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SURVIVAL ANALYSIS FOR DIAGNOSING TUBERCULOSIS PATIENTS

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ABSTRACT. The nature of survival analysis is modeling of time to failure considering the time until death or failure. Kaplan-Meier estimate is one of the best options used to measure the portion of subjects who living for a certain period of time after treatment. This technique is extremely useful in survival analysis at the same time it is used by the researchers to determine or analyze the patients who lost to follow up of the study, those who developed the disease of attention or survived it. It's also used to comparation two group of subjects such as the control group, ie., placebo, and the other treatment group ie., true drug. This context was devised to analyze the Log-rank (Mantel-Cox) distribution that has been comparative to the Survival time serving as Gender and Treatment diagnose the prognostic cause patients for survival time of the patients. In this paper, the treatment indicated a significant difference, while gender has not shown any significant difference in the survival of the Tuberculosis (TB) patients. The SPSS software package performs information analysis.

♣ Note to author: Use 2000 Survival Analysis.

1. INTRODUCTION

Tuberculosis (TB) is an infectious disease that usually affects the lungs, though it can affect any member element in the body. It can develop when Legionella bacteria spread through droplets in the air. TB can be mortal, but in several cases, it is preventable and treatable. In the past, TB, or consumption, was a chief cause of death around the world. Following improvements in living conditions and the development of antibiotics, the prevalence of TB fell dramatically in technical countries. However, in the 1980s, numbers started to hike again. The World Health Organization (WHO) describes it as an epidemic. They statement that it is among the top 10 causes of death globally and the leading cause of expiry from a single infectious agent.

The WHO estimates that in 2018, nearly 10 million people around the world developed TB and 1.5 million people died from the disease, including 251,000 people who also had HIV. A majority of the people affected in Asia. However, TB remains a matter of concern in several other areas, with the United States. The same year, doctors reported 9,025 cases of TB in the U.S., according to the

2000 *Mathematics Subject Classification.* SURVIVAL ANALYSIS, TUBERCULOSIS PATIENTS.

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Centre for Disease Control and Prevention (CDC). Presently, antibiotic resistance is causing renewed concerns about TB among experts. Some strains of the disease are not responding to the most effective treatment options in such cases TB is difficult to be treated.

In 1867, tuberculosis (TB) was the foremost cause of death in Canada. The bacterium that causes TB, the tubercle bacillus, was discovered by a German scientist, Robert Koch, in 1882. Proof that TB was infectious led to organized efforts to isolate those infected in sanatoria special hospitals where patients could rest and get fresh air and a good diet. The "rest cure" was the most common treatment for TB till antibiotic treatment was developed in the 1950s. Another form of treatment was "collapse treatment. "Physicians pumped air into the chest cavity, so the lung could reduce and the tuberculosis lesion could heal. The use of collapse therapy was first recorded in Ingersoll, Ontario, in 1898, but it did not become standard Canadian training until 1919.

The first-time tuberculosis survey conducted in Canada in 1921 by the Saskatchewan Antituberculosis Commission to determine the rate of infection among school children. The study was found that more than half of the children were infected with TB. Travelling TB clinics began in Ontario in 1923 and were soon used in each province. The clinics could diagnose, treat, and follow-up with TB patients then their contacts. Mobile X-ray machines were adopted could find TB before people showed external symptoms, which made treatment far more effective. The woman being tested for tuberculosis on the Ontario Tuberculosis Association Chest X-ray Train, Northern Ontario Streptomycin was discovered in 1946 the first specific antibiotic that could kill the TB causing bacterium. This too other antibiotics became widely used against TB in the 1950s. Antibiotic treatment and a gradual decline in the incidence of tuberculosis led to quicker stays in Sanatoria. The number of TB beds in Canada dropped from 18,977 in 1953 to 9,722 in 1963 and by the 1970s, only a few numbers of TB patients were admitted to hospital. Nowadays, drug therapy is the only type of treatment prescribed by doctors. However, ensuring that patients take the full course of drugs, which usually require several months, remains a problem.

