Available online at http://scik.org
Commun. Math. Biol. Neurosci. 2026, 2026:75
https://doi.org/10.28919/cmbn/9997
ISSN: 2052-2541

MODELING DEPENDENT TIME TO VISUAL ACUITY RECOVERY USING A BIVARIATE COPULA COX APPROACH: A STUDY OF BILATERAL CATARACT SURGERY

WAHYU DWI RAHMAWATI, JERRY DWI TRIJOYO PURNOMO*, BAMBANG WIDJANARKO OTOK

Department of Statistics, Institut Teknologi Sepuluh Nopember, Surabaya 60111, Indonesia

Abstract: Survival analysis is a statistical framework for modeling time-to-event data. In the context of bilateral diseases such as cataracts, the two eyes may exhibit dependent event times, thereby reducing the suitability of univariate approaches for capturing this dependence. This study aims to model the dependence between the times to achieve a minimum visual acuity of 6/18 in the right and left eyes of patients following cataract surgery using a Cox proportional hazards model with a bivariate copula approach. The data consists of patients who underwent bilateral cataract surgery at an eye hospital in Surabaya, between January 1 and October 31, 2025. Parameter estimation was conducted using a two-stage procedure based on maximum pseudo-likelihood, with numerical optimization performed via the Berndt–Hall–Hall–Hausman (BHHH) algorithm. Four Archimedean copula families (Clayton, Frank, Gumbel, and Joe) were considered to model the dependence structure. Based on the Akaike Information Criterion (AIC), the Joe copula provided the best model fit, yielding an AIC value of 2975.158. The estimated dependence parameter was 3.934, corresponding to Kendall's tau of 0.609, indicating a moderately strong positive dependence between the times to achieve the minimum visual acuity in both eyes. Additionally, age and the history of cardiovascular disease were

*Corresponding author
E-mail address: jerry@its.ac.id
Received May 23, 2026

found to have significant effects on the event times in both eyes.

Keywords: Archimedean; BHHH-iteration; cataract; copula; Cox PH; dependency; Kendall's tau.

2020 AMS Subject Classification: 62N01.

1. INTRODUCTION

Time-to-event data are commonly analyzed using survival regression frameworks, including both parametric and semiparametric approaches. In practice, semiparametric methods such as the Cox proportional hazards model are more widely used due to their flexibility about the distribution of event times [1]. However, the standard Cox model is primarily developed for univariate data under the assumption of independence between observations. In many applications, this independence assumption is not satisfied. Time-to-event data often appears in paired or clustered form, such as in studies involving twins, married couples, or paired organs [2]. In such cases, survival times within a pair are likely to be dependent, and univariate approaches may overlook the underlying dependence structure [3].

To address this issue, various extensions of bivariate survival models have been proposed. Common approaches include shared frailty models, which account for dependence through latent random effects that capture unobserved heterogeneity among clustered survival times, as well as marginal models that incorporate dependence structures at the population level [4]. Within the Cox-based framework, an increasingly popular approach is the copula-based method, which links marginal survival functions into a joint distribution, allowing flexible modeling of dependence without altering the marginal specifications [5].

A two-stage estimation approach is frequently adopted for parameter estimation, such as the Inference Functions for Margins (IFM) method, in which the first stage estimates the marginal parameters and the second stage focuses on the dependence parameter [6]. Beyond the classical IFM scheme, Sun et al. [7] propose a joint estimation procedure in the second stage that simultaneously estimates both regression and copula parameters, while imposing the restriction that the regression coefficients are identical across the two margins.

Bivariate copula-based survival models have been widely applied in medical studies involving dependent time-to-event data. Previous studies, such as Gari and Gelcho [8] and Shewa et al. [9], demonstrate the flexibility of Archimedean copulas under both semiparametric and parametric marginal specifications. These approaches have been successfully used to model paired organs, including kidneys, breasts, and eyes. However, their application to cataract data remains limited, despite the inherently bilateral nature of the disease. World Health Organization [10] state that cataract is a leading cause of visual impairment worldwide, affect millions of individuals, with a substantial burden reported in developing countries, including Indonesia. This highlights the need for appropriate statistical models that can capture the dependence structure between the two eyes in cataract patients.

Table 1. Description of Study Variables

Variable	Variable's Name	Description	Scale
Y_1	Observed Time for Left Eye	Time from surgery to achieving a minimum visual acuity of 6/18 in the left eye or to censoring (in days)	Ratio
Y_2	Observed Time for Right Eye	Time from surgery to achieving a minimum visual acuity of 6/18 in the right eye or to censoring (in days)	Ratio
δ	Event Indicator	0: Censore 1: Event	Nominal
X_1	Sex	0: Man 1: Woman	Nominal
X_2	Age	Patient's age at surgery in year	Ratio
X_3	Hypertension	0: No 1: Yes	Nominal
X_4	Diabetes	0: No 1: Yes	Nominal
X_5	Cholesterol	0: No 1: Yes	Nominal
X_6	Cardiovascular disease	0: No 1: Yes	Nominal
X_7	Gastric disease	0: No 1: Yes	Nominal

To address this issue, this study applies to a Cox proportional hazards model with a bivariate copula framework to analyze recovery times in bilateral cataract patients. Parameter estimation is performed using a two-stage maximum pseudo-likelihood approach. Unlike existing methods that impose equality constraints on regression parameters across margins, such restrictions may limit the flexibility of the model in capturing heterogeneous covariate effects between the two eyes. Therefore, this study relaxes this assumption, allowing for a more flexible specification within the copula-based bivariate survival framework. Several Archimedean copulas, including Clayton, Frank, Gumbel, and Joe, are considered.

