

Empirical Likelihood Ratio Test for Mean and Median Residual Lifetime

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Abstract

Prompted by a recent paper in Biometrics, we point out here that the testing involving mean or median residual life times with censored data can be obtained by an easy application of the general empirical likelihood ratio test (Owen 2001). This approach has several advantages: (1) there is no need to estimate the variance/covariance at all, which may become prohibitively complicated for other procedures that requires the estimation of such. (2) When inverting the tests to obtain confidence regions/intervals, this procedure inherits all the good properties of a likelihood ratio test. (3) Free software implementing the test is readily available.

KEY WORDS: Censored data; Chi square distribution; Wilks theorem.

1 Introduction

Jeong, Jung and Costantino in a recent Biometrics paper (2008) proposed a score type test for the median residual life time. They argue that “the need for such estimates is becoming more critical in breast cancer as long-term courses of secondary therapies are now being considered for patients who remain recurrence free after several years of initial treatment”.

They noted that the score test proposed is easier to use since it does not involve nonparametric estimation of the density of the unknown failure time distribution, like in the Berger et al. (1988). But it still involve the estimation of the variance of score. We point out that an even more simpler test is available via the empirical likelihood ratio test for the censored data. It do not require the estimation of any variance at all. This empirical likelihood ratio test can also handle more general types of censored data.

There are also a couple of recent papers dealing with the mean residual life time by Qin and Zhao (2007) Zhao and Qin (2006). They used an estimating function that involves

nuisance parameter. The empirical likelihood they proposed do not have a regular chi squared distribution under null hypothesis, while ours does.

2 Median Residual Life

By definition the median residual lifetime at age x is the number θ that solve the following

$$\frac{1 - F(x + \theta)}{1 - F(x)} = 0.5.$$

Other quantiles of the residual life distribution can be defined similarly. The test developed below can be easily modified to test a quantile. But we shall focus on the median here.

Let us denote the median residual lifetime at age x as $Med(x)$. Clearly θ is also the solution to

$$1 - F(x + \theta) = 0.5[1 - F(x)] .$$

After easy calculation we see that θ is the solution to

$$0.5 = F(x + \theta) - 0.5F(x) .$$

Define a function $g_\theta(t)$ as

$$g_\theta(t) = I_{[t \leq (x+\theta)]} - 0.5I_{[t \leq x]} \tag{1}$$

then the hypothesis $H_0 : Med(x) = \theta$ can be tested by testing

$$H_0 : \int_0^\infty g_\theta(t) dF(t) = 0.5 .$$

This, in turn, can be accomplished by an empirical likelihood ratio test.

The empirical likelihood ratio tests, first proposed by Thomas and Grunkemeier (1975) and Owen (1988), attracted many attentions since then. The empirical likelihood methods developed in the last 20 years has emerged as a very competitive nonparametric test procedure for quite general settings, including the test of a parameter defined by $\int g(t)dF(t)$ with censored data. It parallels the theory of the parametric likelihood ratio test, except the parametric likelihood is replaced by a nonparametric one – the empirical likelihood. The

book of Owen (2001) summarized many of the results (Chapter 6 in particular). Other relevant papers include Murphy and van der Vaart (1997) Pan and Zhou (2001).

A free software implementation of the empirical likelihood ratio test with censored data is available as function `e1.cen.EM2()` inside the R (R Development Core Team 2008) contributed package `emplik`.

Due to the discrete nature of the quantile function, some have advocated for a smoothed quantile empirical likelihood ratio test (Chen and Hall 2001). One way of smoothing the residual median is to replace the indicator functions in (1) by a smoothed version. A 90% confidence interval can be obtained as those θ values that results a p-value larger then 0.1, etc.

Remark 1: Since `e1.cen.EM2()` can handle doubly censored data as well, the same test procedure outlined above can test median residual lifetime with doubly censored data. Left truncated and right censored data can be treated similarly. But we will have to use another function `emplikH2.test()` inside `emplik` package and reformulate the hypothesis in terms of cumulative hazard.

Remark 2: Testing the equality (or the ratio) of two median residual times from two samples (or from one sample at two different ages) can be carried out similarly as outlined in the Jeong, Jung and Costantino (2008).

