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Statistical Issues in Public Health Monitoring- A Review and Discussion

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SUMMARY

A review of methods, suggested in the literature, for sequential detection of changes in public health surveillance data is presented. Many authors have noticed the need for prospective methods and there has been an increased interest in both the statistical as well as epidemiological literature on this type of problem in the recent years. However, most of the vast literature in public health monitoring deals with retrospective methods. This is especially apparent dealing with spatial methods. Evaluations with respect to the statistical properties of special interest for on-line surveillance are rare. The special aspects of prospective statistical surveillance as well as different ways of evaluating such methods are described. Attention is given to methods including only the time domain as well as methods for detection where observations have a spatial structure. In the case of surveillance of a change in a Poisson process the likelihood ratio method and the Shiryaev-Roberts method are derived.

Key Words: DETECTION; EXPECTED DELAY; INCIDENCE RATE; MONITORING; PUBLIC HEALTH SURVEILLANCE; SEQUENTIAL METHODS; SPATIAL CLUSTER

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1 INTRODUCTION

An important issue in public health is the timely detection and prevention of various types of adverse health events. An example of this is an increased birth rate of babies with congenital malformations. This was especially apparent during the thalidomide tragedy in the early 1960's. An increased incidence rate of diseases, such as asthma or influenza is another example. Other examples include, the increase in bacterial resistance to antimicrobial agents, the spatial clustering of various forms of cancer and different side effects of drugs newly released on the market. In all of these examples, quick detection and prevention is beneficial both at an individual level as well as to society, for example in terms of reduced medical expenditures. Public health surveillance is defined as the ongoing, systematic collection, analysis, and interpretation of out-come specific data essential to the planning, implementation and evaluation of public health programmes, closely integrated with the timely dissemination of these data to those responsible for prevention and control (Thacker and Berkelman, 1988). The need for this type of systems is reflected in the vast and diverse literature of the subject. For example, Blindauer et al. (1999) discuss the need for a nationwide surveillance system for the prevention and control of pesticide-related illness and injury. The risk for adverse health outcomes related to chemical exposures is discussed in Hertz-Picciotto (1996) where the use of an environmental health surveillance system is suggested. Thacker et al. (1996) propose a framework to enhance the practice of surveillance in the United States and discusses current and future surveillance needs.

To be able to control various adverse health events, large amounts of data are collected in various nationwide public health programs such as the National Notifiable Diseases Surveillance System (NNDSS) in the United States controlled by the Centers for Disease Control and Prevention (CDC). In this case 52 different diseases (as of 1 January 1999, Centers for Disease Control and Prevention, 1998) are tracked and data are reported weekly both at state and national level. In England and Wales, the Communicable Disease Surveillance Center (CDSC) and the Public Health Laboratory Service (PHLS) handle these issues. In Hannoun and Tumova (2000), a survey of influenza surveillance systems in 24 European countries is reported. An example is the Groupe Régional d'Observation de la Grippe (GROG) in France, described in Hannoun et al. (1989). Salmonella is also under surveillance in many countries including France and the National Salmonella Reference Centre (NSRC) at the Pasteur Institute in Paris. Another example is bacterial food borne infections. In the United States, collaboration between CDC, Food and Drug Administration (FDA) and the US Department of Agriculture (USDA) has led to the Foodborne Diseases Active Surveillance Network known as FoodNet (Stephenson, 1997). Another type of surveillance system concerns with the safety of marketed drugs. Different type of regulations controls the reporting of drug-related adverse events.

Two examples of this is the Guideline for post marketing reporting of adverse drug experiences by the FDA in the United States (Food and Drug Administration, 1992) and the SAMM Guidelines by the Medicines Control Agency in the UK (Medicines Control Agency, 1993).

Also international networks of centers are in use. An example of this is the World Health Organization (WHO) network of influenza surveillance, FluNet. Other examples include European collaboration of influenza surveillance described in Fleming and Cohen (1996). The International Clearinghouse for Birth Defects Monitoring Systems (ICBDMS) (Erickson, 1991) and EUROCAT are two networks for surveillance of birth defects. For salmonella surveillance an example is the Enter-Net network founded by the European Union under the BIOMED 2 programme. These are only a few examples of the various systems in use today. Further reading can be found in Flahault et al. (1998). In Thacker and Berkelman (1988), a general review of the history and development of public health surveillance in the United States can be found.