2. PRELIMINARIES

2.1 Data

Based on medical records from the eye hospital in Surabaya, a total of 4071 cataract surgeries were performed between January 1 and October 31, 2025. However, 3127 of these cases involved patients who underwent surgery in only one eye during the study period, leaving 944 observations from 472 patients who received bilateral surgery. After applying the inclusion criteria, 912 observations (corresponding to 456 patients) were retained for further analysis. A detailed description of the variables used in this study is provided in Table 1.

2.2 Copula-Based Bivariate Survival Model

Copula functions are used to construct a joint distribution from marginal survival functions without altering their individual specifications. In the context of bivariate survival analysis, let $S_1(t_1|\boldsymbol{x}_1)$ and $S_2(t_2|\boldsymbol{x}_2)$ denote the marginal survival functions with covariates [6], [11]. The joint survival function can be expressed as Eq. (1).

$$S(t_1, t_2|\boldsymbol{x}_1, \boldsymbol{x}_2) = C\{S_1(t_1|\boldsymbol{x}_1), S_2(t_2|\boldsymbol{x}_2); \theta\} \quad (1)$$

Where $C(\cdot,\cdot)$ is a copula function with dependence parameter θ. This approach allows the dependence structure to be modeled flexibly and separately from the marginal specifications. The corresponding joint density function is given by [12]:

$$f(t_1, t_2|\boldsymbol{x}_1, \boldsymbol{x}_2) = c\big(S_1(t_1|\boldsymbol{x}_1), S_2(t_2|\boldsymbol{x}_2)\big) f_1(t_1|\boldsymbol{x}_1) f_2(t_2|\boldsymbol{x}_2);\ t_1, t_2 \geq 0. \quad (2)$$

Where $c(u_1, u_2) = \partial^2 C(u_1, u_2)/\partial u_1 \partial u_2$ denotes the second-order partial derivative of the copula function, θ denotes the dependence parameter and $f_k(t_k) = h_{0k}(t_k)S_k(t_k)$ is the marginal density function.

2.3 Archimedean Copula

In this study, several Archimedean copula families are considered, including Clayton, Frank, Gumbel, and Joe copulas, each capturing different dependence characteristics, particularly in the tails of the distribution. The choice of copula is based on its suitability to the observed dependence pattern [13], [14]. The four copula functions are given below with copula parameter θ represents the strength of dependency between event times and can be related to dependence measures such as Kendall's tau [15].

The Clayton copula model has an asymmetric form, exhibiting stronger lower-tail dependence than upper-tail dependence. The Clayton copula is defined as follows, with $\theta > 0$ and Kendall's tau $\tau = \theta/(\theta + 2)$.

$$C(u_1, u_2) = \left(u_1^{-\theta} + u_2^{-\theta} - 1\right)^{-\frac{1}{\theta}} \tag{3}$$

The Gumbel copula is an asymmetric copula that exhibits stronger upper-tail dependence than lower-tail dependence, making it suitable for modeling extreme co-movements in the upper tail. It is defined as follows, with $\theta \geq 1$ and Kendall's tau $\tau = (\theta - 1)/\theta$.

$$C(u_1, u_2) = \exp\left(-\left((-\log u_1)^{\theta} + (-\log u_2)^{\theta}\right)^{\frac{1}{\theta}}\right) \tag{4}$$

The Frank copula is a symmetric copula that does not exhibit tail dependence, making it suitable for modeling moderate dependency. It is clearly defined here as follows, with $\theta \neq 0$ and also Kendall's tau $\tau = 1 - \frac{4}{\theta}\left(1 - \frac{1}{\theta}\int_0^{\theta} \frac{t}{e^t - 1} dt\right)$.

$$C(u_1, u_2) = -\frac{1}{\theta}\log\left(1 + \frac{(e^{-\theta u_1} - 1)(e^{-\theta u_2} - 1)}{e^{-\theta} - 1}\right) \tag{5}$$

The Joe copula is an asymmetric copula that exhibits stronger upper-tail dependence than lower-tail dependence. The formal definition is explicitly stated below, under the conditions that $\theta > 1$ and Kendall's tau $\tau = 1 - 4\int_0^{\infty} \frac{t(1-e^{-t})^{\frac{2}{\theta} - 2} e^{-2t}}{\theta^2} dt$.

$$C(u_1, u_2) = 1 - \left((1-u_1)^\theta + (1-u_2)^\theta - (1-u_1)^\theta(1-u_2)^\theta\right)^{\frac{1}{\theta}} \tag{6}$$

