



Research article

Estimation of monotone bivariate quantile inactivity time with medical applications

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Abstract: In most lifetime models, the bivariate α -quantile inactivity time is a vector of increasing functions. A novel estimator of this vector was created and investigated under this assumption. It was expected that the application of this knowledge would improve the efficiency of the estimator. It was proven that the proposed estimator is consistent and converges weakly to a bivariate Gaussian process under a suitable transformation. A simulation study was conducted to compare the performance of the proposed estimator with that of the usual estimator. Finally, the application of the proposed estimator is illustrated by analyzing a dataset comprising the time to blindness in patients with diabetic retinopathy.

Keywords: inactivity time; monotone bivariate quantile inactivity time; empirical distribution function; estimation

Mathematics Subject Classification: 62N01, 62N05

1. Introduction

Great progress has been made in the field of statistics and probability theory for interdisciplinary research. New techniques and methods have been developed to meet the challenges of data analysis. Statistical methods are becoming increasingly important in various areas of science. The increasing complexity of scientific problems requires the development of new and suitable statistical methods for interdisciplinary research. Current challenges include, ecology: Quantifying biodiversity; the epidemiology of infectious diseases: Disease outbreak detection; financial mathematics: stock option

valuation; industrial engineering: Stochastic optimization; and genomics: Personalized medicine, to name a few.

For a random lifetime T , the conditional inactivity time is defined as $T_t = t - T | T \leq t$, and $t > 0$. An important measure developed based on the conditional inactivity time is the α -quantile inactivity time (α -QIT), which is the α -quantile of T_t . Assuming that the distribution function of T is denoted by F , the α -QIT can be expressed by the following relationship:

$$q_\alpha(t) = t - F^{-1}(\bar{\alpha}F(t)), \quad t > 0,$$

where $\bar{\alpha} = 1 - \alpha$ and $F^{-1}(p) = \inf\{x: F(x) = p\}$ is the inverse function of F . Let T be the event time referring to the instances of a species. Among all instances experienced the event at a time before t , we expect $100\alpha\%$ of these instances to have experienced the event after time $t - q_\alpha(t)$. In this sense, a smaller $q_\alpha(t)$ means larger T . The α -QIT is a competitor for the mean inactivity time (MIT) function. The MIT has been intensively studied by researchers in the field of reliability theory and survival analysis, e.g., refer to Finkelstein [1] and Kayid and Izadkhah [2]. However, when the moments of the underlying model are infinite or heavily skewed to right, α -QIT is preferred over MIT (see Schmittlein and Morrison [3] for a detailed justification of quantile-based than moment-based measures). The α -QIT concept was formally defined and studied by Unnikrishnan and Vinesh Kumar [4]. Shafaei [5] showed that how the underlying model can be characterized by α -QIT function. Shafaei and Izadkhah [6] stated some properties of a parallel system in terms of the α -QIT measure. For a sample T_1, T_2, \dots, T_n of iid lifetimes, the α -QIT can be estimated by

$$q_{\alpha,n}(t) = t - F_n^{-1}(\bar{\alpha}F_n(t)), \quad t \geq T_{(1)},$$

where $F_n(t)$ is the empirical distribution function, i.e.,

$$F_n(t) = \frac{1}{n} \sum_{i=1}^n I(T_i \leq t),$$

and

$$F_n^{-1}(p) = \inf\{x: F_n(x) \geq p\} = \begin{cases} 0 & p = 0, \\ T_{(1)} & 0 < p \leq \frac{1}{n}, \\ T_{(2)} & \frac{1}{n} < p \leq \frac{2}{n}, \\ \dots & \dots \\ T_{(n)} & 1 - \frac{1}{n} < p \leq 1. \end{cases}$$

Then, $q_{\alpha,n}$ can be written as in the following.

$$q_{\alpha,n}(t) = \begin{cases} t & 0 \leq t < t_1, \\ t - T_{(1)} & t_1 \leq t < t_2, \\ t - T_{(2)} & t_2 \leq t < t_3, \\ \dots & \dots \\ t - T_{(n-1)} & t_{k-1} \leq t < t_k, \\ t - T_{(n)} & t \geq t_k, \end{cases} \quad (1)$$

where

$$t_i = \inf\{y: \bar{\alpha}F_n(y) > \frac{i-1}{n}\} = \inf\{y: F_n^{-1}(\bar{\alpha}F_n(y)) = T_{(i)}\}.$$

Note that $F_n^{-1}(\bar{\alpha}F_n(t_i)) = T_{(i)}$, for every $i = 1, 2, \dots, k$ for some $k \leq n$ $t_1 = T_{(1)}$ and $t_i \geq T_{(i)}$ for $i = 2, \dots, k$. The expression (1) shows that $q_{\alpha,n}(t)$ consists of line segments with slope 1 on intervals (t_i, t_{i+1}) , $i = 1, \dots, k-1$ and falls at each point t_i by $T_{(i)} - T_{(i-1)}$, $i = 1, 2, \dots, k$ where $T_{(0)} = 0$. Figure 1 shows a schematic plot of $q_{\alpha,n}(t)$.

