Subj	Survt	Relapse	Sex	log WBC	*Rx*
27	12	1	0	3.06	1
28	11	1	0	3.49	1
29	11	1	0	2.12	1
30	8	1	0	3.52	1
31	8	1	0	3.05	1
32	8	1	0	2.32	1
33	8	1	1	3.26	1
34	5	1	1	3.49	1
35	5	1	0	3.97	1
36	4	1	1	4.36	1
37	4	1	1	2.42	1
38	3	1	1	4.01	1
39	2	1	1	4.91	1
40	2	1	1	4.48	1
41	1	1	1	2.80	1
42	1	1	1	5.00	1

a. Suppose we wish to describe KM curves for the variable logwbc. Because logwbc is continuous, we need to categorize this variable before we compute KM curves. Suppose we categorize logwbc into three categories—low, medium, and high—as follows:

   low (0 – 2.30), n = 11;
   medium (2.31–3.00), n = 14;
   high (> 3.00), n = 17.

   Based on this categorization, compute and graph KM curves for each of the three categories of logwbc. (You may use a computer program to assist you or you can form three tables of ordered failure times and compute KM probabilities directly.)

b. Compare the three KM plots you obtained in part a. How are they different?

c. Below is a printout of the log–rank test and the Peto test for comparing the three groups.

Group	Size	% Cen	LQ	Median	UQ	0.95	Med CI
1	11	63.636	15			15.000	
2	14	28.571	8	17	22	8.000	17
3	17	5.882	4	6	8	4.000	7

df: 2, log–rank: 26.391, P-value: 0, Peto: 16.067, P-value: 0.

What do you conclude about whether or not the three KM curves are the same?

Test

To answer the questions below, you will need to use a computer program (from SAS, BMD, SPIDA, EGRET, S+ or any other package you are familiar with) that computes and plots KM curves and computes the log–rank test.

1. For the vets.dat data set described in the presentation (and listed in Appendix B at the end of this book):
   a. Obtain KM plots for the two categories of the variable cell type 1 (1 = large, 0 = other). Comment on how the two curves compare with each other. Carry out the log–rank and/or Peto tests, and draw conclusions from the test(s).
   b. Obtain KM plots for the four categories of cell type—large, adeno, small, and squamous. Note that you will need to recode the data to define a single variable which numerically distinguishes the four categories (e.g., 1 = large, 2 = adeno, etc.). As in part a, compare the four KM curves. Also, carry out the log–rank and/or Peto tests for the equality of the four curves and draw conclusions.
2. The following questions consider a data set from a study by Caplehorn et al. ("Methadone Dosage and Retention of Patients in Maintenance Treatment," *Med. J. Aust.*, 1991). These data comprise the times in days spent by heroin addicts from entry to departure from one of two methadone clinics. There are two further covariates, namely, prison record and methadone dose, believed to affect the survival times. The data set name is addicts.dat. A listing of the data as stored in a SPIDA file is given in Appendix B. A listing of the variables is given below:

   Column 1: Subject ID
   Column 2: Clinic (1 or 2)
   Column 3: Survival status (0 = censored, 1 = departed from clinic)
   Column 4: Survival time in days
   Column 5: Prison record (0 = none, 1 = any)
   Column 6: Methadone dose (mg/day)

a. Compute and plot the KM plots for the two categories of the "clinic" variable and comment on the extent to which they differ.
b. A printout of the log–rank and Peto tests (using SPIDA) is provided below. What are your conclusions from this printout?

Group	Size	% Cen	LQ	Median	UQ	0.95	Med CI
1	163	25.153	192	428	652	341.000	504
2	75	62.667	280			661.000	

df: 1, log–rank: 27.893, P-value: 0, Peto: 11.078, P-value: 0.001.

c. Compute and evaluate KM curves and the log–rank and/or Peto test for comparing suitably chosen categories of the variable "Methadone dose." Explain how you determined the categories for this variable.

Answers to Practice Exercises

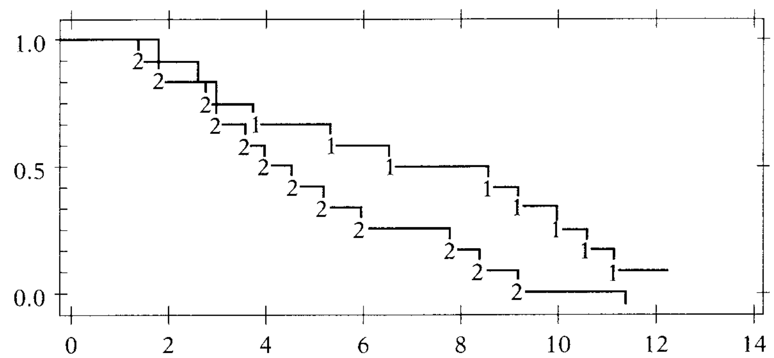
1. a.