TB is still considered one of the deadliest infectious diseases, especially in developing states. A person can have TB bacteria in their body and never develop indications. In utmost people, the immune system can contain the bacteria so that they do not replicate and cause disease. Doctors refer to this as latent TB. A person may never experience symptoms and be unaware of that they have the infection. There is too no risk of passing on a latent infection to another person. Nevertheless, a person with latent TB still requires treatment.

The Centre for Disease Control and Prevention (CDC) estimates show that as many as 13 million people in the U.S. have latent TB. The body may be unable to contain TB bacteria. This is more common when the immune system is weakened due to illness or the use of certain medications. When is happens, the bacteria can be replicated and cause symptoms, resulting in active TB? People with active TB can spread the infection. Without medical intervention, TB becomes active in five to ten percentages (5–10%) of people with the infection. In nearby 50% of

these people, the progression occurs within two to five (2–5) years of getting the infection, according to the CDC.

The risk of developing active TB is higher in:

- Someone with a weakened immune system
- Anybody who first developed the infection in the past 2–5 years
- Older young children and adults
- Who use injected recreational drugs in people?
- People who have not received appropriate treatment for TB in the past

2. REVIEW OF LITERATURE

Zubair Kabir, et al., (2014) we are discussed was a survival analysis of adult tuberculosis disease we are conducted a survival analysis of all the confirmed cases of adult Tuberculosis (TB) patients treated in cork-city, Ireland. This aim study was to estimate survival time (ST), enclosed the median time of survival, and to assess the association and impact of covariance (TB risk factors) to event status and ST. The survival analysis is reported in this paper.

Apeksha et al., (2019) the proposed Survival Analysis of Treatment Defaulters among Tuberculosis Patients in Government Medical College and Hospital, Aurangabad to determine the duration TB patients stay in the treatment before default. Factor associated with defaulters who had been treated in Government Medical College and Hospital (GMCH).

Sandhu (2011) Study of the status of tuberculosis control program based on the implementation of the directly observed treatment short-course strategy (DOTS) Ascendant trend of tuberculosis in the world introduces this disease to be one of the most important infectious diseases in the world. So that every year, 9 million people are afflicted with active TB, and about a 5.1million people die of the disease. As the HIV-contaminated cases are increased, the emergence and spread of tuberculosis (MDR-TB) bacilli have been provided. Diagnostic theses in pulmonary tuberculosis Since the time of Hippocratic, many medical aphorisms have been published, and as they convey a concise and at times a clear manner the experience of the writer, they are often read. Such theses must include many well-known facts to which all subscribe, for the beginner in work in pulmonary tuberculosis, succinct opinions on diagnosis are of great assistance.

Kabtamu Tolosie1 and M. K. Sharma (2014) have proposed an application of the Cox Proportional Hazards Model in Case of Tuberculosis Patients in Selected Addis Ababa Health Centers, Ethiopia Tuberculosis (TB) is a chronic infectious disease and frequently caused by mycobacterium tuberculosis (MTB). It has been one of the major causes of mortality in Ethiopia. The object of the study was to identify factors that affect the survival of the patients with tuberculosis who started treatment for tuberculosis.

3. METRICAL AND METHODS

3.1. DATA.

- 100 patients, we are collected from www.uci.edu.

- The patients are admitting in the age group between 41 to 67 years and two different types of treatments we are given. The covariance is an examination in this study.
- Treatment-(placebo-1, new drug-2)
- Gender-(male-1, female-0)
- Health-(fair-1, poor-2, good-3)

3.2. KAPLAN MEIER METHOD. The Kaplan–Meier estimator, also known as the product-limit estimator, is a non-parametric statistic used to estimate the survival function from lifetime data. In medical research, it is often using to measure the fraction of patients living for a certain amount of time after treatment. In other fields, Kaplan–Meier estimators may be used to measure the length of time people remain unemployed after a job loss, the time-to-failure of machine parts, or how long fleshy fruits remain on plants before they are removed by frugivorous. The estimator of the survival function (the probability that life is longer than) is with a time when at least one event happened, di the number of events (e.g., deaths) that happened at time and the individuals known to have survived up to time.

