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Research article

Dynamic multivariate quantile inactivity time and applications in investigation of a treatment effect

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Abstract: To investigate potentially dependent lifetimes, it is necessary to extend the α-quantile inactivity time to bivariate and multivariate frameworks. To extend this measure to a dynamic multivariate framework, all possible trajectories at time t are considered. The behavior of the extended α-quantile of inactivity time was investigated in relation to the corresponding multivariate hazard rate function. The α-quantile of the inactivity order is defined and discussed for the multivariate case. The difference between the two bivariate α-quantile functions of inactivity, which is an important measure for studying the effect of treatment on lifespan, was also investigated. This measure was used to analyze the effect of laser treatment on the delay of blindness. Two bootstrap approaches were implemented to construct confidence bounds for the difference measure.

Keywords: multivariate quantile inactivity time; reversed hazard rate; stochastic orders; bootstrap method

1. Introduction

For a random lifetime T, the conditional inactivity time is $T_t = t - T|T < t,\ t > 0$. In the reliability theory and survival analysis literature, some proper measures are defined based on the conditional inactivity time, e.g., the reversed hazard rate (RHR), the mean inactivity time (MIT) and the α-quantile inactivity time (α-QIT) functions. The later, which we will focus on it, gives the α quantile of the T_t, $q_\alpha(t) = Q_\alpha(T_t),\ t \geq 0$ and for a continuous random lifetime T, could be written as in the following.

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

where F represents the distribution function of T and $F^{-1}(p) = \inf\{x: F(x) = p\}$ is the inverse of F. Let T be an event time related to some identical objects, and at a time $t > 0$, it is revealed that some instances experienced the event previously. Then, we expect that $100(1-\alpha)\%$ $(100\alpha\%)$ of these instances experiencethe event before (after) time $t - q_\alpha(t)$. The α-QIT is a rival for the MIT and when the data are highly right-censored or skewed, it is preferred to MIT. Also, the MIT is infinite for some lifetime models and the α-QIT or its special case $\alpha = 0.5$, the median inactivity time function, is recommended. Refer to Schmittlein and Morrison [1] for a detailed discussion about preference of quantile based rather than moment based measures in survival analysis.

For a univariate random lifetime T with density function f and distribution function F, the RHR function is

$$r(t) = \frac{f(t)}{F(t)},\ \ t \geq 0,$$

and computes the instantaneous risk of failure at $(t-\delta, t]$ given that it has occured at $[0, t]$. It was introduced by Barlow et al. [2] and explored by many authors, e.g., Block et al. [3], Di Crescenzo [4], Chandra and Roy [5], Finkelstein [6], Kundu et al. [7], Li et al. [8], Burkschat and Torrado [9], Esna-Ashari et al. [10], and Contreras-Reyes et al. [11].

Since α-QIT does not depend on the density function, it is prefered to the RHR function when analyzing lifetime data. The α-QIT function was considered by Unnikrishnan and Vineshkumar [12]. They studied its basic properties and discussed how it can characterize the underlying distribution. Also, they investigated its connection with the RHR function as

$$q'_\alpha(t) = 1 - \frac{r(t)}{r(t - q_\alpha(t))}.$$

Mahdy [13] estimated α-QIT function applying simple empirical estimator of the distribution function. Shafaei [14] focused on the problem of characterizing a lifetime model by its α-QIT functions. Shafaei and Izadkhah [15] discussed attributes of parallel systems by the α-QIT concept. Balmert and Jeong [16] considered right censored data and provided a nonparametric inference on the median inactivity time function. A log-linear quantile regression model for inactivity time was the topic worked out by Balmert et al. [17]. Kayid [18] proposed an estimator of the α-QIT function for right censored data, applying the Kaplan-Meier survival estimator.

However, the univariate α-QIT function is proven to be quite useful, but in some situations, we encounter two or more dependent events, e.g., subsequent tumor recurrences, events related to pairs of organs like eyes, ears, hands, legs, and so on. In such cases, we need to extend the concepts to multivariate settings. In this way, Basu [19] and Johnson and Kotz [20] proposed multivariate hazard rate function as a gradient vector. Nair and Nair [21] proposed bivariate mean residual life vector. Shaked and Shanthikumar [22] proposed a dynamic version of the multivariate MRL measure. The α-quantile residual life function was extended to multivariate settings by Shafaei et al. [23] and Shafaei and Kayid [24]. Kayid [25] developed the multivariate MIT function. Also, Buono et al. [26] used the multivariate RHR concept to study inactivity times of systems. Recently, Kayid extended the α-QIT function for multivariate random lifetimes. They assumed a vector $\boldsymbol{T} = (T_1, T_2, \ldots, T_m)$ of lifetimes and considered the history to be of the form $T_1 < t_1, T_2 < t_2, \ldots, T_m < t_m$, succinctly $\boldsymbol{T} < \boldsymbol{t}$. They considered the following RHR gradient.

$$\tilde{r}(\boldsymbol{t}) = \left(\frac{\partial}{\partial t_1}, \frac{\partial}{\partial t_2}, \ldots, \frac{\partial}{\partial t_m}\right) \log F(\boldsymbol{t}),\ \ \boldsymbol{t} = (t_1, t_2, \ldots, t_m) \in R^{+m}.$$

