

## RESEARCH ARTICLE



# The Fuzzified Log-Rank Test Procedure for Comparing More Than Two Groups

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## Abstract

**Objectives:** To extend the conventional log-rank test to handle fuzzy data, accommodating the inherent uncertainty and vagueness in illustrative data. To create a statistical procedure that can compare survival distributions across more than two groups. **Methods:** The log-rank test is a familiar non-parametric methodology used to compare the survival experiences of two or more groups of subjects. This study applies fuzzification procedures to survival data, transforming precise survival times and event indicators into fuzzy numbers. **Findings:** When fuzziness is attributed to the survival data, the proposed method shows less potential and is unable to produce reliable results. However, the fuzzified log-rank test outperforms conventional methods when dealing with uncertain or imprecise data, providing more reliable results. **Novelty:** Unlike conventional log-rank tests that are typically limited to two groups, the proposed method can simultaneously compare survival distributions across three groups, providing a more comprehensive survival analysis. This article suggests a new procedure that can accommodate the fuzziness in the data. The fuzzified log-rank test enhances the analytical capability of survival analysis and represents a novel contribution to statistical methodologies in medical and survival research.

**Keywords:** Fuzziness; Survival Data; Log-Rank Test; Three Groups; Defuzzification

## 1 Introduction

One among the main focuses of survival analysis is to study the survival behavior and compare the same of two groups by means of comparing the respective survival curves. However, the survival curves are not linear because most of the survival data are skewed. They are not smooth curves instead with steps because of censoring. Hence, it is impossible to compare them by normal means. Special types of procedures are required for the same. Various scientists suggest many methods and the log-rank test is one among them which is familiar by its applicability. A comprehensive comparison of alternatives to the log-rank test, the traditional method in detecting differences under certain conditions and proposing more robust alternatives<sup>(1)</sup>. Adaptive group sequential survival comparisons using log-rank and point-wise test statistics, which allow for

interim analyses and early stopping, thus improving the efficiency of clinical trials while addressing the issue of maintaining statistical power<sup>(2)</sup>. The practical aspects of sample size calculation for the log-rank test and developed methods to predict the number of events over time, provide crucial insights into trial design and resource allocation<sup>(3)</sup>. The integrated log-rank test, which aims to improve the power and flexibility of survival comparisons by integrating over a range of time points<sup>(4,5)</sup>. However, as fuzziness may present in the survival data, the log-rank test should be remodeled to accommodate that fuzziness<sup>(2)</sup>. This paper is intended for the same and a procedure is proposed<sup>(6,7)</sup>.

An extension of the log-rank test by including stratification variables to be adjusted for categorical covariates was suggested by various authors. The main drawback of this method is that then the strata are many the test could have poor power. Further extension of the log-rank test was given by stratified log-rank test and weighted log-rank test in which the weights are given for the times add which the event happens<sup>(8)</sup>. The log-rank test, the test developed for the comparison of survival experiences among different groups is named after its developers, David R. Cox and David Oakes, who introduced it in the 1970s. It is also known as the Mantel-Cox test, as Nathan Mantel independently proposed a similar method around the same time<sup>(9)</sup>. The log-rank test has become a basis in the field of survival analysis, as it contributes a powerful and widely accepted means to evaluate whether there are significant differences in survival times between groups<sup>(10)</sup>.

The log-rank test for multiple groups is an extension of the classic log-rank test, which is commonly used in survival analysis to compare the survival experiences of more than two groups. In scenarios where investigations are dealing with more than two groups<sup>(11)</sup>, such as in clinical trials with multiple treatment arms or epidemiological studies involving several exposure categories, the log-rank test for multiple groups becomes a valuable statistical tool<sup>(12)</sup>. This test allows for the simultaneous comparison of survival curves across multiple categories and helps researchers determine whether there are statistically significant differences in survival experiences among these groups.

## 2 Methodology

### 2.1 The Fuzzified Log-Rank Test Procedure for Comparing More than Two Groups

Consider the comparison of Kaplan-Meier survival curves which provide a graphical representation of survival probabilities over time for each group or category being studied. These curves are constructed by estimating the probability of survival at various time points while considering censored observations. Consider that there are  $p$  cohorts for which the survival experiences are to be compared. The null hypothesis to be tested is that the survival experiences of the  $p$  groups are homogeneous. In contrast, the alternative hypothesis suggests that at least one group's survival experience differs from the others. The log-rank test quantifies the degree of difference between these survival experiences and determines whether it is statistically significant.

