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Original article

A semi-parametric estimator of the quantile residual life for heavily censored data

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ABSTRACT

The p-quantile residual life function summarizes the lifetime data in a useful and simple concept and in units of time. For uncensored data or when the upper tail of the observations is not censored, this function can be estimated by applying the well-known Kaplan-Meier survival estimator. But, when research terminates in heavy right-censored lifetime data which is the case of many biomedical and survival studies, the p-quantile residual life function is not estimable in this way. In this paper, we propose a novel semi-parametric estimator of the p-quantile residual life function in such cases. It combines the nonparametric Kaplan-Meier survival estimator with an approximated tail model motivated by the extreme value theory. The proposed estimator has been examined by a simulation study and applied to a lifetime data set in the sequel.

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1. Introduction

In many fields such as epidemiology, biology, medicine, and survival analysis, the researcher's interest is on time to event data, e.g., the survival time of a creature or time of tumor recurrence. The most familiar measure for induction and analyzing such data is the survival function, which for every time $t \geq 0$ computes the probability of the event to occur beyond time t. The p-quantile residual life (p-QRL) function, $0 < p < 1$, is another relevant measure in this context providing an intuitive meaning. For example, in the case $p = 0.5$, we have a median residual life which at time t captures the remaining time that half of the survived population at t will experience the event. This fact that unlike the survival function, the p-QRL is expressed in the time units by which the observations are measured makes its interpretation easier.

Besides, in reliability analysis, the p-QRL measure is quite useful for describing the lifetime of manufactured devices. For instance, it is very likely for some devices to fail in the early stages of their work. It is the case especially when the failure rate has a bathtub shape. Then we can consider a burn-in time t_0 that every produced device should pass before releasing to field operation. We can find such t_0 that maximizes the p-QRL function. For more details, we refer to Conboy et al. (2020).

Sometimes, time events may be invisible due to some censoring mechanism which cannot be naturally avoided. During the study, some items may be lost to follow-up before experiencing the event or reaching the end-time of the study. They are said to be right-censored. However, items passing the end-time of the study are referred to be Type I censored.

Given a right-censored data set, the survival function can be estimated using Kaplan-Meier (KM) estimator proposed by Kaplan and Meier (1958). The KM survival plot, which summarizes the possibly censored data graphically, has been vastly used in the aforementioned areas. On the other hand, taking account of right censoring, many authors focused on the problem of estimating the p-QRL function. Among them, we refer to Jeong et al. (2008), Franco-Pereira and de Uña-Álvarez (2013), Jeong and Fine (2013), Lin et al. (2015), Zhang et al. (2015), and Lin et al. (2016).

One drawback in right-censored data corresponds to the case that the upper tail and especially last observations are censored.

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In this case, the KM survival estimator does not vanish to zero in the support tail. Thus, the inverse of the survival function at small values will not be estimable by the KM estimator. Therefore, we cannot estimate the p-QRL function especially at large values (cf. Franco-Pereira and de Uña-Álvarez (2013)). The results of many types of research consist of highly censored data sets in which major of their large observations are censored. For such data sets, we may not estimate the p-QRL function, namely, qp(t), (for example, the median residual life) even at rather small ts. Therefore, our idea is to provide an approach to estimate the p-QRL function for all t values.

In this paper, we propose a new semi-parametric method for estimating the p-QRL function that overcomes the problem of dealing with high censored lifetimes. It applies the KM estimator of the survival function in a proper threshold time u, and the generalized Pareto distribution (GPD) as an approximated tail model (Coles (2001)). The approximation of the tail model is motivated by the results of the extreme value theory, refer to Castillo et al. (2005) and Coles (2001). Then, the uncensored observations in the tail (which we suppose to be greater than the threshold u) are used to provide the maximum likelihood estimation of the model parameters.

The paper has been organized as follows. Section 2 provides preliminaries and states the problem. In Section 3, the new estimator of the p-QRL function has been proposed. The attributes of this estimator are investigated through a simulation study in Section 4. In Section 5, the results of a research investigation of the effect of some treatments on the colon recurrence time are considered. Then the first quartile residual life (0.25-QRL) and the median residual life functions are estimated. Finally, a conclusion is drawn in Section 6.