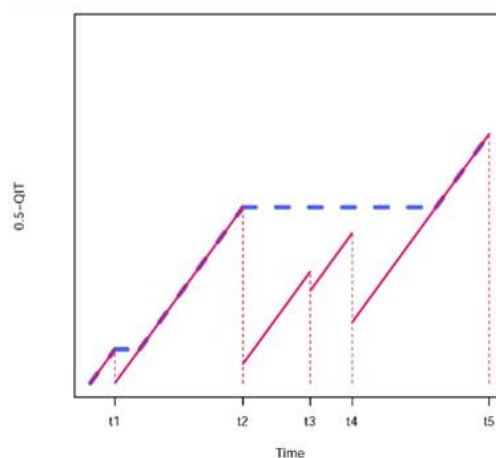


Figure 1. A schematic plot of the univariate 0.5-QIT function and its increasing version. The figure shows t_i points which are useful in computing and plotting both usual and increasing function.

For the univariate case, Mahdy [7] proposed the estimator (2) for the α -QIT function and investigated its asymptotic properties. Balmert and Jeong [8] created a nonparametric inference of the median inactivity time function for right-censored data. Balmert et al. [9] applied a log-linear quantile regression model to the inactivity time for right-censored data. Kayid [10] applied the Kaplan-Meiere survival estimator to the α -QIT function for estimation and inference.

We can have two or more dependent events. For example, if successive events of the same person/instance are tracked, the event times depend on each other. Another example is that researchers are interested in determining the effect of a treatment on specific event times related to the eyes, ears, hands or legs. One organ was randomly selected for treatment and the other was a control organ. The events associated with these organs depend on their progression. In such cases, we need to extend the measures in question to bivariate or multivariate settings. In the following section, I refer to the authors who have implemented this idea. Basu [11] and Johnson and Kotz [12] examined the multivariate hazard rate function as a gradient vector. The mean residual lifetime was extended by Nair and Nair [13] to obtain a vector of dependent lifetimes. Shaked and Shanthikumar [14] introduced the dynamic multivariate MRL concept. Kayid [15] developed the multivariate MIT concept. Navarro [16]

characterized the basic model by the bivariate hazard rate function. The concept of the α -quantile residual lifetime (α -QRL) was extended to the multivariate context by Shafaei and Kayid [17]. Shafaei et al. [18] discussed the multivariate α -QRL concept in a dynamic way. Buono et al. [19] applied multivariate RHR for discussing reliability attributes of systems. Kayid [20] extended the α -QIT concept to bivariate context and discussed its estimation.

Let F be the distribution function of a random pair $\mathbf{T} = (T_1, T_2)$. Then, the α -QIT vector at point $\mathbf{t} = (t_1, t_2)$ is defined to be $(q_{\alpha,1}(\mathbf{t}), q_{\alpha,2}(\mathbf{t}))$. The first element of this vector is

$$\begin{aligned} q_{\alpha,1}(\mathbf{t}) &= \sup\{x: P(t_1 - T_1 > x | \mathbf{T} \leq \mathbf{t}) = \bar{\alpha}\} \\ &= \sup\{x: F(t_1 - x, t_2) = \bar{\alpha}F(\mathbf{t})\} \\ &= \inf\{t_1 - z: F(z, t_2) = \bar{\alpha}F(\mathbf{t})\} \\ &= t_1 - F_1^{-1}(\bar{\alpha}F(\mathbf{t}); t_2), \end{aligned}$$

where $\bar{\alpha} = 1 - \alpha$ and

$$F_1^{-1}(p; t_2) = \inf\{z: F(z, t_2) = p\},$$

is the partial inverse of F in terms of the T_1 . The second element of the α -QIT vector is defined similarly.

$$q_{\alpha,2}(\mathbf{t}) = t_2 - F_2^{-1}(\bar{\alpha}F(\mathbf{t}); t_1),$$

where $F_2^{-1}(p; t_1) = \inf\{z: F(t_1, z) = p\}$ is the partial inverse of F in terms of the second element. The reversed hazard rate vector of \mathbf{T} is $(r_1(\mathbf{t}), r_2(\mathbf{t}))$ and

$$r_i(\mathbf{t}) = \frac{\partial}{\partial t_i} \log F(\mathbf{t}), \quad i = 1, 2.$$

The RHR satisfies the following relation.

$$\begin{cases} \frac{\partial}{\partial t_1} F(t_1, t_2) = r_1(t_1, t_2)F(t_1, t_2), \\ \frac{\partial}{\partial t_2} F(t_1, t_2) = r_2(t_1, t_2)F(t_1, t_2). \end{cases}$$

Kayid [20] showed that if $r_i(\mathbf{t})$ is decreasing (increasing) in t_i , then $q_{\alpha,i}(\mathbf{t})$ is increasing (decreasing) in t_i . It is a surprising fact that for most of the standard bivariate models, $r_i(\mathbf{t})$ is decreasing in t_i (Finkelstein [1]). For example, bivariate Gumbel, Pareto, normal, and gamma models have decreasing reversed hazard rate functions. This implies that $q_{\alpha,i}(\mathbf{t})$ is increasing in t_i . For some examples of such models, refer to Kayid [20]. This motivates me to introduce a new estimator of $q_{\alpha,1}(\mathbf{t})$ and $q_{\alpha,2}(\mathbf{t})$ under the assumption that they are increasing with respect to t_1 and t_2 , respectively. It is expected that applying this knowledge, I have a more accurate estimator than the usual estimator defined by Kayid [20]. Such monotone estimators are defined and studied by Kochar et al. [21], Franco Pereira and Una-Alvarez [22], and Shafaei and Franco Pereira [23].

The rest of this paper is structured as follows. In Section 2, the promised increasing estimator of the bivariate α -QIT function is proposed and its asymptotic properties are discussed. Then, the performance of the new estimator is compared with that of the usual estimator in a simulation study. In Section 4, the proposed estimator is applied to investigate the effect of laser treatment on the time to blindness. In Section 5, I summarize the results.