It is clear from the meanning of the component i of vector $\tilde{r}(\boldsymbol{t})$ that

$$\tilde{r}_i(\boldsymbol{t}) = \lim_{\delta\to 0} P(t_i - \delta < T_i < t_i | \boldsymbol{T} < \boldsymbol{t}).$$

Also, they defined the α-QIT vector as in the following.

$$q_\alpha(\boldsymbol{t}) = (\tilde{q}_{\alpha,1}(\boldsymbol{t}), \tilde{q}_{\alpha,2}(\boldsymbol{t}), \dots, \tilde{q}_{\alpha,m}(\boldsymbol{t})),$$

in which

$$\tilde{q}_{\alpha,i}(\boldsymbol{t}) = \sup\{x: P(t_i - T_i > x | \boldsymbol{T} < \boldsymbol{t}) = \bar{\alpha}\}, \;\; \bar{\alpha} = 1 - \alpha, i = 1,2, \dots, m.$$

This form of extended α-QIT is not a dynamic measure. In this paper, we propose a dynamic multivariate α-QIT version. The proposed dynamic α-QIT functions consider all possible histories, which could be observed at a time $t > 0$ and could be quite useful from theoretical and applied points of view. Evaluating the effect of a treatment on some event times related to eyes, ears, hands, or legs may be the major goal of a research. Based on the proposed α-QIT function, we define a new measure for investigation the effect of a treatment on event times.

The rest of this article is organized as follows. In Section 2, we introduce the dynamic multivariate α-QIT functions and their basic properties and explore their connection with the dynamic RHR function. In Section 3, we extend the RHR and α-QIT orders to a dynamic multivariate context and examine their relationships. In Section 4, we discuss the difference measure d_α, which is useful for detecting the treatment effect. A simulation study was conducted to investigate the behavior of the d_α function. In Section 5, we analyze a dataset of patients with diabetic retinopathy at risk of blindness. Confidence limits for the d_α function are calculated using two bootstrap approaches. The final results are presented in Section 6.

2. Dynamic multivariate α-QIT

In the first step, assume a bivariate random lifetime $\boldsymbol{T} = (T_1, T_2)$. An observer that starts screening at any time $t > 0$ may observe one of three different histories. The observer may find that both elements experienced the event before t, i.e., $h_t = \{T_1 < t, T_2 < t\}$, the first element experienced the event before t and the second element experienced it at a time $t_2 \ge t$, $h^1_{t,t_2} = \{T_1 < t, T_2 = t_2\}$, or the second element experienced it before t and the first elemet experiences it at a time $t_1 \ge t$, $h^2_{t,t_1} = \{T_1 = t_1, T_2 < t\}$. In light of these histories, the following three functions define the α-QIT concept in the bivariate framework and in a dynamic manner.

$$q^*_{\alpha,i}(t) = Q_\alpha(t - T_i | h_t) = Q_\alpha(t - T_i | T_1 < t, T_2 < t), \;\; ,i = 1,2, \quad (1)$$

$$q^*_{\alpha,1}(t|t_2) = Q_\alpha(t - T_1 | h^1_{t,t_2}) = Q_\alpha(t - T_1 | T_1 < t, T_2 = t_2), \;\; t_2 \ge t,$$

and

$$q^*_{\alpha,2}(t|t_1) = Q_\alpha(t - T_2 | h^2_{t,t_1}) = Q_\alpha(t - T_2 | T_1 = t_1, T_2 < t), \;\; t_1 \ge t. \quad (2)$$

These relations could be simplified as in the following.

$$q^*_{\alpha,i}(t) = t - F_i^{-1}(\bar{\alpha}F(t,t);t), \quad ,i = 1,2,$$

$$q^*_{\alpha,1}(t|t_2) = t - F_1^{*-1}(\bar{\alpha}f_2(T_1 \le t, T_2 = t_2);t_2), \quad t_2 \ge t,$$

and

$$q^*_{\alpha,2}(t|t_1) = t - F_2^{*-1}(\bar{\alpha}f_1(T_1 = t_1, T_2 \le t);t_1), \quad t_1 \ge t,$$

where

$$F_1^{-1}(p;t) = \sup\{x: F(T_1 \le x, T_2 \le t) = p\},$$

$$F_2^{-1}(p;t) = \sup\{x: F(T_1 \le t, T_2 \le x) = p\},$$

$$F_1^{*-1}(p;t_2) = \sup\{x: f_2(T_1 \le x, T_2 = t_2) = p\},$$

$$F_2^{*-1}(p;t_1) = \sup\{x: f_1(T_1 = t_1, T_2 \le t) = p\},$$

$$f_2(T_1 \le t, T_2 = t_2) = \lim_{\delta \to 0^+} \frac{1}{\delta} P(T_1 \le t, t_2 - \delta < T_2 \le t_2),$$

and

$$f_1(T_1 = t_1, T_2 \le t) = \lim_{\delta \to 0^+} \frac{1}{\delta} P(\, t_1 - \delta < T_1 \le t_1, T_2 \le t).$$

The functions defined in (1) to (2) computes the quantile of inactivity time of components conditioning on the observed history from time $t > 0$. As stated, the α-QIT is defined based on different histories, which may be the case. For the next result, we need to review the dynamic bivariate RHR concept from Buono et al. [26], which is defined by the following relations.