2. Preliminaries: Non-parametric estimation of *p*-QRL

Let the random variable T which represents the lifetime of an object follows the survival function $S(t) = P(T > t)$. The p-QRL function is defined as

$$q_p(t) = S^{-1}(\overline{p}S(t)) - t, t \geq 0, \tag{1}$$

where $S^{-1}(\alpha) = \inf\{x : S(x) \geq \alpha\}$ is the inverse function of S and $\overline{p} = 1 - p$. Let T_i, $i = 1, 2, \cdots, n$ stand for n independent realizations of T and are right-censored by random variable C_i, i.e., T_i will be observable if $T_i \leq C_i$. Let $X_i = \min\{T_i, C_i\}$ and $\delta_i = I(T_i \leq C_i)$. We count the number of items failed up to or at time t by

$$\overline{N}(t) = \sum_{i=1}^{n} N_i(t),$$

where $N_i(t) = I(X_i \leq t, \delta_i = 1)$ and the number of items at risk at t by

$$\overline{Y}(t) = \sum_{i=1}^{n} Y_i(t),$$

where $Y_i(t) = I(X_i \geq t)$. Then the KM estimator of the survival function is given by

$$\widehat{S}(t) = \prod_{s \leq t} \left(1 - \frac{\Delta \overline{N}(s)}{\overline{Y}(s)}\right), t \geq 0,$$

where $\Delta \overline{N}(s) = \overline{N}(s) - \overline{N}(s-)$which represents the number of failures at time s. When $P(X_i \geq t) = \pi_i(t) = \pi(t)$ we have

$$E\left(\widehat{S}(t) - S(t)\right) \leq (1 - S(t))(1 - \pi(t))^n,$$

which shows that the KM estimator is asymptotically unbiased and has a sharper slope for earlier times and/or in the case of greater censoring variable. See Fleming and Harrington (1991) for more details. We can estimate the p-QRL function by

$$\widehat{q}_p(t) = \widehat{S}^{-1}\left(\overline{p}\widehat{S}(t)\right) - t, t \leq X^*, \tag{2}$$

where X^* be the largest uncensored observation and $\widehat{S}$ is the KM survival function estimator. It is asymptotically consistent and under proper normalization converges in distribution to a zero-mean normal process. For more information, refer to Franco-Pereira and de Uña-Álvarez (2013).

When the last observation has not been censored, the estimator (2) is well-defined for all $t \leq X^*$. Otherwise, it is not defined for all values $t > t^*$ where t^* stands for $\widehat{S}^{-1}\left(\frac{1}{\overline{p}}\widehat{S}(X^*)\right)$. When $t > t^*$, $\overline{p}\widehat{S}(t) < \widehat{S}(X^*)$ that is $\overline{p}\widehat{S}(t)$ falls below the computable range of the inverse of KM survival function. Fig. 1 explains the issue graphically.

3. Semi-parametric estimation of *p*-QRL

This section aims to propose a semi-parametric estimator of $q_p(t)$ for $t > t^*$. Note that if $0 < p_2 < p_0 < p_1 < 1$, then

$$S^{-1}(p_2) = u + S_u^{-1}(p_2/p_1), \tag{3}$$

where $S(u) = p_1$ and $S_u(t) = P(T - u > t \mid T > u)$ shows the survival of the remaining lifetime given survival to time u. Moreover, let u be properly given and p_2 be $\overline{p}S(t)$, then we estimate p_1 and p_2 by the KM estimate $\widehat{S}(u)$ and $\overline{p}\widehat{S}(t)$. So, to estimate $S^{-1}(p_2)$ it is sufficient to estimate the survival function S_u^{-1}. In the following, we will argue that when u is sufficiently large, S_u can be approximated by the GPD. This approximation is motivated by an asymptotic result concerning the weak convergence of the sample maximum to the generalized extreme value distribution (GEV). Therefore, our proposed estimation of $q_p(t)$ combines the nonparametric KM estimation of the survival function u with the maximum likelihood estimation of the GPD model.

