UNIT 16 LOG-RANK TEST

Structure

16.1 INTRODUCTION

In Unit 15, we studied various methods of estimation of the survival functions for complete as well as censored data. We have learned how comfortably summarize the survival experience of follow-up data. We studied how the Kaplan and Meier method works and uses the complete as well as censored observations to estimate the survival function at various time points with their standard error and confidence interval. We are now in a position to plot and summarized the Kaplan and Meier survival curve and locate the median survival time on the curve.

All, we have done is with the assumption that we have only one group of patients and this much analysis is enough in such a situation. But there are various situations in our survival studies where we have two or more groups. For example, two groups of breast cancer patients where the first group received surgical treatment whereas the second group received surgery and chemotherapy. In such situations, we are concerned not only with summarizing survival data but our interest will be more to make an inference about which treatment option is doing better? We can compare the groups using the Kaplan-Meier survival curves. But the weakness of this approach is that it does not provide a comparison of the total survival experience of the two groups, but rather gives a comparison at some arbitrary time point(s). In short, we move to compare the survival experiences by using testing of hypothesis.

In this unit, we will discuss comparisons of survival experiences according to the inferential approach when we deal with censored survival data. We start with the log-rank test. In Sec. 16.2 and 16.3, we discuss the log-rank tests for two and more than two groups, respectively. The tests are based on some assumptions so, in Sec. 16.4, we give the assumptions of the log-rank test. A brief summary of what we have covered in this unit is described in Sec. 16.5. If you will face some problems in the solution of the exercises then you can go through Sec. 16.6 in which we provide the solutions/answers to the exercises.

Objectives

After studying this unit, you should be able to:

- describe the concept of hypothesis testing for survival data;
- explain the situation in which the log-rank test is used;
- apply the log-rank test for two groups comparison;
- use the log-rank test for more than two groups; and

- discuss the assumptions of the log-rank test.

16.2 LOG-RANK TEST FOR COMPARISON OF TWO GROUPS

In the biomedical field, we are concerned not only with estimating the survival function but more often with the comparison of survival distributions/ experiences when we deal with two or more groups of patients/subjects. For example, a laboratory researcher may want to compare the tumour-free times of two or more groups of rats exposed to carcinogens, a diabetologist may want to compare the retinopathy free times of two groups of diabetic patients, an oncologist may be interested in comparing the ability of two or more treatments for controlling cancer. We may compare two or more groups either estimated medians or drawing survival functions curves but these give only a rough idea of the differences between them. Also, these do not reveal whether the differences are significant or due to chance causes. Therefore, we require statistical tests for that.

In the course MST004: Statistical inference, you have studied that the statistical tests are broadly classified into two categories: parametric and non-parametric tests. For applying the parametric tests, we have to know the form of the characteristic under study(normal) but in the biological fields, it is extremely difficult to have prior knowledge about the distribution of the survival experiences. Therefore, we cannot use parametric tests for the comparison of survival experiences. As you know, the non-parametric tests are not based on the distribution of the characteristic under study so we can apply non-parametric tests for comparison. In Block 4 of MST-004: Statistical Inference, you have studied various non-parametric tests. For comparing two independent groups, we may use the Mann Whitney U test and for paired data (before and after) we may use the paired sign test when data are at least in the ordinal scale and the Wilcoxon matched-pair signed-rank test when survival data are at least interval scale. But these tests require the complete data of each patient/subject. Therefore, we can apply these non-parametric tests for survival data if we deal with complete/ uncensored data. For example, if we compare the time to liver failure for several dose levels of a new drug on animals and follow every animal until the event occurs then we may use the Mann Whitney U test (Wilcoxon rank-sum test) to compare two groups of different levels. However, if some animals may die or we terminate the study before the event occurs to all animals (the data is censored) then the actual time of the event is unknown because the event does not occur while understudying observation. In such cases, the Mann Whitney U test can be highly biased in the presence of censored data. Therefore, the standard statistical tests cannot usually be applied because the underlying distribution is rarely normal and the data are often 'censored'. In this unit, we will discuss the log-rank test that is used for such situations.

We start our discussion with two hypothetical data sets coming from a randomized controlled trial. The first set is the group of 15 breast cancer patients described in Unit 15. Let us assume that this is the group of breast cancer patients who had surgical treatment and were then followed up for 20 months with mortality as an event or outcome of interest. We name this group as **Surgery group** and the survival data of this group is:

Surgery group:

Survival time (in months): 3, 4, 4^+, 6, 7, 9, 9^+, 11, 12, 14, 16, 18, 18, 20^+, 20^+

+ sign represents censored observations.