3.2.1. *ASSUMPTIONS.*

- Assume that at any time patients who are censored have the same survival prospects forecast as those who continue to be followed.
- We assume that the probabilities of survival are the same for subjects recruited early and late in the study.
- We assume that the event will take place at a specific time

3.2.2. *VARIABLES IN STUDY.*

- Time variables (duration variables): must be a continuous variable.
- Status variable: categorical or continuous variable, represents the event of interest (taken in the event or not).
- Factor variable categorical variable represents a causal effect (for ‘example: type of treatment
- Stratification variable: categorical variables.

3.3. LOG RANK TEST. The log-rank test is a hypothesis test for comparing the survival distributions of two sample groups. It is a nonparametric test and appropriate to use when the data are right-skewed and censored (technically, the censoring must be non-informative). It 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 occurs (such as the time from initial treatment to a heart attack). This test also called the Mantel-Cox test, and the log-rank test can also be view as a time-stratified Cochran–Mantel–Hansel test.

3.4. COX PROPORTIONAL HAZARDS MODEL. The Cox proportional-hazards model is fundamentally a regression model generally used statistical in medical research for investigating the average association between the survival time of patients and one or more predictor variables.

4. RESULTS AND DISCUSSION

The estimated mean time until death is 4.389 months for a new drug. In survival analysis, the survival probabilities are usually reported at certain time points on the curve (e.g., 1 year and 5-year survival); otherwise, the median survival time (the time at which 50% of the subjects have reached the events) can be reported. The median time between admission for tuberculosis infarction and death is 4.600 months for the new drug compared to 2.700 months for placebo.

TABLE 1. Comparison of Newdrug group and Placebo group using Kaplan–Meier

Treatment	Estimate	Std.Error	95%L Bound	95%U Bound	Estimate	Std.Error	95% LB	95%UP
New drug	4.389	0.187	4.021	4.756	4.600	0.270	4.071	5.129
Placebo	3.076	0.222	2.642	3.511	2.700	0.101	2.503	2.897
Overall	3.741	0.159	3.429	4.053	3.700	0.247	3.215	4.185

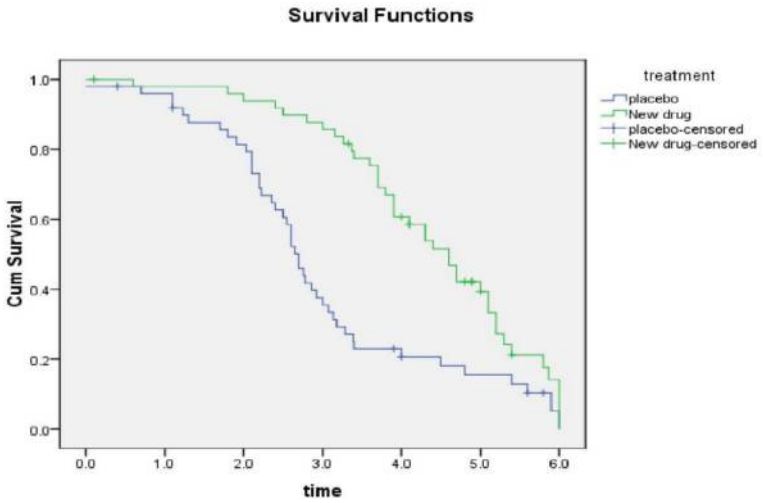

FIGURE 1. Kaplan–Meier curves Shows that the survival probability is lower for placebo at all-time points so they are less likely to survive

TABLE 2. This table show that overall comparisons of the Log rank test (Mantel-Cox)

Overall Comparisons	Chi square	df	Sig
Log Rank (Mantel-Cox)	12.512	1	0.0001

As the p-value (0.000) is less than 0.05. The p-value (sig) is the probability of getting a test statistic of at least 12.512. If there is really difference in survival

times for new drug and Placebo. Conclude that there is significant evidence of a difference in survival times for new drug and placebo groups. The estimated time until death is 4.389 months for new drug and 3.076 month for placebo, i.e. new drug group have an increased chance of survival.

TABLE 3. Comparison of Gender (using Kaplan–Meier)

Means and Medians for Survival Time

Gender	Meana				Median			
	Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Inter	
			Lower Bound	Upper Bound			Lower Bound	Upper
Male	3.849	0.227	3.404	4.294	3.7	0.392	2.933	4.467
Female	3.644	0.224	3.206	4.083	3.4	0.34	2.734	4.066
Overall	3.741	0.159	3.429	4.053	3.7	0.247	3.215	4.185

a. Estimation is limited to the largest survival time if it is censored.