The total amount of data collected in these systems is enormous. The data collected can be handled in different ways in order to use the provided information. Common to all applications mentioned and to all public health surveillance systems is that a decision of whether to take preventive actions or not has to be made sequentially based on the data collected so far. From a statistical point of view, this is a much more complicated situation than in a fixed sample situation. For example, traditional hypothesis testing cannot be used. Instead sequential methods such as statistical surveillance should be used.

Different definitions and use of the term surveillance exist in different types of literature. In most of the literature it is not necessary to declare that the term surveillance is used for a prospective situation where observations are gathered sequentially. This is in opposite to a retrospective or fixed sample situation were observations are not accumulating over time. For clarification, by statistical surveillance we mean the prospective or online observation of a stochastic process $X = \{X(t); t = 1,2...\}$ with the aim of detecting an important change in the process at an unknown time-point τ, as quickly as possible. Much of the research on statistical surveillance was originally done with focus on applications in industrial production control. How commonly these methods are used in practice in public health surveillance systems today can be questioned. For example, Hilsenbeck (1990) reported that none of the examined cancer registers in North America used any statistical control procedure. Instead some informal process control was used. However, the usefulness of statistical surveillance methods also in public health related settings are reported in many papers.

The context of public health surveillance implies specific problems not generally present in the case of an industrial production control. Stroup et al. (1993) notes the problems of seasonal effects and reporting delays in the National Notifiable Diseases Surveillance System. Thacker and Berkelman (1988) discuss problems of incomplete or inaccurate reporting. In Lui and Rudy (1989) and Hillson et al. (1998), the problem of how to handle time lags in case reporting is discussed. Farrington et al. (1996) also address these problems and point out the need for a statistical surveillance system with properties suitable for dealing with problems common in epidemiological data such as bias, delay, lack of accuracy and seasonality. In Thacker et al. (1995), the surveillance of chronic diseases and the requirements for the surveillance system are discussed. It is argued that the characteristics of chronic diseases make the surveillance situation in many aspects different from the one of infectious diseases. In Morabia (1996), the question of what to monitor is raised and the author argues that not only the cases of disease, but also rather the risk factors should be monitored. This type of questions is not exclusive for public health surveillance. The problem of seasonality and delays in reporting was discussed in Andersson et al. (2001) in the case of surveillance of economic time-series. The need for leading indicators was discussed in Andersson et al. (2001) for business cycle surveillance and in Royston (1991) and Andersson (2000) for the use of leading indicators in natural family planning. Although these questions are crucial for a successful statistical surveillance method in a public health context, these issues will not be further discussed here. The review is instead focused on the inferential aspects of proposed statistical surveillance methods. We limit the discussion to the methodological and quantitative part of the surveillance problem and exclude further review of the epidemiological discourse.

Many authors have addressed the problem of constructing methods suitable for public health surveillance. The literature of this subject is found both in statistical as well as in epidemiological journals. The purpose of many papers has been the development of an online monitoring system. However, many of the studies have not taken into account the special statistical aspects of prospective surveillance. Instead the problem has been treated in as if fixed sample situation where data are not accumulating over time. These types of papers are not reviewed here. Some reviews of surveillance methods are already available (Barbujani, 1987) and Farrington and Beale, 1998). However, in Barbujani (1987), the focus is narrowed to methods suggested for surveillance birth effects. In Farrington and Beale (1998), much attention is on key problems when using large surveillance databases. Instead we focus on the inferential part of the surveillance problem including methods for evaluating surveillance methods. A notable feature of many of the methods suggested in the literature is the lack of evaluation by other means then in different case studies. The main purpose of this paper is thus to summarize the current position of surveillance methods in public health related settings and to enhance the use of proper evaluation of methods for surveillance.