2.4 Marginal Survival Function under the Cox Proportional Hazards Model

The marginal survival function $S_k(t_k|\boldsymbol{x}_k)$ under the Cox proportional hazards model with covariates $\boldsymbol{x}_k$ is given by [16]:

$$S_k(t_k|\boldsymbol{x}_k) = \exp\left(-\int_0^{t_k} h_{0k}(u)\exp(\boldsymbol{x}_{\boldsymbol{k}}^T\boldsymbol{\beta}_{\boldsymbol{k}})\,du\right) = \exp(-H_{0k}(t_k)\exp(\boldsymbol{x}_{\boldsymbol{k}}^T\boldsymbol{\beta}_{\boldsymbol{k}})) \tag{7}$$

Where $h_{0k}(t_k)$ denotes the baseline hazard function for the k-th margin, $H_{0k}(t_k)$ represents the cumulative baseline hazard function for the k-th margin, with $k = 1,2$, and $\boldsymbol{\beta}_k$ is a $p \times 1$ vector of regression parameters associated with the covariates $\boldsymbol{x}_k$.

Consider V distinct event times from n observed individuals, denoted by the ordered sequence $t_1 < t_2 < \cdots < t_V$. At each event time t_v, the risk set $R(t_v)$ includes all individuals who remain under observation and are at risk just prior to t_v. The regression coefficients $\boldsymbol{\beta}_k$ are estimated via the partial likelihood [17] (see Eq. (8)), followed by estimation of the cumulative baseline hazard $H_{0k}(t_k)$ using the Breslow estimator in Eq. (9) [18]:

$$L(\boldsymbol{\beta}_k) = \prod_{i=1}^{n}\left(\frac{\exp(\boldsymbol{x}_{ki}^T\boldsymbol{\beta}_k)}{\sum_{r\in R(t_{kv})}\exp(\boldsymbol{x}_{kr}^T\boldsymbol{\beta}_k)}\right)^{\delta_{ki}}; k = 1, 2. \tag{8}$$

$$\widehat{H}_{0k}(t_k) = \sum_{v:t_{kv}\le t_k}\frac{d_{kv}}{\sum_{r\in R(t_{kv})}\exp\left(\boldsymbol{x}_{kr}^T\widehat{\boldsymbol{\beta}}_k\right)}; k = 1, 2. \tag{9}$$

Here, $\delta_{ki} = I(T_{ki} \le C_{ki})$ is an indicator function that takes the value 1 if the event is observed and 0 otherwise. The vector $\boldsymbol{x}_{kr}$denotes the covariates for the k-th margin corresponding to an individual in the risk set at time t_{kv}, with $r = 1,2, \dots, N(R(t_{kv}))$. The term d_{kv} represents the number of events occurring at time t_{kv}, and $\widehat{\boldsymbol{\beta}}_k$ denotes the estimated regression coefficients obtained from the partial likelihood of the Cox proportional hazards model.

2.5 Estimation Algorithm

This section describes the estimation procedure for the proposed bivariate copula-based Cox survival model. The formulation begins with the specification of observed data and model assumptions, followed by the construction of the likelihood and pseudo-likelihood functions used for parameter estimation.

1. Suppose that there are n subjects, where the bivariate event times for the i-th individual are denoted by (T_{1i}, T_{2i}), and the corresponding censoring times are denoted by (C_{1i}, C_{2i}). The observed times are defined as $Y_{ki} = \min(T_{ki}, C_{ki})$, for $i = 1, 2, \ldots, n$ and $k = 1,2$. The censoring indicators are given by $\delta_i = (\delta_{1i}, \delta_{2i})$, where $\delta_{ki} = I(T_{ki} \leq C_{ki})$, taking the value 1 if the event is observed and 0 otherwise.
2. It is assumed that the survival times (T_{1i}, T_{2i}) are independent of the censoring times (C_{1i}, C_{2i}).
3. The joint survival function is defined in Eq. (1), and the corresponding joint density function is given in Eq. (2). The Archimedean copula functions considered in this study are specified in Eq. (3) - Eq. (6).
4. The marginal survival functions are modeled using the Cox proportional hazards model, as presented in Eq. (7). The likelihood function for estimating the regression parameters $\boldsymbol{\beta}_k$ is defined in Eq. (8), and its logarithmic form can be written as $\ell(\beta_k) = \log L(\beta_k)$.
5. Let $\boldsymbol{\psi} = (\boldsymbol{\beta}_1^T, \boldsymbol{\beta}_2^T, \theta)^T$ denote the vector of unknown parameters and let (H_{01}, H_{02}) represent the baseline cumulative hazard functions for the two margins.
6. The pseudo log-likelihood function for the bivariate copula-based Cox survival model is then defined as $\ell = \sum_i \ell_i$, where ℓ_i denotes the contribution of the i-th individual based on the marginal survival functions specified in Eq. (7).

$$\begin{aligned}
\ell(\boldsymbol{\psi}) = \sum_{\boldsymbol{i=1}}^{\boldsymbol{n}} \Bigg(& d_{1i} d_{2i} \left(\log \frac{\partial^2 C(u_{1i}, u_{2i})}{\partial u_{1i} \partial u_{2i}} + \log f_{1i} + \log f_{2i} \right) \\
& + d_{1i}(1 - d_{2i}) \left(\log \frac{\partial C(u_{1i}, u_{2i})}{\partial u_{1i}} + \log f_{1i} \right) \\
& + d_{2i}(1 - d_{1i}) \left(\log \frac{\partial C(u_{1i}, u_{2i})}{\partial u_{2i}} + \log f_{2i} \right) \\
& + (1 - d_{1i})(1 - d_{2i}) \log C(u_{1i}, u_{2i}) \Bigg)
\end{aligned} \tag{10}$$

where $(\delta_{1i}, \delta_{2i}) \in \{(0,0), (0,1), (1,0), (1,1)\}$.