Case I: If we are to test $H_0 : Med_1(x_1)/Med_2(x_2) = c$, where $Med_i(x_i)$ denote the median residual time from sample i at age x_i , we shall first obtain two empirical likelihood ratio statistics for testing the two auxiliary hypothesis: $H_{01} : Med_1(x_1) = c\theta$ and $H_{02} : Med_2(x_2) = \theta$. Let us denote the two resulting test statistic by $W_1(\theta)$ and $W_2(\theta)$. The test for the original hypothesis $H_0 : Med_1(x_1)/Med_2(x_2) = c$, can then be obtained by using the test statistic $W = \inf_{\theta}\{W_1(\theta) + W_2(\theta)\}$, which will have a chi square distribution, degree of freedom 1, under H_0 .

Case II: If we are to test the ratio of two median residual times from the same sample but at two different ages x_1 and x_2 , i.e. $H_0 : Med(x_1)/Med(x_2) = c$, we may proceed

similarly as above, except we need to replace the two auxiliary hypothesis by $H_{00} : Med(x_2) = \theta, Med(x_1) = c\theta$. Empirical likelihood ratio test for this type of hypothesis is also available via the `e1.cen.EM2()` function. Denote the Wilks likelihood ratio statistic for H_{00} by $W_3(\theta)$. Then the test of $H_0 : Med(x_1)/Med(x_2) = c$ can be obtained by using $W = \inf_{\theta} W_3(\theta)$. This statistic again will have a chi square distribution, degree of freedom 1, under H_0 .

Remark 3: For the score test, this last case would be much more involved, since the covariance between $Med(x_1)$ and $Med(x_2)$ needs to be estimated. This is even more so when we are dealing with the mean residual time.

Remark 4: The advantage of a likelihood ratio based confidence region, i.e. range respecting and transform invariant, is inherited in the empirical likelihood ratio inference.

3 Mean Residual Life Time

The mean residual time of random variable T , at a given age x , is defined as

$$M(x) = E(T|T \geq x) - x = \frac{\int_x^{\infty} s dF(s)}{1 - F(x)} - x = \frac{\int_x^{\infty} 1 - F(s) ds}{1 - F(x)}.$$

For a given x value, we first notice that the hypothesis

$$H_0 : M(x) = \mu$$

is equivalent to the following hypothesis

$$H_0 : \frac{\int_x^{\infty} s dF(s)}{1 - F(x)} = (x + \mu),$$

and also equivalent to

$$H_0 : \int_x^{\infty} s dF(s) = [1 - F(x)](x + \mu).$$

This in turn can be written as (since $\int_x^{\infty} dF(s) = 1 - F(x)$)

$$H_0 : \int_x^{\infty} [s - (x + \mu)] dF(s) = 0.$$

Now this test can be done easily by a one sample empirical likelihood test (Owen 2001) for censored data, with a hypothesis of mean type. Software is readily available via the

`el.cen.EM2()` function from the R contributed package `emplik`. We first define the function

$g(s) = [s - (x + \mu)]I_{[s > x]}$ in R code as

```
mygfun <- function(s, age, muage) {as.numeric(s >= age)*(s - (age+muage))}
```

and then to test a hypothesis like $M(50) = 25$ we do

```
el.cen.EM2(x=times, d=status, fun=mygfun, mu=0, age=50, muage=25)
```

TWO GENERALIZATIONS: testing the ratio of two mean residual times from two independent samples (or from the same sample but at two different ages) can be done following the same procedure outlined in the end of previous section in remark 2.

4 Examples

We take the data set `cancer` from the R package `survival`. It contains 228 survival times of lung cancer patients with 63 right censored observations.

We shall find the 90% confidence interval for the mean and median residual life at one year (365.25 days) i.e. confidence interval for $M(365.25)$ and $Med(365.25)$.

When inverting the empirical likelihood ratio tests to get the confidence intervals, it is often very helpful to know where is the ‘center’ of that confidence interval, i.e. when testing for this value, you should get a P-value of one. For the empirical likelihood ratio tests, the ‘center’ is given by the nonparametric maximum likelihood estimator based on the Kaplan-Meier estimator.