$$r_i^*(t) = \lim_{\delta \to 0^+} \frac{1}{\delta} P(t - \delta < T_i \le t | T_1 \le t, T_2 \le t), \quad t \ge 0, i = 1,2,$$

$$r_1^*(t|t_2) = \lim_{\delta \to 0^+} \frac{1}{\delta} P(t - \delta < T_1 \le t | T_1 \le t, T_2 = t_2), \quad t_2 > t,$$

and

$$r_2^*(t|t_1) = \lim_{\delta \to 0^+} \frac{1}{\delta} P(t - \delta < T_2 \le t | T_1 = t_1, T_2 \le t), \quad t_2 > t.$$

Theorem 1. Assume that the $\tilde{q}_{\alpha,i}(t,t)$ has continuous differentiation with respect to their both coordinates. Then, we can write

$$\begin{aligned} 1 - \frac{d}{dt} q^*_{\alpha,1}(t) \quad &= \frac{\tilde{r}_1(t,t)}{\tilde{r}_1(t - \tilde{q}_{\alpha,1}(t,t), t)} \\ &+ \frac{f_2(T_1 \le t - q^*_{\alpha,1}(t|t), T_2 = t) - f_2(T_1 \le t - \tilde{q}_{\alpha,1}(t,t), T_2 = t)}{f_1(T_1 = t - \tilde{q}_{\alpha,1}(t,t), T_2 \le t)}, \end{aligned} \tag{3}$$

$$\begin{aligned} 1 - \frac{d}{dt} q^*_{\alpha,2}(t) \quad &= \frac{\tilde{r}_2(t,t)}{\tilde{r}_2(t, t - \tilde{q}_{\alpha,2}(t,t))} \\ &+ \frac{f_1(T_1 = t, T_2 \le t - q^*_{\alpha,2}(t|t)) - f_1(T_1 = t, T_2 \le t - \tilde{q}_{\alpha,2}(t,t))}{f_2(T_1 \le t, T_2 = t - \tilde{q}_{\alpha,2}(t,t))}, \end{aligned} \tag{4}$$

$$1-\frac{d}{dt}q^*_{\alpha,1}(t|t_2)=\frac{r^*_1(t|t_2)}{r^*_1(t-q^*_{\alpha,1}(t|t_2)|t_2)}, \tag{5}$$

and

$$1-\frac{d}{dt}q^*_{\alpha,2}(t|t_1)=\frac{r^*_2(t|t_1)}{r^*_2(t-q^*_{\alpha,2}(t|t_1)|t_1)}. \tag{6}$$

Proof. To prove (3), note that $q^*_{\alpha,1}(t)=\tilde{q}_{\alpha,1}(t,t)$, so we have

$$\frac{d}{dt}q^*_{\alpha,1}(t)=\frac{d}{dt_1}\tilde{q}_{\alpha,1}(t_1,t)|_{t_1=t}+\frac{d}{dt_2}\tilde{q}_{\alpha,1}(t,t_2)|_{t_2=t}. \tag{7}$$

Applying Theorem 2 of Kayid [18], the first derivative of (7) is

$$\frac{d}{dt_1}\tilde{q}_{\alpha,1}(t_1,t)|_{t_1=t}=1-\frac{\tilde{r}_1(t,t)}{\tilde{r}_1(t-\tilde{q}_{\alpha,1}(t,t),t)}. \tag{8}$$

It could be checked that $\tilde{q}_{\alpha,1}(t_1,t_2)$ verifies the following relation.

$$P(T_1\le t_1-\tilde{q}_{\alpha,1}(t_1,t_2),T_2\le t_2)=\bar{\alpha}P(T_1\le t_1,T_2\le t_2).$$

Thus, for the second derivative of (7), we differentiate both sides of the following relation in terms of t_2.

$$P(T_1\le t-\tilde{q}_{\alpha,1}(t,t_2),T_2\le t_2)=\bar{\alpha}P(T_1\le t,T_2\le t_2).$$

Then, we have

$$\begin{aligned}\frac{d}{dt_2}\tilde{q}_{\alpha,1}(t,t_2)|_{t_2=t}&=\frac{f_2(T_1\le t-\tilde{q}_{\alpha,1}(t,t),T_2=t)-\bar{\alpha}f_2(T_1\le t,T_2=t)}{f_1(T_1=t-\tilde{q}_{\alpha,1}(t,t),T_2\le t)}\\&=\frac{f_2(T_1\le t-\tilde{q}_{\alpha,1}(t,t),T_2=t)-f_2(T_1\le t-q^*_{\alpha,1}(t|t),T_2=t)}{f_1(T_1=t-\tilde{q}_{\alpha,1}(t,t),T_2\le t)}.\end{aligned} \tag{9}$$

Now, (3) is followed by (7), (8), and (9). The proof of (4) is completely similar. To prove (5), we check that $q^*_{\alpha,1}(t|t_2)$ satisfies the relation

$$f_2(T_1\le t-q^*_{\alpha,1}(t|t_2),T_2=t_2)=\bar{\alpha}f_2(T_1\le t,T_2=t_2),$$

and by differentiation from both sides of this relation in terms of t, it follows that

$$1-\frac{d}{dt}q^*_{\alpha,1}(t|t_2)=\frac{\bar{\alpha}f_{12}(T_1=t,T_2=t_2)}{f_{12}(T_1=t-q^*_{\alpha,1}(t|t_2),T_2=t_2)},$$