The vector of the observed number of failures  $O_j$  in all the groups at the time  $t_j$  and the corresponding expected number of failures  $E_j$  with variance  $V_j$  are given below.

$$O_j = \begin{pmatrix} D_{1j} \\ D_{2j} \\ D_{3j} \\ \vdots \\ D_{kj} \end{pmatrix}, E_j = \begin{pmatrix} E_{1j} \\ E_{2j} \\ E_{3j} \\ \vdots \\ E_{kj} \end{pmatrix}, \text{ where } E_{ij} = \frac{N_j(t_j)}{N(t_j)} \cdot D_j$$

$$V_j = (V_{kl}^{(j)}),$$

$$V_{kl}^{(j)} = \frac{D_{kj} N_k(t_j) (N(t_j) - D_j) (N(t_j) - N_k(t_j))}{N(t_j)^2 (N(t_j) - 1)}$$

Now let  $O = \sum_{j=1}^k O_j$ ,  $E = \sum_{j=1}^k E_j$  and  $V = \sum_{j=1}^k V_j$ , then the test statistic for testing the homogeneity of survival curves of  $p$  cohorts given by,

$$\chi^2 = (O - E)^T V^{-1} (O - E) \sim \chi_p^2 \text{ under } H_0.$$

The fuzzified version of the test consists of fuzzifying the survival times by means of trapezoidal fuzzy numbers and the survival times are obtained through the respective alpha ( $\alpha$ ) cuts using the centroid method<sup>(13)</sup>. The number of failures that occurred by time  $t_j$  is also fuzzified by trapezoidal fuzzy numbers. The Chi-square test statistic for the log-rank test has been formulated according to the  $\alpha$ -cut intervals of trapezoidal fuzzy numbers. Having the upper limit of the alpha cut interval, the upper-level crisp log-rank test statistic was obtained, and using the lower limit of the alpha cut interval, the lower-level crisp log-rank test statistic was obtained<sup>(14)</sup>. Thus, in this approach, the test statistic is split into two parts according to the lower-level and upper-level  $\alpha$ -cut intervals,

$$A_\alpha = [A_L(\alpha), A_U(\alpha)]$$

Where,  $A_L(\alpha) = [a_i + \alpha(b_i - a_i)]$  and  $A_U(\alpha) = [d_i + \alpha(d_i - c_i)]$ ;  $i = 1, 2, \dots, n$ ;  $\alpha \in [0, 1]$ .

The test statistic provided by,

$$\chi^2_L = \sum_{i=1}^n \frac{(O_i^L - E_i^L)^2}{E_i^L} \text{ and } \chi^2_U = \sum_{i=1}^n \frac{(O_i^U - E_i^U)^2}{E_i^U}$$

where,  $O_i^L = [a_i + \alpha(b_i - a_i)]$  and  $O_i^U = [d_i + \alpha(d_i - c_i)]$ ;  $i = 1, 2, \dots, n$ ;  $\alpha \in [0, 1]$ .

$E_i^L = [a_i + \alpha(b_i - a_i)]$  and  $E_i^U = [d_i + \alpha(d_i - c_i)]$ ;  $i = 1, 2, \dots, n$ ;  $\alpha \in [0, 1]$ .

The crisp value of the chi-square test statistic for the log-rank test is obtained by the defuzzification of the chi-square values obtained as above through the centroid method. The resultant value is compared with the Chi-square table value at p degrees of freedom and the null hypothesis of homogeneity of survival curves is rejected at a particular level of significance if the calculated Chi-square value is greater than the table value.

### 3 Result and Discussion

The data was collected from the Boronophenylalanine (BPA) as the capture agent, a study was conducted to evaluate the effectiveness of Boron Neutron Capture Treatment (BNCT) is a branch of radiation science that is showing potential as a cancer treatment method. In treating the therapeutically refractory F98 glioma. Rats' brains were implanted with F98 glioma cells. Three rat groups were investigated. Three groups got different forms of treatment: radiation alone, radiation plus a suitable concentration of BPA, and no treatment at all for one group.

#### 3.1 The Conventional Log-Rank Test for More Than Two Groups

The frequency of the failure and at risk with their corresponding totals are included in the contingency table, which is created for three groups, namely, untreated, radiated, and radiated+BPA.

Table 1. Results for Conventional Log-Rank Test

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
Untreated	10	10	2.2723	26.281	6.7537
Radiated	10	9	8.697	0.011	0.01
Radiated+BPA	10	8	16.031	0.01	7.2934