The second set is the group of breast cancer patients randomized to those who receive surgery followed by chemotherapy. This group of patients receive both the treatment namely surgery and chemotherapy. There were 13 patients who received this intervention. We name it as **Chemotherapy group**. They were followed up to 22 months to observe mortality experience. The survival data obtained from this group is:

Chemotherapy group:

Survival time (in months): 5, 7, 8, 10^+, 12, 14, 14^+, 17, 19, 20, 20^+, 21, 22^+

Now, we show the data of both the groups in a more structured way in Table 1(a) and (b) respectively as we have done in Unit 15.

Table 1 (a): Structured data of Surgery group

Follow up time (in months)	Number still in the study at start of month t	Deaths during month t	Censored during month t	Number after month t
0	15	0	0	15
3	15	1	0	14
4	14	1	0	13
4^+	13	0	1	12
6	12	1	0	11
7	11	1	0	10
9	10	1	0	9
9^+	9	0	1	8
11	8	1	0	7
12	7	1	0	6
14	6	1	0	5
16	5	1	0	4
18	4	2	0	2
20^+	2	0	2	0

Table 1 (b): Structured data of Chemotherapy group

Follow up time (in months)	Number still in the study at start of month t	Deaths during month t	Censored during month t	Number after month t
0	13	0	0	13
5	13	1	0	12
7	12	1	0	11
8	11	1	0	10
10^+	10	0	1	9
12	9	1	0	8
14	8	1	0	7
14^+	7	0	1	6
17	6	1	0	5
19	5	1	0	4
20	4	1	0	3
20^+	3	0	1	2
21	2	1	0	1
22^+	1	0	1	0

We estimate the survival probabilities/function for both the groups using the Kaplan and Meier method which is described in Unit 15. The survival distribution and summary statistics of both groups of patients are as follows:

Table 2: Survival probabilities of Surgery and Chemotherapy groups

Surgery group		Chemotherapy group	
Follow up time (in months)	**Cumulative probability of surviving of month t**	**Follow up time (in months)**	**Cumulative probability of surviving of month t**
t	**S**	**t**	**S**
0	1	0	1.000
3	0.933	5	0.923
4	0.867	7	0.846
6	0.794	8	0.769
7	0.722	12	0.684
9	0.650	14	0.598
11	0.569	1	0.499
12	0.488	19	0.399
14	0.406	20	0.299
16	0.325	21	0.150
18	0.163		

For interpretation purposes, we can also plot the Kaplan and Meier survival curve for both groups of patients as follows:

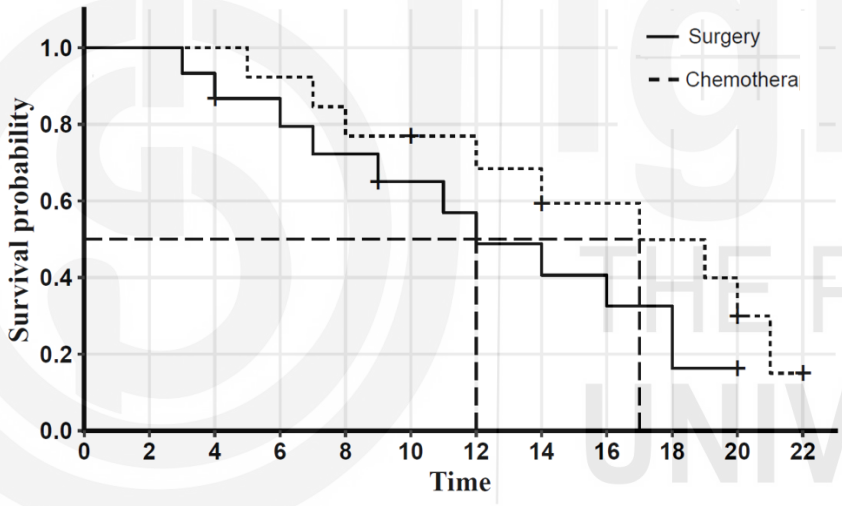

Fig. 16.1: Kaplan and Meier survival curves for Surgery and Chemotherapy groups.

From Table 2 and Fig 16.1, we observe that the approximate median survival time for the Surgery group is 12 months whereas for the Chemotherapy group is 17 months which is at first look longer. We can also get a visual comparison of these graphs also gives an impression that among Surgery patients events happened slightly faster than chemotherapy patients.