Then, the result follows by applying

$$f_{12}(T_1=t,T_2=t_2)=r^*_1(t|t_2)f_2(T_1\le t,T_2=t_2).$$

The proof of (6) is completely similar. □

The relations (3) to (6) show how the dynamic RHR and αQIT at bivariate context are related. For example (5) shows that if the RHR function $r^*_1(t|t_2)$ is increasing (decreasing) in t, then $q^*_{\alpha,1}(t|t_2)$ is decreasing (increasing). Similarly, if $r^*_2(t|t_1)$ is increasing (decreasing) in t, then $q^*_{\alpha,2}(t|t_1)$ is decreasing (increasing)

To extend the concept to more than two elements, assume a lifetime vector $\boldsymbol{T} = (T_1, T_2, \ldots, T_m)$ and let the history at time $t > 0$, denoted by $h_{t,I}$, where $I = \{i_1, i_2, \ldots, i_k\}$ and $t_I = (t_1, t_2, \ldots, t_k)$, $t_1 > t, \ldots, t_k > t$, determines that $T_i < t$ for every $i \in I'$ and $T_{i_1} = t_1, \ldots, T_{i_k} = t_k$. This means that the history at t determines that which elements have their events before or after t and if the event is after t, its time is known. Note that I can be an empty set or refer to all element indexes exluding just one. Notationally,

$$h_{t,I} = \{T_{I'} < t1, T_I = t_I\},$$

where 1 is a vector of 1's with propoer length. For simplicity we denote this history by h_t hereafter. For a fixed history h_t, the dynamic multivariate RHR function of a comonent $j \in I'$, is defined to be (see Buono et al. [26])

$$r_j^*(t|h_t) = \lim_{\delta \to 0^+} \frac{1}{\delta} P(t - \delta < T_j \leq t|h_t), \ \ t \geq 0.$$

We define the dynamic multivariate α-QIT function for index $j \in I'$ at time t by

$$q_{\alpha,j}^*(t|h_t) = Q_\alpha(t - T_j|h_t), \ \ t \geq 0,$$

which can be written as in the following.

$$\begin{aligned} q_{\alpha,j}^*(t|h_t) &= \inf\{y: P(t - T_j > y|T_{I'} < t1, T_I = t_I) = \bar{\alpha}\} \\ &= \inf\{y: P_I(T_j \leq t - y, T_{I'} \leq t1, T_I = t_I) = \bar{\alpha} P_I(T_{I'} \leq t1, T_I = t_I)\}, \ \ t \geq 0, \end{aligned}$$

where

$$P_I(T_{I'} \leq t1, T_I = t_I) = \lim_{\delta \to 0^+} \left(\prod_{i \in I} \frac{1}{\delta} \right) P(T_{I'} \leq t_{I'}, t_I - \delta < T_I \leq t_I).$$

It is trivial to extend Theorem 1 to multivariate cases to investigate the relation between the RHR and the multivariate α-QIT.

Example 1. Let T_1 and T_2 follow the power models with distribution functions $F_1(t_1) = t_1^a$, $a > 0$, $0 < t_1 < 1$ and $F_2(t_2) = t_2^b$, $b > 0$, $0 < t_2 < 1$. Using the comonotonocity copula (refer to Nelsen [27]), we have the bivariate model with the following distribution.

$$F(t_1, t_2) = t_1^a \wedge t_2^b, \ \ 0 < t_1 < 1, 0 < t_2 < 1.$$

Then, we have

$$q_{\alpha,1}^*(t) = \begin{cases} t\left(1 - \bar{\alpha}^{\frac{1}{a}}\right) & a \geq b, \\ t - \bar{\alpha}^{\frac{1}{a}} t^{\frac{b}{a}} & a < b, \end{cases}$$

which is increasing for $a < b$, and for $a > b$, it is decreasing and then increasing with a minimum at the following point:

$$t = \left(\frac{b}{a}\right)^{\frac{a}{a-b}} \bar{\alpha}^{\frac{1}{a-b}}.$$

3. Stochastic order in terms of α-QIT

It is said that T_1 is smaller than T_2 in RHR, with $T_1 \leq T_2$ in RHR, if $r_1(t) \leq r_2(t)$ where r_i

shows the RHR of T_i. It is justified by the sense that for a small random lifetime T, when we know that $T \leq t$, we expect small instantaneous risk of T near t. Also, $T_1 \leq T_2$ in MIT if $m_1(t) \geq m_2(t)$ and m_i is the MIT of T_i. Refer to Finkelstein [6] for a connection between RHR and MIT orders.

Similarly, let $q_{\alpha,i}(t)$ be the α-QIT function of T_i, then we say that $T_1 \leq T_2$ in α-QIT order, if $q_{\alpha,1}(t) \geq q_{\alpha,2}(t)$ for every t.

Theorem 2.

i. For two univariate random lifetimes T_1 and T_2, the RHR order implies the α-QIT order.

ii. Moreover, $T_1 \leq T_2$ in RHR if and only if $T_1 \leq T_2$ in α-QIT for every $\alpha \in (0,1)$.