The estimated mean time until death is 3.849 months for Males and 3.644 months for Females. The median time between admission for tuberculosis infarction and death is 3.700 months for Males compared to 3.400 months for Females.

TABLE 4. this table show that log rank test (Mantel-cox)

Overall Comparisons

	Chi-Square	Df	Sig.
Log Rank (Mantel-Cox)	0.106	1	0.745

Test of equality of survival distributions for the different levels of gender.

As the p-value (0.745) is greater than 0.05, The p-value (sig) is the probability of getting a test statistic of at least 0.106. If there really is no difference in survival times for Male and Female conclude that there is no significant evidence of a difference in survival times for Males and Females. The estimated time until death is 3.849 months for Male and 3.644 months for Female.

TABLE 5. Relationship between Survival Time and Overall (score), Change from Previous Step and Change from Previous Block (-2 Log likelihood)

	Overall (score)			Change from Previous Step			Change from Previous Block		
-2 Log Likelihood	Chi-square	df	Sig.	Chi-square	df	Sig.	Chi-square	df	Sig.
	17.679	8	0.023	21.736	8	0.005	21.736	8	0.005

- For Gender, the p-value is 0.722 is greater than 0.05, so there is no evidence of a greater risk of death following acute Tuberculosis disease in either sex.
- For Health, there is no significant difference between the fair, poor and good.

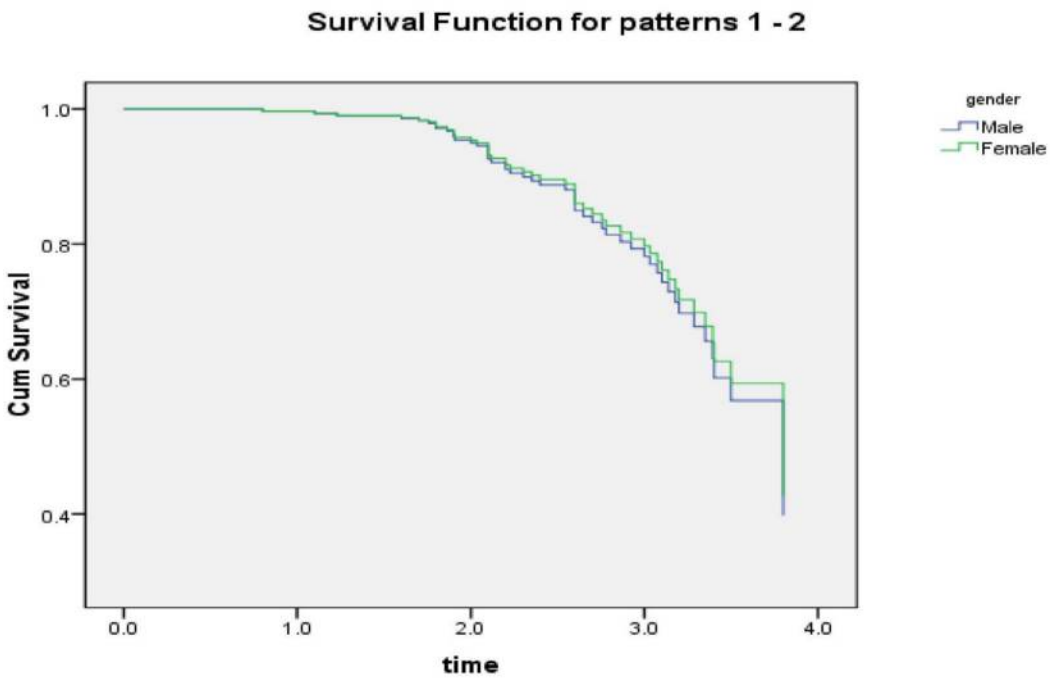

FIGURE 2. Kaplan–Meier curves Shows that the survival probability no difference for both gender

- For Age Group, the reference category is 41- 45 which means that all the other categories are compared to the group containing patients under the age of 41- 45. The next category is 46-50, 51-55, 56-60, then61-65, and lastly 66-67. There is no evidence of a difference between 51-55, 61-65 years old, and under 41-50's but there is a difference between the other three age groups and the under 41-45's.