Our immediate question and interest will be to find out

Do these curves are significantly different?

Is there any significant difference between the median survival times of the two groups?

However, this question has to be answered statistically. As we have studied in Unit 9 of the course MST-004: Statistical Inference that for testing any statement regarding one group/population or two or more groups/populations we have to use **testing of hypothesis**. There are inferential approaches for it. In simple terms, we try to evaluate the hypothesis through a test of significance.

There are many tests designed for comparing survival functions/curves. Among them, the most popular and simple is the **log-rank test** or otherwise known as **Mantel- Haenszel** test for comparison of the survival curve.

The log-rank is a non-parametric test and is appropriate to use when the data are right-skewed and censored. It does not make any assumption about the form of survival distributions. The test is widely used in clinical trials to establish the efficacy of a new treatment in comparison with a control treatment when the measurement is the time to event. The log-rank test is designed to detect a difference between two or more survival distributions/functions/curves especially when the event rate in one group is consistently higher than the other group. This test compares the whole survival experience between groups and may be viewed as a test of whether the survival distributions/curves are similar or not. The log-rank test statistic has multiple variants that are provided by various statistical computing packages (e.g., SPSS, SAS, R). We describe one variant that is closely related to the chi-square test statistic in which we compare the observed to the expected number of events at each time point over the follow-up period.

In the log-rank test tests, we test the null hypothesis that the event time distribution among groups is equal. i.e.

H_0: There is no significant difference in survival probabilities between the two groups or there is no difference between the populations in the probability of death at any point.

H_1: There is a significant difference in survival probabilities between two groups or there is a significant difference between the populations in the probability of death at any point.

Symbolically, If $S_1(t)$ and $S_2(t)$ are the survival functions of the first and second groups respectively then the null and alternative hypotheses are

$$H_0 : S_1(t) = S_2(t)$$

$$H_1 : S_1(t) \neq S_2(t)$$

The log-rank test is based on the times of events (here deaths) and also considers the information of the censored observations in determining the number at risk as we have seen in the Kaplan-Meier method.

For each time of event occur, we compute the observed number of events (deaths) in each group and the expected number of events if there were in reality no difference between the groups. The principle behind computing the expected number of events in the log-rank test is straightforward. For example, in our case, there were 15 patients in the Surgery group and 13 patients in the Chemotheraphy group. Therefore, there was a total of 28 patients. The first event (death) occurred in 3rd month in the Surgery group. Therefore, the overall risk of death in this month was 1/28. Since there were 15 patients in group 1, so, if the null hypothesis was true, the expected number of deaths in the Surgery group is

$$15 \times \frac{1}{28} = 0.538$$

Similarly, for the Chemotheraphy group, the expected number of deaths during this month is

$$13 \times \frac{1}{28} = 0.464$$

We make a similar calculation for each time of the event (death) and then we add all results of such calculations for Group 1. After that we obtain a single number, called the extent of exposure (E_1), which represents the expected number of deaths in that group Similarly, we obtain the expected number of deaths (E_2) for Group 2. The basic procedure of the log-rank test is that at each point where an event happens, we calculate expected frequencies and using these individual expected frequencies we make the total expected frequencies. Similarly, we note down the number of events at each time point that we have observed for both groups then we add all for each group. These totals are called observed frequencies (O_1 and O_2). After that, we look at the proportional discrepancy of the expected number of deaths(frequency) with observed frequency and we define test statistic as the sum of squares of these proportional discrepancies as in the general chi-square test.

Procedure of the Log-rank Test:

As usual first step in the testing of hypothesis is to set up null and alternative hypotheses, so our null and alternative hypotheses are setup, below in Step 1.

Step 1: In the log-rank test tests, we test the null hypothesis that the event time distribution among groups is equal. i.e.

H_0: There is no significant difference between the survival functions/curves of the two groups

H_1: There is a significant difference between the survival functions/curves of the two groups

If $S_1(t)$ and $S_2(t)$ are the survival functions of the first and second groups respectively then the null and alternative hypotheses in the symbolical form are

$$H_0 : S_1(t) = S_2(t)$$

$$H_1 : S_1(t) \neq S_2(t)$$

Step 2: After setting the null and alternative hypotheses, we arrange the time (t) in increasing order at which the event (not censored) occur after combining both groups.