Consider an arbitrary sequence of i.i.d. random variables T_1, T_2,... following the same distribution of T and let M_n be maximum of the first n elements of this sequence. Let there exist sequences $a_n > 0$ and b_n of constants such that the normalized random sequence $a_n(M_n - b_n)$ converges weakly to non-degenerate distribution G. Then, G accommodates GEV

$$G(x) = \exp\left\{-\left[1 + \xi\left(\frac{x - \mu}{\sigma}\right)\right]^{-\frac{1}{\xi}}\right\}, \tag{4}$$

with the support $\{x : 1 + \xi(\frac{x-\mu}{\sigma}) > 0\}$ where $\xi, \mu \in \mathbb{R}$ and $\sigma > 0$. This result ensures that for some sufficiently large but fixed n, the approximation

$$F_T^n\left(\frac{x}{a_n} + b_n\right) \approx G(x),$$

where G is given in (4) and F_T is the distribution function of the lifetime T. So F_T^n shows the distribution function of the largest order statistics of i.i.d. sample of lifetimes with size n. Note that b_n which centralizes growing maximum increases with n and makes the whole expression $\frac{x}{a_n} + b_n$ to be larger than some threshold u. By taking $t = \frac{x}{a_n} + b_n$ we have

$$F_T(t) \approx G^{\frac{1}{n}}(a_n(t - b_n)), t \geq u.$$

On the other hand, the max-stability property of the GEV model states that $G^{\frac{1}{n}}(a_n(t - b_n))$ equals with $G\left(a_n'\left(t - b_n'\right)\right)$. Thus, for $t \geq u$, $F_T(t)$ belongs to this family too, notationally, $F_T(t) = G(t)$, $t \geq u$. In the light of the preceding discussion, we can approximate $S_u(t)$ for some threshold u by:

$$S_u(t) = \frac{S(t+u)}{S(u)} \approx \frac{\overline{G}(t+u)}{\overline{G}(u)} = \frac{1 - \exp\left\{-\left[1 + \xi\left(\frac{u+t-\mu}{\sigma}\right)\right]^{-\frac{1}{\xi}}\right\}}{1 - \exp\left\{-\left[1 + \xi\left(\frac{x-\mu}{\sigma}\right)\right]^{-\frac{1}{\xi}}\right\}}.$$

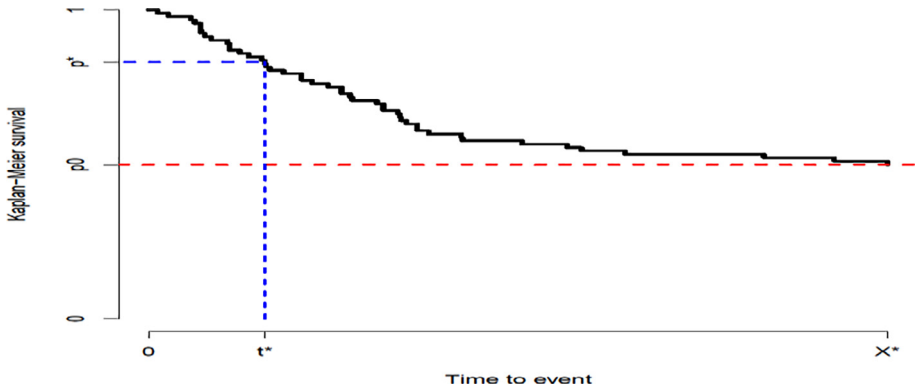

Fig. 1. This illustrative plot shows that when large observations have been censored the QRL function $q_p(t)$ is not estimable for $t > t^*$ by the inverse of the KM survival function. Here, p^* and p_0 equal to $\frac{1}{p}\widehat{S}(X^*)$ and $\widehat{S}(X^*)$ respectively.