In the reliability theory and survival analysis, various measures are applied for comparing two random lifetimes. Two univariate random lifetimes, T_1 and T_2, with reliability functions, $\bar{F}_1$ and $\bar{F}_2$, could be compared by their reliability functions in the sense that if $\bar{F}_1(t) \leq \bar{F}_2(t)$ for each t in the support, then we say that $T_1 \leq T_2$ in ordinary stochastic order. Refer to Shaked and Shantikumar [28] for detailed discussion about various stochastic orders and related results. The comparsion could be done by the hazard rate, RHR, the mean residual life, MIT, α-quantile residual life, α-QIT, or other proper measures.

In the multivariate context, a vector of lifetimes T_1 is said to be smaller than T_2 in stochastic order if $E\phi(T_1) \leq E\phi(T_2)$ for all nondecreasing functions $\phi: \mathbb{R}^{+m} \to \mathbb{R}^{+}$ which these expectations exist for them. To extend the RHR and α-QIT orders to multivariate context, we compare different histories of T_1 and T_2 in the sense that $\bar{h}_t^2$ of T_2 is said to be more severe than h_t^1 of T_1, $h_t^1 \leq \bar{h}_t^2$, if every component passed time t in h_t^1, it passed t in $\bar{h}_t^2$ too. Also, the common components in both histories, the event times of $\bar{h}_t^2$ are greater than the correspondings in h_t^1. Notationally,

$$h_t^1 = \{T_{I'}^1 < t1, T_I^1 = t_I^1\},$$

and

$$\bar{h}_t^2 = \{T_{(I \cup J)'}^2 < t1, T_I^2 = t_I^2, T_J^2 = t_J^2\},$$

and every element of t_I^2 is greater than the corresponding element of t_I^1, i.e., $t_I^1 \leq t_I^2$, and J could be an empty or non-empty set.

Definition 1. The multivariate random lifetime T_1 is said to be smaller than T_2 in RHR if for every $t > 0$, $k \in (I \cup J)'$ and $h_t^1 \leq \bar{h}_t^2$,

$$r_k^{*1}(t|h_t^1) \leq r_k^{*2}(t|\bar{h}_t^2).$$

Definition 2. The multivariate random lifetime T_1 is said to be smaller than T_2 in α-QIT if for every $t > 0$, $k \in (I \cup J)'$ and $h_t^1 \leq \bar{h}_t^2$,

$$q_{\alpha,k}^{*2}(t|\bar{h}_t^2) \leq q_{\alpha,k}^{*1}(t|h_t^1).$$

Suppose that T consists of positively dependent components in the sense that for a failed element k before t, the more severe history it belongs to, the larger lifetime T_k, and specially the smaller α quantile of $t - T_k$ conditional to its history it has. It is equivalent to say that $T \leq T$ in α-QIT. This means that the proposed multivariate order in α-QIT is not reflexive. In other words, $T \leq T$ in α-QIT may not be true generally. Similarly the multivariate RHR order is not reflexive, and $T \leq T$ in RHR may not be the true in general. In fact, $T \leq T$ in RHR implies positive dependency between components too, see Shaked and Shanthikumar [29,30] for similar discussions in the case of multivariate hazard rate function.

The following theorem shows that how the multivariate RHR and α-QIT orders are related.

Theorem 3. $T_1 \le T_2$ in RHR if and only if $T_1 \le T_2$ in α-QIT order for every $\alpha \in (0,1)$.

Proof. In the univariate case, it is straightforward to show that $T_1 \le T_2$ in RHR if and only if the fraction $\frac{F_1(t)}{F_2(t)}$ is decreasing in $t > 0$. Similarly, we conclude that $T_1 \le T_2$ in RHR if and only if the following expression decreases as z increases.

$$\frac{P_I(T_k^1 \le z, h_t^1)}{P_{I\cup J}(T_k^2 \le z, \bar{h}_t^2)}.$$

Assume that $T_1 \le T_2$ in RHR, then for any $t > 0$ and $0 < x < t$,

$$\frac{P_I(T_k^1 \le t - x, h_t^1)}{P_{I\cup J}(T_k^2 \le t - x, \bar{h}_t^2)} \ge \frac{P_I(h_t^1)}{P_{I\cup J}(\bar{h}_t^2)}. \tag{10}$$

On the other hand, by definition of multivariate α-QIT, we have

$$\frac{P_I(T_k^1 \le t - q_{\alpha,k}^{*1}(t|h_t^1), h_t^1)}{P_I(h_t^1)} = \frac{P_{I\cup J}(T_k^2 \le t - q_{\alpha,k}^{*2}(t|\bar{h}_t^2), \bar{h}_t^2)}{P_{I\cup J}(\bar{h}_t^2)} = \bar{\alpha},$$

which implies that

$$\frac{P_I(T_k^1 \le t - q_{\alpha,k}^{*1}(t|h_t^1), h_t^1)}{P_{I\cup J}(T_k^2 \le t - q_{\alpha,k}^{*2}(t|\bar{h}_t^2), \bar{h}_t^2)} = \frac{P_I(h_t^1)}{P_{I\cup J}(\bar{h}_t^2)}.$$