Step 3: After that, we find the number at risk (N_{1t} and N_{2t}) at each time when the event happens as we have found in the Kaplan-Meier method. That is, we have to consider the censored observations also to find the number at risk.

Step 4: Next, we find the total number at risk in both groups as the sum of numbers at risk in both groups, i.e., $N_t = N_{1t} + N_{2t}$.

Step 5: After calculating the total number at risk, we mention the number of events/deaths (observed frequency) that happen at each time in both groups, i.e., O_{1t} and O_{2t}.

Step 6: Next, we find the total number of events as the sum of the numbers of events in both groups, i.e., $O_t = O_{1t} + O_{2t}$.

Step 7: After that, we find the expected number of events (expected frequency) that have to occur in both groups, i.e., E_{1t} and E_{2t} under the assumption that the null hypothesis is true means the event is equally distributed to both groups. We use the formula as

$$E_{1t} = N_{1t} \times \frac{O_t}{N_t} \text{ and } E_{2t} = N_{2t} \times \frac{O_t}{N_t}$$

Step 8: Finally, we find

O_1 = Total observed number of deaths in Group 1

O_2 = Total observed number of deaths in Group 2

E_1 = Total expected number of deaths in Group 1

E_2 = Total expected number of deaths in Group 2

Step 9: Test statistic

Since this test compares observed frequencies with the corresponding expected frequencies, therefore, we are interested in the magnitudes of the differences between the observed and expected frequencies. Specifically, we wish to know whether the differences are small enough to be attributed to chance or they are largely due to some other factors. With the help of observed and expected frequencies, we may compute a test statistic that reflects the magnitudes of differences between these two quantities when H_0 is true. The test statistic is given by

$$\chi^2 = \frac{(O_1 - E_1)^2}{E_1} + \frac{(O_2 - E_2)^2}{E_2}$$

The χ^2-statistic follows approximately the chi-square distribution with one degree of freedom.

Step 10: We obtain the critical value of the test statistic at a given level of significance under the condition that the null hypothesis is true. **Table 1** in the Appendix at the end of this course provides critical values of the test statistic (χ^2) for various degrees of freedom and different level of significance.

Step 11: Take the decision on the null hypothesis

To take the decision on the null hypothesis, We compare the test statistic (calculated in Step 9) with the chi-square critical (tabulated) value (observed in Step 10) for a given level of significance (α) under the condition that the null hypothesis is true.

If the calculated value of the test statistic is greater than or equal to the critical value with one degree of freedom at α level of significance then we reject the null hypothesis H_0 at α level of significance, otherwise, we do not reject H_0.

After understanding the procedure of the log-rank method, let us test the survival distribution for the Surgery and Chemotherapy groups patients differ significantly or not using this test.

If $S_1(t)$ and $S_2(t)$ are the survival functions of the Surgery and Chemotherapy groups patients then we can formulate the null and alternative hypotheses as

$H_0 : S_1(t) = S_2(t)$

$H_1 : S_1(t) \neq S_2(t)$

After setting the null and alternative hypotheses, we arrange the time (t) in increasing order at which the event (not censored) occurs after combining both groups. The survival times for both groups are as follows:

Surgery group: 3, 4, 4^+, 6, 7, 9, 9^+, 11, 12, 14, 16, 18, 18, 20^+, 20^+

Chemotherapy group: 5, 7, 8, 10^+, 12, 14, 14^+, 17, 19, 20, 20^+, 21, 22^+

Consider the time of death (not censored) of the patients in both groups and arrange in ascending order as

3, 4, 5, 6, 7, 8, 9, 11, 12, 14, 16, 17, 18, 19, 20 21

Now, we find the number at risk in both groups. There were 15 patients in the Surgery group and 13 patients in the Chemotherapy group at the beginning of the follow-up. Both groups together the first event happened in 3rd month and that event was in the Surgery group. Hence, in 3rd month, there were 15 patients at risk in the Surgery group and 13 in the Chemotherapy group.

The second event (death) happened in the 4th month and that event again was in the Surgery group. Hence, at the time 4th month, there are 14 patients at risk in the Surgery group whereas 13 were in the Chemotherapy group because there was no death or no censored observation in the Chemotherapy group till the 4th month. The third event happened in the 5th month and that event was in the Chemotherapy group. Hence in time 5th month, there are 12 patients at risk in the Surgery group because there was one death and one censored in the 4th month whereas 13 in the Chemotherapy group.