2. Estimation of increasing bivariate α -QIT

Let \dots, \dots, T_n be an iid random sample from bivariate distribution F . The empirical distribution function is defined by

$$F_n(t_1, t_2) = n^{-1} \sum_{i=1}^n I(T_{1i} \leq t_1, T_{2i} \leq t_2),$$

and the partial inverse of F_n , with respect to the first and second elements, are as in the following respectively:

$$F_{1,n}^{-1}(p; t_2) = \inf\{x: F_n(x, t_2) \geq p\},$$

and

$$F_{2,n}^{-1}(p; t_1) = \inf\{x: F_n(t_1, x) \geq p\}.$$

Kayid [20] proposed the following estimator of the bivariate α -QIT vector.

$$q_{\alpha,n}(\mathbf{t}) = (q_{\alpha,1,n}(\mathbf{t}), q_{\alpha,2,n}(\mathbf{t})),$$

where

$$\begin{cases} q_{\alpha,1,n}(\mathbf{t}) = t_1 - F_{1,n}^{-1}(\bar{\alpha}F_n(\mathbf{t}); t_2), \\ q_{\alpha,2,n}(\mathbf{t}) = t_2 - F_{2,n}^{-1}(\bar{\alpha}F_n(\mathbf{t}); t_1), \end{cases}$$

with the knowledge of increasing bivariate α -IQT, we define the natural estimator

$$iq_{\alpha,n}(\mathbf{t}) = (iq_{\alpha,1,n}(\mathbf{t}), iq_{\alpha,2,n}(\mathbf{t})),$$

where

$$\begin{cases} iq_{\alpha,1,n}(\mathbf{t}) = \sup_{y \leq t_1} q_{\alpha,1,n}(y, t_2), \\ iq_{\alpha,2,n}(\mathbf{t}) = \sup_{y \leq t_2} q_{\alpha,2,n}(t_1, y), \end{cases}$$

Let $t_2 > 0$ be fixed and define $T_1[t_2] = T_1|T_2 \leq t_2$, then the distribution function of $T_1[t_2]$ is

$$F_1^*(x; t_2) = P(T_1[t_2] \leq x) = \frac{F(x, t_2)}{F_2(t_2)},$$

where $F_2(t_2) = P(T_2 \leq t_2)$. Denote α -QIT of $T_1[t_2]$ by $q_{\alpha,1}^*(t_1; t_2)$, then it can be shown that

$$q_{\alpha,1}^*(t_1; t_2) = q_{\alpha,1}(t_1, t_2). \quad (2)$$

Similarly, for every fixed $t_1 > 0$, we define $T_2[t_1] = T_2|T_1 \leq t_1$ following distribution $F_2^*(\cdot; t_1)$. Let $q_{\alpha,2}^*(t_2; t_1)$ be the α -QIT of $T_2[t_1]$, then we can investigate that

$$q_{\alpha,2}^*(t_2; t_1) = q_{\alpha,2}(t_1, t_2). \quad (3)$$

Given a bivariate iid random sample (T_{1i}, T_{2i}) , $i = 1, 2, \dots, n$ from distribution F , and for every fixed t_2 , consider the following univariate random sample which follows from $F_1^*(\cdot; t_2)$.

$$\chi(1, t_2) = \{T_{1ij} : \text{when } T_{2ij} \leq t_2, j = 1, \dots, k_1(t_2)\}.$$

I can apply this sample to estimate $q_{\alpha,1}^*(t_1; t_2)$, as in the following.

$$q_{\alpha,1,n}^*(t_1; t_2) = t_1 - F_{1,n}^{*-1}(\bar{\alpha}F_{1,n}^*(t_1; t_2)),$$

where

$$F_{1,n}^*(t_1; t_2) = \frac{\#(T_{1ij} \leq t_1)}{k_1(t_2)},$$

and

$$F_{1,n}^{*-1}(p) = \inf\{x : F_{1,n}^*(x; t_2) \geq p\}.$$

Applying the knowledge of increasing $q_{\alpha,1}^*(t_1; t_2)$ in terms of t_1 , it is natural to use the following estimator.

$$iq_{\alpha,1,n}^*(t_1; t_2) = \sup_{y \leq t_1} q_{\alpha,1,n}^*(y; t_2).$$

Again, for a bivariate iid random sample $(T_{1i}, T_{2i}), i = 1, 2, \dots, n$ from distribution F , and for every fixed t_1 , consider the following sample.

$$\chi(2, t_1) = \{T_{2ij} : \text{when } T_{1ij} \leq t_1 \dots = 1, 2, \dots, k_2(t_1)\},$$

which follows from $F_2^*(\cdot; t_1)$. Then, the estimator of $q_{\alpha,2}^*(t_2; t_1)$ is defined by

$$q_{\alpha,2,n}^*(t_2; t_1) = t_2 - F_{2,n}^{*-1}(\bar{\alpha}F_{2,n}^*(t_2; t_1)),$$

where

$$F_{2,n}^*(t_2; t_1) = \frac{\#(T_{2ij} \leq t_2)}{k_2(t_1)},$$

and

$$F_{2,n}^{*-1}(p) = \inf\{x : F_{2,n}^*(x; t_1) \geq p\}.$$

In an increasing context,

$$iq_{\alpha,2,n}^*(t_2; t_1) = \sup_{y \leq t_2} q_{\alpha,2,n}^*(y; t_1).$$

It is clear that

$$\begin{cases} iq_{\alpha,1,n}(\mathbf{t}) = iq_{\alpha,1,n}^*(t_1; t_2), \\ iq_{\alpha,2,n}(\mathbf{t}) = iq_{\alpha,2,n}^*(t_2; t_1). \end{cases} \quad (4)$$

Theorem 1. Let us assume that the following two conditions are fulfilled.

