

Cumulative Incidence Function in Competing Risks: A Case Study of Primary Biliary Cirrhosis in Liver Disease

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ABSTRACT

Competing risks have a potential to cause biased estimates in the context of survival analysis using both traditional tools like the Kaplan-Meier estimator and Cox proportional hazards model. This is especially applicable in Primary Biliary Cirrhosis (PBC) which is a chronic liver disease where the patients can die or undergo liver transplantation as a mutually exclusive outcome. This study used the cumulative incidence function (CIF) and Fine-Gray sub-distribution hazard model to measure competing risks in patients with PBC using data in the Mayo Clinic randomised trial of 312 patients. The likelihoods of death and liver transplantation as time progressed were estimated using CIFs which adequately considered competing events, and Fine-Gray was also used to determine the impact of D-penicillmain therapy versus placebo and the important prognostic factors. The findings revealed that, the cumulative death rates were always higher than the cumulative transplantation rates of the liver during the follow-up time. Even though the patients who were treated with D-penicillmain reported a slightly low mortality and slightly higher rate of transplantation compared to the patients provided with placebo; the difference was considered insignificant. Competing outcomes were found to be significantly predicted by age, ascites, disease stage, and platelet count and not by sex, bilirubin, and albumin. Altogether, the research proves that the competing risks approach is better in terms of its accuracy and clinical significance of assessment outcomes in PBC and the significance of CIF-based methodology in the assessment of treatment effects and prognosis in chronic liver disease.

Keywords: D-penicillmain, Placebo, Mortality, Transplant, Death.

1.0 INTRODUCTION

Competing risk analysis is a significant area of analysis in the field of survival analysis especially in the medical research area (Nijman *et al.*, 2021; Lee *et al.*, 2018). Competing risks involve the fact that an individual is capable of having multiple possible outcomes, and the presence of a particular event prevents the occurrence of another (Schmid *et al.*, 2021; D'Amico *et al.*, 2018). The concept is especially significant in long-term diseases such as Primary Biliary Cirrhosis (PBC), which is an autoimmune condition of the liver whereby the small bile ducts are gradually destroyed causing liver issues, cirrhosis, and ultimately liver failure or transplantation (Lleo *et al.*, 2016; Li *et al.*, 2022). Knowledge of the competing risks transformations in PBC is highly essential, as it gives a deeper picture of patient prognosis and outcome of treatment (Tanaka *et al.*, 2018; Kragh *et al.*, 2021). The conventional methods of survival analysis do not usually extend beyond the time of the occurrence of a specific event, which is usually censored by a method such as Kaplan-Meier estimates (Rossello & González-Del-Hoyo, 2022; Dauda *et al.*, 2019; Dauda, 2022). There are however issues with these methods as they may give misleading results in case of competing risks, since they fail to recognize the fact that occurrence of other events

may affect the event of interest (Austin & Fine, 2017; Dauda, 2022). Thus, it would be essential to use a cumulative incidence function approach. The cumulative incidence function is used to estimate the likelihood of the event of interest to happen at a certain time point with the probability of competing events taken into adequate consideration to give a clearer picture of the risk edge of people with PBC (Paukner *et al.*, 2025). The critical role of proper risk modelling in PBC is also explained by complex aetiology and heterogeneous clinical course of the condition (Dauda, 2022). PBC is mostly women-dominant disease and is characterized by gradual but fatal progression whereby there is gradual degradation in liver functioning (Haredasht *et al.*, 2023). The disease can present itself to patients in a broad spectrum, starting with asymptomatic progression of the disease, and ending with severe liver damage, thus requiring an individual approach to treatment and follow-up (Anstee *et al.*, 2022). Moreover, PBC may be related to a number of complications, such as the hepatic decompensation and formation of other liver related illnesses, putting patients at risk and making the treatment plan more complicated (Harms *et al.*, 2018; Hofer *et al.*, 2024). Considering these complications, competing risk modelling methods

