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Assessing Treatment Methods via Testing Exponential Property for Clinical Data

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Abstract: This paper tries to pay the attention of researchers in the medical field to the use of the statistical tests as good tools for assessing the efficacy of the treatment methods, especially the non- parametric statistical tests. A statistical test is designed to judge the behavior of clinical data, whether these data have exponential property or not. Laplace transform technique and aging classes concept of life distributions are used to design the proposed test. Knowing the behavior of clinical data helps statisticians and researchers to make the right decision about the problem under study. To guarantee the right assessment using the proposed statistical test, Its efficiency and power are calculated and compared with other tests. The proposed statistical test is applied to real clinical data. Finally, concluding remarks are formulated to summarize the main results.

Keywords: Clinical Data Analysis, Assessing Treatment Methods, Testing Hypotheses, Non-Parametric Statistical Tests, Monte Carlo Simulation.

1 Introduction

A person is attacked by a virus and this virus settles in some cells for a time interval $(0,x)$. In this period the person carries the disease and suffers from it. At time x, a treatment method is applied to resist the attacked virus for a period y as shown in Figure 1. Then, at time $x+y$, we need to assess if the used treatment has a positive effect on this person or not. To answer this question, a random sample must be chosen from patients who suffer from the same disease and a statistical test also must be applied to make a decision about the efficacy of the proposed treatment method. Often, the statistical tests are prepared based on the classes of life distributions, where each class contains lifetime probability distributions that have common features and satisfy the mathematical definition of this class. Statisticians defined a lot of classes such as increasing failure rate and new better than used (NBU).

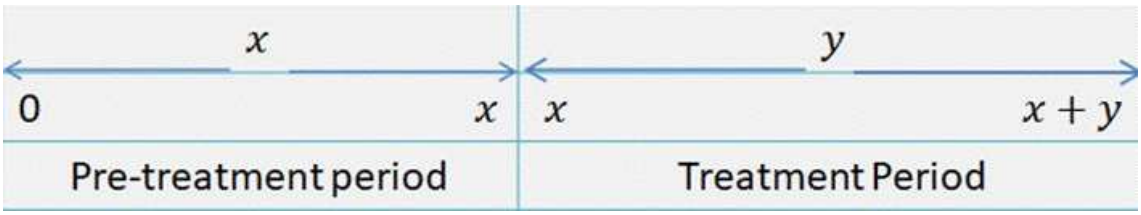

Fig. 1: Treatment period scheme

The basis behind the definition of these classes is to analyse the failure of engineering systems. While, in this paper, the proposed test is prepared to test the Exponential (new is as good as used) against the NBU property depending on a random sample of patients suffering from a certain disease. If the selected sample has exponential property, then the used

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treatment has positive effects due to the new (healthy person) is as good as (a person who was cured of disease). But, if the selected sample has NBU property, then the used treatment has a negative effect. Now, a data set is collected and two claims are supposed, the first is the data is exponential and the second is the data is not exponential and has NBU property. To support one of the two hypotheses, a statistical test is needed to show that which of the two claims is true. Recently, the classification of life probability distributions contributed to set-up new statistical tests with high efficiency, for details see Barlow and Proschan [1], Abouammoh et al. [2], Ahmad et al. [3] and Mahmoud et al. [4]. Atallah et al. [5] and Mansour [6] developed a new technique called Laplace transform to get on test with high efficiency for testing Exponential property for some clinical data. The Laplace transform technique is the generalization of the goodness of fit technique which has been used in setting-up statistical tests. In Section 2 based on U- statistic our test is developed and its asymptotic properties are studied. In that section, Monte Carlo null distribution critical points are simulated for different sample sizes and the power estimates are also calculated and tabulated. Finally, in Section 3 we discuss some applications to demonstrate the utility of the proposed statistical test.

2 The Statistical Test

In this section, a test statistic is constructed to test Exponentiality against NBU based on Laplace transform technique. A life distribution with cumulative distribution function (CDF), $F(0)=0$, survival function $\bar{F}$ and finite mean μ is said to be NBU if

$$\bar{F}(x_1+x_2)\leq \bar{F}(x_1)\bar{F}(x_2),\ \text{for any } x_1,x_2>0. \tag{1}$$