(C1). $F(t_1, t_2)$ be twice differentiable with respect each element.

(C2). $\frac{\partial}{\partial t_1} F(\mathbf{t})$ and $\frac{\partial}{\partial t_2} F(\mathbf{t})$ are bounded from zero on the intervals $(0, F_1^{-1}(\bar{\alpha}; t_2))$ and $(0, F_2^{-1}(\bar{\alpha}; t_1))$, respectively, for every $t_1 > 0$ and $t_2 > 0$.

Then, $(iq_{\alpha,1,n}(\mathbf{t}), iq_{\alpha,2,n}(\mathbf{t}))$ is consistent for $(iq_{\alpha,1}(\mathbf{t}), iq_{\alpha,2}(\mathbf{t}))$.

Proof. By Theorem 7 from Kayid [24], we have

$$|iq_{\alpha,1,n}^*(t_1; t_2) - iq_{\alpha,1}^*(t_1; t_2)| \rightarrow 0, \text{ almost every where,}$$

and

$$|iq_{\alpha,2,n}^*(t_2; t_1) - iq_{\alpha,2}^*(t_2; t_1)| \rightarrow 0, \text{ almost every where.}$$

Thus, the result follows from (2)–(4).

To state the next theorem, I need two following conditions.

(C3) $\frac{\partial}{\partial t_1} q_{\alpha,1}(\mathbf{t})$ and $\frac{\partial}{\partial t_2} q_{\alpha,2}(\mathbf{t})$ exist and there are $c_1 > 0$ and $c_2 > 0$ such that $\frac{\partial}{\partial t_1} q_{\alpha,1}(\mathbf{t}) > c_1$

and $\frac{\partial}{\partial t_2} q_{\alpha,2}(\mathbf{t}) > c_2$ for all $0 < t_1 < b_1$ and $0 < t_2 < b_2$ for some positive b_1 and b_2 .

(C4) $\frac{\partial^2}{\partial t_1 \partial t_1} q_{\alpha,1}(\mathbf{t})$ and $\frac{\partial^2}{\partial t_2 \partial t_2} q_{\alpha,2}(\mathbf{t})$ exist and

$$\sup_{0 < t_1 < b_1} \left| \frac{\partial^2}{\partial t_1 \partial t_1} q_{\alpha,1}(\mathbf{t}) \right| \leq c_3 < \infty \text{ and } \sup_{0 < t_2 < b_2} \left| \frac{\partial^2}{\partial t_2 \partial t_2} q_{\alpha,2}(\mathbf{t}) \right| \leq c_4 < \infty.$$

Theorem 2. Assume that C1–C4 are satisfied. Then, we have

$$\sqrt{n} \left| \left(iq_{\alpha,1,n}(\mathbf{t}), iq_{\alpha,2,n}(\mathbf{t}) \right) - \left(q_{\alpha,1}(\mathbf{t}), q_{\alpha,2}(\mathbf{t}) \right) \right| \rightarrow 0, \text{ in probability.}$$

Proof. By Theorem 5 from Kayid [21], we have

$$\sup_{0 < t < b_1} |iq_{\alpha,1,n}^*(t_1; t_2) - q_{\alpha,1}^*(t_1; t_2)| \rightarrow 0, \text{ in probability,}$$

and

$$\sup_{0 < t < b_2} |iq_{\alpha,2,n}^*(t_2; t_1) - q_{\alpha,2}^*(t_2; t_1)| \rightarrow 0, \text{ in probability.}$$

Thus, the result follows from relations (2)–(4) and the concept of convergence in probability in bivariate setting.

The following lemma, which is the result of the well-known Slutsky theorem, is used in the proof of the next theorem (see Van der Vaart [25] for Slutsky's theorem and related results).

Lemma 1. If $\sqrt{n}(X_n - Y_n) \rightarrow 0$ in probability and $\sqrt{n}X_n$ converges, in distribution, to a random variable X with distribution F , then $\sqrt{n}Y_n$ converges, in distribution, to a random variable Y with the same distribution F .

Theorem 3. Under the conditions C1–C4, we have

$$\sqrt{n} \left| \left(iq_{\alpha,1,n}(\mathbf{t}), iq_{\alpha,2,n}(\mathbf{t}) \right) - \left(q_{\alpha,1}(\mathbf{t}), q_{\alpha,2}(\mathbf{t}) \right) \right| \rightarrow N(0, C\Sigma C), \text{ in distribution,}$$

where

$$C = - \begin{bmatrix} \frac{\partial}{\partial p} F_1^{-1}(p; t_2)|_{p=\bar{\alpha}F(t)} & 0 \\ 0 & \frac{\partial}{\partial p} F_2^{-1}(p; t_1)|_{p=\bar{\alpha}F(t)} \end{bmatrix},$$

and elements of Σ are

$$\sigma_{11} = \sigma_{22} = \alpha \bar{\alpha} F(\mathbf{t}),$$

and

$$\sigma_{12} = \sigma_{21} = F(F_1^{-1}(\bar{\alpha}F(\mathbf{t}); t_2), F_2^{-1}(\bar{\alpha}F(\mathbf{t}); t_1)) - \bar{\alpha}^2 F(\mathbf{t}).$$

Proof. Theorem 7 of Kayid [20] states that under some mild conditions:

$$\sqrt{n} \left| \left(q_{\alpha,1,n}(\mathbf{t}), q_{\alpha,2,n}(\mathbf{t}) \right) - \left(q_{\alpha,1}(\mathbf{t}), q_{\alpha,2}(\mathbf{t}) \right) \right| \rightarrow N(0, C\Sigma C), \text{ in distribution,}$$

where C and Σ are defined in this theorem. Thus, applying Lemma 1, the result follows immediately.