Since u is sufficiently large, we have

$$\frac{1-\exp\left\{-\left[1+\xi\left(\frac{u+t-\mu}{\sigma}\right)\right]^{-\frac{1}{\xi}}\right\}}{1-\exp\left\{-\left[1+\xi\left(\frac{x-\mu}{\sigma}\right)\right]^{-\frac{1}{\xi}}\right\}} \approx \frac{\left[1+\xi\left(\frac{u+t-\mu}{\sigma}\right)\right]^{-\frac{1}{\xi}}}{\left[1+\xi\left(\frac{x-\mu}{\sigma}\right)\right]^{-\frac{1}{\xi}}}.$$

Then, by simplifying the right side of this approximation, it follows that

$$S_u(t) \approx \left[1+\frac{\xi t}{\sigma^*}\right]^{-\frac{1}{\xi}}, 1+\frac{\xi t}{\sigma^*} \geq 0, t \geq 0, \tag{5}$$

where $\sigma^* = \sigma + \xi(u-\mu)$. This relation shows that $S_u(t)$ approximately follows a GPD for sufficiently large u. Depending on the shape parameter ξ, three distinct cases can be described by this model.

- $\xi < 0$: light tail with finite upper bound $-\frac{\sigma_u}{\xi}$.
- $\xi = 0$: exponential tail.
- $\xi > 0$: heavy tail.

When $\xi > \frac{1}{s}$, the sth moment of GPD is infinite. So, when we are confident of finite mean and/or variance it may be useful to restrict the parameter space by $0 < \xi \leq 1$ and/or 0.5. However, such restriction is not recommended in a neat semi-parametric framework. For GDP(5), the inverse of the survival function equals with

$$S_u^{-1}(p) = \frac{\sigma^*}{\xi}\left(p^{-\xi}-1\right), 0 < p < 1. \tag{6}$$

To implement the method for censored data, let T_i, $C_i^{'}$ and T^* be true survival time, random right censoring time, and a constant time presenting end of the study, respectively. Taking $C_i = \min\left(C_i^{'}, T^*\right)$, we observe $X_i = \min(T_i, C_i)$ and $\delta_i = I(T_i \leq C_i)$. To estimate $q_p(t)$ for $t > t^*$, we suggest the following steps.

- At first we should select a proper value for u which is a trade-off between the accuracy of the tail model approximation and the share of the observations available for estimating the model parameters. Large values of u improve the approximation of the model but limit the volume of the observations for estimation of the parameters. Yet, there is not any standard approach for finding an optimum value for u. Nevertheless, it seems that the 80 percent quantile of the observed (uncensored) times be a proper value for threshold u. That is 20 percent of observed and uncensored events lie between u and T^* (see Alvarez-Iglesias et al. (2015) for a similar discussion).
- Construct new sample $x_i = t_i - u$ for all censored or uncensored observations t_i grater than u and let k denote the count of them. Applying this data set, we obtain the maximum likelihood estimation of the parameters of GPD model (5). The likelihood function is

$$L(\xi, \sigma^*) = \prod_{i=1}\left(\frac{1}{\sigma^*}\left(1+\frac{\xi x_i}{\sigma^*}\right)^{-\frac{1}{\xi}-1}\right)^{\delta_i}\prod_{i=1}^{k}\left(\left(1+\frac{\xi x_i}{\sigma^*}\right)^{-\frac{1}{\xi}}\right)^{1-\delta_i},$$

where δ_i equals 1 for uncensored items and zero for censored ones. We can find the maximum likelihood estimation $\widehat{\xi}$ and $\widehat{\sigma}^*$ by maximizing this expression numerically.

- Now, in the light of Relations (3) and (6), we propose the estimator

$$\widehat{q}_p(t) = u + \widehat{S}_u^{-1}\left(\frac{\overline{p}\widehat{S}(t)}{\widehat{S}(u)}\right) - t$$

$$= u + \frac{\widehat{\sigma}^*}{\widehat{\xi}}\left(\left(\frac{\overline{p}\widehat{S}(t)}{\widehat{S}(u)}\right)^{-\widehat{\xi}} - 1\right) - t, t^* \leq t \leq t_{(n)}, \tag{7}$$

where $\widehat{S}$ refers to KM estimator of S and $\widehat{\sigma}^*$ and $\widehat{\xi}$ show the maximum likelihood estimations.