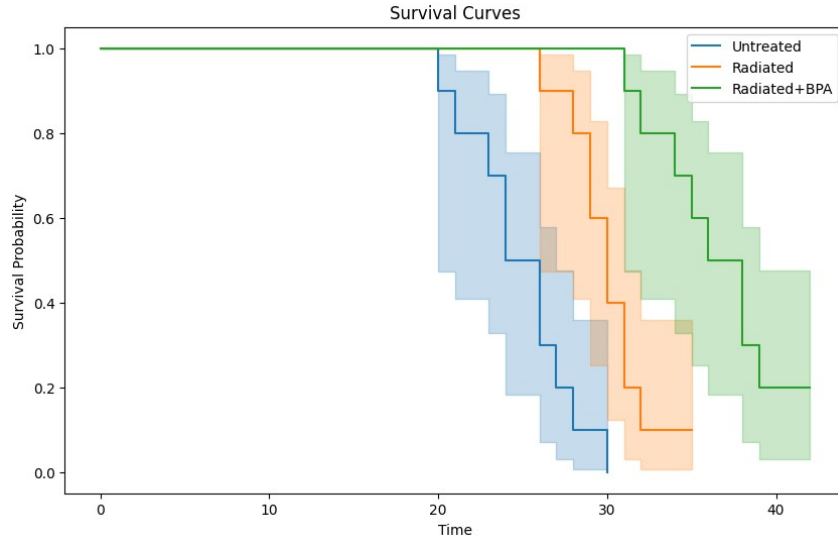
$\chi^2 = 6.7537$  on 3 degrees of freedom.

The test statistic follows a chi-square distribution with 3 degrees of freedom. The critical value  $\chi^2$  distribution at 0.05 level of significance is 7.815, and hence then the decision rule for this test is to accept the null hypothesis. Hence, there is no significant difference is identified between the three survival curves.

For comparing the survival curves, the survival probabilities are calculated using the Kaplan-Meier estimator, and the corresponding graphs were plotted for the three groups.

#### 3.2 The Fuzzified Log-Rank Test

The log-rank test in order to modify for imprecise measurements of survival times. This test works best when the event of interest happens inside a predetermined specified time as different survival curves from being exactly observed. Although the conventional log-rank test works on precisely defined time points of event occurrences, the fuzzy log-rank test aims to overcome the intrinsic vagueness of fuzzy data. As a result, in fuzzy circumstances when the event time is uncertain but falls inside an interval, the fuzzy log-rank test can be applied.



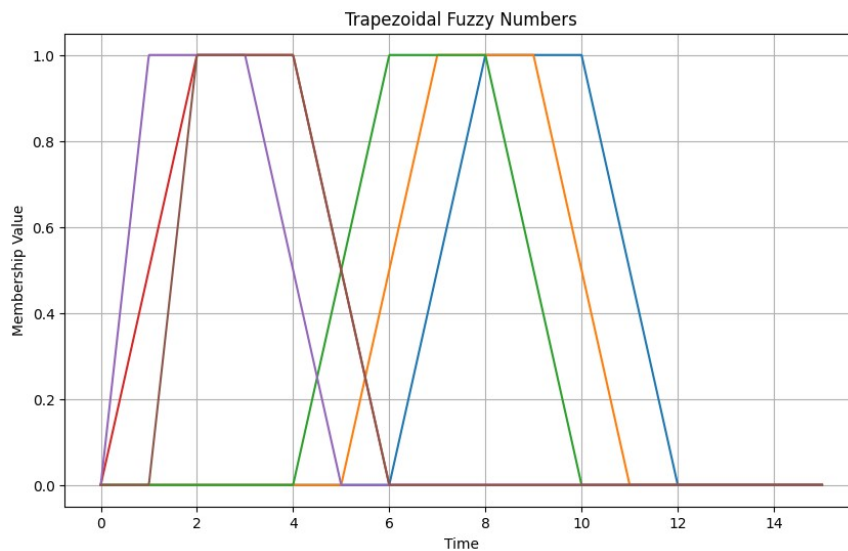
**Fig 1. Survival curve of the Conventional Log-Rank Test**

**Table 2. Trapezoidal fuzzy numbers**

Groups	Failures	At Risk
Untreated	(6,8,10,12)	(0,2,4,6)
Radiated	(5,7,9,11)	(0,1,3,5)
Radiated+BPA	(4,6,8,10)	(1,2,4,6)

The following table is a construction of the trapezoidal membership function used to fuzzify each element, yielding the associated alpha cuts.

The following plot visualizes the membership functions of different trapezoidal fuzzy numbers over the construction table, the membership value of each fuzzy number changes with the construction table.



**Fig 2. Trapezoidal fuzzy numbers**

The survival time is made as fuzzy as stated and the corresponding survival times are obtained using the fuzzy survival curves method. Note that the survival curves obtaining so are intersecting which is contrary to the conventional methodology.