In the real world, lifetime random pairs $\mathbf{T}_1, \mathbf{T}_2, \dots, \mathbf{T}_n$ may be censored by a random censorship C_i , in the sense that the observations are $\tilde{T}_{1i} = T_{1i} \wedge C_i$, $\tilde{T}_{2i} = T_{2i} \wedge C_i$, $\delta_{1i} = I(T_{1i} > C_i)$ and $\delta_{2i} = I(T_{2i} > C_i)$. Note that $a \wedge b = \min\{a, b\}$. Let censorship random variable C_i be independent from desired lifetimes and follows from distribution G and the reliability function $\bar{G} = 1 - G$, i.e., $\bar{G}(t) = P(C_i > t)$. Also, let $\tilde{R}(t_1, t_2) = P(\tilde{T}_{1i} > t_1, \tilde{T}_{2i} > t_2)$ and $R(t_1, t_2) = P(T_{1i} > t_1, T_{2i} > t_2)$. Then, we have

$$R(t_1, t_2) = \frac{\tilde{R}(t_1, t_2)}{\bar{G}(t_1 \vee t_2)},$$

where $t_1 \vee t_2 = \max\{t_1, t_2\}$. So, we can estimate the reliability function R by

$$R_n(t_1, t_2) = \frac{1}{n} \frac{\sum_{i=1}^n I(\tilde{T}_{1i} > t_1, \tilde{T}_{2i} > t_2)}{\bar{G}_n(t_1 \vee t_2)}.$$

Under this censoring scheme, Lin and Ying [26] showed that $R_n(t_1, t_2)$ is strongly consistent and weakly converges to a Gaussian process. Thus, when we have such censored data, the empirical distribution function could be replaced by the following estimate:

$$F_n(t_1, t_2) = 1 - R_n(t_1, 0) - R_n(0, t_2) + R_n(t_1, t_2).$$

3. Simulations

To investigate the performance of the proposed (increasing) estimator and comparing it with the usual estimator, a simulation study is conducted. The bivariate Gumbel and Pareto distributions with respectively the following reliability functions are selected for the baseline models:

$$\bar{F}(t_1, t_2) = \exp\{-t_1 - t_2 - \beta t_1 t_2\}, \quad \beta > 0, t_1 \geq 0, t_2 \geq 0,$$

and

$$\bar{F}(t_1, t_2) = (t_1 + t_2 - 1)^{-c}, \quad c > 0, t_1 \geq 1, t_2 \geq 1.$$

Both models are important from practical and theoretical points of view. The Gumbel distribution was introduced by Gumbel [27], and the Pareto model was used by Jupp and Mardia [28] to analyze income data for consecutive years. Some proper values for β and c were selected. In each simulation run, $r = 1000$ replicates of bivariate samples of size n were generated, where n was set to 25, 50 or 100. For each sample, $q_{0.5,1,n}()$ and its increasing version, $iq_{0.5,1,n}()$, are calculated at four appropriate time points t_1, t_2, t_3 and t_4 according to the following rules: Let F_1 be the marginal distribution of the first element and $\mathbf{t}_i = (t_{1i}, t_{2i})$. The equations $F_1(t_{11}) = 0.25, F_1(t_{12}) = 0.40, F_1(t_{13}) = 0.50$ and $F_1(t_{14}) = 0.75$ are solved to find t_{11} to t_{14} and given them, the equations $F(t_{11}, t_{21}) = 0.2, F(t_{12}, t_{22}) = 0.3, F(t_{13}, t_{23}) = 0.4,$ and $F(t_{14}, t_{24}) = 0.6$ are solved for t_{21} to t_{24} . After calculating the objective functions for r replicates, the bias (B) and mean squared error (MSE) were calculated and are shown in Tables 1 and 2 for the Gumbel and Pareto models, respectively. All simulations and calculations were performed in R (statistical programming language). The results show small values for B and MSE for both the conventional estimator and the proposed increasing estimator. As expected, the MSE increases with $F(t)$ (see Theorem 3). The MSE values for the increasing estimator are smaller in all cases, indicating that the increasing estimator performs better than the conventional estimator. See Figures 2 and 3 for a graphical representation of the ratio of MSE values related to the usual to the increasing estimator.