7. The first step in the two-stage estimation procedure is to obtain initial estimates of the regression parameters $\boldsymbol{\beta}_k$ using the partial likelihood, and to estimate H_{0k} using the Breslow estimator. Subsequently, the pseudo log-likelihood $\ell(\boldsymbol{\psi})$ is maximized with respect to the dependence parameter θ, using the estimated $\boldsymbol{\beta}_k$ and H_{0k} as initial values for the second stage. More specifically, the procedure can be described as follows:
   a. Estimate $\boldsymbol{\beta}_k$ using the log function of Eq. (8) and save the results as $\widehat{\boldsymbol{\beta}}_k^{(0)}$.
   b. Estimate $\widehat{H}_{0k}(t_k)$ using Eq. (9) where the $\widehat{\boldsymbol{\beta}}_k$ is the result from 7.a.
   c. Estimate θ using the pseudo log-likelihod function in Eq. (10) under the condition that $\boldsymbol{\beta}_k = \widehat{\boldsymbol{\beta}}_k^{(0)}$ and $\widehat{H}_{0k}$ are treated as fixed values which can be written as $\ell(\boldsymbol{\psi}|\widehat{\boldsymbol{\beta}}_1^{(0)}, \widehat{\boldsymbol{\beta}}_2^{(0)}, \widehat{H}_{01}, \widehat{H}_{02})$ where $\ell(\boldsymbol{\psi})$ is the. The resulting estimate is denoted as $\eta^{(0)}$.
8. In the second step, the parameter vector $\boldsymbol{\psi}$ is estimated jointly by maximizing the joint log-likelihood function, using $\boldsymbol{\psi}^{(0)} = (\widehat{\boldsymbol{\beta}}_1^{(0)}, \widehat{\boldsymbol{\beta}}_2^{(0)}, \theta^{(0)})$ as the initial values to obtain the final parameter estimates. The estimation uses the B-HHH algorithm as follows:

1. Define the gradient function $\boldsymbol{U}(\boldsymbol{\psi}) = \frac{\partial \ell(\boldsymbol{\psi})}{\partial \boldsymbol{\psi}} = \sum_i \frac{\partial \ell_i(\boldsymbol{\psi})}{\partial \boldsymbol{\psi}} = \sum_i \boldsymbol{U}_i(\boldsymbol{\psi})$ and the Hessian as $\boldsymbol{H}(\boldsymbol{\psi}) = -\sum_{\boldsymbol{i=1}}^{\boldsymbol{n}} \boldsymbol{U}_i(\boldsymbol{\psi}) \boldsymbol{U}_i(\boldsymbol{\psi})^T$.
2. Define the initial value with $\boldsymbol{\psi}^{(0)}$.
3. The parameter $\boldsymbol{\psi}$ is iteratively optimized using the following updating formula:

$$\boldsymbol{\psi}^{(m+1)} = \boldsymbol{\psi}^{(m)} - \boldsymbol{H}(\boldsymbol{\psi})^{-1} \boldsymbol{U}(\boldsymbol{\psi}^{(\boldsymbol{m})});\ m = 0, 1, 2, \ldots \tag{11}$$

4. Convergence is achieved when $\| \widehat{\boldsymbol{\psi}}^{(m+1)} - \widehat{\boldsymbol{\psi}}^{(m)} \| < \varepsilon$, with ε denoting a small tolerance level near zero.
5. Save the result as $\widehat{\boldsymbol{\psi}}$ then re-estimate $\widehat{H}_{0k}$ using the value of $\widehat{\boldsymbol{\beta}}_k$ in $\widehat{\boldsymbol{\psi}}$.

3. MAIN RESULTS

3.1 Description of Covariates

The data used in this study consists of 912 observations from 456 patients. The following presents the distribution of event occurrences and censoring for the right and left eye.