Taking $x = q_{\alpha,k}^{*1}(t|h_t^1)$ in (10), we conclude that

$$\frac{P_I(T_k^1 \le t - q_{\alpha,k}^{*1}(t|h_t^1), h_t^1)}{P_{I\cup J}(T_k^2 \le t - q_{\alpha,k}^{*1}(t|h_t^1), \bar{h}_t^2)} \ge \frac{P_I(h_t^1)}{P_{I\cup J}(\bar{h}_t^2)} = \frac{P_I(T_k^1 \le t - q_{\alpha,k}^{*1}(t|h_t^1), h_t^1)}{P_{I\cup J}(T_k^2 \le t - q_{\alpha,k}^{*2}(t|\bar{h}_t^2), \bar{h}_t^2)},$$

which shows that $P_{I\cup J}(T_k^2 \le t - q_{\alpha,k}^{*1}(t|h_t^1), \bar{h}_t^2) \le P_{I\cup J}(T_k^2 \le t - q_{\alpha,k}^{*2}(t|\bar{h}_t^2), \bar{h}_t^2)$ and implies that $q_{\alpha,k}^{*1}(t|h_t^1) \ge q_{\alpha,k}^{*2}(t|\bar{h}_t^2)$. This completes the "if" part. The "only if" part is completely similar to Theorem 1 of Kayid [25] and is ommited. □

4. Inference on a treatment effect

The difference

$$d_\alpha(t) = q_{\alpha,1}^*(t) - q_{\alpha,2}^*(t), \quad t \ge 0,$$

could be considered as a measure of difference between two dependent random lifetimes, T_1 and T_2, and could reveal the effect of a treatment. As a special ordering based on the α-QIT concept, we say that $T_1 \le T_2$ in identity QIT if $d_\alpha(t) \ge 0$, $t > 0$. This measure applied for investigating the effect of a laser treatment on the time to blindness of diabetic retinopathy patients. For a sample of bivariate lifetimes $\boldsymbol{T}_i = (T_{1i}, T_{2i})$, $i = 1,2,\dots,n$, we can estimate $q_{\alpha,1}^*(t)$ by

$$q_{\alpha,n,1}^*(t) = t - F_{1,n}^{-1}(\bar{\alpha}F(t,t); t), \quad t \ge 0,$$

where $F_{1,n}^{-1}(p;t) = \inf\{x: F(x,t) = p\}$ is the inverse of the empirical distribution function F_n with respect to the first element. Similarly, we can estimate $q_{\alpha,2}^*(t)$ by

$$q^*_{\alpha,n,2}(t) = t - F^{-1}_{2,n}(\bar{\alpha}F(t,t);t), \ \ t \geq 0.$$

Then, the difference $d_\alpha(t)$ is estiamted by the following relation.

$$d_{\alpha,n}(t) = q^*_{\alpha,n,1}(t) - q^*_{\alpha,n,2}(t), \ \ t \geq 0. \tag{11}$$

Due to the results about the estimator vector $(q^*_{\alpha,n,1}(t), q^*_{\alpha,n,2}(t))$, it is clear that $d_{\alpha,n}(t) \to d_\alpha(t)$ almost surely. The variance of $d_{\alpha,n}(t)$ could be written as in the following:

$$\mathrm{var}(d_{\alpha,n}(t)) = \frac{1}{n}(c_{11}^2\sigma_{11} + c_{22}^2\sigma_{22} - 2c_{11}c_{22}\sigma_{12}),$$

where

$$c_{11} = \frac{\partial}{\partial p}F_1^{-1}(p;t)|_{p=\bar{\alpha}F(t,t)},$$

$$c_{22} = \frac{\partial}{\partial p}F_2^{-1}(p;t)|_{p=\bar{\alpha}F(t,t)},$$

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

and

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

In practice, estimating this variance is a drawback since c_{11} and c_{22} are not simple. In the next section, we use resampling bootstrap methods for obtaining a confidence band of d_α.

4.1. Simulation study

In a simulation study, the consistency and efficiency of $d_{\alpha,n}$ is investigated. To implement the simulation study, we consider the bivariate well-known Gumbel and Pareto distributions with the following reliability functions, respectively,

$$\bar{F}(x_1,x_2) = \exp\{-x_1 - x_2 - \beta x_1x_2\}, \ \ \beta > 0, x_1 \geq 0, x_2 \geq 0,$$

and

$$\bar{F}(x_1,x_2) = (x_1 + x_2 - 1)^{-\lambda}, \ \ \lambda > 0, x_1 \geq 1, x_2 \geq 1.$$

Let (X_1, X_2) follows from Gumbel (Pareto), then we simulate r replicates of samples of size n from $(T_1 = X_1, T_2 = X_2 + c)$, $c > 0$. As reliability functions show, X_1 and X_2 are symmetric and we shift X_2 by c to make a difference to their related quantile functions. In each run, $r = 1000$ replicates of size $n = 25$ or 50 are generated. Then, for each sample, $d_{\alpha,n}(t)$ is computed at three points on the identity line (t_i, t_i), $i = 1,2,3$. These points are selected to be 0.3, 0.5 and 0.7 quantiles of the underlying distribution. Provided $d_{\alpha,n}$ values for r replicates, their bias (B) and mean squared error (MSE) are computed and reported in Tables 1 and 2. The results show small B and MSE values for all runs which indicates that $d_{\alpha,n}$ is a good estimator of d_α. Since the true values of $d_\alpha(t)$ are small values, the MSE values shows small values too. As n increases, MSE decreases which means that $d_{\alpha,n}$ is consistent for d_α. Biases are usually negative, which means that $d_{\alpha,n}$ tends to be smaller than the true value of d_α.

Table 1. Simulation results about $d_{0.5,n}$ for Gumbel model.