based on the cumulative incidence function can go a long way in complementing our knowledge of the prognosis of patients with PBC (Crowther, 2020). It allows identifying the risk factors that are linked to various outcomes and enables clinicians to make knowledgeable decisions regarding the surveillance and intervention measures. Moreover, by specifying the personal likelihood of various competing events, these models can explain how various outcomes interact with each other, helping to devise specific therapeutic interventions that may help clinically manage them (Dauda & Lamidi, 2025; Sanni *et al.*, 2025). Both the ordinary survival analysis and competing risk models have been earlier used to identify the patterns in PBC progression. In their studies, studies have reported the occurrence of liver transplantation, liver-related mortality, and the occurrence of other complications as the endpoints. Nevertheless, most of these studies have been facing issues associated with the shortcomings of the selected methodologies. The call of paradigm shift in a more thorough analysis to apply cumulative incidence functions to competing risk environments has been increased by the fact that the knowledge of PBC is increasingly gaining insight. Various researches have explored ways of analyzing the competing risks data in various areas. Based on a four-year retrospective cohort study, (Guo *et al.*, 2024) constructed and developed a competing risk nomogram to determine the cumulative incidence of hepatocellular carcinoma (HCC) among patients with hepatitis B virus (HBV)-related cirrhosis. (Thomadakis *et al.*, 2024), suggested a flexible shared parameter model of longitudinal and competing risks, using cumulative incidence functions to analyze the possibility of misclassification of possible causes of failure using doubling. The model of a competing risk presented by (Lai *et al.*, 2017) was a bivariate random effects model that was specifically aimed at clustered survival data. They are an effective way of taking into consideration the random hospital or cluster effects, and the estimation of the parameters is carried out by an iterative algorithm. A new estimation method of discrete time survival analysis with competing events was proposed by (Meir & Gorfine, 2025) It is a faster estimation technique and it is easy to combine regularized regression and screening techniques. (Lee, 2022; Kalu *et al.*, 2025) centered on semi parametric analysis of the recurrent discrete-time data with competing risks, and introduced a method with which the model parameters and cumulative incidence functions can be successfully estimated. Discrete competing risks analysis was studied by (Schmid & Berger, 2021) which made use of cause specific hazards and sub distribution hazard models to address discrete failure times with competing events. (Berger *et al.*, 2023) constructed a competitive risks

model in the discrete time to predict the mortality of older patients in the postoperative period, and six prominent risk factors that were considered to be linked to the outcome of postoperative. In medical decision-making, (Heyard *et al.*, 2020), suggested a new methodology of validation of discrete time-to-event prediction models with competing risks, which improves the evaluation of discrimination, calibration, and prediction error. Lastly, (Poguntke *et al.*, 2018) examined the use of cause-specific hazard analysis and odds ratio to process competing risks data when time-dependent covariates are considered and recommended against using sub distribution methods until these issues are resolved. This study aims at exploring the competing risks between death and liver transplantation in patients with Primary Biliary Cirrhosis (PBC) employing Cumulative Incidence Function (CIF) and the fine-gray sub-distribution hazard model.

2.0 METHODOLOGY

2.1. Data Description

Mayo Clinic trial on primary biliary cirrhosis (PBC) and liver transplant was carried out between 1974 and 1984 (Murtaugh *et al.*, 1994), where 424 PBC patients were enrolled who fulfilled the criteria in qualifying as a randomized placebo-controlled trial of D-penicillmain. Out of them, 312 patients were enrolled in the trial, and their information was quite comprehensive. The paper uses the cumulative incidence function (CIF) model and its data set consists of 312 persons and 3 events (Censored, Transplant, and Death). Also, there are 17 covariates in the dataset, age, sex, treatment (trt), ascites, hepato, spiders, edema, bilirubin (bili), cholesterol (chol), albumin, copper, alkaline phosphatase (alk.phos), AST, triglycerides (trig), platelet count, prothrombin time (protime), and disease stage. This paper uses a competing risks model based on Cumulative Incidence Function (CIF) model to examine three event outcomes:

$$j = \begin{cases} 1, & \text{if the patient experiences transplant} \\ 2, & \text{if the patient died of disease} \\ 3, & \text{if the patient was censored} \end{cases}$$

The results of 312 liver patients by the treatment group are given in Table 1. Patients might have one of three possible outcomes: being censored (0), liver transplant (1), and dying (2). There were 83 censored, 10 liver transplant and 65 dead in the D-penicillmain group ($n = 158$). Among the placebo ($n=154$) 85 were censored, 9 were transplanted, and 60 died. Among response rate, 168 were censored, 19 were transplanted, and 125 died. Table 1 below shows that the PBC datasets can be obtained in the survival package.

Table 1: Summary of the Characteristics of 312 Liver Patients in the Study.