Through the above repeated computational steps, we understood the mechanism of obtaining the number at risk in each group at each event time. Hence using the same methodology, we can compute N_{1t} and N_{2t}. We calculate the same in Columns 2 and 3 respectively of Table 3.

After that, we find the total number at risk, the number of events in the Surgery and Chemotherapy groups, and the total number of events. We calculate $N_t = N_{1t} + N_{2t}$ in Column 4, O_{1t} and O_{2t} in Columns 5 and 6 and $O_t = O_{1t} + O_{2t}$ in Column 7 of Table 3.

Now, we find the expected number of events (expected frequency) that have to occur in both groups, i.e., E_{1t} and E_{2t} under the assumption that the null hypothesis is true means the event is equally distributed to both groups. In the 3rd month, there were 15 and 13 patients in both groups and one death among 28 patients, hence we would expect the number of deaths has to occur in the Surgery group is

$$E_{1t} = N_{1t} \times \frac{O_t}{N_t} = 15 \times \frac{1}{28} = 0.536$$

and in the Chemotherapy group is

$$E_{2t} = N_{2t} \times \frac{O_t}{N_t} = 13 \times \frac{1}{28} = 0.464$$

Hence using the same methodology, we can find the expected death at each time of the event. We calculate the same in Columns 8 and 9 respectively in Table 3.

Table 3: Observed and expected frequencies computed at event time

Combined follow up time (in months)	Number at risk in		Total number at risk $N_t = N_{1t} + N_{2t}$	Number of events in		Total number of events $O_t = O_{1t} + O_{2t}$	Expected number of events in	
	Surgery N_{1t}	Chemotherapy N_{2t}		Surgery O_{1t}	Chemotherapy O_{2t}		Surgery $E_{1t} = N_{1t} \times (O_t/N_t)$	Chemotherapy $E_{2t} = N_{2t} \times (O_t/N_t)$
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
3	15	13	28	1	0	1	0.536	0.464
4	14	13	27	1	0	1	0.519	0.481
5	12	13	25	0	1	1	0.480	0.520
6	12	12	24	1	0	1	0.500	0.500
7	11	12	23	1	1	2	0.957	1.043
8	10	11	21	0	1	1	0.476	0.524
9	10	10	20	1	0	1	0.500	0.500
11	8	9	17	1	0	1	0.471	0.529
12	7	9	16	1	1	2	0.875	1.125
14	6	8	14	1	1	2	0.857	1.143
16	5	6	11	1	0	1	0.455	0.545
17	4	6	10	0	1	1	0.400	0.600
18	4	5	9	2	0	2	0.889	1.111
19	2	5	7	0	1	1	0.286	0.714
20	2	4	6	0	1	1	0.333	0.667
21	0	2	2	0	1	1	0.000	1.000
				$O_1 = 11$	**$O_2 = 9$**	**20**	**$E_1 = 8.532$**	**$E_2 = 11.468$**

From the above calculations, we have

$$\chi^2 = \frac{(O_1 - E_1)^2}{E_1} + \frac{(O_2 - E_2)^2}{E_2} = \frac{(11 - 8.532)^2}{8.532} + \frac{(9 - 11.468)^2}{11.468} = 1.245$$

The critical value of chi-square with one degree of freedom at 5% level of significance is 3.84.

Since the calculated value of the test statistic (= 1.245) is smaller than the critical value (= 3.84) so we do not reject the null hypothesis.

Thus, we conclude that the survival times are not different or there is not enough evidence to conclude that the survival times are different.

For better understanding, you may like to apply the log-rank test yourself on the following exercise.

E1) A group of patients diagnosed with a disease and kept randomized to receive either standard treatment or new treatment. They were followed

for 72 days to observe mortality experience. The survival data obtained from this group is given as follows:

Patient number	Survival time (days)	Outcome	Treatment
1	2	Died	2
2	4	Died	2
3	5	Died	2
4	6	Unknown	1
5	9	Died	2
6	9	Unknown	2
7	12	Died	2
8	12	Died	1
9	15	Unknown	2
10	15	Unknown	1
11	22	Died	2
12	30	Died	1
13	37	Died	1
14	55	Died	1
15	72	Survived	1

Test whether there is a significant difference between the survival times of the patients under standard and new treatments at 5% level of significance.