Tabel 2. Frequency Distribution of Events by Eye

	Right Cataract Eye (OD) (Proportion)	**Left Cataract Eye (OS) (Proportion)**
Event ($\delta = 1$)	350 (76,75%)	334 (73,25%)
Censored ($\delta = 0$)	106 (23,25%)	122 (26,75%)
Total	456 (100,00%)	456 (100,00%)

Table 2 shows that more than 70% of patients who underwent cataract surgery at the eye hospital in Surabaya achieved a favorable outcome (visual acuity ranging from 6/18 to 6/6), while the remaining patients had not reached this outcome by the end of the study period. Some patients who did not achieve a minimum visual acuity of 6/18 had a history of other ocular conditions that may affect surgical outcomes, such as diabetic retinopathy, myopia, and glaucoma [19], [20]. Furthermore, the comparison of Kaplam-Meier survival curves based on the covariates used in this study are presented by Fig.1

The outcome of cataract surgery may be influenced by patient age and can vary across different age groups. Consistent with this, a recent study reported significant differences in surgical outcomes between patients aged below 55 years and those aged 55 years and above [21]. In line with these findings, a clear separation between age groups is observed in both eyes, where patients aged <55 years consistently exhibit higher survival probabilities, indicating a longer time to achieve the target visual acuity compared to older patients. A distinct pattern is also observed for patients with a history of cardiovascular disease, whose survival curves show a more rapid decline, particularly in the early postoperative period, suggesting earlier event occurrence.

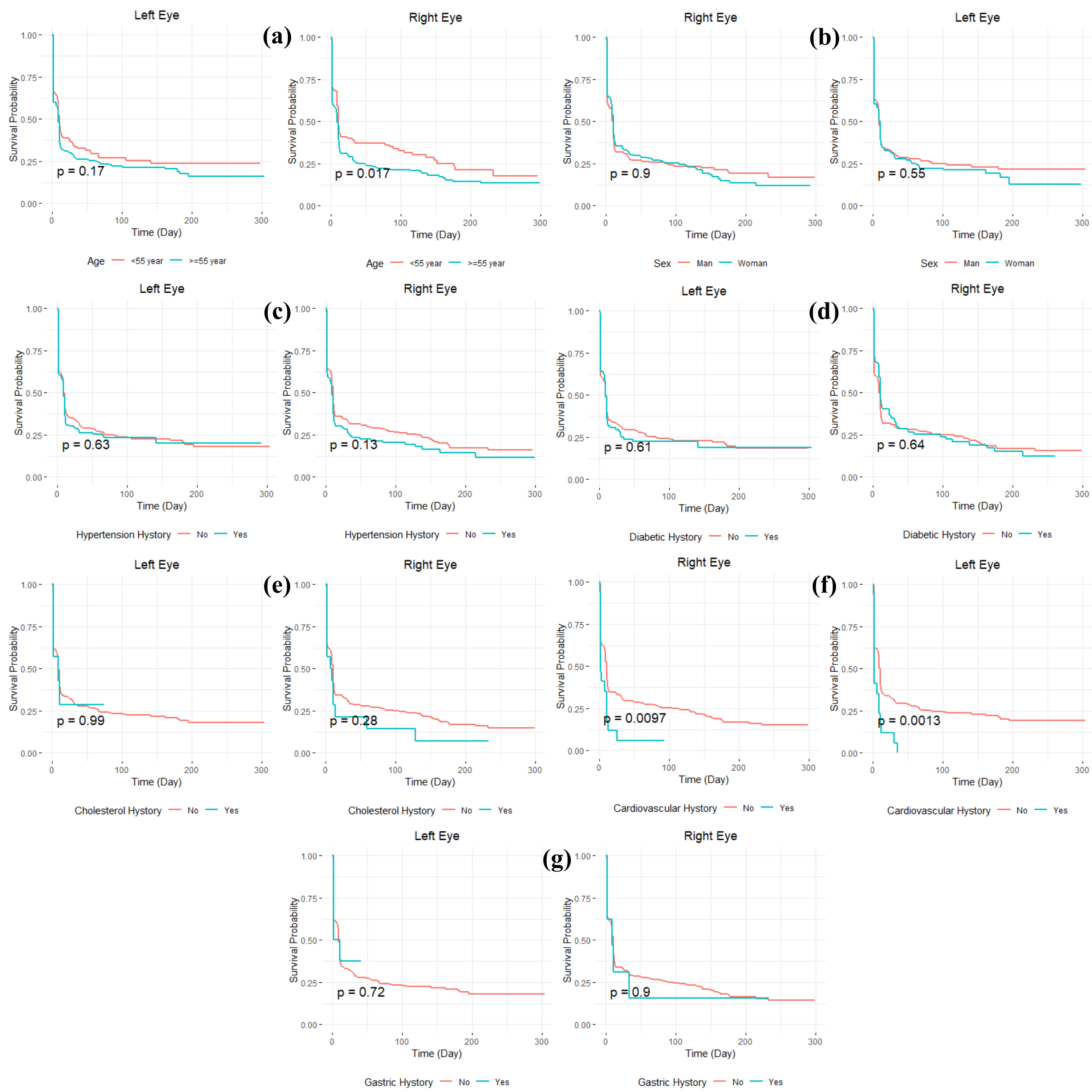

Figure 1. Kaplan–Meier survival curves of time to achieving visual acuity ≥6/18, stratified by covariatesde for the left and right eyes: (a) age, (b) sex, (c) hypertension, (d) diabetic, (e) cholesterol, (f) cardiovascular disease, and (g) gastric disease

Differences by sex display varying patterns between the two eyes, indicating potential heterogeneity across margins. Specifically, the relative positions of the survival curves differ between the right and left eye over time. In contrast, other covariates, including hypertension, diabetes mellitus, cholesterol, and gastric disease, show largely overlapping curves or inconsistent separation, suggesting a weaker dependency with the time to achieve the target visual acuity.