Event (Outcome/Status) by Treatment

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Treatment	Censored (0)	Transplant (1)	Death (2)	Total	
D- Penicillamine	83	10	65	158	$\hat{F}_j(t/X) = 1 - \exp\left(-\int_0^t \hat{\lambda}_{j0}(s) \exp(X^T \hat{\beta}) ds\right) \quad (4)$
Placebo	85	9	60	154	
Total	168	19	125	312	

2.2. Model Specification

Competing risks, they happen when an individual has the ability to undergo several events, which cannot be performed simultaneously, and the presence of one event does not allow another to occur. The conventional models of survival such as the Kaplan-Meier estimator and Cox proportional hazards model do not take the rival risks into account and tend to overestimate the probability of an occurrence (Dauda *et al.*, 2018; Dauda *et al.*, 2023; Dauda *et al.*, 2025). In this paper, the Cumulative Incidence Function (CIF) is the main approach to competing risk modeling. Event *j* at time *t* CIF is defined as:

$$F_j(t) = P(T \leq t, J=j) \quad (1)$$

where *T* is the time to event, and *J* denotes the type of event. The CIF can be estimated as:

$$\hat{F}_j(t) = \sum_{t_i \leq t} \hat{h}_j(t_i) \hat{S}(t_i-1) \quad (2)$$

Where $\hat{h}_j(t_i)$ is the cause-specific hazard for event *j* at time *t*, $\hat{S}(t_i)$ is the overall survival probability just before *t*.

2.3. Fine and Gray’s Proportional Sub-distribution Hazard Model

In order to determine the influence of covariates on the risk of an event, this research will use the proportional sub distribution hazard model developed by Fine and Gray (Austin *et al.*, 2021) which is a model that models the hazard function of the CIF instead of cause specific hazards. The event *j* sub distribution hazard function is defined as:

$$\lambda_j(t/X) = \lambda_{j0}(t) \exp(X\beta) \quad (3)$$

where $\lambda_{j0}(t)$ is the baseline sub-distribution hazard, *X* is a vector of covariates, β represents the regression coefficients. This model estimates the direct effect of covariates on the cumulative incidence of an event while properly accounting for competing risks.

2.4. Estimation of the CIF Using Fine & Gray’s Model

The CIF for a given covariate profile *X* can be estimated as:

This formula provides a direct probability estimate of the event occurring by time *t* while considering competing events. The cumulative baseline hazard function is estimated using a Breslow-type estimator:

$$\hat{\Lambda}_{j0}(t) = \sum_{t_i \leq t} \frac{1}{\sum_{k \in R(T_i)} \exp(X_k^T \hat{\beta})} \quad (5)$$

where $R(T_i)$ is the risk set at time *T_i*.

2.5. Software Implementation

Statistical software packages like R (cmprsk, survival packages) can be used to perform the analysis of CIF and competing risks. The packages offer CIFs estimation, Fine and Gray model estimation and hypothesis testing functions. In this study, we performed all the analyses with version 4.4.1 of R, which uses the cmprsk package to estimate CIF and to do regression modelling.

3.0 RESULTS

3.1 Cumulative incidence probabilities

Table 2 gives cumulative incidence data at 1000, 2000, 3000 and 4000 days. The probability is a likelihood to the occurrence of a given event at a particular time with reference to the competing risks. The cumulative incidence probabilities in transplant have a steady upward trend with time. On day 1000, it is 0.0193, increasing to 0.0441 and 0.0705 and 0.0792 on day 3000 and 4000. This implies that there are minimal chances of getting a transplant during the period under observation. Comparatively, there is a significant and faster increase in cumulative incidence of death. Probability begins with 0.1735 on day 1000, increases to 0.2966, 0.4108, to 0.5719 on day 4000. This means that dying is more probable with time than transplantation happening. The outcomes indicate that death is a more prominent phenomenon in the considered period, which may indicate the such problems as the increase of mortality rates, inaccessibility to transplants, or transplant delays.

Table 2: Cumulative incidence probabilities at the specified time points

Days	1000	2000	3000	4000
1 Transplant	0.0192	0.0440	0.070	0.079
2 Death	0.1735	0.2966	0.410	0.571
	9	6	5	2
	0	0	8	9

Table 3 contains the amount of variance between the cumulative incidence of two competing events, transplant (1 transplant) and death (2 death) at various time (days 1000, 2000, 3000, and 4000). Variance is the

measure of uncertainty or variability of cumulative incidence estimates and the larger it is, the lower the precision. In the case of transplant, the variance is comparatively small at every time point indicating that estimates of Cumulative incidence of the event are valid. Variance is $6.105397e-05$ at day 1000 which increases to 0.000343 at day 4000. Although there is this increase, the variance is still low, which indicates that there is no change in cumulative incidence estimates of transplant over time and thus that they are consistent and consistent. In the case of death, the variance is significantly bigger meaning that there is increased uncertainty in the cumulative incidence estimates of the event. At day 1000 the variance is $4.626481E-04$ and at day 4000, the variance is 0.0019. It indicates an increased variance that is larger and higher which indicates that the estimate of death is less specific, which might be attributed to more instances or less variance in the data associated with mortality. The values of the variances indicate that transplant has more accurate estimates as compared to death. The two estimates indicate that the variance increases with time, as the cumulative incidence estimates are becoming less certain. Nevertheless, the higher variance related to death highlights the difficulty of proper estimation of mortality, probably because it is more complex and variable.