16.3 LOG-RANK TEST FOR COMPARISON OF MORE THAN TWO GROUPS

In Section 16.2, you understood the methodology and computation procedure of the log-rank test for comparing survival functions/ distributions/ curves in the case of two groups. There are many situations where we have to compare more than two groups. For example, in our case of the Surgery and Chemotherapy groups if we introduce one more group who received surgery combined with radiotherapy and want to test whether the survival time of the patients is the same or not in all groups.

For comparison of three or more groups, we may use one-way ANOVA if the assumptions such as populations are normal, data measured at least in interval scale, etc. are fulfilled. But the underlying distribution is rarely normal. Therefore, we may use a non-parametric test Kruskal-Wallis. But we can apply this test when we have complete data. Therefore, the standard statistical tests cannot usually be applied because the underlying distribution is rarely normal and the data are often 'censored'.

The log-rank test can also be used to compare more than two survival distributions. The null hypothesis for this more general situation is that all survival distributions are the same. For three or more groups, we use just a

simple extension of the log-rank test for two groups and use the same tabular layout to carry out the calculations.

If the number of groups which we have to compare is k (> 2), then the test statistic of the log-rank test for more than two groups is given as follows:

$$\chi^2 = \sum_{i=1}^{k} \frac{(O_i - E_i)^2}{E_i}$$

The log-rank test statistic has approximately a chi-square distribution with k – 1 degrees of freedom. Therefore, we make the decision about significance using the chi-square tables with the appropriate degrees of freedom.

For illustration purposes, in our considered example, two groups of breast cancer treatment situation, we introduce one more group surgery combined with radiotherapy. There are another fifteen subjects who underwent surgery and radiotherapy. We name it as **radiotherapy group**. They were also followed for 25 months to observe mortality experience. The survival data obtained from this group are:

Radiotherapy group:

Survival time (in months): 4^+, 6^+, 8, 9^+,10^+, 13^+, 14, 15, 17^+,18^+, 19^+, 20, 21^+, 22^+, 24, 25^+

Now, we show the data of the radiotherapy group in a more structured way in Table 4.

Table 4: Structured data of radiotherapy group

Follow up time (in months)	Number still in study at start of month t	Deaths during month t	Censored during month t	Number after month t
0	15	0	1	15
4^+	15	0	1	14
6^+	14	0	1	13
8	13	1	0	12
9^+	12	0	1	11
10^+	11	0	1	10
13^+	10	0	1	9
14	9	1	0	8
15	8	1	0	7
17^+	7	0	1	6
18^+	6	0	1	5
19^+	5	0	1	4
20	4	1	0	3
22^+	3	0	1	2
24	2	1	1	1
25^+	1	0	1	0

We can also plot the Kaplan and Meier survival curve for all groups as

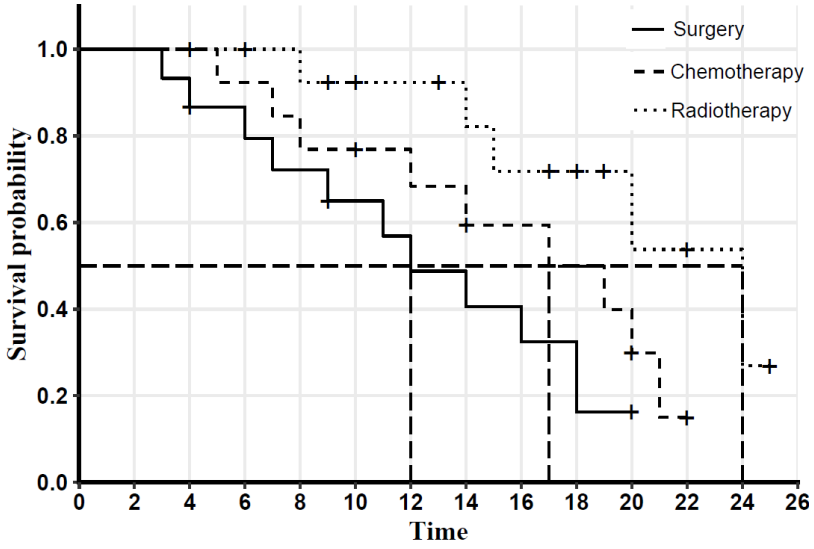

Fig. 16.2: Kaplan and Meier survival curves for Surgery, Chemotherapy and Radiotherapy groups.

From the above Tables and Fig 16.2, we observe that the approximate median survival time radiotherapy group is 24 months. In the log-rank test tests, we test the null hypothesis that the event time distribution among groups is equal. i.e.