Variance (bias) of this estimator is comprised of variation (bias) due u, and $\widehat{S}_u^{-1}\left(\overline{p}\widehat{S}(t)/\widehat{S}(u)\right)$ along with their covariance and seems to be more complicated than to be expressed by a closed expression. In the case of the heavy tail of the true lifetime model which causes that $\widehat{\xi} > 0$, it's variance increases with t. Fortunately, we can use the bootstrap method to estimate its bias and variance and in turn approximate confidence intervals. However, simulation studies heuristically imply that bias and variance reduce strongly by sample size.

4. Simulation study

To design a simulation framework, we consider gamma, lognormal, and Weibull models along with four censoring schemas. Both right censoring and Type I censoring have been taken in account. Once the model and the censoring scheme determined, $r = 100$ replicates of samples of sizes $n = 500$ and 1000 have been drawn and censored. Then for two values $p = 0.5$ (corresponding to the median residual life function) and $p = 0.75$ the proposed esti-

mator $\widehat{q}_p(t)$ has been computed by each of r replicates. For each replicates the bias is computed by the difference $\widehat{q}_p(t) - q_p(t)$. We report their mean and standard deviation as *bias* and *sd* in Tables 1–3. In addition, $M\widehat{q}_p$ that shows the mean of the estimation values $\widehat{q}_p(t)$ has been entered in the tables.

To provide censored random samples, some proper combinations of right censoring and Type I censoring have been selected. Let α_1 and α_2 represent the proportions of Type I censoring and random right censoring respectively. The simulation process starts withdrawing a sample of size n from the true model that is the distribution of T following survival function S. We take the distribution of the right censoring random variable C to be uniform on the interval $(0, M)$. Moreover, according to type I censoring, the observations will be censored if they are greater than T^*. For fixed values α_1 and α_2, we should compute M and T^* through the equations $P(C < \min\{T, T^*\}) = \alpha_2$ and $P(\{T^* < T < C\} \cup \{T^* < C < T\}) = \alpha_1$. It is straightforward to show that these equations can be simplified to the system equations

$$\begin{cases} S(T^*)(M - T^*) = M\alpha_1, \\ \int_0^{T^*} S(x)dx = M\alpha_2, \end{cases}$$

which can be solved in terms of M and T^* by standard numerical methods. Then, we can pursue the procedure according to the bellow steps.

- Generate a random sample $t_1, t_2, \cdots, t_n$ from the true model with the survival function S.
- Generate a random sample $c_1, c_2, \cdots, c_n$ of uniform $(0, M)$ as random censoring times.
- Compute the observable data $x_i = \min\{t_i, c_i, T^*\}$ and $\delta_i = I(t_i \le c_i, t_i \le T^*)$ for $i = 1, 2, \cdots, n$.
- Repeat steps 1 to 3 r times.
- Let t_{0j} be the maximum observed (uncensored) lifetime of the sample in the jth replication, $j = 1, 2, \cdots, r$. Then, take t_0 to be the mean of t_{0j}. Of course, t_0 is suitable for applying in the simulation, since it is expected that $\widehat{S}^{-1}\left(\overline{p}\widehat{S}(t_0)\right)$ will not be computed by the KM estimator $\widehat{S}$.
- For each replication, compute $\widehat{q}_p(t_0)$ introduced by (7).

Results of simulations have been gathered in Tables 1–3. All tables agree on the fact that the bias and sd values show a strong reduction from $p = 0.75$ to 0.5.

5. Applications

Moertel et al (1995) reported a data set related to one trial for investigation of the effectiveness of Fluorouracil (5-FU) and Levamisole (Lev) in reducing the recurrence rate of stage B/C colon cancer. The trial involves three treatments for Observation (Obs), Levamisole (Lev), and Levamisole plus 5-FU (Lev + 5-FU). Under right censoring, for every person, both events of recurrence of cancer and death have been recorded. We focus on the recurrence times which near 50 percent of them have been censored. For each of the three treatments and the overall data, the KM survival function has been drawn in Fig. 2, which reveals high censoring rates.