The paper is organized as follows. First, in Section 2, some general concepts of statistical surveillance are described. Also different ways of evaluating such a system is presented. In Section 3, the problem of detection of an increased incidence rate is discussed and reviewed. The use of the LR method and the Shiryaev- Roberts method is suggested and the alarm criteria are derived when it is assumed that a Poisson process generates data. In Section 4, the problem of detection of a change in a spatial structure is discussed and reviewed. The current situation is summarized and some concluding remarks are given in Section 5.

2 GENERAL CONCEPTS OF STATISTICAL SURVEILLANCE

By statistical surveillance we mean the online monitoring of a stochastic process $X = \{X(t); t = 1,2...\}$ with the aim of detecting an important change in the process at an unknown time-point τ, as quickly and as accurately as possible. At each time-point, s, we want to discriminate between two states of the monitored system; the in-control and the out-of-control state, here denoted by $D(s)$ and $C(s)$ respectively. To do this we use the accumulated observations $X_s = \{X(t); t \leq s\}$ to form alarm sets, $A(s)$, such that if $X_s \in A(s)$, this is an indication that the process is in state $C(s)$ and an alarm is triggered. Usually this is done by using an alarm function, $p(X_s)$, and a control limit, $g(s)$, where the time of an alarm, t_A, is written as:

$$t_A = \min\{s; p(X_s) > g(s)\}$$

Different types of in- and out-of-control states are used depending on the application. The most frequently studied case is when $D(s) = \{\tau > s\}$ and $C(s) = \{\tau \leq s\}$. The change to be detected also differs depending on the application. Often a change in a parameter in the distribution of X will be of interest. For example, a change in a parameter can correspond to a changed level, a changed variation or possibly a combined change in the level and variation at the same time. Mostly studied in the literature is the step change, where a parameter changes from one constant level to another constant level. Different types of changes are of interest in different applications. Other type of changes includes a gradual, linear change or an exponential increase.

The alarm function together with the alarm limit constitutes a statistical surveillance method that is a method that tells us when to trigger an alarm, based on the accumulated observations. Thacker et al. (1995) used the term 'surveillance system' to describe a system which include a functional capacity for data collection, analysis and dissemination linked to public health programmes. Here, we concentrate on the statistical issues of how to handle the information in the data collected, while the term surveillance system is used in a broader sense. For the evaluation of a method of surveillance, different types of measures are used to characterize the behavior both when the process is in- and out-of-control. When the process is in-control, all alarms are false alarms. The distribution of the false alarms is often summarized in the average in-control run length, denoted by $\mathrm{ARL}^0=\mathrm{E}[t_A \mid \tau = \infty]$. Another common measure is the probability of a false alarm, $P(t_A < \tau) = \sum_{t=1}^{\infty} P(\tau = t) P(t_A < \tau \mid \tau = t)$. However this requires an assumption of the distribution of τ, which often is assumed to be geometric. This assumption is suitable when the probability of a shift at each time point conditioned on no shift before is constant for each time-point.

When evaluating the effectiveness of different types of surveillance methods, one has to face a trade off between false alarms and short delay times for true alarms. The way to handle this is usually in the same way as in a hypothesis-testing situation, where the type 1 error is fixed and evaluations of the power is made for various situations. The translation to the surveillance situation has traditionally been to characterize the type 1 error by the ARL^0. Then different types of methods have been compared for a fix value of the ARL^0. Another way of characterizing the type 1 error is by the probability of a false alarm.

The measures of evaluation with respect to a true shift can be made in many different ways. In the vast literature on quality control the average out-of-control run length, $\mathrm{ARL}^1=\mathrm{E}[t_A \mid \tau = 1]$ is usually used. This implies that the change occurred at the same time as the surveillance started. This can be useful in a manufacturing process where one expects various start-up problems. However in a public health situation this is in general not an appropriate approach. In this case one should focus on other measures of evaluation, which takes into account also the possibilities of later changes, since the ability of detection depends on the time-point of the change. One such example is the conditional expected delay as a function of the change point τ:

$$CED(t) = \mathrm{E}[t_A - \tau \mid t_A \geq \tau = t]$$

Assuming a distribution of τ, one could also consider the expected delay:

$$ED_\tau = \sum_{t=1}^{\infty} P(\tau = t) \cdot CED(t)$$

In some applications only a limited delay-time can be tolerated. An example is the outbreak of an infectious disease, where an epidemic could be prevented if the outbreak is detected within a given time-interval. In this case we can consider the probability of successful detection:

$$PSD(d,t) = \mathrm{P}(t_A - \tau \leq d \mid t_A \geq \tau = t)$$

If an alarm is triggered various preventive actions should be taken. To be able to choose what actions to take, it is desirable to know how much trust to put in an alarm. Different surveillance methods have different false alarm distributions as a function of time. Therefore, the proportion of false compared to justified alarms at a specific time point will differ between the methods, that is the trust of an alarm will differ between methods. For choosing what actions to take if an alarm is triggered, the predictive value of an alarm can be used:

$$PV(s) = P(C(s) \mid t_A = s)$$

In Chen et al. (1993), the same type of problem was handled and a method for confirming or rejecting alarms was suggested based on data subsequent to an alarm. However, knowledge of the predictive value could solve this problem without the extra data and thus shorten the time for actions. In general a constant predictive value would be desirable since it would imply that the same actions would be taken whenever the alarm is triggered.

These kinds of measures of evaluation concern the on-line features of the surveillance method. In CDC's guidelines for evaluating surveillance systems (Centers for Disease Control and Prevention, 1988) the timeliness is mentioned as one important aspect when evaluating a surveillance system. It is stated that the timeliness of the surveillance system should be evaluated in terms of availability of information for disease control. This includes both the delay in reporting as well as the time required for the identification of outbreaks. However, no specific measurements for the timely evaluation are provided in the guidelines. Some measures of evaluation are stated, such as the sensitivity and the predicted value positive. These kinds of measures concerns with the ability of correct classification of cases and requires an external source of correct classifications which can be used to validate the data collected by the system. German (2000) gives a review of the use of such measures. These measurements concerns with the quality of the data collected by the surveillance system and do not address the effectiveness of the system to detect adverse events. Therefore they cannot be used as substitutes for the measures of evaluation suggested above.

Further reading on general statistical surveillance can be found in various papers (Shiryaev, 1963; Shiryaev, 1978; Pollak, 1985; Moustakides, 1986; Frisén and de Maré, 1991; Frisén, 1992; Srivastava and Wu, 1993; Siegmund and Venkatraman; 1995; Lai, 1995; Frisén and Wessman, 1999 and Frisén, 1999).

In the following sections, a review of articles covering the topic of statistical surveillance in a public health context is presented. The intention is to summarize the current situation for online surveillance, thus excluding papers dealing with the problem retrospectively. Often the data collected in public health surveillance is represented by counts of cases for example of a disease. This type of data is less studied in most areas of surveillance, where continuous variables are more common. One example though is the case of monitoring the fractions of non-conforming products in an industrial process. A review of methods suggested in this situation can be found in Woodall (1997).

3 DETECTION OF INCREASED INCIDENCE RATES

One major field of research in environmental epidemiology concerns incidence rates. A vast literature covers the production of maps of incidence rates as well as various retrospective tests (Marshall, 1991; Lawson et al., 1999 and Lawson and Cressie, 2000). The literature is rather sparse when it comes to prospective methods of surveillance.

When constructing a surveillance method for detection of an increased incidence rate, different assumptions concerning the underlying process can be made depending on the setting and the data collected. Often, a Poisson process for the cases of disease is assumed. In the case when this assumption has not been considered appropriate, more complex time dependent processes have been used to model the cases of disease. A critical aspect for the system is also whether the base-line rate of the disease is assumed known or not. Based on these assumptions and the type of available data, different types of methods have been suggested for the surveillance, such as the Poisson CUSUM, the Exponential CUSUM, the Sets method and different window methods, which will be further discussed in the coming sections. However, common to all these situations is the sequential decisions to be made at each time point, which make the inferential situation the same.