H_0: There is no significant difference among the survival functions of the three groups

H_1: There is a significant difference among the survival functions of the three groups

If $S_3(t)$ be the survival function of the radiotherapy group then the null and alternative hypotheses in the symbolical form are

$$H_0 : S_1(t) = S_2(t) = S_3(t)$$

$$H_1 : \text{At least two are different}$$

To test the hypothesis, we follow the same methodology which we used in the case of two groups and find the observed and expected frequencies at each time of the event. We calculate the same in the following table.

From the calculations, we have

$$\chi^2 = \frac{(O_1 - E_1)^2}{E_1} + \frac{(O_2 - E_2)^2}{E_2} + \frac{(O_3 - E_3)^2}{E_3}$$

$$= \frac{(11 - 6.275)^2}{6.275} + \frac{(9 - 8.295)^2}{8.295} + \frac{(5 - 10.430)^2}{10.430} = 6.443$$

The critical value of chi-square with 3 –1 = 2 degrees of freedom at 5% level of significance is 5.99.

Since the calculated value of the test statistic (= 6.443) is greater than the critical value (= 5.99) so we reject the null hypothesis.

Thus, we conclude that the three treatments are not equally effective at 5% level of significance.

You may like to apply the log-rank test yourself for a better understanding of the following exercise.

E2) A group of patients diagnosed with a disease and kept randomized to receive either any one of the treatments A, B and C. They were followed up to 72 days to observe mortality experience. The survival data obtained from this group is given as follows:

Patient number	Survival time (days)	Outcome	Treatment
1	2	Died	B
2	4	Died	B
3	5	Unknown	B
4	6	Unknown	A
5	9	Unknown	B
6	10	Died	C
7	12	Died	B
8	12	Died	A
9	15	Unknown	B
10	18	Unknown	A
11	22	Died	B
12	26	Died	C
13	30	Died	A
14	35	Unknown	C
15	37	Died	C
16	55	Died	C
17	72	Died	A
18	80	Survived	C

Test whether all treatments are equally effective at 5% level of significance.

16.4 COMMENTS ON LOG-RANK TEST

The log-rank test is designed to detect a difference between two or more survival distributions/curves with the assumption that the chance of an event happening in a small interval in one group is a constant time more than in the other group. This ratio continues to be the same throughout the follow-up time.

The log-rank test is based on the some assumptions as of the Kaplan Meier survival curve:

1. The censoring is not related to prognosis.
2. The survival probabilities are the same for participants enrolled early and late in the study,
3. The events happened at the times specified.

In the case where we have the knowledge that the survival experiences in groups changes based on a third prognostic factor, for example, age of patients, then stratify the groups according to different age categories and then the log-rank test should be applied in each category.

We now end this unit by giving a summary of what we have covered in it.

Table 5: Observed and expected frequencies computed at event time

Combined follow up time (in months)	Number at risk in			Total number at risk $N_t = N_{1t} + N_{2t} + N_{3t}$	Number of events in			Total number of events $O_t = O_{1t} + O_{2t} + O_{3t}$	Expected number of events in		
	Surgery N_{1t}	Chemotherapy N_{2t}	Radiotherapy N_{3t}		Surgery O_{1t}	Chemotherapy O_{2t}	Radiotherapy O_{3t}		Surgery $E_{1t} = N_{1t} \times (O_t/N_t)$	Chemotherapy $E_{2t} = N_{2t} \times (O_t/N_t)$	Radiotherapy $E_{3t} = N_{3t} \times (O_t/N_t)$
3	15	13	15	43	1	0	0	1	0.349	0.302	0.349
4	14	13	15	42	1	0	0	1	0.333	0.310	0.357
5	12	13	14	39	0	1	0	1	0.308	0.333	0.359
6	12	12	14	38	1	0	0	1	0.316	0.316	0.368
7	11	12	13	36	1	1	0	2	0.611	0.667	0.722
8	10	11	13	34	0	1	1	2	0.588	0.647	0.765
9	10	10	12	32	1	0	0	1	0.313	0.313	0.375
11	8	9	11	28	1	0	0	1	0.286	0.321	0.393
12	7	9	10	26	1	1	0	2	0.538	0.692	0.769
14	6	8	9	23	1	1	1	3	0.783	1.043	1.174
15	5	8	8	21			1	1	0.238	0.381	0.381
16	5	6	7	18	1	0	0	1	0.278	0.333	0.389
17	4	6	7	17	0	1	0	1	0.235	0.353	0.412
18	4	5	6	15	2	0	0	2	0.533	0.667	0.800
19	2	5	5	12	0	1	0	1	0.167	0.417	0.417
20	2	4	4	10	0	1	1	2	0.400	0.800	0.800
21	0	2	3	5	0	1	0	1	0.000	0.400	0.600
24			2	2	0	0	1	1	0.000	0.000	1.000
					$O_1 = 11$	**$O_2 = 9$**	**$O_3 = 5$**	25	**$E_1 = 6.275$**	**$E_2 = 8.295$**	**$E_3 = 10.430$**

We now end this unit by giving a summary of what we have covered in it.