Table 3: Variance of the cumulative incidence estimates at the corresponding time points.

Days	1000	2000	3000	4000
1 Transplant	6.105397e-05	0.000144	0.000274	0.000343
2 Death	4.626481E-04	0.000723	0.001077	0.00192

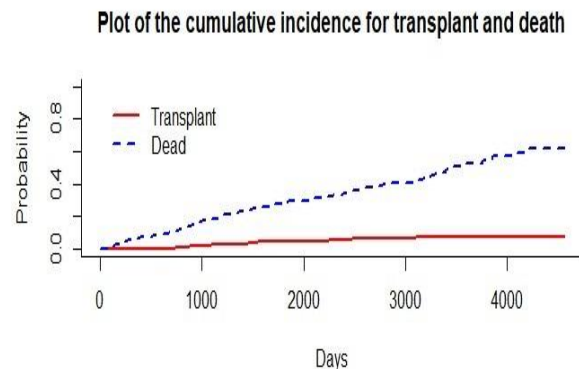


Figure 1: Cumulative incidence functions (CIF) for two clinical outcomes in PBC patients, excluding censored observations. The plot shows the CIF for each event type (transplant and death) against patients' survival times (in days)

Table 4 shows the cumulative incidence (transplant and death) of both D-penicillmain and placebo in 4 times (1000, 2000, 3000 and 4000 days). The likelihood estimates of any event happening at a given time take into consideration all rival risks. Cumulative incidences of transplant increase by 0.0317 (3.17) on day 1000 to 0.0759 (7.59) on day 3000, whilst they do not change at the D-penicillmain group. Death cumulative incidence begins with 0.1460 (14.60) at day 1000, and then increases to 0.5424 (54.24) at day 4000. Cumulative incidence in the placebo group starts with 0.0065 (0.65) on day 1000 followed by an increment to 0.0822 (8.22) on day 4000. The cumulative incidence of death begins to rise at 0.2017 (20.17%), at day 1000, to 0.5989 (59.89) at day 4000. As a rule, cumulative incidences of transplant and death are greater in the placebo group than in D-penicillmain one. At day 4000 the rate of transplant is greater in the placebo group and there is also an increased incidence of death especially past day 2000. The findings indicate that the D-penicillmain group is less prone to the increasing rate of transplant, but it is also less likely to have an accumulated death in comparison to placebo group. This disparity can be an indication that the use of D-penicillmain has been linked to the lower mortality rates, as compared to the placebo group which is characterized by increased incidences of transplant and death in the long run.

Table 4: Cumulative Incidence Estimates for Events in Treatment Groups

Days	1000	2000	3000	4000
Transplant in D-penicillmain	0.0317	0.0459	0.0759	0.0759
Transplant in placebo	0.0065	0.0422	0.0650	0.0822
Death in D-penicillmain	0.1460	0.3010	0.4373	0.5424
Death in placebo	0.2017	0.2912	0.3829	0.5989

Table 5 contains the estimates of the variances of the cumulative incidence of two events, namely, transplant and death among patients undergoing either the D-penicillmain or placebo treatment in four time points (1000, 2000, 3000, and 4000 days). Variance used to measure the uncertainty of the cumulative incidence estimates as a larger value implies more variation and less accuracy. In transplant, D-penicillmain group variance is at 0.000196 in day 1000 and at 0.000570 in days 3000 and 4000. This means that the estimate is quite constant in the long-run with a slight greater variability. Under placebo group, variance of transplant begins with lower value of 0.000043 on day 1000, and then increase to 0.000811 on day 4000. This is an indication that the

cumulative incidence estimates of the transplant in placebo group are more variable especially after the 3000 day mark, which suggests that the results were less accurate with the passage of time. In the case of death, the D-penicillmain group variance begins at 0.000797 at the 1000 day, followed by an increase in variance of 0.003307 at 4000 day. This is an indication of growing uncertainty in the death estimates with time, due to increased number of death events and increased variability of the data. Variance of death in placebo group starts at 0.001056 at day 1000 and increases in 0.004321 at day 4000. At every time point, variance is larger in D-penicillmain group, and also, it increases with time. This implies that cumulative incidence estimates of death in placebo group are more valid and less precise especially in later periods.