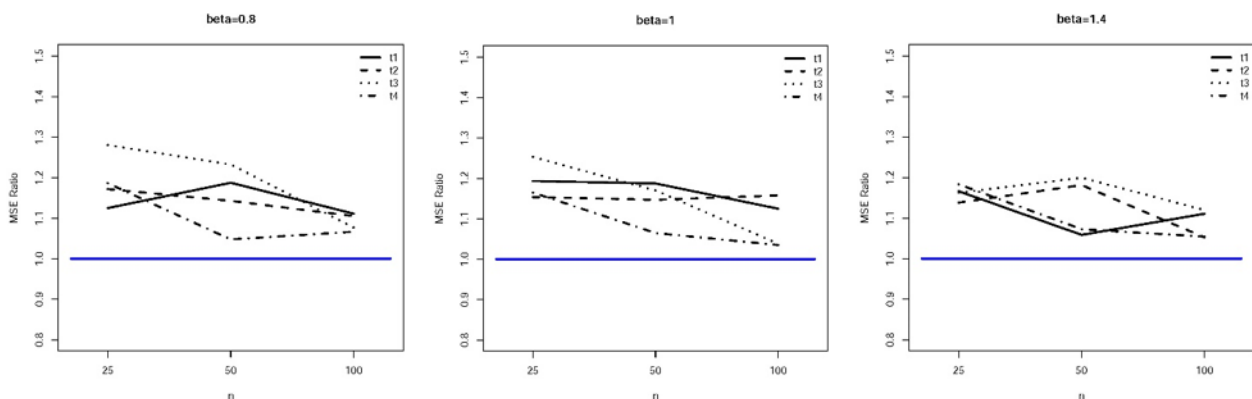


Figure 2. The MSE ratio of the usual estimator to the increasing version for Gumbel distribution reported in Table 1. All points lies above horizontal line 1 indicating a better performance for increasing estimator rather than the usual one.

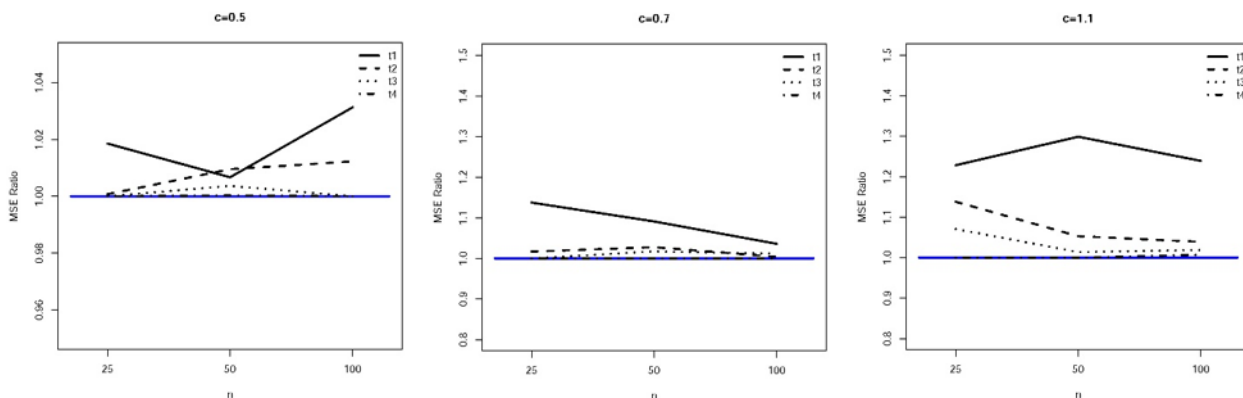


Figure 3. The MSE ratio of the usual estimator to the increasing one for Pareto model. All points lies above horizontal line and shows that the increasing estimator provides a smaller MSE.

Table 1. Simulation results for the bivariate Gumbel distribution.

Estimator	n	point	β					
			0.8		1		1.4	
			B	MSE	B	MSE	B	MSE
Usual	25	t_1	0.0133	0.0036	0.0120	0.0037	0.0115	0.0035
		t_2	0.0146	0.0075	0.0096	0.0075	0.0144	0.0074
		t_3	0.0113	0.0105	0.0086	0.0099	0.0157	0.0100
		t_4	0.0118	0.0242	0.0150	0.0212	0.0203	0.0232
	50	t_1	0.0071	0.0019	0.0068	0.0019	0.0062	0.0018
		t_2	0.0093	0.0040	0.0074	0.0039	0.0071	0.0039
		t_3	0.0055	0.0053	0.0069	0.0055	0.0050	0.0054
		t_4	0.0070	0.0110	0.0050	0.0115	0.0059	0.0118
	100	t_1	0.0057	0.0010	0.0049	0.0009	0.0043	0.0010
		t_2	0.0033	0.0021	0.0035	0.0022	0.0035	0.0020
		t_3	0.0017	0.0028	0.0058	0.0027	0.0022	0.0028
		t_4	-0.0010	0.0064	0.0027	0.0059	0.0009	0.0058
Increasing	25	t_1	0.0395	0.0032	0.0388	0.0031	0.0386	0.0030
		t_2	0.0480	0.0064	0.0466	0.0065	0.0503	0.0065
		t_3	0.0440	0.0082	0.0435	0.0079	0.0473	0.0086
		t_4	0.0370	0.0204	0.0392	0.0182	0.0455	0.0196
	50	t_1	0.0224	0.0016	0.0232	0.0016	0.0238	0.0017
		t_2	0.0286	0.0035	0.0282	0.0034	0.0268	0.0033
		t_3	0.0244	0.0043	0.0252	0.0047	0.0238	0.0045
		t_4	0.0192	0.0105	0.0175	0.0108	0.0163	0.0110
	100	t_1	0.0145	0.0009	0.0141	0.0008	0.0139	0.0009
		t_2	0.0140	0.0019	0.0141	0.0019	0.0148	0.0019
		t_3	0.0103	0.0026	0.0137	0.0026	0.0115	0.0025
		t_4	0.0063	0.0060	0.0058	0.0057	0.0082	0.0055

Table 2. Simulation results for the bivariate Pareto distribution.