After loading the package `emplik` and `survival` [package `survival` is only needed here to supply the data `cancer`. Version 0.9.4 of `emplik` contain the estimation `MMRtime()`, while the testing below is available in earlier versions of `emplik`], estimation can be easily obtained as in

```
> time <- cancer$time
> status <- cancer$status-1
> MMRtime(x=time, d=status, age=365.25)
$MeanResidual
[1] 275.9997

$MedianResidual
[1] 258.75
```

The following are R results when testing the mean/median residual times. For confidence interval of mean residual time we do

```

> mygfun <- function(s, age, muage) {as.numeric(s >= age)*(s-(age+muage))}
> el.cen.EM2(x=time, d=status, fun=mygfun, mu=0, age=365.25, muage=234.49389)$Pval
[1] 0.1000000
> el.cen.EM2(x=time, d=status, fun=mygfun, mu=0, age=365.25, muage=323.1998)$Pval
[1] 0.1

```

therefore the 90% confidence interval for mean residual time is [234.49389, 323.1998]. For the testing of median residual time, we first need to code the g_θ function defined in (1) and then use `el.cen.EM2` to test.

```

> mygfun2 <- function(s, age, Mdage) {as.numeric(s<=(age+Mdage))-0.5*as.numeric(s<=age)}
> el.cen.EM2(x=time, d=status, fun=mygfun2, mu=0.5, age=365.25, Mdage=184.75)$Pval
[1] 0.1135797
> el.cen.EM2(x=time, d=status, fun=mygfun2, mu=0.5, age=365.25, Mdage=321.7499)$Pval
[1] 0.1192006

```

Therefore the 90% confidence interval for the median residual time is [184.75, 321.7499]. Notice due to the discrete nature of the quantile function, we do not get exactly a P-value of 0.1. Smoothing the indicator function in (1) would solve this problem. Another benefit of smoothing is (potentially) a more accurate P-value, as argued by Chen and Hall (1991).

If we use the linear smooth function [bandwidth 1/20], we get 90% confidence interval [184.7416765, 321.71153607].

If we use the cubic smoother function [with bandwidth 1/20] we get the 90% confidence interval [184.77410217, 321.73115592]. These intervals are practically the same as before, but you get exact P-value of 0.1.

The empirical likelihood ratio test of median residual time can also be done in terms of hazard, we also leave this to reader.

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REFERENCES

- Berger, R. L., Boos, D. D., and Guess, F. M. (1988). Tests and confidence sets for comparing two mean residual life functions. *Biometrics* 44, 103115.
- Chen, S.X. and Hall, P. (1991). Smoothed empirical likelihood confidence-intervals for quantiles. *Ann. Statist.* **21** 11661181.

- Guess, F. and Park, D.H. (1991) Nonparametric confidence bounds, using censored data, on the mean residual life. *IEEE Transactions on Reliability* **40**, 78-80.
- Jeong, Jong-Hyeon, Jung, Sin-Ho and Costantino, Joseph P. (2008) Nonparametric Inference on Median Residual Life Function. *Biometrics* **64**, 157-163. March 2008
- Murphy, S., and van der Vaart, A. (1997), Semi-Parametric Likelihood Ratio Inference. *Annals of Statistics* **25**, 1471–1509.
- Owen, A. (1988), Empirical Likelihood Ratio Confidence Intervals for a Single Functional. *Biometrika*, **75**, 237–249.
- Owen, A. (2001). *Empirical Likelihood*. Chapman & Hall, London.
- Qin, G. and Zhao, Y. (2007) Empirical likelihood inference for the mean residual life under random censorship. *Statistics and Probability Letters*, **77**, 549-557.
- Thomas, D. R., and Grunkemeier, G. L. (1975), “Confidence Interval Estimation of Survival Probabilities for Censored Data,”
- R Development Core Team (2008). *R: A Language and Environment for Statistical Computing*. R Foundation for Statistical Computing, Vienna, Austria. <http://www.R-project.org>
- Zhao, Y. and Qin, G. (2006) Inference for the Mean Residual Life Function via Empirical Likelihood. *Communications in Statistics: Theory and Methods*, **35**, Number 6, 1025-1036.