3.2 Estimation Results of the Bivariate Copula Cox Model

The modified two-stage method is applied to cataract eye data obtained from patient medical records at an eye hospital. The survival time is defined as the duration from the date of surgery to the time when visual acuity reaches a minimum outcome of 6/18. Table 3 presents the estimated regression parameters for the bivariate survival model under four copula families, namely Clayton, Frank, Gumbel, and Joe. The estimation is performed for two margins, the left and right eyes. In general, the signs of the coefficients are relatively consistent across copula models, although their magnitudes vary. This suggests that different dependence structures do not substantially alter the direction of covariate effects but may influence the strength of these effects.

Table 3. Estimation Results

	Estimated Parameter							
Copula	Clayton		Frank		Gumbel		Joe	
Margin	Left	Right	Left	Right	Left	Right	Left	Right
Sex	0.105	- 0.017	0.068	- 0.015	0.043	- 0.044	0.019	- 0.059
Age	0.001	0.000	0.004	0.003	0.003	0.002	0.004	0.003
Hypertension	0.007	0.108	0.039	0.142	0.029	0.129	0.041	0.133
Diabetes	0.116	- 0.062	- 0.052	- 0.234	- 0.001	- 0.164	- 0.061	-0.207
Cholesterol	- 0.226	0.013	0.103	0.239	0.086	0.224	0.300	0.412
Cardiov. Disease	0.842	0.827	0.644	0.641	0.640	0.605	0.538	0.487
Gastric disease	- 0.065	0.130	- 0.195	- 0.073	-0.152	- 0.074	- 0.269	- 0.243
θ	2.116		7.310		2.619		3.934	

Among the covariates, age shows a consistently positive effect across all models, indicating an increasing hazard of achieving the visual acuity outcome with higher age. A covariate with the largest coefficient is also observed across all copula models, reflecting a relatively strong dependency with shorter time to visual recovery. Some variability in coefficient signs across margins is observed for certain variables, indicating potential heterogeneity that may be influenced by the assumed dependence structure. The dependence parameter θ is positive for all copula models, indicating positive dependency between event times in the two eyes.

Table 4 shows a comparison of the AICC values and Kendall's tau of the four models. Among the four models, the Joe copula yields the smallest AIC value (2975.158), indicating the best balance between model complexity and goodness-of-fit compared to the other copula specifications. Based on the AIC criterion, the Joe copula is therefore selected as the most appropriate model to represent the dependence structure between the times to achieve the minimum visual acuity of 6/18 in both eyes of post-cataract surgery patients. Subsequently, the significance of the estimated parameters under the Joe copula model is evaluated.

Table 4. Model Evaluation

Copula	AIC	Kendall's Tau
Clayton	3102.347	0.514
Frank	3050.282	0.576
Gumbel	2990.995	0.618
Joe	2975.158	0.609

The significance test result showed by Table 5. There is a discrepancy in the results of the partial significance tests for the covariates of diabetes and cholesterol history between the right and left eye. These covariates are not statistically significant for the survival time of the left eye but are significant for the right eye. Several factors may explain this difference, including the non-simultaneous cataract surgery and the preoperative requirements that must be met by patients. Cataract surgery is generally performed sequentially rather than simultaneously for both eyes, following the guidelines of the Asia-Pacific Association of Cataract and Refractive Surgeons, which recommend delayed sequential surgery for bilateral cases. This approach allows for the evaluation of postoperative outcomes, particularly the risk of inflammation or other complications, before proceeding with surgery on the second eye.

Additionally, delays between surgeries may occur due to healthcare coverage policies, such as those of BPJS Kesehatan, which require a minimum visual acuity threshold (e.g., <6/18) for eligibility. As a result, surgery on the second eye may be postponed if it does not meet this criterion. Systemic conditions also play a critical role, such as diabetes mellitus, as poor glycemic control increases the risk of postoperative complications and necessitates preoperative stabilization. These factors contribute to variations in surgical timing and may affect the analysis results, including differences in significance and the direction of regression coefficients between the two eyes.

Based on the regression coefficients obtained from the bivariate copula Cox survival model with the Joe copula, most of the analyzed covariates exhibit different directions of association with theoretical expectations. However, this finding is consistent with the initial covariate exploration using Kaplan–Meier curves, where the curves for patients with a history of the disease tend to lie above those for patients without such a history. This indicates that patients with a history of the disease tend to experience the event earlier than those without a history of the disease.