Estimator	n	point	c					
			0.5		0.7		1.1	
			B	MSE	B	MSE	B	MSE
Usual	25	t_1	-0.0040	0.1866	0.0149	0.0686	0.0018	0.0242
		t_2	0.0030	0.2704	-0.0067	0.1025	-0.0042	0.0346
		t_3	-0.0412	0.4076	-0.0285	0.1508	-0.0082	0.0469
		t_4	-0.0591	0.5858	-0.0349	0.2085	-0.0156	0.0620
	50	t_1	0.0017	0.0903	-0.0100	0.0407	0.0040	0.0113
		t_2	-0.0152	0.1273	-0.0178	0.0554	0.0005	0.0159
		t_3	-0.0312	0.1913	-0.0296	0.0816	-0.0025	0.0221
		t_4	-0.0534	0.3003	-0.0345	0.1103	-0.0004	0.0273
	100	t_1	-0.0086	0.0461	-0.0017	0.0172	0.0008	0.0057
		t_2	-0.0089	0.0577	-0.0030	0.0253	-0.0010	0.0080
		t_3	-0.0137	0.0823	-0.0057	0.0343	-0.0037	0.0107
		t_4	-0.0222	0.1243	-0.0086	0.0495	-0.0035	0.0141
Increasing	25	t_1	0.0004	0.1832	0.0271	0.0603	0.1125	0.0197
		t_2	0.0032	0.2702	-0.0018	0.1008	0.0049	0.0304
		t_3	-0.0411	0.4076	-0.0285	0.1508	-0.0043	0.0438
		t_4	-0.0591	0.5858	-0.0349	0.2085	-0.0155	0.0620
	50	t_1	0.0057	0.0897	0.0009	0.0373	0.0830	0.0087
		t_2	-0.0135	0.1261	-0.0142	0.0539	0.0048	0.0151
		t_3	-0.0307	0.1906	-0.0286	0.0802	-0.0012	0.0218
		t_4	-0.0534	0.3002	-0.0343	0.1103	-0.0004	0.0273
	100	t_1	-0.0046	0.0447	0.0014	0.0166	0.0631	0.0046
		t_2	-0.0072	0.0570	-0.0017	0.0252	0.0008	0.0077
		t_3	-0.0137	0.0823	-0.0042	0.0339	-0.0029	0.0105
		t_4	-0.0222	0.1243	-0.0085	0.0495	-0.0033	0.0140

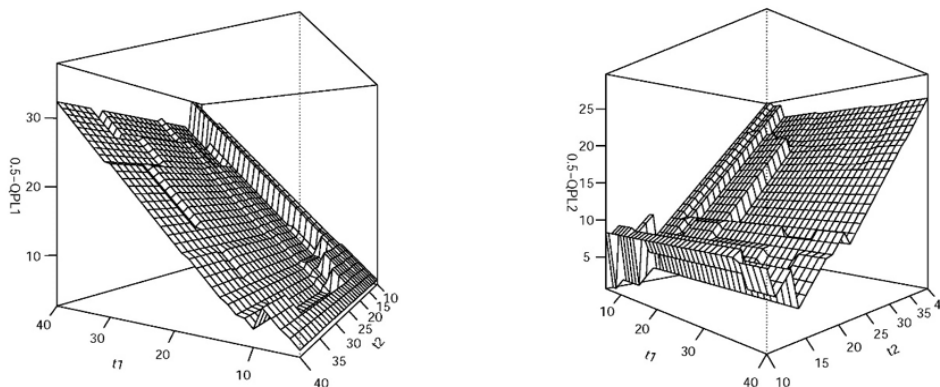
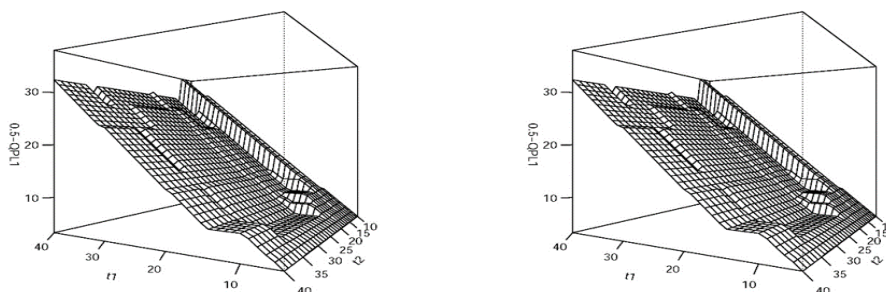
4. Effect of laser treatment on blindness

In a study that began in 1971, researchers were interested in the effect of laser photocoagulation on delaying blindness in patients with DR. Patients with visual acuity $\geq 20/100$ in both eyes were selected for the study. One eye of each patient was randomly selected for laser photocoagulation (treatment) and the other eye was observed without treatment (control). The time from the start of treatment to blindness is given in months. Blindness means that visual acuity fell below 5/200 on two consecutive visits. The data for this study is available in the “diabetic” dataset in the “survival” package in R. Table 3 shows part of the dataset relating to adolescents (under 20 years of age). For patient i , T_{1i} and T_{2i} indicate the observed time to blindness in the control and treated eyes, respectively.

Table 3. Survival times to blindness in months for juveniles.