FIGURE 1 GOES HERE

3.1 Detection of a Changed Intensity in a Poisson Process

If a Poisson process for the cases of an adverse health event is assumed, an increased incidence rate corresponds to an increased intensity of the Poisson process. The possibility of detecting such an increased intensity depends both on the way the process is observed as well as the surveillance method used to monitor the process.

3.1.1 Using the Time between Events to Study the Poisson Process

In some cases the intervals between the adverse events have been of focus. These intervals can be measured by either the continuous time between the events, which are exponentially distributed, or by using a discrete time scale measuring the number of acceptable events between adverse events. Both these ways includes no loss of information about the process. The increased intensity would then be recognized as shorter intervals between the adverse events and fewer acceptable events between adverse events respectively.

Using the continuous, exponentially distributed time between adverse events, methods like the Exponential CUSUM and the Exponential EWMA can be used. The CUSUM and EWMA methods are two standard methods in statistical process control. Their names come from the way the alarm statistic is formed. For CUSUM, the alarm statistic is based on the cumulative sum of differences between the observations and their expected values. The alarm statistic of the EWMA method is based on an exponentially weighted moving average of the observations. These methods for exponentially distributed variables have not been used in a public health context, but studies have been made in other areas (Vardeman and Ray, 1985; Gan and Choi, 1994; Gan, 1994 and Gan, 1998).

Within the area of surveillance of congenital malformations, the Sets method was proposed in Chen (1978). It focuses on the lengths of the intervals between successive births with malformed babies, measured by the number of healthy babies born between malformed babies. The lengths of these intervals will be geometrically distributed. The method signals an alarm if n consecutive intervals are shorter than some threshold value. In various papers, the Sets method has been further studied (Chen, 1986; Gallus et al., 1986; Radaelli and Gallus, 1989; Sitter et al., 1990; Gallus et al., 1991; Lie et al., 1991; Arnkelsdottir, 1995 and Chen et al., 1997). In Arnkelsdottir (1995) evaluation was made with respect to the probability of successful detection and the predictive value. In Wolter (1987) and Radaelli (1992), the Cuscore method was studied. In this method a score is assigned of +1 or –1 to each interval between adverse events depending on whether it is longer or not then some threshold value. The alarm statistic is formed from the cumulative score.

However, this type of reporting of the observations means a direct loss of information and a sub optimal method can be expected.

3.1.2 Using the Number of Events in Fixed Intervals to Study the Poisson Process

If the number of events is recorded for fixed time intervals, information of the process will be lost and the resulting surveillance method will be sub-optimal for detecting the change in the process as quickly as possible. Therefore, using fixed intervals could be motivated only by practical restrictions of the reporting system. For fixed time intervals a commonly used method is the Poisson CUSUM method. It compares the actual number of events in each time period with the expected number and uses the cumulated sum of deviations to form an alarm statistic. A general review of the Poisson CUSUM method can be found in Lucas (1985). The Poisson CUSUM was early applied to congenital malformations in England and Wales (Hill et al., 1968 and Weatherall and Haskey, 1976). In many papers the method has been used to compare and evaluate the performance of alternative methods, for example the Sets method in the previous section (Barbaujani and Calzolari, 1984; Pollak and Kenett, 1983; Gallus et al., 1986; Chen, 1987 and Radaelli, 1992). In Barbujani (1987), these comparisons are reviewed and further described. A sequential binomial likelihood ratio test of the probability that an infant has Down's syndrome was proposed in Lie et al. (1993). In this case the alarm limits were chosen to yield a certain ARL^0 instead of a certain α-level. Comparison with the Poisson CUSUM method was also made with respect to the ARL^1. In Radaelli (1992), the Poisson CUSUM was compared with the Cuscore method. As an alternative to the Poisson CUSUM, Rossi et al. (1999) evaluated different normal approximations to a Poisson process, in order to improve the method. Other articles discussing the Poisson CUSUM includes Praus et al. (1993) for the use in post-marketing surveillance of adverse drug reactions and Hutwagner et al. (1997) for the case of Salmonella outbreaks. In Bjerkesal and Bakketeig (1975), an early application of the Poisson Shewart method for the case of congenital malformations in Norway can be found.

