence intervals (LIFETEST), 4339, 4361,	LIFETEST procedure, 4328, 4415
4362	product-limit estimates
log-rank test for association	LIFETEST procedure, 4328, 4330, 4355, 4375,
105 Turns test for association	4376

```
Scheffe's adjustment
    LIFETEST procedure, 4350
SDF, see survival distribution function
Sidak's adjustment
    LIFETEST procedure, 4350
simulated adjustment
    LIFETEST procedure, 4350
stratified tests
    LIFETEST procedure, 4328, 4329, 4335, 4337,
         4352, 4367, 4379
studentized maximum modulus adjustment
    LIFETEST procedure, 4350
survival distribution function
    LIFETEST procedure, 4328, 4355, 4374
survivor function, see survival distribution function
Tarone-Ware test for homogeneity
    LIFETEST procedure, 4328, 4353
traditional graphics
    LIFETEST procedure, 4381
transformations for confidence intervals
    LIFETEST procedure, 4339
trend tests
    LIFETEST procedure, 4328, 4352, 4353, 4369,
         4379
Tukey's adjustment
    LIFETEST procedure, 4350
Wilcoxon test for association
    LIFETEST procedure, 4329
Wilcoxon test for homogeneity
    LIFETEST procedure, 4328, 4353, 4365
```

# Syntax Index

ADJUST= option	INTERVALS= option
STRATA statement (LIFETEST), 4350	PROC LIFETEST statement, 4340
ALPHA= option	
PROC LIFETEST statement, 4339	LANNOTATE= option
ALPHAQT= option	PROC LIFETEST statement, 4383
PROC LIFETEST statement, 4339	LIFETEST procedure, 4327
ANNOTATE= option	BY statement, 4347
PROC LIFETEST statement, 4382	FREQ statement, 4348
ATRISK option	ID statement, 4348
PROC LIFETEST statement, 4339	PROC LIFETEST statement, 4337
,,,	STRATA statement, 4348
BANDMAX= option, see BANDMAXTIME= option	syntax, 4337
BANDMAXTIME= option	TEST statement, 4353
PROC LIFETEST statement, 4339	TIME statement, 4354
BANDMIN= option, see BANDMINTIME= option	LIFETEST procedure, BY statement, 4347
BANDMINTIME= option	LIFETEST procedure, FREQ statement, 4348
PROC LIFETEST statement, 4339	NOTRUNCATE option, 4348
BY statement	LIFETEST procedure, ID statement, 4348
LIFETEST procedure, 4347	LIFETEST procedure, PROC LIFETEST statement, 4337
CENSOREDSYMBOL= option	ALPHA= option, 4339
PROC LIFETEST statement, 4382	ALPHAQT= option, 4339
CONFBAND= option	ANNOTATE= option, 4382
PROC LIFETEST statement, 4339	ATRISK option, 4339
CONFTYPE= option	BANDMAXTIME= option, 4339
PROC LIFETEST statement, 4339	BANDMINTIME= option, 4339
,	CENSOREDSYMBOL= option, 4382
DATA= option	CONFBAND= option, 4339
PROC LIFETEST statement, 4340	CONFTYPE= option, 4339
DESCRIPTION= option	DATA= option, 4340
PROC LIFETEST statement, 4382	DESCRIPTION= option, 4382
DIFF= option	EVENTSYMBOL= option, 4382
STRATA statement (LIFETEST), 4351	FORMCHAR= option, 4383
	GOUT= option, 4383
EVENTSYMBOL= option	INTERVALS= option, 4340
PROC LIFETEST statement, 4382	LANNOTATE= option, 4383
	*
FORMCHAR= option	LINEPRINTER option, 4383
PROC LIFETEST statement, 4383	MAXTIME= option, 4340, 4383
FREQ statement	METHOD= option, 4340
LIFETEST procedure, 4348	MISSING option, 4341
	NELSON option, 4341
GOUT= option	NINTERVAL= option, 4341
PROC LIFETEST statement, 4383	NOCENSPLOT option, 4383
GROUP= option	NOLEFT option, 4341
STRATA statement (LIFETEST), 4352	NOPRINT option, 4341
-	NOTABLE option, 4341
ID statement	OUTSURV= option, 4342
LIFETEST procedure, 4348	OUTTEST= option, 4342

PROC LIFETEST statement, 4342	
OUTTEST= option	
PROC LIFETEST statement, 4342	
PLOTS= option	
PROC LIFETEST statement, 4342, 4384	
PROC LIFETEST statement	
LIFETEST procedure, 4337	
•	
REDUCEOUT option	
PROC LIFETEST statement, 4346	
SINGULAR= option	
PROC LIFETEST statement, 4346	
STDERR option	
PROC LIFETEST statement, 4346	
STRATA statement	
LIFETEST procedure, 4348	
•	
TEST statement	
LIFETEST procedure, 4353	
TEST= option	
STRATA statement (LIFETEST), 4353	
TIME statement	
LIFETEST procedure, 4354	
TIMELIM= option	
PROC LIFETEST statement, 4347	
TIMELIST= option	
PROC LIFETEST statement, 4347	
TREND option	
STRATA statement (LIFETEST), 4352	
~ · · · · · · · · · · · · · · ·	
WIDTH= option	
PROC LIFETEST statement, 4347	