We are interested in the estimation of the first QRL function and the median residual life function respectively corresponding to $p = 0.25$ and 0.5. As before, let t^* stand for the minimum of t values where the QRL can not be computed directly by inverting the KM

Table 1
Simulation results for the log-normal (1, 0.5).

n	p		(0.1,0.3)	(0.2, 0.2)	(0.2, 0.1)	(0.1, 0.05)
500		$M_{\widehat{q}_p}$	2.5821	3.7561	2.6533	2.3134
	0.75	bias	0.5342	1.7089	0.6085	0.2380
		sd	1.9196	4.2724	2.4804	2.6121
		$M_{\widehat{q}_p}$	1.2076	1.2915	1.1338	1.1159
	0.50	bias	0.1893	0.2644	0.1124	0.0619
		sd	0.5883	0.9855	0.5585	0.3956
1000		$M_{\widehat{q}_p}$	2.2879	2.2565	2.3828	2.0106
	0.75	bias	0.2397	0.2049	0.3381	−0.0652
		sd	1.4182	1.4428	2.0186	0.7124
		$M_{\widehat{q}_p}$	1.0744	1.1491	1.0932	0.9911
	0.50	bias	0.0562	0.0222	0.0718	−0.0337
		sd	0.3949	0.4405	0.3540	0.2237

Table 2
Simulation results for the gamma (0.9, 2).

n	p		(0.1, 0.3)	(0.2, 0.2)	(0.2, 0.1)	(0.1, 0.05)
500		$M_{\widehat{q}_p}$	0.5533	0.5014	0.4852	0.4907
	0.75	bias	0.1305	0.0832	0.0631	0.0586
		sd	0.3290	0.3003	0.2453	0.2078
		$M_{\widehat{q}_p}$	0.2460	0.2494	0.2369	0.2276
	0.50	bias	0.0364	0.0426	0.0276	0.0126
		sd	0.1427	0.1129	0.0778	0.0809
1000		$M_{\widehat{q}_p}$	0.5003	0.4807	0.4664	0.4528
	0.75	bias	0.0773	0.0624	0.0438	0.0204
		sd	0.2793	0.1903	0.1600	0.1349
		$M_{\widehat{q}_p}$	0.2212	0.2128	0.2197	0.2334
	0.50	bias	0.0114	0.0059	0.0103	0.0183
		sd	0.0657	0.0609	0.0604	0.0608

Table 3
Simulation results for the Weibull (1.2, 3).

n	p		(0.1,0.3)	(0.2,0.2)	(0.2,0.1)	(0.1,0.05)
500		$M_{\widehat{q_p}}$	5.3993	5.9644	4.5763	3.3337
	0.75	bias	2.3480	2.8360	1.5028	0.4228
		sd	7.5687	8.3373	5.9047	2.0737
		$M_{\widehat{q_p}}$	1.8733	2.0957	1.8772	1.5307
	0.50	bias	0.3073	0.4824	0.2973	0.0435
		sd	1.1001	1.1999	0.9687	0.5527
1000		$M_{\widehat{q_p}}$	3.6093	3.9250	3.8343	3.1620
	0.75	bias	0.5612	0.7976	0.7619	0.2489
		sd	2.4968	3.4923	2.9527	1.0536
		$M_{\widehat{q_p}}$	1.7904	1.9712	1.6409	1.5194
	0.50	bias	0.2255	0.3588	0.0618	0.0333
		sd	0.6970	0.9163	0.5111	0.3830

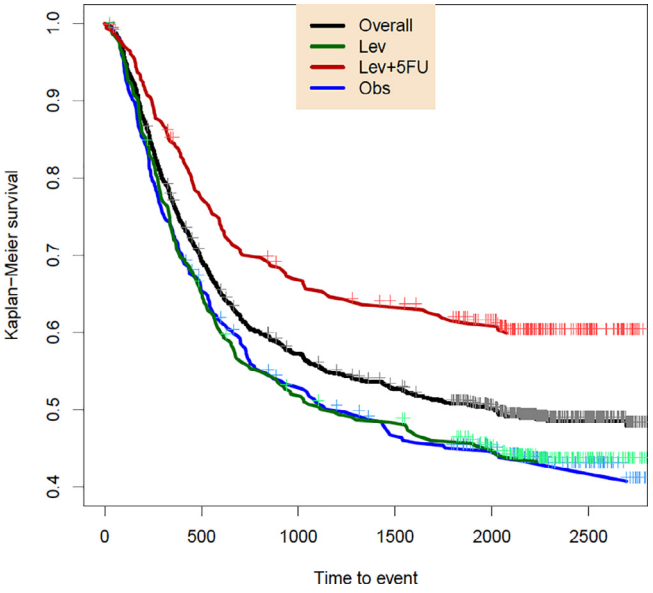

Fig. 2. The KM survival plot for three treatments and the overall data. Every censored item is included by a+.