		Parameters			
		$\beta = 0.5, c = 0.1$		$\beta = 1.2, c = 0.3$	
n	point	B	MSE	B	MSE
25	t_1	-0.00898	8.07e-05	-0.01567	2.45e-04
	t_2	-0.01645	2.70e-04	-0.00768	5.90e-05
	t_3	-0.01455	2.11e-04	-0.00505	2.55e-05
50	t_1	0.00231	5.33e-06	-0.00760	5.79e-05
	t_2	0.00498	2.48e-05	-0.00537	2.89e-05
	t_3	0.00689	4.75e-05	-0.00750	5.62e-05
100	t_1	-0.00680	4.62e-05	-0.00234	5.49e-06
	t_2	-0.00561	3.15e-05	-0.00251	6.30e-06
	t_3	-0.00569	3.24e-05	-0.00147	2.18e-06
200	t_1	-0.00076	5.87e-07	0.00138	1.91e-06
	t_2	-0.00073	5.40e-07	0.00117	1.37e-06
	t_3	-0.00114	1.31e-06	0.00166	2.78e-06

Table 2. Simulation results about $d_{0.5,n}$ for Pareto model.

		Parameters			
		$\lambda = 1, c = 2$		$\lambda = 1.2, c = 5$	
n	point	B	MSE	B	MSE
25	t_1	-0.00608	3.70e-05	-0.01311	0.00017
	t_2	-0.01069	1.14e-04	-0.01824	0.00033
	t_3	-0.01473	2.17e-04	-0.01214	0.00014
50	t_1	-0.00917	8.41e-05	-0.00335	1.12e-05
	t_2	-0.00796	6.34e-05	-0.00118	1.40e-06
	t_3	-0.00671	4.50e-05	-0.00634	4.02e-05
100	t_1	-0.01136	1.29e-04	-0.00537	2.88e-05
	t_2	-0.00672	4.52e-05	-0.00468	2.19e-05
	t_3	-0.00400	1.60e-05	-0.00164	2.71e-06
200	t_1	-1.45e-03	2.12e-06	-0.00556	3.10e-05
	t_2	-4.70e-05	2.21e-09	-0.00354	1.25e-05
	t_3	-1.84e-04	3.39e-08	-0.00303	9.24e-06

5. Effect of laser treatment on blindness

In a study started in 1971, researchers were curious about the effect of laser photocoagulation on delaying the blindness in diabetic retinopathy patients. Every diabetic retinopathy patient with visual acuity of 20/100 or better in their both eyes were eligible to take part in the study. For each participant, one eye was randomly selected for as treatment (laser photocoagulation) and the other eye was considered to be the control eye. The time from treatment initiation to blindness was of interest and recorded. The blindness means visual acuity be smaller than 5/200 in two consecutive visits. The "survival" package of R software contains the complete data of this experiment. We extracted the event times to blindness of both eyes for juvenile patients (the age less than 20 years). Table 3, shows the data in which for each patient i, T_{1i} and T_{2i} give the observed time to blindness for control and treated eyes, respectively.

Table 3. For juvenile patients, T_{1i} and T_{2i} show times (in months) to blindness for control and treated eyes, respectively.

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			

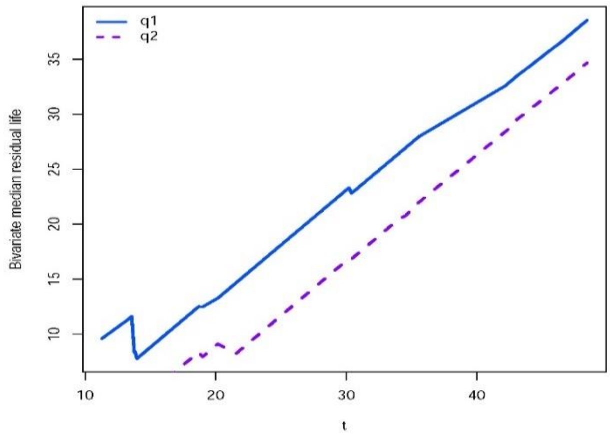

Figure 1. The bivariate median inactivity time functions $q^*_{n,0.5,1}$ and $q^*_{n,0.5,2}$.

Figure 1 draws $q^*_{0.5,n,1}$ and $q^*_{0.5,n,2}$ functions and shows that both functions are increasing. The difference $d_{0.5,n}$, defined by (11), is also plotted in Figure 2 by a solid blue line which reveals positive values. Positive values of $d_{0.5}$ means that T_1 is smaller than T_2 in identity QIT. Then, it concludes that the laser treatment causes delay to blindness. We apply two approaches to provide confidence bounds for $d_{0.5}$. In the first approach, each point t is considered separately. Assume that we want to compute a confidence interval for $d_\alpha(t_i)$. This approach consists of the following steps.

• Let B be the bootstrap resampling size. Generate B samples with replacement from the pairs (T_{1i}, T_{2i}), $i = 1,2,\ldots,n$, namely $(T_{1i}, T_{2i})_{*b}$, $i = 1,2,\ldots,n$, $b = 1,2\ldots,B$.

• Applying the sample b, compute the difference $d_{\alpha,n,b}(t_i)$, $b = 1,\ldots,B$.