Lemma 2.1. Let X_1 and X_2 be two independent random variables with the same CDF satisfy NBU property, then

$$\left(E[e^{-sX_1}]\right)^2 \geq E[e^{-sX_1}(1-sX_1)]. \tag{2}$$

Proof. Multiplying both sides in Inequality (1) by $e^{-s(x_1+x_2)}$ and the following integrals are considered:

$$\int_0^\infty\int_0^\infty e^{-s(x_1+x_2)}\bar{F}(x_1+x_2)dx_1dx_2 \leq \int_0^\infty\int_0^\infty e^{-s(x_1+x_2)}\bar{F}(x_1)\bar{F}(x_2)dx_1dx_2,\ \text{say } I_1\leq I_2,$$

now,

$$I_1=\int_0^\infty\int_0^\infty e^{-s(x_1+x_2)}\bar{F}(x_1+x_2)dx_1dx_2=\int_0^\infty\int_u^\infty \bar{F}(v)e^{-sv}dvdu=\int_0^\infty ue^{-su}\bar{F}(u)du$$
$$=\frac{1}{s^2}E\int_0^{sX_1}ye^{-y}dy=\frac{1}{s^2}E[1-sX_1e^{-sX_1}-e^{-sX_1}],$$

and

$$I_2=\int_0^\infty\int_0^\infty e^{-s(x_1+x_2)}\bar{F}(x_1)\bar{F}(x_2)dx_1dx_2=\frac{1}{s^2}(1-E[e^{-sX_1}])^2, \tag{3}$$

which completes the proof.

Let $X_1,X_2,...,X_n$ be a random sample from a distribution with CDF $F(x)$. The following issue will be deliberated, $H_\circ$: F is exponential versus H_1 : F is IFR and not exponential. From Inequality (2), δ can be defined as:

$$\delta(s)=\left(E[e^{-sX_1}]\right)^2-E[e^{-sX_1}(1-sX_1)],\delta(s)\geq 0. \tag{4}$$

It is noted that, under $H_\circ$, $\delta=0$, while it is positive under H_1. A direct empirical estimate of δ is

$$\hat{\delta}_n(s)=\frac{1}{n(n-1)}\sum_{i_1\neq i_2}\{e^{-s(X_{i_1}+X_{i_2})}+sX_{i_1}e^{-sX_{i_1}}-e^{-sX_{i_1}}\}=\frac{1}{n(n-1)}\sum_{i_1\neq i_2}\phi(X_{i_1},X_{i_2}),\ \text{say}\ . \tag{5}$$

Theorem 2.2. As $n\to\infty$, $(\hat{\delta}_n(s)-\delta(s))$ is asymptotically normal with mean equal zero and variance $\sigma^2(s)/n$, where $\sigma^2(s)$ is given in (8). Under $H_\circ$, the variance reduces to (9).

Proof. Using the standard U-statistic theory,cf. Lee [7], one can see that

$$\sigma^2=V\{E[\phi(X_1,X_2)\mid X_1]+E[\phi(X_2,X_1)\mid X_1]\}. \tag{6}$$

Remember the definition of $\phi(X_i,X_j)$ in (5), thus it is not difficult to show that

$$E[\phi(X_1,X_2) \mid X_1] = e^{-sX_1}\int_0^\infty e^{-sx}dF(x) + sX_1e^{-sX_1} - e^{-sX_1}. \tag{7}$$

Similarly,

$$E[\phi(X_2,X_1) \mid X_1] = e^{-sX_1}\int_0^\infty e^{-sx}dF(x) + s\int_0^\infty xe^{-sx}dF(x) - \int_0^\infty e^{-sx}dF(x).$$

Hence,

$$\sigma^2(s) = Var\left\{2e^{-sX_1}\int_0^\infty e^{-sx}dF(x) + s\int_0^\infty xe^{-sx}dF(x) - \int_0^\infty e^{-sx}dF(x) + sX_1e^{-sX_1} - e^{-sX_1}\right\}. \tag{8}$$

Under $H_\circ$,

$$\sigma_\circ^2(s) = \frac{s^2\left(2s^2+2s+1\right)}{(s+1)^4(2s+1)^3}. \tag{9}$$

To estimate the efficiency of this procedure, the Pitman asymptotic efficiency (PAE) of our test has been compared with some previous tests for the following alternatives :

Table 1. Comparison between the PAE of our test and some other tests.

Test	Weibull	LFR	Makeham
Kango [8]	0.132	0.433	0.144
Ahmad et al. [3]	0.855	0.554	0.236
Mugdadi and Ahmad [9]	0.170	0.408	0.039
Our test $\Delta_n(0.0001)$	19206.4	19204.5	4801.6

It is noticed that the proposed test $\Delta_n(0.0001)$ enjoys with efficiency better than other tests for all alternatives as shown in Table 1, where our test was computed at different values of $s \geq 0$, till obtaining the best efficiency for all alternatives. The Monte Carlo null distribution critical values of our test $\Delta_n(0.0001)$ has been implemented for generation 10000 random samples from the standard exponential distribution. These values will be the criteria for dividing the samples space into acceptance or rejection region for $H_\circ$.