Table 6: Observed and expected frequencies computed at event time

Combined follow up time (in months)	Number at risk in		Total number at risk $N_t = N_{1t} + N_{2t}$	Number of events in		Total number of events $O_t = O_{1t} + O_{2t}$	Expected number of events in	
	Standard N_{1t}	New N_{2t}		Standard O_{1t}	New O_{2t}		Standard $E_{1t} = N_{1t} \times (O_t/N_t)$	New $E_{2t} = N_{2t} \times (O_t/N_t)$
2	7	8	15	0	1	1	0.467	0.533
4	7	7	14	0	1	1	0.500	0.500
5	7	6	13	0	1	1	0.538	0.462
9	6	5	11	0	1	1	0.545	0.455
12	6	3	9	1	1	2	1.333	0.667
22	4	1	5	0	1	1	0.800	0.200
30	3	0	3	1	0	1	1.000	0.000
37	2	0	2	1	0	1	1.000	0.000
55	1	0	1	1	0	1	1.000	0.000
				$O_1 = 4$	**$O_2 = 6$**	**10**	**$E_1 = 7.184$**	**$E_2 = 2.816$**

E2) We can formulate the null and alternative hypothesis as

H_0: All treatments are equally effective

H_1: All treatments are not equally effective

Now, we do the calculation for observed and expected frequency in Table 7.

From the calculations, we have

$$\chi^2 = \frac{(O_1 - E_1)^2}{E_1} + \frac{(O_2 - E_2)^2}{E_2} + \frac{(O_3 - E_3)^2}{E_3}$$

$$= \frac{(3 - 2.728)^2}{2.728} + \frac{(4 - 4.115)^2}{4.115} + \frac{(4 - 4.157)^2}{4.157} = 0.036$$

The critical value of chi-square with 3 –1 = 2 degrees of freedom at 5% level of significance is 5.99.

Since the calculated value of the test statistic (= 0.036) is less than the critical value (= 5.99) so we do not reject the null hypothesis.

Thus, we conclude that all treatments are equally effective on the diseases at 5% level of significance.

Table 7: Observed and expected frequencies computed at event time

Combined follow up time (in months)	Number at risk in			Total number at risk $N_t = N_{1t} + N_{2t}+N_{3t}$	Number of events in			Total number of events $O_t = O_{1t} +O_{2t}+O_{3t}$	Expected number of events in		
	Surgery N_{1t}	Chemotherapy N_{2t}	Radiotherapy N_{3t}		Surgery O_{1t}	Chemotherapy O_{2t}	Radiotherapy O_{3t}		Surgery $E_{1t} = N_{1t}\times(O_t/N_t)$	Chemotherapy $E_{2t} = N_{2t}\times(O_t/N_t)$	Radiotherapy $E_{3t} = N_{3t}\times(O_t/N_t)$
2	5	7	6	18	0	1	0	1	0.278	0.389	0.333
4	5	6	6	17	0	1	0	1	0.294	0.353	0.353
10	4	3	6	13	0	0	1	1	0.308	0.231	0.462
12	4	3	5	12	1	1	0	2	0.667	0.500	0.833
22	2	1	5	8	0	1	0	1	0.250	0.125	0.625
26	2	6	5	13	0	0	1	1	0.154	0.462	0.385
30	2	6	4	12	1	0	0	1	0.167	0.500	0.333
37	1	5	3	9	0	0	1	1	0.111	0.556	0.333
55	1	4	2	7	0	0	0	0	0.000	0.000	0.000
72	1	2	1	4	1	0	1	2	0.500	1.000	0.500
					$O_1 = 3$	**$O_2 = 4$**	**$O_3 = 4$**	**11**	**$E_1 = 2.728$**	**$E_2 = 4.115$**	**$E_3 = 4.157$**