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Comparison of Two Statistical Techniques for the Surveillance of Birth Defects

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Research Article

Abstract: A surveillance system for detecting increases in congenital malformation such as cleft lip and palate is applied for a single hospital. For the cleft lip and palate congenital malformation data which was collected from the government organization for the period of 2000 to 2012, we applied the sets method and the cumulative sum technique (CUSUM) and both methods compared. The sets method is shown to be more efficient than the CUSUM technique to detect sudden shift from the normal rate of the cleft lip and palate congenital malformation to an increased rate.

Keywords: Congenital malformation; Sets method; CUSUM technique; Surveillance of rare events; Cleft lip and palate; Birth defect.

1. Introduction

The problem of monitoring the incidence rate of an event of interest where the baseline probability of the event is small arises in medical and epidemiological settings. One example is monitoring the incidence of a rare type of congenital malformation. In this paper, we focus on cleft lip and palate. Cleft lip and palate are birth defects that happen while a baby is developing in the uterus. Researchers believe that most cases of cleft lip and palate are caused by an interaction of genetic and environmental factors. Environmental factors thought to contribute to clefting include: fetal exposure to cigarette smoke, alcohol, certain medications, illicit drugs and certain viruses. A relatively large increase of such diseases may involve a small number of cases and may not be easily be recognized. Use of a routine monitoring system may permit earlier detection. The causative factors may then be investigated and control measures more readily initiated. Moreover, quite frequently very low level increase rate may occur unnoticed. Detection of such increase rate may eventually lead to a better understanding of the etiology of the particular diseases. Several surveillance techniques have been devised for the identification of an increase in malformation rates. In this paper, two of the statistical techniques most widely used for the surveillance of congenital malformations are compared. Indeed one of the two principal statistical techniques suggested for the analysis of data which are collected within the framework of a diseases monitoring system originally proposed for and has been widely used in, quality control systems. This is the CUSUM technique. The other principal method for disease monitoring is the sets technique. The sets method for monitoring adverse clinical outcomes was first introduced by Chen (1978) using geometric model. This method was later developed by Gallus *et al*. (1986). The CUSUM method is a well-known method originally developed in the field of quality control (1954). The Poisson assumption leads naturally to the idea of monitoring the number of events per unit of time using a CUSUM chart based on the Poisson CUSUM. Many researchers have compared the Poisson CUSUM to the sets method. Barbujani (1984) found that the Poisson CUSUM has faster signal times and greater sensitivity, greater specificity and better accuracy than the sets method. Gallus *et al*. (1986) found that the Poisson CUSUM signals an alarm more quickly than the sets method when there is less than a four-fold increase in the incidence rate. Chen (1987) determined that the sets method signals an alarm more quickly than the Poisson CUSUM when the number of incidents per year is 5 or less and when the increase in the incidence rate is low. Grigg *et al*. (2004) developed risk-adjusted method of the sets method. Sego *et al*. (2008) compared the performance of the sets method and its modifications with that of the Bernoulli CUSUM chart under a wide variety of circumstances. Except in a very few instances, they suggested that the Bernoulli CUSUM chart has better than the sets method and its modifications for the extensive number of cases considered. In this paper, the sets method is shown to be more efficient than the CUSUM technique to detect sudden shift from the normal rate of the cleft lip and palate congenital malformation to an increased rate

2. The Sets method

The sets method, proposed by Chen (1978) is based on the interval between the births of two individuals carrying the same specific malformation. Let we take the problem of monitoring cleft lip and palate malformation in a single hospital. Consider the set of births occurring between two consecutive malformed cases. Its size denoted by X, is assumed to follow a geometric distribution. The following notations are used:

π_0 - The normal rate of the specific monitored malformation.

$\pi_1 = \gamma\pi_0$ - The increased rate of the specific malformation.

P_i - The probability under H_i that a given sequence signals an alarm, for i = 0, 1.

λ - The number of false alarms expected during a given interval of time.

β - The number of births expected during a given interval of time.

Let $\pi (0 < \pi < 1)$ be the malformation rate. The expected value of X is

$$E(X) = \frac{1-\pi}{\pi} = \eta \qquad (2.1)$$

We denote the baseline values of π and η by π_0 and η_0, respectively. We define a threshold $T = k\eta_0 (k > 0)$, and say that if an observation of X is less than T it gives an A-event; otherwise it gives a B-event. It can be shown that, when π_0 is small,

$$P_0(A) = \Pr(X < k\eta_0) \approx 1 - e^{-k} \qquad (2.2)$$

where $P_0(A)$ indicates the probability of an A-event under baseline conditions. Analogously, if the frequency of malformations is given by $\pi_1 = \gamma\pi_0$, $(0 < \gamma < \frac{1}{\pi_0})$, then

$$P_1(A) = \Pr(X < k\eta_0) \approx 1 - e^{-k\gamma} \qquad (2.3)$$

where $P_1(A)$ gives the A-event probability under increased malformation rate π_1. According to Chen, an alarm is defined by the consecutive appearances of n A-events. Thus, after n consecutive sets, the alarm probability is given by

$$P_0(alarm) = P_0^n(A) \approx (1 - e^{-k})^n \qquad (2.4)$$

under baseline condition.

$$P_1(alarm) = P_1^n(A) \approx (1 - e^{-ky})^n \qquad (2.5)$$

under increased rate.