5. CONCLUSION

In this study, the Kaplan-Meier method was used to estimate the survival curves of TB patients. The log-rank statistic was also used to test whether there is a significant difference in the survival experience of TB patients with respect to the different groups and gender being considered. p ¡0.05 was considered a significant difference. In this paper, the Kaplan-Meier survival analysis of the new drug group

TABLE 6. Relationship between Survival Time and Gender, Health and Age groups (95% CI for Exp (B))

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95 % CI for Exp(B)	
							Lower	Upper
Gender	-0.081	0.229	0.127	1	0.722	0.922	0.589	1.443
Health			0.633	2	0.729	-	-	
Health (1)	0.216	0.287	0.57	1	0.45	1.242	0.708	2.178
Health (2)	0.125	0.269	0.216	1	0.642	1.133	0.669	1.919
Age Group	-	-	4.589	5	0.468*	-	-	-
Age Group (1)	-0.82	0.484	3.867	1	0.049*	0.931	0.867	0.997
Age Group (2)	-0.443	0.474	0.875	1	0.349	0.642	0.254	1.625
Age Group (3)	-0.751	0.474	.505	1	0.034*	2.745	1.131	6.665
Age Group (4)	-0.321	0.514	0.391	1	0.532	0.725	0.265	1.986
Age Group (5)	-0.758	0.526	4.074	1	0.043*	2.475	1.012	6.058

had a significantly better event than the Placebo group, whereas the gender of the TB patients does not have a significant difference in the survival experience. Cox proportion is used to find the overall relationship in tuberculosis and Cox proportion is used to find the relationship between age and survival time.

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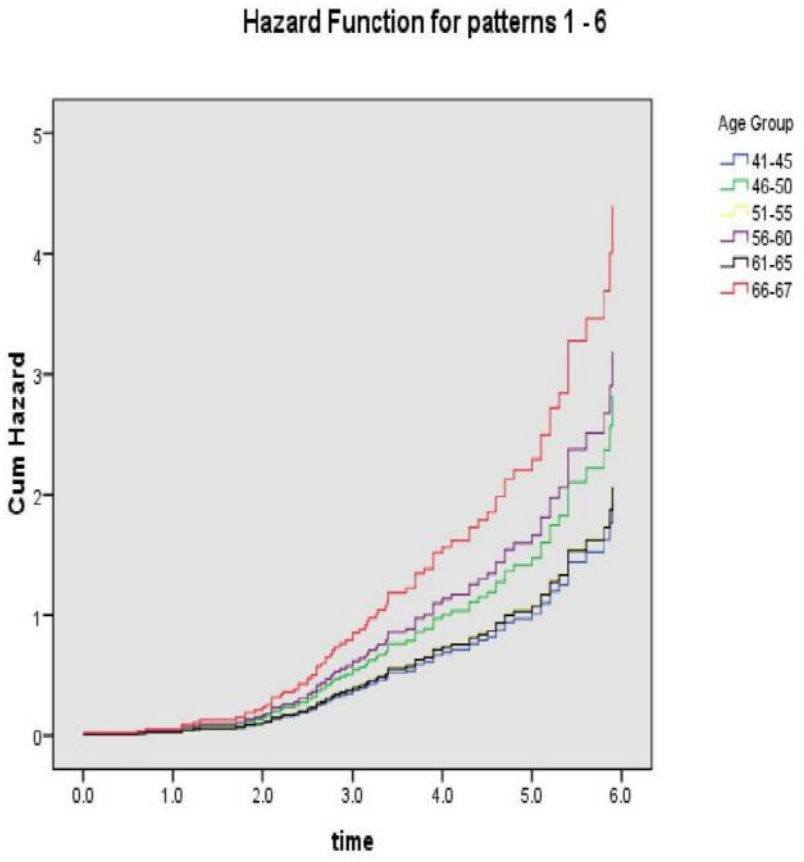

FIGURE 3. Hazard curves Shows that the probability of survives is a difference for Age Group

♣ Note to author: Proceedings articles should be formatted as in reference 1 above, journal articles as in reference 2 above, and books as in reference 3 above.

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