Table 5: Variance Estimates for Events in Treatment Groups

Days	1000	2000	3000	4000
Transplant in D-penicillmain	0.0002 0	0.0002 9	0.0005 7	0.0005 7
Transplant in placebo	0.0000 4	0.0002 9	0.0005 3	0.0008 1
Dead in D-penicillmain	0.0008 0	0.0014 5	0.0021 5	0.0033 1
Dead in placebo	0.0010 7	0.0014 4	0.0022 0	0.0043 2

The findings of the statistical tests used to compare the cumulative incidence in transplant and death events in the two treatment groups are provided in Table 6. The tests were being done in order to find out whether there is a significant difference between the treatment groups regarding the occurrence of the events. Transplant has a test value of 0.0194 and a p-value of 0.8891. This p-value is significantly higher than the level of significance of 0.05 which shows that there is no significant difference in cumulative incidence of transplant between two treatment groups. The finding indicates that there are no significant differences in likelihood of transplant between the groups with time. The test statistic and p-value of death are 0.0666 and 0.7964 respectively. Like in transplant event, the p-value is far greater than 0.05 indicating that there is no significant difference in the cumulative death incidence between two treatment groups. This implies that there is no significant difference in treatment group in regards to mortality risk in the study period.

Table 6: Tests for Differences in Cumulative Incidence by Treatment Group

Event	Stat	P-value	df
Transplant	0.0194	0.8891	1
Death	0.0666	0.7964	1

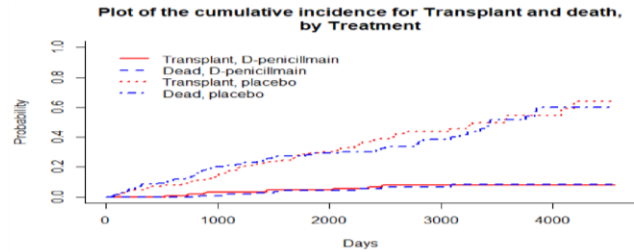


Figure 2: Plots of the estimated cumulative incidence function (CIF) for two event types (clinical outcomes) in PBC patients, with censored observations excluded. The plots are categorized by the treatment received (D-penicillamine and placebo) and are presented against the patients' survival times (in days).

The results of the cumulative hazards under the sub-distribution regression model are indicated in Table 7 that is applied to determine the impact of covariates on the occurrence of interest in the presence of competing risks. The regression coefficients, the relative risks (RR) thus obtained, the standard errors and p-values explain the direction of the effect of each covariate on the sub-distribution hazard and the statistical significance of such effects. Age show a statistically significant relationship with cumulative hazard ($p < 0.001$). The negative coefficient and the relative risk which is less than one ($RR = 0.883$) implies that as age increases, the sub-distribution hazard of the event of interest is lower implying that age is protective in the competing risks model. The value of ascites is also very crucial ($p < 0.001$) and imply a negative significant impact on the sub-distribution hazard. The very low relative risk ($RR 0.00003$) suggests that the occurrence of ascites significantly lowers the cumulative occurrence of the event of interest, which ascites is a significant determinant in competing risks process. Sex have a positive coefficient and a high relative risk ($RR = 4.063$), which has a greater cumulative hazard of one category of sex compared to the reference category. Nevertheless, it is not statistically significant at the standard level ($p = 0.054$) which shows only slight evidence of the association. The coefficient of treatment is negative but statistically insignificant ($p = 0.42$) which gives no support that there is a statistically significant exposure on incurring treatment which affects the sub-distribution hazard of the event. In the same vein, hepatomegaly, spiders, edema, bilirubin, cholesterol, albumin, copper, AST, triglycerides, platelet count, protein level, and stage

of the disease do not exhibit statistically significant effects ($p > 0.05$), which implies that there is little evidence that they contribute cumulatively to the cumulative incidence, having considered the competing risks. Alkaline phosphatase shows a borderline association ($p = 0.084$), the relative risk is less than unity, so there is a potential weak negative correlation with the sub-distribution hazard, but this effect is not statistically significant.

Table 7: Results of the cumulative hazards of the sub-distribution regression model for testing the covariate effects

Covariates	Coefficients	Relative risk (RR)	Standard errors	P-Value
Treatment	-4.701e-01	6.624	0.5884	4.2e-01
Age	-1.246e-01	0.883	0.0227	4.2e-08
Sex	1.403e+01	4.063	0.7285	5.4e-02
Ascites	-1.028e+01	0.00003	1.7660	5.9e-09
Hepto	6.866e-01	1.933	0.6386	2.8e-01
Spiders	-4.726e-01	0.624	0.6886	4.9e-01
Edema	1.256e+00	3.516	1.5250	4.1e-01
Bili	-8.017e-02	0.923	0.1232	5.2e-01
Chol	1.575e-03	1.002	0.0018	3.9e-01
Albumin	-9.642e-01	0.381	0.9320	3.0e-01
Copper	5.753e-04	1.001	0.0019	7.6e-01
Alk. Phos	-6.226e-04	0.999	0.0004	8.4e-02
AST	-4.687e-04	1.000	0.0046	9.2e-01
Trir	2.242e-03	1.002	0.0057	6.9e-01
Platelet	6.890e-03	1.007	0.0031	2.8e-01
Protine	-6.222e-01	0.537	0.3918	1.1e-01
Stage	1.160e+00	3.198	0.5380	3.1e-01