Group 1					Group 2				
$t_{(j)}$	n_j	m_j	q_j	$S(t_{(j)})$	$t_{(j)}$	n_j	m_j	q_j	$S(t_{(j)})$
0.0	25	0	0	1.00	0.0	25	1	0	1.00
1.8	25	1	0	.96	1.4	25	1	0	.96
2.2	24	1	0	.92	1.6	24	1	0	.92
2.5	23	1	0	.88	1.8	23	1	0	.88
2.6	22	1	0	.84	2.4	22	1	0	.84
3.0	21	1	0	.80	2.8	21	1	0	.80
3.5	20	1	0	.76	2.9	20	1	0	.76
3.8	19	1	0	.72	3.1	19	1	0	.72
5.3	18	1	0	.68	3.5	18	1	0	.68
5.4	17	1	0	.64	3.6	17	1	0	.64
5.7	16	1	0	.60	3.9	16	1	0	.60
6.6	15	1	0	.56	4.1	15	1	0	.56
8.2	14	1	0	.52	4.2	14	1	0	.52
8.7	13	1	0	.48	4.7	13	1	0	.48
9.2	12	2	0	.40	4.9	12	1	0	.44
9.8	10	1	0	.36	5.2	11	1	0	.40
10.0	9	1	0	.32	5.8	10	1	0	.36
10.2	8	1	0	.28	5.9	9	1	0	.32

(Continued on next page)

Group 1					Group 2				
$t_{(j)}$	n_j	m_j	q_j	$S(t_{(j)})$	$t_{(j)}$	n_j	m_j	q_j	$S(t_{(j)})$
10.7	7	1	0	.24	6.5	8	1	0	.28
11.0	6	1	0	.20	7.8	7	1	0	.24
11.1	5	1	0	.16	8.3	6	1	0	.20
11.7	4	1	3	.12	8.4	5	1	0	.16
					8.8	4	1	0	.12
					9.1	3	1	0	.08
					9.9	2	1	0	.04
					11.4	1	1	0	.00

b. KM curves for CHR data:



Group 1 appears to have consistently better survival prognosis than group 2. However, the KM curves are very close during the first four years, but are quite separate after four years, although they appear to come close again around twelve years.

c. Using the expanded table format, the following information is obtained:

$t_{(j)}$	m_{1j}	m_{2j}	n_{1j}	n_{2j}	e_{1j}	e_{2j}	$m_{1j}-e_{1j}$	$m_{2j}-e_{2j}$
1.4	0	1	25	25	.500	.500	–.500	.500
1.6	0	1	25	24	.510	.490	–.510	.510
1.8	1	1	25	23	1.042	.958	–.042	.042
2.2	1	0	24	22	.522	.478	.478	–.478
2.4.	0	1	23	22	.511	.489	–.511	.511
2.5.	1	0	23	21	.523	.477	.477	–.477
2.6	1	0	22	21	.516	.484	.484	–.484

(Continued on next page)

$t_{(j)}$	m_{1j}	m_{2j}	n_{1j}	n_{2j}	e_{1j}	e_{2j}	$m_{1j}-e_{1j}$	$m_{2j}-e_{2j}$
2.8	0	1	21	21	.500	.500	−.500	.500
2.9	0	1	21	20	.512	.488	−.512	.512
3.0	1	0	21	19	.525	.475	.475	−.475
3.1	0	1	20	19	.513	.487	−.513	.513
3.5	1	1	20	18	1.053	.947	−.053	.053
3.6	0	1	19	17	.528	.472	−.528	.528
3.8	1	0	19	16	.543	.457	.457	−.457
3.9	0	1	18	16	.529	.471	−.529	.529
4.1	0	1	18	15	.545	.455	−.545	.545
4.2	0	1	18	14	.563	.437	−.563	.563
4.7	0	1	18	13	.581	.419	−.581	.581
4.9	0	1	18	12	.600	.400	−.600	.600
5.2	0	1	18	11	.621	.379	−.621	.621
5.3	1	0	18	10	.643	.357	.357	−.357
5.4	1	0	17	10	.630	.370	.370	−.370
5.7	1	0	16	10	.615	.385	.385	−.385
5.8	0	1	15	10	.600	.400	−.600	.600
5.9	0	1	15	9	.625	.375	−.625	.625
6.5	0	1	15	8	.652	.348	−.652	.652
6.6	1	0	15	7	.682	.318	.318	−.318
7.8	0	1	14	7	.667	.333	−.667	.667
8.2	1	0	14	6	.700	.300	.300	−.300
8.3	0	1	13	6	.684	.316	−.684	.684
8.4	0	1	13	5	.722	.278	−.722	.722
8.7	1	0	13	4	.765	.235	.335	−.335
8.8	0	1	12	4	.750	.250	−.750	.750
9.1	0	1	12	3	.800	.200	−.800	.800
9.2	2	0	12	2	1.714	.286	.286	−.286
9.8	1	0	10	2	.833	.167	.167	−.167
9.9	0	1	9	2	.818	.182	−.818	.818
10.0	1	0	9	1	.900	.100	.100	−.100
10.2	1	0	8	1	.888	.112	.112	−.112
10.7	1	0	7	1	.875	.125	.125	−.125
11.0	1	0	6	1	.857	.143	.143	−.143
11.1	1	0	5	1	.833	.167	.167	−.167
11.4	0	1	4	1	.800	.200	−.800	.800
11.7	1	0	4	0	1.000	.000	.000	.000
Totals	22	25			30.79	16.21	−8.690	8.690