Table 5. Significance Test Result for the Chosen Model

Covariat	Estimated Par.	SE	Stat	p-value
		Left Eye		
Sex	0.019	0.057	0.329	0.742
Age	0.004	0.002	2.753	0.006***
Hypertension	0.041	0.076	0.541	0.588
Diabetes	-0.061	0.081	-0.746	0.455
Cholesterol	0.300	0.161	1.867	0.062*
Cardiov. disease	0.538	0.209	2.577	0.010**
Gastric disease	-0.269	0.273	-0.984	0.325
		Right Eye		
Sex	-0.059	0.056	-1.047	0.295
Age	0.003	0.001	2.174	0.030**
Hypertension	0.133	0.075	1.779	0.075*
Diabetes	-0.207	0.084	-2.482	0.013**
Cholesterol	0.412	0.176	2.334	0.020**
Cardiov. disease	0.487	0.185	2.642	0.008***
Gastric disease	-0.243	0.272	-0.891	0.373

*significant at 10%; **significant at 5%; ***significant at 1%

These findings suggest the presence of other factors that may influence the observed relationships. Based on the available data, one of the primary possibilities is the limitation in patient data recording. Visual acuity measurements are highly dependent on patients' adherence to postoperative follow-up visits after cataract surgery. Patients who fail to attend follow-up visits, or who do not adhere to the recommended schedule, may give substantial variability in observation times and potentially result in censored data. This condition may increase the proportion of patients classified in the group at risk of not achieving the minimum visual acuity, thereby potentially affecting the direction of the estimated coefficients and leading to inconsistencies with theoretical expectations. Nevertheless, the influence of other unobserved factors not included in the analysis cannot be ruled out, as they may also contribute to the discrepancies in the direction of the estimated coefficients.

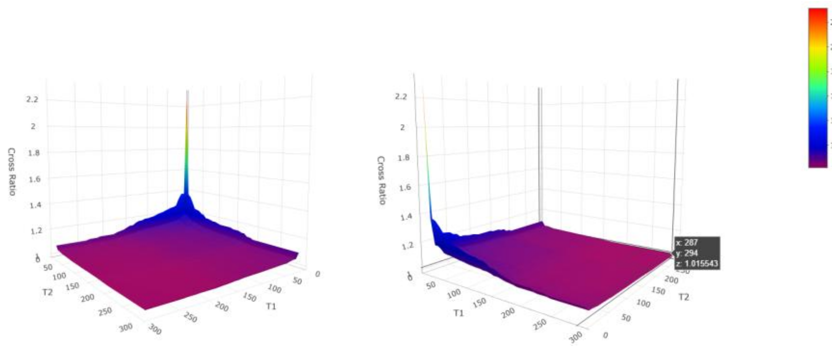

Figure 2. Cross rasio t_1 and t_2

Figure 2 presents the hazard curves for the event occurrence in the left and right eyes. The estimated cross-ratio curve indicates that the level of dependence between the two events is relatively high at the early stage, as reflected by a cross-ratio value of 2.315 at $T_1 = T_2 = 7$. This suggests that the occurrence of an event in one unit is strongly associated with the occurrence in the other unit during the initial phase of observation. As time progresses, the cross-ratio value decreases but remains relatively stable at a level slightly above one. This indicates that although the strength of dependence weakens over time, a positive association between the two events persists throughout the later observation period.

4. CONCLUSION

This study employed a two-stage maximum pseudo-likelihood approach to estimate the parameters of a bivariate copula-based Cox survival model. In the first stage, marginal regression parameters were estimated using partial likelihood, and the baseline survival functions were obtained nonparametrically. These estimates were then used as initial values in the second stage, where the regression and dependence parameters were jointly optimized using the BHHH algorithm. Among the copula families considered, the Joe copula provided the best fit based on the Akaike Information Criterion (AIC = 2975.158). The estimated dependence parameter ($\theta = 3.934$) and Kendall's tau (0.609) indicate a moderately strong positive dependency between the two eyes.

In terms of covariate effects, age and history of cardiovascular disease were found to significantly increase the hazard of achieving the event in both eyes. Additionally, cholesterol was significant in the right eye with a positive effect, while diabetes mellitus showed a negative dependency, indicating a lower event rate among affected patients. Future studies should further explore the role of ocular comorbid conditions to enhance the representativeness of the findings. Moreover, the consideration of alternative copula families may offer greater flexibility in modeling the dependence between visual acuity outcomes in bilateral eyes.

ACKNOWLEDGEMENTS

The authors are grateful to Undaan Eye Hospital for institutional support and access to retrospective clinical data. This research was fully funded by Ministry of Higher Education, Science, and Technology (BIMA) 2026 with contract number: 2171/PKS/ITS/2026.

ETHIC STATEMENT

This study was approved by the Ethics Committee of RSUD Haji East Java Province Approval No. 445/182/KOM.ETIK/2025. The study was conducted in accordance with the principles of the Declaration of Helsinki. This research used secondary data obtained from patients' medical records. All data were anonymized prior to analysis to ensure patient confidentiality. Informed consent was waived by the Ethics Committee due to the retrospective nature of the study and the use of de-identified data.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests.

REFERENCES

[1] F. Emmert-Streib, M. Dehmer, Introduction to Survival Analysis in Practice, Mach. Learn. Knowl. Extr. 1 (2019), 1013-1038. https://doi.org/10.3390/make1030058.

[2] D.D. Hanagal, Correlated Compound Poisson Frailty Models Based on Reversed Hazard Rate, Commun. Stat. Theory Methods 53 (2024), 1312-1330. https://doi.org/10.1080/03610926.2022.2098336.