Table 8 reveals the findings of the refitted sub-distribution regression model, which estimates the impact of the major covariates on the cumulative hazards in the competing risk outcomes. The age coefficient is equal to -0.1042, and its relative risk (RR) is equal to 0.900. This implied that age reduced the likelihood of the occurrence by 10 percent with every unit increase in age. The statistical evidence of the effect is very strong ($P = 1.0e-06$), which demonstrates that older age is a protective factor. The coefficient of ascites is 0.598 2/3 and that of RR is 0.0001 and this means that the risk will be nearly reduced by the presence of ascites. The result is very statistically significant ($P = 0.000$) which proves the protective effect of ascites. The platelet coefficient is 0.003996 and RR coefficient is 1.004, which implies that on an increment in platelet count by one unit, the event risk goes up by 0.4. The difference is statistically significant ($P = 3.0e-02$) indicating that the increase in platelet counts correlates with a low risk increment. The

disease stage coefficient is 0.7955 and the RR coefficient is 2.219 which means that with a one unit increase in the disease stage, the risk of the event increases more than two times. The statistical significance of the effect is statistically significant ($P = 9.5e-03$), meaning that the risk is significantly increased by the advanced stages of the disease.

Table 8: Results of the Refitted Sub-Distribution Regression Model for Key Covariates on Competing Risk Outcomes

Covariate	Coefficients	Relative Risk (RR)	Standard Errors	P-Value
Age	-0.104200	0.900	0.021320	1.0e-06
Ascites	-9.598000	0.0001	0.469300	0.000
Platelet	0.003996	1.004	0.001837	3.0e-02
stage	0.795500	2.219	0.306900	9.5e-03

4.0 DISCUSSION

The paper has used cumulative incidence functions and the Fine-Gray sub-distribution hazard model to investigate the dynamics of competing events death and liver transplantation in patients with Primary Biliary Cirrhosis (PBC). The analysis found out that the cumulative incidence of mortality was always higher than the cumulative incidence of transplantation over the period. time frame, and highlighting its preeminence as the main outcome. Although patients who were subjected to D-penicillmain treatment had a slightly lower mortality and slightly higher rate of transplant than their control group who were on placebo, none of that was statistically significant. This implies that D-penicillmain does not provide any significant benefit of survival in the PBC management. Covariate analysis revealed that age, ascites, disease stage and platelet count were the significant predictors of the event. Ascites and getting older. had a lower risk correlation, and higher platelet counts and high stage of the disease were correlated with risks of events. Notably, estimates of the variances showed that transplantation probabilities were more precise when compared to mortality and this could have been due to the complexity and heterogeneity of data on deaths in chronic liver disease.

5.0 CONCLUSION

The study presents a detailed analysis of data from Mayo Clinic trial on primary biliary cirrhosis (PBC) patients, focusing on competing risks of death and liver transplantation. By using cumulative incidence functions (CIFs) and regression models, the results show that death is the main event, while transplantation occurs less often. Comparisons between the D-penicillmain and placebo groups show slightly reduced mortality and increased transplantation rates for the treatment group, though these differences are not statistically significant, suggesting small impact of the treatment on event probabilities. Key risk factors identified for competing events include age, ascites, disease stage, and platelet count, while other variables, such as sex, bilirubin, and albumin, did not show significant associations. Variance analysis highlighted greater consistency in transplantation estimates, which indicate potential limitations in mortality data accuracy. The findings show that including competing risks in survival analysis is important for understanding treatment effects and influence of risk factors. The study provides useful insights for clinical decisions and shows that more findings are needed for better treatment options for PBC patients.