survival function. Values of t^* computed for these data sets have been gathered in Table 4.

The first quartile residual life function and the median residual life function have been plotted in Figs. 3 and 4, respectively. For $t < t^*$ these functions have been estimated by (2) and have been plotted by a thinner line.

These figures distinguish larger median residual life and first quartile residual life functions for Lev + 5-FU treatment, which are even noticeably above the QRL functions related to overall data. However, for two treatments Obs and Lev, both of these QRL functions are comparable and lie below the QRL functions of the overall group.

6. Conclusion

The p-quantile residual life function summarizes the lifetime data in a useful and simple concept and in units of time. For uncen-

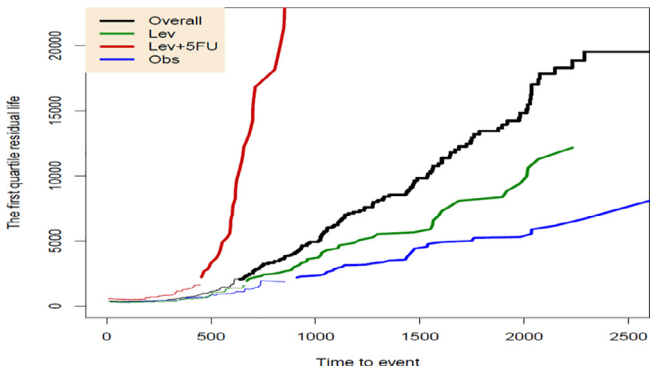

Fig. 3. The first quartile residual life function for three treatments and the overall data.

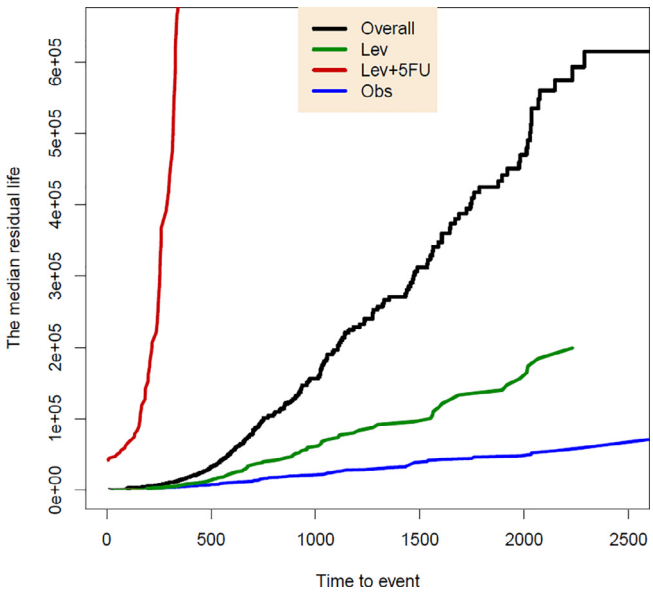

Fig. 4. The median residual life function for three treatments and the overall data.

Table 4
Values of t^*.

		Obs	Lev	Lev + 5-FU	Overall
p	0.25	871	668	449	636
	0.5	230	191	0	99

sored data or when the upper tails of the observations are not censored, this function can be estimated by applying the well-known Kaplan-Meier survival estimator. However, when research terminates in heavy right-censored lifetime data, which is the case of many biomedical and survival studies, the p-quantile residual life function is not estimable in this way. In the current investigation, we proposed a novel semi-parametric estimator of the p-quantile residual life function in such cases. The proposed estimator has been examined by a simulation study and applied to a real lifetime data set in the sequel.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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