Patient (i)	1	2	3	4	5	6	7	8	9
T_{1i}	6.9	1.63	13.83	35.53	14.8	6.2	22	1.7	43.03
T_{2i}	20.17	10.27	5.67	5.90	33.9	1.73	30.2	1.7	1.77
Patient (i)	10	11	12	13	14	15	16	17	18
T_{1i}	6.53	42.17	48.43	9.6	7.6	1.8	9.9	13.77	0.83
T_{2i}	18.7	42.17	14.3	13.33	14.27	34.57	21.57	13.77	10.33
Patient (i)	19	20	21	22	23	24			
T_{1i}	1.97	11.3	30.4	19	5.43	46.63			
T_{2i}	11.07	2.1	13.97	13.80	13.57	42.43			

Figures 4 and 5 draw the bivariate median inactivity time functions and their increasing versions, $iq_{n,0.5,1}(\mathbf{t})$ and $iq_{n,0.5,2}(\mathbf{t})$, respectively.

**Figure 4.** The bivariate median inactivity time functions $q_{n,0.5,1}(\mathbf{t})$ (left) and $q_{n,0.5,2}(\mathbf{t})$ (right).**Figure 5.** The bivariate increasing median inactivity time functions $iq_{n,0.5,1}(\mathbf{t})$ (left) and $iq_{n,0.5,2}(\mathbf{t})$ (right).

The comparison of the proposed increasing median inactivity time functions $iq_{n,0.5,1}(t)$ and $iq_{n,0.5,2}(t)$ at different points is informative in investigating the treatment effect. To provide a simple and powerful statistics, we can consider the points on the identity line and use the following statistics

$$d_n(t) = iq_{n,0.5,1}(t, t) - iq_{n,0.5,2}(t, t), \quad t \geq 0. \quad (5)$$

If I assume that the treatment dose not effect the time length to blindness, $d_n(t)$ should be positive or negative values near zero, reflecting some random errors. However, if the treatment causes longer time to blindness, I expect relatively larger values for $iq_{n,0.5,1}(t, t)$ than $iq_{n,0.5,2}(t, t)$, i.e., positive values for $d_n(t)$. Figure 6 plots $d_n(t)$ in all points of the observed T_1 or T_2 . The plot shows positive values that increase with t and indicates that the treatment causes longer time to blindness. The effect of treatment also increases with time. The bivariate median inactivity functions are on the right side of Figure 6 to provide a better comparison of these functions.

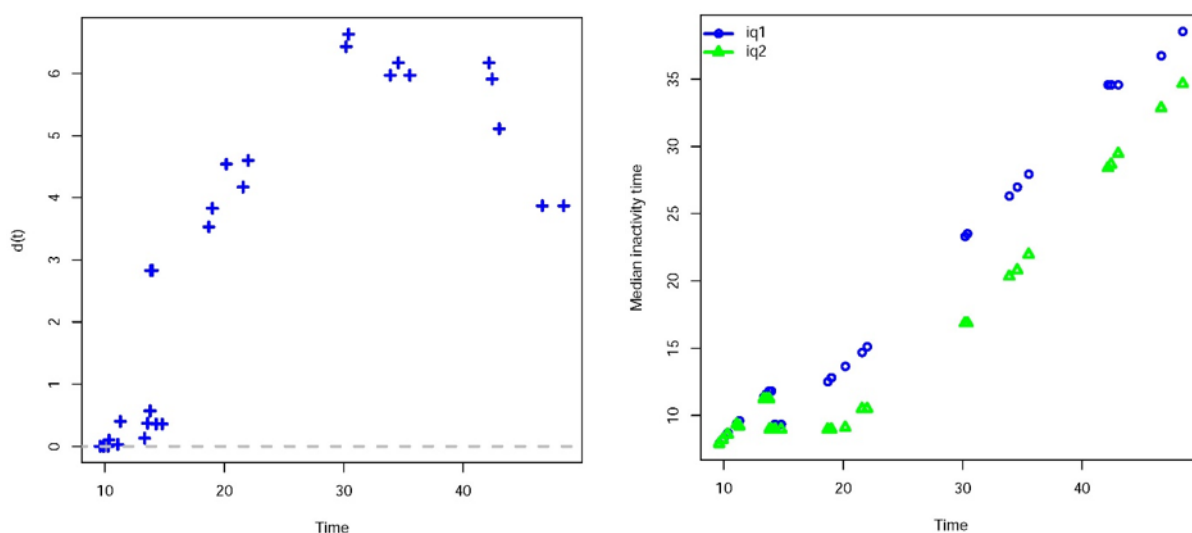


Figure 6. The left side plot shows the differences of bivariate increasing median inactivity times defined in (5). The plot indicates that the laser treatment causes a longer time to blindness. The right side plot draws identical bivariate median inactivity time functions for some identical values.

5. Conclusions

Assuming an increasing α -QIT function, I define a new estimator for this function. It is proven that the proposed estimator is consistent. It is asymptotically close to the usual estimator in the sense that the difference to the usual estimator converges to zero with high probability. It is also shown that the proposed estimator converges weakly to a Gaussian process when normalized. Interestingly, none of the asymptotic results assume that the true α -QIT function increases, which increases the applicability of the estimator in general. The simulation results show that the MSE for the proposed increasing estimator is smaller than that of the conventional estimator. When using the proposed estimator, it was found that the laser treatment causes a delay in glare.

Acknowledgements

The author thanks the two anonymous reviewers for their careful reading of our manuscript and their many insightful comments and suggestions.

This work was supported by Researchers Supporting Project number (RSP2024R392), King Saud University, Riyadh, Saudi Arabia.

Data availability statement

The data for this study is available in the “diabetic” dataset in the “survival” package in R.

Conflict of interest

The author declares that there is no conflict of interest.

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