REFERENCES

- Anstee, Q. M., Castera, L., & Loomba, R. (2022). Impact of non-invasive biomarkers on hepatology practice: Past, present and future. *Journal of Hepatology*, *76*(6), 1362–1378. <https://doi.org/10.1016/j.jhep.2022.03.026>
- Austin, P. C., & Fine, J. P. (2017). Practical recommendations for reporting Fine–Gray model analyses for competing risk data. *Statistics in Medicine*, *36*(27), 4391–4400. <https://doi.org/10.1002/sim.7501>
- Austin, P. C., Steyerberg, E. W., & Putter, H. (2021). Fine–Gray subdistribution hazard models to simultaneously estimate the absolute risk of different event types: Cumulative total failure probability may exceed 1. *Statistics in Medicine*, *40*(19), 4200–4212. <https://doi.org/10.1002/sim.9023>
- Berger, M., Kowark, A., Rossaint, R., Coburn, M., Schmid, M., & POSE-Study Group. (2023). Modeling postoperative mortality in older patients by boosting discrete-time competing risks models. *Journal of the American Statistical Association*, *118*(544), 2239–2249. <https://doi.org/10.1080/01621459.2023.2208388>
- Crowther, M. J. (2020). *merlin*—A unified modeling framework for data analysis and methods development in Stata. *The Stata Journal*, *20*(4), 763–784. <https://doi.org/10.1177/1536867X209763>
- D’Amico, G., Morabito, A., D’Amico, M., Pasta, L., Malizia, G., Reborja, P., & Valsecchi, M. G. (2018). Clinical states of cirrhosis and competing risks. *Journal of Hepatology*, *68*(3), 563–576. <https://doi.org/10.1016/j.jhep.2017.10.020>
- Dauda, K. (2022). Development and modeling of decision tree for survival data with multiple events using deviance and Cox–Snell residuals within node homogeneity technique. *International Journal of Advanced Health Science and Technology*, *2*(3), 183–190. <https://doi.org/10.35882/ijahst.v2i3.9>
- Dauda, K. A., Adeniyi, E. J., Lamidi, R. K., & Wahab, O. T. (2025). Exploring flexible penalization of Bayesian survival analysis using beta process prior for baseline hazard. *Computation*, *13*(2), 21. <https://doi.org/10.3390/computation13020021>
- Dauda, K. A., & Lamidi, R. K. (2025). Consistency and stability in feature selection for high-dimensional microarray survival data in diffuse large B-cell lymphoma cancer. *Data*, *10*(2), 26. <https://doi.org/10.3390/data10020026>
- Dauda, K. A., Lamidi, R. K., Dauda, A. A., & Yahya, W. B. (2023). A new generalized gamma–Weibull distribution with applications to time-to-event data. *bioRxiv*. <https://doi.org/10.1101/2023.11.18.567670>
- Dauda, K. A., Pradhan, B., Shankar, B. U., & Mitra, S. (2019). Decision tree for modeling survival data with competing risks. *Biocybernetics and Biomedical Engineering*, *39*(3), 697–708. <https://doi.org/10.1016/j.bbe.2019.05.001>
- Dauda, K. A., Yahya, W. B., Banjoko, A. W., & Oloredo, K. O. (2018). Competing risk modeling using cumulative incidence function: Application to recurrent bladder cancer data. <https://doi.org/10.46792/fuoyejt.v3i1.180>
- Dauda, K. A. (2022). Optimal tuning of random survival forest hyperparameter with an application to liver disease. *The Malaysian Journal of Medical Sciences: MJMS*, *29*(6), 67.
- Guo, D., Li, J., Zhao, P., Mei, T., Li, K., & Zhang, Y. (2024). The hepatocellular carcinoma risk in patients with HBV-related cirrhosis: A competing risk nomogram based on a 4-year retrospective cohort study. *Frontiers in Oncology*, *14*, 1398968. <https://doi.org/10.3389/fonc.2024.1398968>
- Haredasht, F. N., Dauda, K. A., & Vens, C. (2023). Exploiting censored information in self-training for time-to-event prediction. *IEEE Access*, *11*, 96831–96840. <https://doi.org/10.1109/ACCESS.2023.3312310>
- Harms, M. H., Lammers, W. J., Thorburn, D., Corpechot, C., Invernizzi, P., Janssen, H. L., et al. (2018). Major hepatic complications in ursodeoxycholic acid-treated patients with primary biliary cholangitis. *American Journal of Gastroenterology*, *113*(2), 254–264. <https://doi.org/10.1038/ajg.2017.440>