The alarm system requires the specification of the two parameters, k and n. To specify the parameters Chen suggested that

$$k = \frac{-\ln 0.01}{\gamma} \qquad (2.6)$$

$$n \approx \frac{\ln P_0}{\ln(1 - e^{-k})} \qquad (2.7)$$

P_0 is determined by λ, the number of false alarms to be expected in a given interval of time, during which we expect β newborns.

$$P_0 = \frac{\lambda}{(\beta\pi_0 - n + 1)} \qquad (2.8)$$

n and P_0 can be calculated through an iterative procedure.

3. The Cumulative sum technique

In Statistical process control, suitable system to detect small shift is the CUSUM technique. In CUSUM, the analyses are carried out at the end of the regular periods. In this work the analyses were carried out at monthly intervals. The CUSUM statistic calculated by the following formula:

$$S_t = S_{t-1} + x - K \qquad (3.1)$$

A constant value K is subtracted from the number of diagnoses made at each month. The remainder is added to the sum of remainders accumulated over previous analyses. Whenever the sum is negative, then the value zero is assumed. The value of parameters H and K are obtained with respect to the baseline frequency from Ewan and Kemp published table (1960). The parameters K and H value can be determined by another method. In this method Setting K and H values are dependent on the baseline frequency of the particular malformation. K value can be taken to be the positive integer immediately greater than the mean baseline malformation frequency. H value can be calculated from the following formula:

$$H = 1 + 2\sqrt{(s^2 / (K - m)}$$

where m is the mean baseline malformation rate and s^2 is the variance. H is constant in time for each considered malformation.

4. Comparisons and Results

Let us consider the sets method. A surveillance method is applied to a hospital with nearly 250 births per month, with a baseline rate, π_0 , equal to 0.0009 malformations per month. The given sequence will signal an alarm depend on the values of n and $k\eta_0$. It is assumed that the system can be able to detect an increase rate five times the normal rate. The data were analyzed with γ equal to 5. The values of $k\eta_0$, n, P_0, P_1 are determined for the given data.

Table 1. Threshold dimension of sets ($k\eta_0$), number of sets(n) in a sequence that signals an alarm, probability of a true alarm(P_0) and probability of a true alarm when increase γ = 5(P_1) for the set based system.

Name of the Malformation	$k\eta_0$	n	P_0(A)	P_1(B)
Cleft palate/lip	1024	5	0.0792	0.9512

The value of n and P_0 can be evaluated by an iterative procedure. For different values for n, P_0 value was calculated. Using this P_0 value again the n value was calculated. The values for n and P_0 tabulated in the below table.

n	P_0	N	P_0
1	0.0588	6	0.0833
2	0.0624	5	0.07688
3	0.0666	5	0.07688
4	0.0714	5	0.00760
5	0.7688	5	0.07688

For n = 5, we get P_0 = 0.7688 by using (2.4). By using this value for P_0, we get n=5 by using (2.8). So the value is 5. That is, an alarm would be signaled after the appearance of 5 consecutive sets, each smaller than $K\eta_0$ or 1024 births. The value of P_1 (B) = 0.9512 probability that an increased rate five times the normal rate would be detected after a sequence of 5 sets. If the size of the set is less than the threshold dimension of set (i.e 1024) then an alarm would be signaled. Let us considered the CUSUM technique. The parameter value K and H are determined with respect to the baseline rate and the average time length. In this study K and H values are determined using the Ewan and Kemp published tables. For the given data K = 1 and H= 3 are recommended. Applying this parameter to the given data, the alarm is not signaled. Because there is no point not exceed the H=3 value. The visual representation of the set method and the CUSUM method values are presented in the Figure 1 and Figure 2.

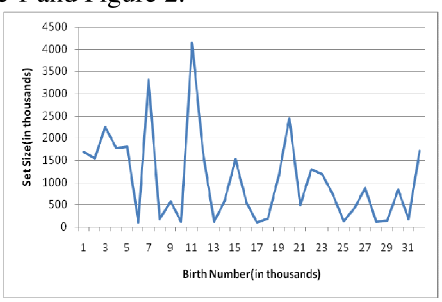

Figure 1: Line Chart for set Method

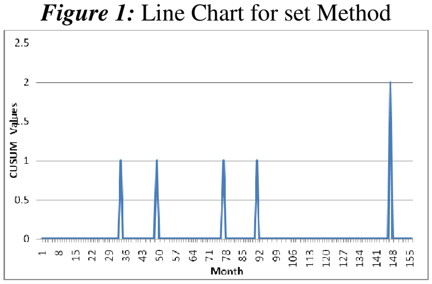

Figure 2: Line Chart for CUSUM Method

From the Figure 1, we conclude that the sets method is signaled an alarm after the fifth set which size is less than 1024 and from the Figure 2, the CUSUM technique is not signaled. So the sets method may be the best monitoring system for the small increased rate for the given monitoring system.

5. Conclusion

Based on the comparison of set method and CUSUM technique, the set method is better than the CUSUM technique and which is given an alarm when there is an increase in the cleft lip and palate malformation. Such an investigation gives search for clues leading to the factor(s) responsible for the increased risk of cleft lip and palate malformation. Similar comparison may also be worked out for monitoring any other rare diseases, since the calculations are simple and the surveillance system can be maintained by local staff of the hospital.

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