On Independent Copies of Negative Binomial Distribution

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- Short title: Limit Points of vector sequences
- AMS classification: Primary 60F15; secondary 60G17

Abstract

This paper finds a limiting region for the number of subjects required and hence number of failed in screening test in multi-centric clinical trials. This situation follows a properly normalized independent vector sequences comprising of moving maxima ($Y^m_{k(n)}$) for m (>1) multi centric set up in clinical trials, where $1 \le k(n) \le n$. Results are given for bi-centric and multi-centric situations , under certain conditions on k(n) for $p=\infty$ case.

Keywords: *Almost sure limit set; Clinical trial; Moving maxima; Independent copies; Vector sequence*

1. Introduction

The number of failure subjects to make it to the clinical trial till the fixed number of inclusions is reached on the j^{th} day follows Negative Binomial Distribution (NBD). Consider k(n) number of days, and hence the maximum failures moves and hence screening subjects , as and when k(n) changes. This is exactly the moving maxima, which is due to Rothmann and Russo (1991) . The scheme of finding number of failures for fixed number of inclusion of subjects on each day is adopted at each center , The moving maxima of number of screening subjects, that include failures and test passed subjects, on j^{th} day at each centre constitute vector sequence of independent components of i^{th} centre moving maxima. Thus to provide optimum resources at the centre to minimize the cost involved , doctors /company might be interested to know the strong limiting regions in which the moving maxima of number of screening subjects of multi-centre lie.

Let r be the number of subjects passes the screening tests i.e. the sample size required for the multi-centric trial. Let $\{X_n , n \ge 1\}$ be a sequence of number of screening subjects required to meet r and is independent identically distributed random variables (i.i.d.r.v) with common probability mass function

$$P(X=k)=p(k)= {}^{(k-1)}c_{(r-1)}\, a^r (1-a)^{k-r},\ k=r, r+1,\dots, 0<a<1 .$$

Define, moving maxima $Y^i_{k(n)} = \max(X_{n+1} , X_{n+2} , \dots, X_{n+k(n)})$ where k(n) is a sequence of positive integers , $2 \le k(n) \le n$, for i^{th} multi-centre , i=1,2,3,….

Condition on k(n) in Hebbar and Vadiraja(1997) is used in this paper.

k(n) is non-decreasing (1.1)

$\sup [k(n+1) – k(n)] \le \mu$ (finite) (2.1)

and

$K(n) = [n/(\log n)^{t(n)}]$ where $t(n) \to p$, $0 \le p \le \infty$ as $n \to \infty$ (3.1)

Let b_n = - logn/log(1-a) is a real sequence and that (logk(n)/logn) → Δ as n →∞ where Δ Є [0,1)

In view of this, it is planned to get the strong limiting regions for vector sequences of independent copies of moving maxima for Negative Binomial Distribution (NBD). For p Є [0,∞) , Vadiraja and Nagesha (2016) showed the limit sets. Here it is proceeded with p = ∞. Throughout, δ_i's, i=1,2,.. are sufficiently small positive constants. However, for ease of computation, results are proved for bi-centric case only. On similar lines to this, the result of multi-centric vector sequence can be proved. Below the theorems are stated.

Theorem 1. The almost sure limit set of the vector sequence

$\{ Y^1_{k(n)}/ b_n, Y^2_{k(n)} / b_n \}$ n≥1, coincides with the region $S_1=\{(x,y): \Delta\le x,y\le 1+ \Delta , x + y \le 1+ \Delta \}$ where Δ Є [0,1).

Theorem 2. The almost sure limit set of the vector sequence

$\{ Y^1_{k(n)} / b_n, Y^2_{k(n)} / b_n ,\ldots, Y^m_{k(n)} / b_n \}$ n≥1,m>0 coincides with the region $S_1=\{(x,y,\ldots,z): \Delta \le x,y,\ldots,z \le 1+ \Delta , x + y+..+z \le 1+ \Delta \}$ where Δ Є [0,1).

Remark: Let $Y_{k(n)}^* = \max(X_{n+1}, X_{n+2} \ldots X_{n+k(n)})$ be the forward moving maxima. Then the above results hold good.

2. Proofs.

The proof of Theorem 1 is built up through the following lemmas.