- Heyard, R., Timsit, J.-F., Held, L., & COMBACTE-MAGNET Consortium. (2020). Validation of discrete time-to-event prediction models in the presence of competing risks. *Biometrical Journal*, *62*(3), 643–657. <https://doi.org/10.1002/bimj.201800293>
- Hofer, B. S., Burghart, L., Halilbasic, E., Simbrunner, B., Petrenko, O., Mandorfer, M., et al. (2024). Evaluation of potential hepatic recompensation criteria in patients with PBC and decompensated cirrhosis. *Alimentary Pharmacology & Therapeutics*, *59*(8), 962–972. <https://doi.org/10.1111/apt.17908>
- Kalu, U., Rasheed, L. K., Iheme, O. U., Toheeb, A. Y., & Iheme, U. U. (2025). Systematic assessment of Cox proportional hazards, exponential, log-normal survival models in time to event using breast cancer data. *World News of Natural Sciences*, *58*, 163-182.
- Kragh Andersen, P., Pohar Perme, M., van Houwelingen, H. C., Cook, R. J., Joly, P., Martinussen, T., ... & Therneau, T. M. (2021). Analysis of time-to-event for observational studies: guidance to the use of intensity models. *Statistics in medicine*, *40*(1), 185-211.
- Lai, X., Yau, K. K., & Liu, L. (2017). Competing risk model with bivariate random effects for clustered survival data. *Computational Statistics & Data Analysis*, *112*, 215–223. <https://doi.org/10.1016/j.csda.2017.03.011>
- Lee, C., Zame, W., Yoon, J., & Van Der Schaar, M. (2018). Deephit: A deep learning approach to survival analysis with competing risks. In *Proceedings of the AAAI Conference on Artificial Intelligence* (Vol. 32, No. 1). <https://doi.org/10.1609/aaai.v32i1.11842>
- Lee, M. (2022). Semiparametric analysis of recurrent discrete time data with competing risks. *Journal of Statistical Computation and Simulation*, *92*(16), 3301–3316. <https://doi.org/10.1080/00949655.2022.2102171>
- Li, Y., Hwang, W.-T., Maude, S. L., Teachey, D. T., Frey, N. V., Myers, R. M., et al. (2022). Statistical considerations for analyses of time-to-event endpoints in oncology clinical trials. *Clinical Cancer Research*, *28*(18), 3940–3949. <https://doi.org/10.1158/1078-0432.CCR-22-0560>
- Lleo, A., Leung, P. S., Hirschfield, G. M., & Gershwin, E. M. (2020). The pathogenesis of primary biliary cholangitis: A comprehensive review. *Seminars in Liver Disease*, *40*(1), 34–48. <https://doi.org/10.1055/s-0039-1697617>
- Meir, T., & Gorfine, M. (2025). Discrete-time competing-risks regression with or without penalization. *Biometrics*, *81*(2), ujad040. <https://doi.org/10.1093/biomtc/ujaf040>
- Murtaugh, P. A., Dickson, R. E., Van Dam, G. M., Malinchoc, M., Grambsch, P. M., Langworthy, A. L., & Gips, C. H. (1994). Primary biliary cirrhosis: Prediction of short-term survival based on repeated patient visits. *Hepatology*, *20*(1), 126–134. <https://doi.org/10.1002/hep.1840200120>
- Nijman, G., Wientjes, M., Ramjith, J., Janssen, N., Hoogerwerf, J., Abbink, E., et al. (2021). Risk factors for in-hospital mortality in laboratory-confirmed COVID-19 patients in the Netherlands: A competing risk survival analysis. *PLOS ONE*, *16*(3), e0249231. <https://doi.org/10.1371/journal.pone.0249231>
- Paukner, M., Ladner, D. P., Team, C., & Zhao, L. (2025). Measuring disease burden with individual cumulative incidence in patients with cirrhosis. *Journal of Biomedical Informatics*, 104883.
- Poguntke, I., Schumacher, M., Beyersmann, J., & Wolke, M. (2018). Simulation shows undesirable results for competing risks analysis with time-dependent covariates for clinical outcomes. *BMC Medical Research Methodology*, *18*(1), 79. <https://doi.org/10.1186/s12874-018-0535-5>
- Rossello, X., & González-Del-Hoyo, M. (2022). Survival analyses in cardiovascular research, part II: Statistical methods in challenging situations. *Revista Española de Cardiología (English Edition)*, *75*(1), 77–85. <https://doi.org/10.1016/j.rec.2021.07.001>
- Sanni, B. I., Aderoju, S. A., Lamidi, R. K., Adeshola, A. D., Jimoh, A. K., & Adeniyi, E. J. (2025). The New Two-Parameter Exponential-Gamma-Based Distribution: Properties And Application To Non-Communicable Disease Data. *Journal of Science and Technology*, 30(12).
- Schmid, M., & Berger, M. (2021). Competing risks analysis for discrete time-to-event data. *WIREs Computational Statistics*, *13*(5), e1529. <https://doi.org/10.1002/wics.1529>
- Tanaka, A., Leung, P. S., & Gershwin, M. E. (2018). Evolution of our understanding of PBC. *Best Practice & Research Clinical Gastroenterology*, *34*, 3–9. <https://doi.org/10.1016/j.bpg.2018.05.008>
- Thomadakis, C., Meligkotsidou, L., Yiannoutsos, C. T., & Touloumi, G. (2024). Joint modeling of longitudinal and competing-risk data using cumulative incidence functions for the failure submodels accounting for potential failure cause misclassification through double sampling. *Biostatistics*, *25*(1), 80–97. <https://doi.org/10.1093/biostatistics/kxac043>