• Use the computed differences to compute the confidence interval

$$\left(\bar{d}_{\alpha,n}(t_i) - s_d z_{1-\frac{p}{2}}, \bar{d}_{\alpha,n}(t_i) + s_d z_{1-\frac{p}{2}}\right),$$

where z_β represents the β quantile of the standard normal distribution, $\bar{d}_{\alpha,n}(t_i)$ is the mean of b values of $d_{\alpha,n,b}(t_i)$ and s_d is their standard deviation (the square root of their variance).

Applying the first approach with $B = 1000$, Figure 2 plots $d_{0.5,n}$, along with 95% bootstrap confidence intervals. Also, the mean of $d_{0.5,n}$ values are plotted for each selected t_i.

In the second approach, which is described in the following steps, a confidence bound for d_α function is derived.

• Fix the resampling size B and generate B samples with replacement from the pairs (T_{1i}, T_{2i}), $i = 1,2,\ldots,n$, namely $(T_{1i}, T_{2i})_{*b}$, $i = 1,2,\ldots,n$, $b = 1,2\ldots,B$.

• Select a set of points t_i, $i = 1,2,\ldots,k$, at which we are focused. Compute $d_{\alpha,n,b}(t)$, $b = 1,\ldots,B$ for all t_i. These values could be arranged to a $b \times k$ matrix and shows B curves, which all are computed at t_i points.

• For each $d_{\alpha,n,b}$ (row b of the matrix) compute the following score.

$$SD(d_{\alpha,n,b}) = \frac{1}{k}\sum_{j=1}^{k}(d_{\alpha,n,b}(t_j) - \bar{d}_{\alpha,n}(t_j)),$$

where

$$\bar{d}_{\alpha,n}(t_j) = \frac{1}{B}\sum_{b=1}^{B} d_{\alpha,n,b}(t_j).$$

Then, sort all $d_{\alpha,n,b}$ functions in terms of SD, from smallest to largest SD.

• Find largest $d_{\alpha,n,b}$, which atmost $100\frac{p}{2}\%$ of $d_{\alpha,n,b}$ functions lies before it in the sorted list as the lower bound of the confidence band of d_α. Also, find the smallest $d_{\alpha,n,b}$ where most $100\frac{\alpha}{2}\%$ of $d_{\alpha,n,b}$ functions lie after it in the sorted list as the upper bound of the confidence band.

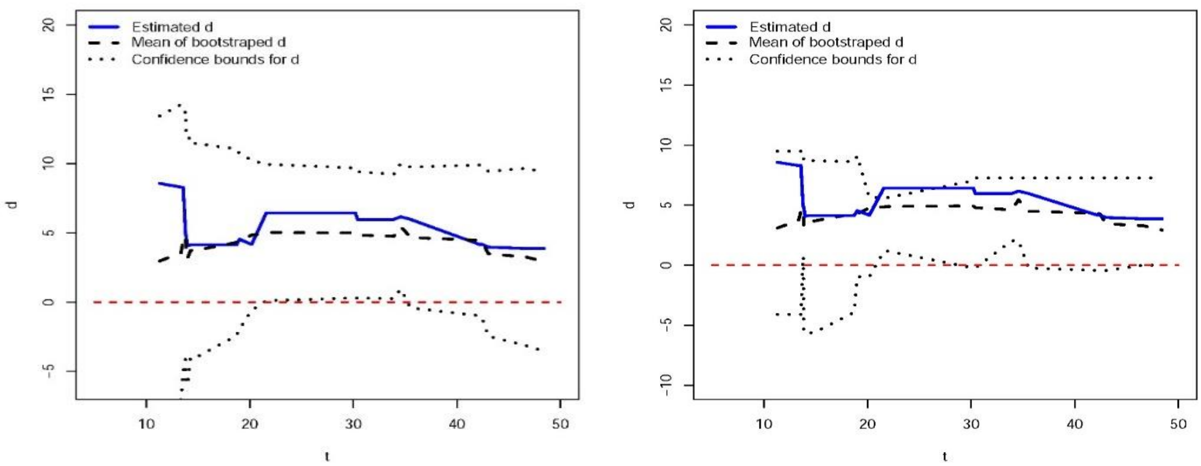

Figure 2. The estimated $d_{0.5,n}$, mean of the bootstraped samples and the 95% confidence bounds applying the first approach (left) and applying the second approach (right).

Figure 2, right side, shows the results of the bootstrap 95% confidence bounds with $B = 1000$. The estimated $d_{0.5,n}$ and mean of $d_{0.5,n,b}$ for all bootstraped samples are plotted too.

6. Conclusions

The α-QIT has been extended to a dynamic multivariate environment. The idea is to consider all possible trajectories at time $t > 0$. It was shown that the dynamic multivariate α-QIT and RHR are related. A new stochastic ordering based on dynamic multivariate α-QIT functions is presented and its relationship with the RHR ordering is demonstrated. It is proven that the proposed ordering is weaker than the corresponding RHR ordering. A difference measure was defined and investigated, which is useful for studying the effects of a treatment. The proposed difference measure was used to illustrate how to infer the effect of a treatment on life expectancy. One important aspect that may open a door for new ideas and future studies is to investigate the possible application of the proposed difference measure in the Rubin casual model.

Use of AI tools declaration

The author declares he has not used Artificial Intelligence (AI) tools in the creation of this article.

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Data availability statement

The data used to support the findings of this research is included in the article.

Conflict of Interest

There is no any conflict of interest.

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