Let for every $a_0 < a < a_1$, there exists a constant c > 0 such that

$c a_0^i < p_i < c a_1^i$ for all i. (1.2)

Lemma 1.2. Let $S_1 = \{(x,y): \Delta \le x,y \le 1+\Delta , x+y \le 1+ \Delta\}$

For every ϵ >0,

$P(Y^1_{k(l_i)} > (x+\epsilon) b_{l_i}, Y^2_{k(l_i)} > y b_{l_i}$ i.o.)=0 (2.2)

$P(Y^1_{k(l_i)} > x b_{l_i}, Y^2_{k(l_i)} > (y+ \epsilon) b_{l_i}$ i.o.)=0 (3.2)

and $P(Y^1_{k(l_i)} > x b_{l_i}, Y^2_{k(l_i)} > y b_{l_i}$ i.o.)=1 (4.2)

where $l_i= [i^\theta]$ and $\theta^{-1}=(x+y-2 \Delta +\epsilon/2)$

Proof:

Note that $\Sigma_{i=x b_{li} \text{ to } \infty} p_i \to 0$ for i large (5.2)

$k(l_i) \cdot \Sigma_{i=x b_{li} \text{ to } \infty} p_i \to 0$ for i large and x> Δ

$k(l_i) \cdot \Sigma_{i=y b_{li} \text{ to } \infty} p_i \to 0$ for i large and y> Δ (6.2)

(2.2) is achieved as follows. For all i large,

$P(Y^1_{k(l_i)} > (x+\epsilon) b_{l_i}, Y^2_{k(l_i)} > y b_{l_i}) =\{\Sigma_{i=(x+\epsilon) b_{li} \text{ to } \infty} p_i^1 \}^{k(l_i)} \{\Sigma_{i=y b_{li} \text{ to } \infty} p_i^2 \}^{k(l_i)}$ =

const. $\{1-\{1-(1-a_0)^{(x+\varepsilon)b_{li}}\}\}^{k(l_i)}\} \{1-\{1-(1-a_0)^{y b_{li}}\}\}^{k(l_i)}\}$

in view of (1.2).

$$= \text{const. } k^2(l_i)\, (1-a_0)^{(x+\varepsilon)b_{li}} * (1-a_0)^{y b_{li}}$$

$=\text{const. } \exp \{ \log (k^2(l_i)\,(1-a_0)^{(x+\epsilon)b}{}_{li} * (1-a_0)^{yb}{}_{li}) \}$

$=\text{const. } \exp \{ 2\log k(l_i) + (x+y+\epsilon)b_{li} * \log(1-a_0) \}$

$=\text{const. } \exp \{ 2\log k(l_i) - (x+y+\epsilon) \log l_i \log(1-a_0)/ \log(1-a_0) \}$

$=\text{const. } \exp \{ - \log l_i ((-2 \log k(l_i)/ \log l_i) + x+y+\epsilon) \}$

$=\text{const. } l_i^{- (x+y-2\Delta+\epsilon)}$

$$= \text{const. } i^{-\theta(x+y-2\Delta+\epsilon)} \qquad (7.2)$$

For every $\epsilon>0$ and i large,

$$\theta(x+y-2\Delta+\epsilon) = 1 + \delta_1 \qquad (8.2)$$

where $\delta_1 = [\theta\, \epsilon/2] > 0$.

In view of (8.2) and (7.2) ,

$\Sigma\, P(Y^1{}_{k(li)} > b_{li}(x+\epsilon),\ Y^2{}_{k(li)} > yb_{li}) < \infty$

Through Borel-Cantelli (B-C) lemma , (2.2) follows. The proof of (3.2) is similar. The proof of (4.2) is established through B-C lemma.

Note that

$$P(Y^1{}_{k(li)} > b_{li}(x),\ Y^2{}_{k(li)} > b_{li}(y)) = \text{const. } k^2(l_i)\, (1-a_1)^{xb}{}_{li} * (1-a_1)^{yb}{}_{li} \qquad (9.2)$$

in view of (1.2). For every $\varepsilon>0$ and i large, we have

$\text{RHS}(9.2) \geq \text{const. } l_i^{- (x+y-2\Delta-\varepsilon)}$

$=\text{const. } i^{-(1-\delta 2)}$

where $\delta_2 = 3\theta\epsilon/2>0$ for every $\epsilon>0$ and i large. To prove (4.2), it is sufficient to show $Y^i{}_{k(li)}$'s are independent for all i large , i =1,2,.. Observe that,

$$l_i - k(l_i) + 1 - l_{i+1} = l_i\, [1-k(l_i)/ l_i + 1/ l_i - l_{i-1}/ l_i] \qquad (10.2)$$

RHS (10.2) $\rightarrow\infty$ for large i and for $\theta > 0$ i.e $x+y \leq 2\Delta$

as $l_{i-1}/ l_i \rightarrow 1$ ($k(l_{i-1}) * l_{i-1}/ l_{i-1*}\, l_i$) $\rightarrow 0$, $1- l_{i-1}/ l_i \sim h\, i^{(\theta-1)}$

Hence, whenever $\theta>1$,i.e. $(x+y-2\Delta)<1$

R.H.S(10.2) is $\sim l_i$ as $i\rightarrow\infty$. Further for $(1- \Delta)^{-1} < \theta \leq 1$, the expression inside the square bracket of (10.2) is $\sim h i^{(\theta-1)}$ as $i\rightarrow\infty$, since $i^{(1-\theta)} * k(l_i)/ l_i \rightarrow 0$

Thus, for $\theta > (1-\Delta)^{-1}$, i.e. for $x+y < 1+ \Delta$, R.H.S (10.2) tends to ∞ as $i \to \infty$.