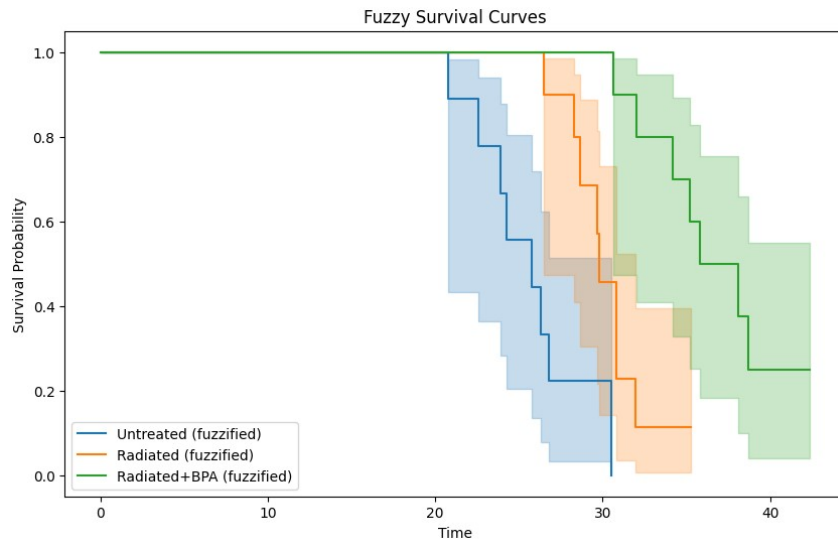


Fig 3. Survival curve of the Fuzzified Log-Rank Test

The fuzzified log-rank test is performed using the alpha cuts of those trapezoidal fuzzy numbers.

Table 3. Alpha Cuts of Trapezoidal Fuzzy Numbers

Groups	Failures	At Risk
Untreated	$[(6 + 2\alpha), (12 - 2\alpha)]$	$[(0 + 2\alpha), (6 - 2\alpha)]$
Radiated	$[(5 + 3\alpha), (11 - 2\alpha)]$	$[(0 + \alpha), (5 - 2\alpha)]$
Radiated+BPA	$[(4 + 2\alpha), (10 - 2\alpha)]$	$[(1 + \alpha), (6 - 2\alpha)]$

**The Lower-Level Alpha Cuts**

The expected number of three groups and the observed number of three groups by the six lower levels are given below respectively,

Table 4. The Lower-Level Alpha Cuts

Groups	Failures	At Risk	Total
Untreated	$(6 + 2\alpha)$	$(0 + 2\alpha)$	$(6 + 4\alpha)$
Radiated	$(5 + 3\alpha)$	$(0 + \alpha)$	$(5 + 4\alpha)$
Radiated+BPA	$(4 + 2\alpha)$	$(1 + \alpha)$	$(5 + 3\alpha)$
Total	$(15 + 7\alpha)$	$(1 + 4\alpha)$	$(16 + 11\alpha)$

From the chi-square table value  $\chi^2_{T(0.05)} (\nu = 6) = 12.592$  and considering that  $\chi^2_L$  exceeds  $\chi^2_{T(0.05)}$  for all  $\alpha \leq 1$ . This test is to reject the null hypothesis  $H_0^L$  at the 0.05 level of significance for all values of  $\alpha$ . This result provides strong evidence that there are significant differences between the three groups being compared.

**The Upper-Level Alpha Cuts**

The expected number of three groups and the observed number of three groups by the six upper levels are given below respectively,

The given chi-square table value  $\chi^2_{T(0.05)} (\nu = 6) = 12.592$  and considering that  $\chi^2_U$  exceeds  $\chi^2_{T(0.05)}$  for all  $\alpha \leq 1$ . This test is to reject the null hypothesis  $H_0^U$  at the 0.05 level of significance for all values of  $\alpha$ . This means that the differences in survival distributions between the three groups are statistically significant.

The decisions from both the lower-level and upper-level models defuzzified, and the null hypothesis was rejected. This indicates that there is a significant difference in survival among the three groups: Untreated, Radiated, and Radiated + BPA.

Table 5. The Upper-Level Alpha Cuts

Groups	Failures	At Risk	Total
Untreated	$(12 - 2\alpha)$	$(6 - 2\alpha)$	$(18 - 4\alpha)$
Radiated	$(11 - 2\alpha)$	$(5 - 2\alpha)$	$(16 - 4\alpha)$
Radiated+BPA	$(10 - 2\alpha)$	$(6 - 2\alpha)$	$(16 - 4\alpha)$
Total	$(33 - 6\alpha)$	$(16 - 6\alpha)$	$(50 - 12\alpha)$

## 4 Conclusion

Finding a reliable solution to every kind of problem requires a comprehensive analysis of all underlying factors, including identifying various causes of variations and vagueness in the observed data. The present work aims to incorporate fuzziness into a statistical test. The illustration shows that the null hypothesis of homogeneity survival curves is not rejected in the conventional log-rank test, but it is rejected in the fuzzy log-rank test. Therefore, it can be concluded that the fuzzified log-rank test is more sensitive than the conventional one. However, the expected amount of fuzziness in the data should be determined with scientific expertise, as completely nullifying the fuzziness may not be appropriate for any sample data observed.

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