Table 2. The critical values of $\Delta_n(0.0001)$.

n	90%	95%	99%
5	0.620272	0.860075	1.5147
10	0.393942	0.513607	0.829577
15	0.305116	0.394968	0.61211
20	0.267903	0.336147	0.503473
25	0.234692	0.296865	0.428615
30	0.21629	0.270721	0.396387
35	0.202761	0.248383	0.360126
39	0.187105	0.23349	0.327356
40	0.190819	0.234956	0.328881
43	0.180877	0.223567	0.310418
45	0.177054	0.221255	0.307769
50	0.170917	0.208788	0.284599

From Table 2, the critical values decrease as the sample size increases and they increase as the confidence level increases. Another criterion was used which is the power of the test to guarantee a good performance for the proposed test. The power of $\Delta_n(0.0001)$ has been computed for the three alternatives Weibull and Gamma distributions based on 10000 samples.

Table 3. The power estimates of the Statistic $\Delta_n(0.0001)$.

n	θ	Weibull	Gamma
	2	0.9589	0.8610
10	3	0.9989	0.9959
	4	1.0000	0.9999
	2	0.9995	0.9584
20	3	1.0000	0.9992
	4	1.0000	1.0000
	2	1.0000	0.9807
30	3	1.0000	0.9999
	4	1.0000	1.0000

The Statistic $\Delta_n(0.0001)$ has a good performance for Weibull and Gamma alternatives and the power estimates increase as the sample size increases as shown in Table 3.

3 Some Applications

In this section, some applications to our statistical test are applied in the medical research field.

Application No. 1

Consider the data in Al-Gashgari et al. [10] which represent 39 liver cancers patients taken from Elminia cancer center Ministry of Health – Egypt, which entered in (1999). The ordered life times (in days)

10	14	14	14	14	14	15	17	18	20
20	20	20	20	23	23	24	26	30	30
31	40	49	51	52	60	61	67	71	74
75	87	96	105	107	107	107	116	150	

In this case, $\hat{\delta}_n(0.0001) = 496.694$ which is greater than the critical value in Table 2 at confidence level 95%, then we accept H_1 which states that the data set have NBU property and hence the used treatment method is not significant.

Application No. 2

Consider the data in Ahmad et al. [3], these data represent set of 40 patients suffering from blood cancer(leukemia) from one of ministry of health hospitals in Saudi Arabia and the ordered values in years are

0.315	0.496	0.616	1.145	1.208	1.263	1.414	2.025	2.036	2.162
2.211	2.370	2.532	2.693	2.805	2.910	2.912	3.192	3.263	3.348
3.348	3.427	3.499	3.534	3.751	3.767	3.858	3.986	4.049	4.244
4.323	4.381	4.381	4.392	4.397	4.647	4.753	4.929	4.973	5.074

In this case, $\hat{\delta}_n(0.0001) = 3.99546$which is greater than the critical value in Table 2 at confidence level 95%, then we reject $H_\circ$ which states that the data set have exponential property and hence the used treatment method is not significant.

Application No. 3

Consider the following data set in Johnson and Kotz [11] and represent the survival times (in years) after diagnosis of 43 patients with a certain kind of leukemia.

0.019	0.129	0.159	0.203	0.485	0.636	0.748	0.781	0.869	1.175	1.206
1.219	1.219	1.282	1.356	1.362	1.458	1.564	1.586	1.592	1.781	1.923
1.959	2.134	2.413	2.466	2.548	2.652	2.951	3.038	3.600	3.655	3.745
4.203	4.690	4.888	5.143	5.167	5.603	5.633	6.192	6.655	6.874	

In this case, $\hat{\delta}_n(0.0001) = 1.39577$ which is greater than the critical value in Table 2 at confidence level 95%, then we accept H_1 which states that the data set have NBU property and hence the used treatment method is not significant.

4 Conclusion

The statistical test is proposed to contribute to the assessment of the quality of proposed treatments of some types of cancer. The decisions based on our test showed that if the proposed treatments have a positive or negative effect on the patients through their survival times. The concept of classes of life distributions is used for preparing the proposed statistical test. To guarantee good results based on the proposed statistical test, its statistical properties are computed and compared with other tests. The proposed test can be applied to assess the efficacy of all treatment methods in all different fields in medical research regardless of knowing the nature of the used treatment method. But it is not recommended to apply this test in case of comparing two treatment methods. It is also recommended to develop new non-parametric statistical tests with high efficiency and using these tests as tools for assessing the different proposed treatments.

Conflict of interest

The authors declare that they have no conflict of interest.

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