3.1.3 Observing the Process in a Moving Window

An approach discussed in a retrospective setting in Stroup et al. (1989) and Stroup et al. (1993) was a window-based method. In this case the number of events in a moving window of fixed length is compared with an expected number based on the previous years. This method was suggested for prospective use in Wharton et al. (1993) using data from the National Notifiable Diseases Surveillance System for a four-month period and in Rigau-Perez et al. (1999) for dengue outbreaks in Puerto Rico. Shore and Quade (1989), proposed the SM-method which is based on a moving window and compared it with the Poisson CUSUM method. However, window based methods are known to be sub-optimal. For example, if one compares two consecutive moving windows of fixed lengths, the ability of detecting a gradual change is low (Svéreus, 1995). Using moving windows will severely reduce the information about the observed process. If the window is wide it will smooth over possible shifts in the process. If, on the other hand, the windows are narrow, the information lost will be larger since only a small amount of the observations are used at each time point. One way of motivating the use of it would be if the base-line rate of the disease were completely unknown.

There are several examples of window-based methods being used in practice. A window-based method was previously in use by the FDA to detect increased frequencies of adverse events related to drugs. In this case the number of reported adverse events in a "report interval" was compared with those of a "comparison interval" and reported to the FDA (Food and Drug Administration, 1992). Recently this type of reporting was revoked (Food and Drug Administration, 1997) with the motivation that the expedited increased frequency reports had not contributed to the timely identification of safety problems. This might be due to the use of a window-based method for detection. Another example of the use is the detection of increased gamma radiation levels in Sweden where two consecutive 24-hour periods are compared by the Swedish Radiation Protection Institute (Kjelle, 1987).

3.1.4 The Likelihood Ratio-Method for a Poisson Process, an Optimal Surveillance Method

The observation of times between events for the Poisson process is preferred to the observation of number of events in fixed intervals if the situation allows for it. However, for the construction of a surveillance method also the alarm statistic and the alarm limits must be considered. The choice of alarm statistic and alarm limits determines the characteristics of the system. The way to choose these is guided by the desired properties of the system, often expressed in terms of an optimality criterion.

In a public health situation, optimality of a surveillance method is not easily determined, due to the complex epidemiological discourse. In our view, the minimization of the expected delay for a fixed probability of a false alarm is a natural choice. Further discussions of optimal surveillance can be found in Frisén and de Maré (1991), Frisén (1999) and Frisén and Sonesson (2000). Consider the case where we want to distinguish between the states $D(s) = \{ \tau > s \}$ and $C(s) = \{ \tau \le s \}$ for the case of a shift in the intensity of the process from λ_0 to λ_1. Then this optimality criterion leads to the likelihood ratio method (Frisén and de Maré, 1991). This method has been studied in some papers, for the case of a positive shift in a normal distribution (Frisén and Wessman, 1999). The time of an alarm for the likelihood ratio method can be expressed as the first time the posterior probability of a change exceeds a constant:

$$t_A = \min\{s; P(\tau \le s \mid X_s = x_s) > K\}$$

An equivalent way is the first time the full likelihood exceeds an alarm limit:

$$\begin{aligned} t_A &= \min\{s; \frac{f_{X_S}(x_s \mid C(s))}{f_{X_S}(x_s \mid D(s))} > \frac{P(\tau > s)}{P(\tau \le s)} \cdot \frac{K}{1-K}\} \\ &= \min\{s; \sum_{t=1}^{s} \frac{P(\tau = t)}{P(\tau \le s)} \cdot L(s,t) > \frac{P(\tau > s)}{P(\tau \le s)} \cdot \frac{K}{1-K}\} \end{aligned}$$

where $L(s,t)$ is the conditional likelihood at time s for the case when $\tau = t$.

The limitation of the likelihood ratio method is that it requires knowledge of the distribution of the change-point, τ. Often a geometric distribution has been used for other situations. If the intensity of a shift is low, that is, the parameter in the geometric distribution is close to zero, the Shiryaev-Roberts method can be used as an approximation of the likelihood ratio method. This was demonstrated in Frisén and Wessman (1999) to be a good approximation for intensities up to 0.20 in the case of a change in the mean of a normal distribution. The Shiryaev-Roberts method can also be regarded as one, which use a non-informative prior for the time of change.