Thus, the events under consideration are independent, for all i large.

Lemma 2.2 . For all $x \geq \Delta$, $y \geq \Delta$ with $x+y > 1+\Delta$ and for every $\epsilon > 0$,

$$P(Y^1_{k(n)} > b_n(x+\epsilon),\ Y^2_{k(n)} > b_n(y+\epsilon)\ \text{ i.o.})=0 \qquad (11.2)$$

Proof:

$$P(Y^1_{k(n)} > b_n(x+\epsilon),\ Y^2_{k(n)} > b_n(y+\epsilon)) = \{\Sigma_{i=(x+\epsilon)\,bli\ to\ \infty}\ p_i^1\}^{k(li)}\ \{\Sigma_{i=(y+\varepsilon)\,bli\ to\ \infty}\ p_i^2\}^{k(li)}$$

$$= \text{const. } \{1-\{1-(1-a_0)^{(x+\varepsilon)b}{}_{li})\}^{k(li)}\}\ \{1-\{1-(1-a_0)(^{y+\varepsilon)b}{}_{li})\}^{k(li)}\}$$

in view of (1.2).

$$= \text{const. } k^2(l_i)\ (1-a_0)^{(x+\varepsilon)b}{}_{li} * (1-a_0)^{(y+\varepsilon)b}{}_{li}$$

$$= \text{const. } i^{-\theta(x+y-2\Delta+2\varepsilon)} \qquad (12.2)$$

For every $\epsilon>0$, $x+y>1+\Delta$ and for n large ,

$$\theta(x+y-2\Delta+2\epsilon) > 1+\delta_3,\ \delta_3=3\theta\epsilon/2 > 0. \qquad (13.2)$$

An appeal to (13.2), (12.2) and B_C lemma, the lemma is proved.

Lemma 3.2 . For every $\epsilon>0$ and $x_0 = \Delta$

$$P(Y^1_{k(n)} < (x_0-\epsilon)b_n\ \text{ i.o.})=0 \qquad (14.2)$$

$$P(Y^2_{k(n)} < (x_0-\epsilon)b_n\ \text{ i.o.})=0 \qquad (15.2)$$

Proof:

(14.2) is established by showing the following and (16.2) follows on similar lines.

$$P(Y^1_{k(n)} \leq (x_0-\epsilon)b_n\ \text{ i.o.})=0 \qquad (16.2)$$

and

$$P(Y^1_{k(n)} \leq (x_0+\epsilon)b_n\ \text{ i.o.})=1 \qquad (17.2)$$

Note that by the independence,

$$P(Y^1_{k(n)} \leq (x_0-\epsilon)b_n) = \{\Sigma_{i=0\ to\ (x0-\epsilon)\ bn}\ p_i^1\}^{k(n)}$$

$$= \exp.\{-k(n)\ \Sigma_{i=(x0-\epsilon)\ bn\ to\ \infty}\ p_i^1\}^{k(n)} \qquad (18.2)$$

in view of (5.2) as $n \to \infty$. From (1.2) for all large i

$$RHS(18.2) \leq \exp.\{-\text{const. } k(n)\ \Sigma_{i=(x0-\epsilon)\ bn\ to\ \infty}\ (1-a_0)^i\}$$

$$\leq \exp.\{-\text{const. } k(n)\ (1-a_0)^{(x0-\varepsilon)bn}\}$$

$$\leq [\text{const.}/\ k(n)\ (1-a_0)^{(x0-\varepsilon)bn}]^M \qquad (19.2)$$

M being a positive integer. Fix M large so that

$RHS(19.2) \leq n^{-M\varepsilon/2} \leq n^{-(1+\delta 4)}, \delta_4 > 0.$ (20.2)

Hence an appeal to B-C lemma, (16.2) is shown.

Next, we show (17.2). Consider,

$P(Y^1_{k(n)} \leq (x_0+\epsilon)b_n) \geq \lim_{N\to\infty} \{\Sigma_{i=0 \text{ to } (x0+\epsilon)bN}\ p_i^1\}^{k(N)}$

$= \lim_{N\to\infty} \exp.\{-(1+o(1))\ k(N)\ \Sigma_{i=(x0+\epsilon)bN \text{ to } \infty}\ p_i^1\}^{k(N)}$

$\geq \lim_{N\to\infty} \exp.\{-\text{const. } k(N)\ (1-a_1)^{(x_0-\varepsilon)bN}\}$

$\geq \lim_{N\to\infty} \exp.\{-\text{const. } N^{-\varepsilon/2}\}$

similar to that at (20.2).

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Hence, (17.2). Thus , the proof of (14.2) is complete. Similarly (15.2) can be shown. Hence the proof of lemma.

Proof of Theorem 1: S is a required limit set by lemmas 2.2 and 3.2. It is concluded with the fact that the limit set is necessarily closed from the lemma1.2 . This completes the proof of theorem1.

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