d. The log-rank statistic can be computed from the totals of the expanded table using the formulae:

$$\text{log-rank statistic} = \frac{(O_i - E_i)^2}{\widehat{\text{Var}}(O_i - E_i)}$$

$$\text{Var}(O_i - E_i) = \sum_j \frac{n_{1j} n_{2j} (m_{1j} + m_{2j})(n_{1j} + n_{2j} - m_{1j} - m_{2j})}{(n_{1j} + n_{2j})^2 (n_{1j} + n_{2j} - 1)}$$

The variance turns out to be 9.448, so that the log–rank statistic is $(8.69)^2/9.448=7.993$.

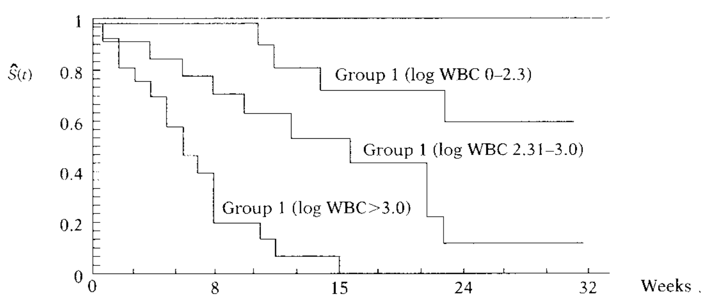
Using SPIDA, the results for the log–rnak and Peto tests are given as follows:

Group	Size	%Cen	LQ	Median	UQ	0.95	Med CI
1	25	12.000	3.8	8.700	10.7	5.300	10.0
2	25	0.000	3.1	4.700	7.8	3.500	5.9

df: 1, log–rank: 7.993, P-value: 0.005, Peto: 3.516, P-value: 0.061.

The log–rank test gives highly significant results, whereas the Peto test is almost significant at the .05 level. These results indicate that there is a significant difference in survival between the two groups.

2. a. For the Anderson dataset, the KM plots for the three categories of log WBC are shown below:



b. The KM curves are quite different with group 1 having consistently better survival prognosis than group 2, and group 2 having consistently better survival prognosis than group 3. Note also that the difference between group 1 and 2 is about the same over time, whereas group 2 appears to diverge from group 3 as time increases.

c. Both the log–rank statistic (26.391) and the Peto statistic (16.067) are highly significant with P-values equal to zero to three decimal places. Because there are three groups being compared, each statistic is approximately chi-square with two degrees of freedom under the null hypothesis that all three groups have a common survival curve.

Appendix: Matrix Formula for the Log–Rank Statistic for Several Groups

For $i = 1, 2, \ldots, G$ and $j = 1, 2, \ldots, k$, where $G =$ # of groups and $k =$ # of distinct failure times,

n_{ij} = # at risk in ith group at jth ordered failure time

m_{ij} = observed # of failures in ith group at jth ordered failure time

e_{ij} = expected # of failures in ith group at jth ordered failure time

$$= \left(\frac{n_{ij}}{n_{1j} + n_{2j}}\right)(m_{1j} + m_{2j})$$

$$n_j = \sum_{i=1}^{G} n_{ij}$$

$$m_j = \sum_{i=1}^{G} m_{ij}$$

$$O_i - E_i = \sum_{j=1}^{k} (m_{ij} - e_{ij})$$

$$\widehat{\text{Var}}(O_i - E_i) = \sum_{j=1}^{k} \frac{n_{ij}(n_j - n_{ij})m_j(n_j - m_j)}{n_j^2(n_j - 1)}$$

$$\widehat{\text{Cov}}(O_i - E_i, O_l - E_l) = \sum_{j=1}^{k} \frac{-n_{ij}n_{lj}m_j(n_j - m_j)}{n_j^2(n_j - 1)}$$

$$\mathbf{d} = (O_1 - E_1, O_2 - E_2, \ldots, O_{G-1} - E_{G-1})'$$

$$\mathbf{V} = ((v_{il}))'$$

where $v_{ii} = \widehat{\text{Var}}\,(O_i - E_i)$ and $v_{il} = \widehat{\text{Cov}}\,(O_i - E_i, O_l - E_l)$ for $i = 1, 2, \ldots, G-1$; $l = 1, 2, \ldots, G-1$.

Then, the log–rank statistic is given by the matrix product formula:

$$\text{Log–rank statistic} = \mathbf{d}'\mathbf{V}^{-1}\mathbf{d}$$

which has approximately a chi-square distribution with $G-1$ degrees of freedom under the null hypothesis that all G groups have a common survival curve.