[3] N.W. Deresa, I. Van Keilegom, K. Antonio, Copula-Based Inference for Bivariate Survival Data with Left

Truncation and Dependent Censoring, Insurance Math. Econom. 107 (2022), 1-21. https://doi.org/10.1016/j.insmatheco.2022.07.011.

[4] M. Gorfine, D.M. Zucker, Shared Frailty Methods for Complex Survival Data: A Review of Recent Advances, Annu. Rev. Stat. Appl. 10 (2023), 51-73. https://doi.org/10.1146/annurev-statistics-032921-021310.

[5] A.A. Ding, W. Wang, Inference for Bivariate Survival Data by Copula Models Adjusted for the Boundary Effect, Commun. Stat. Theory Methods 36 (2007), 2927-2936. https://doi.org/10.1080/03610920701386901.

[6] J.H. Shih, T.A. Louis, Inferences on the Association Parameter in Copula Models for Bivariate Survival Data, Biometrics 51 (1995), 1384-1399. https://doi.org/10.2307/2533269.

[7] T. Sun, Y. Liu, R.J. Cook, W. Chen, Y. Ding, Copula-Based Score Test for Bivariate Time-to-Event Data, with Application to a Genetic Study of AMD Progression, Lifetime Data Anal. 25 (2019), 546-568. https://doi.org/10.1007/s10985-018-09459-5.

[8] F.S. Gari, G.N. Gelcho, Bivariate Survival Copula Analysis of Glaucoma Patients during Blindness: Glaucoma Cases at Alert Hospital in Addis Ababa City of Ethiopia, J. Res. Health Sci. 22 (2022), e00547. https://doi.org/10.34172/jrhs.2022.82.

[9] F. Shewa, S. Endale, G. Nugussu, J. Abdisa, K. Zerihun, et al., Time to Kidneys Failure Modeling in the Patients at Adama Hospital Medical College: Application of Copula Model, J. Res. Health Sci. 22 (2022), e00549. https://doi.org/10.34172/jrhs.2022.84.

[10] World Health Organization, World Report on Vision, World Health Organization, Geneva, 2019. https://iris.who.int/handle/10665/328717.

[11] R.B. Nelsen, An Introduction to Copulas, 2nd ed., Springer Series in Statistics, Springer, New York, 2006. https://doi.org/10.1007/0-387-28678-0.

[12] G.D.C. Barriga, F. Louzada-Neto, E.M.M. Ortega, V.G. Cancho, A Bivariate Regression Model for Matched Paired Survival Data: Local Influence and Residual Analysis, Stat. Methods Appl. 19 (2010), 477-495. https://doi.org/10.1007/s10260-010-0140-1.

[13] J. Größer, O. Okhrin, Copulae: An Overview and Recent Developments, WIREs Comput. Stat. 14 (2022), e1557. https://doi.org/10.1002/wics.1557.

[14] G. Risca, S. Galimberti, P. Rebora, A. Cattoni, M.G. Valsecchi, et al., Archimedean Copulas: A Useful Approach

in Biomedical Data—A Review with an Application in Pediatrics, Stats 8 (2025), 69. https://doi.org/10.3390/stats8030069.

[15] J. Ansari, M. Rockel, Dependence Properties of Bivariate Copula Families, Depend. Model. 12 (2024), 20240002. https://doi.org/10.1515/demo-2024-0002.

[16] H. Zhu, Y. Lan, J. Ning, Y. Shen, Semiparametric Copula-Based Regression Modeling of Semi-Competing Risks Data, Commun. Stat. Theory Methods 51 (2022), 7830-7845. https://doi.org/10.1080/03610926.2021.1881122.

[17] A.J. Turkson, F. Ayiah-Mensah, V. Nimoh, Handling Censoring and Censored Data in Survival Analysis: A Standalone Systematic Literature Review, Int. J. Math. Math. Sci. 2021 (2021), 9307475. https://doi.org/10.1155/2021/9307475.

[18] R.L. Prentice, S. Zhao, The Statistical Analysis of Multivariate Failure Time Data: A Marginal Modeling Approach, Chapman and Hall/CRC, Boca Raton, 2019. https://doi.org/10.1201/9780429162367.

[19] P. Desai, D.C. Minassian, A. Reidy, National Cataract Surgery Survey 1997-8: A Report of the Results of the Clinical Outcomes, Br. J. Ophthalmol. 83 (1999), 1336-1340. https://doi.org/10.1136/bjo.83.12.1336.

[20] M. Grimfors, K. Mollazadegan, M. Lundström, M. Kugelberg, Ocular Comorbidity and Self-Assessed Visual Function after Cataract Surgery, J. Cataract Refract. Surg. 40 (2014), 1163-1169. https://doi.org/10.1016/j.jcrs.2013.11.033.

[21] H. Ben-Eli, Y. Cnaany, M. Halpert, I. Chowers, A. Goldstein, Investigating the Impact of Age and Sex on Cataract Surgery Complications and Outcomes, Sci. Rep. 15 (2025), 1242. https://doi.org/10.1038/s41598-024-84382-4.