The time of an alarm for the Shiryaev-Roberts method is:

$$t_A = \min\{s; \sum_{t=1}^{s} L(s,t) > K\}$$

where K is a constant.

The likelihood ratio method and the Shiryaev-Roberts method have been suggested in other situations, and the extension to a positive shift in a Poisson process is straightforward. The construction of these methods can be done both in the case when data is represented by the time between events and when data is represented by the number of events in fixed intervals. In both cases, the likelihood ratio and the Shiryaev-Roberts method will be preferable to the previously suggested methods for these situations in the sense that the expected delay will be shorter for a fixed value of the probability of a false alarm. In the case with exponentially distributed time intervals denoted by X, the time of an alarm for the likelihood ratio method is, for some constant L:

$$t_A = \min\{s; \sum_{t=1}^{s} P(\tau = t) \cdot \exp\left\{(-\lambda_1 + \lambda_0)\sum_{i=t}^{s} X(i)\right\} \cdot \left(\frac{\lambda_1}{\lambda_0}\right)^{s-t+1} > L \cdot P(\tau > s)\}$$

For the Shiryaev-Roberts method an alarm will be given at:

$$t_A = \min\{s; \sum_{t=1}^{s} \exp\left\{(-\lambda_1 + \lambda_0)\sum_{i=t}^{s} X(i)\right\} \cdot \left(\frac{\lambda_1}{\lambda_0}\right)^{s-t+1} > L\}$$

In the case where the observed data consists of number of events, X, recorded in fixed intervals of length k, for the likelihood ratio method, an alarm will be given at:

$$t_A = \min\{s; \sum_{t=1}^{s} P(\tau = t) \cdot \exp\{(-\lambda_1 + \lambda_0) \cdot k \cdot (s - t + 1)\} \cdot \left(\frac{\lambda_1}{\lambda_0}\right)^{\sum_{i=t}^{s} X(i)} > L \cdot P(\tau > s)\}$$

For the Shiryaev-Roberts method the time of an alarm will be:

$$t_A = \min\{s; \exp\{(-\lambda_1 + \lambda_0) \cdot k \cdot (s - t + 1)\} \cdot \sum_{t=1}^{s} \left(\frac{\lambda_1}{\lambda_0}\right)^{\sum_{i=t}^{s} X(i)} > L\}$$

If the counts are recorded for intervals of different length, a slight modification has to be done, but again this is straightforward.

For use in an epidemiological context also other properties of these methods needs to be examined properly. A desirable property, which was demonstrated by Frisén and Wessman (1999) to be fulfilled for the Shiryaev-Roberts method, at least in the case of a normal distribution, is that the predictive value is almost constant as a function of time. This would be particularly useful in an epidemiological context and the investigations to follow an alarm as this implies that an alarm could be interpreted in the same way regardless on whether it is late or early. If that is the case also for a shift in a Poisson process could be expected but remains to be verified.

3.2 Processes with Time Dependencies

If the assumption of a Poisson distribution for the cases of disease cannot be motivated, another approach must be taken. Noting that time series of a number of diseases exhibit time dependence (autocorrelation, seasonality etc) a series of papers have been devoted to model these time series. Properly modelled, deviations from the modelled series can be thought as an indication of a change in the disease pattern. Watier et al. (1991) propose an ARIMA type model based warning system where the alert threshold value is a function of the upper side of the prediction interval. The idea was applied to data for Salmonella in France. Nobre and Stroup (1994) use the forecast errors to calculate a probability index function to detect deviation from past observations applied to data for measles cases reported through the NNDSS. In Farrington et al. (1996) a regression algorithm was developed to assist in detecting outbreaks of infectious diseases reported to the CDSC. A threshold for the number of cases was constructed by using prediction intervals for the modeled base-line rate. Evaluation of the detection probability was made. The timely modeling of diseases was also the focus in Williamson and Hudson (1999), where ARIMA models were used on data for various diseases both on national and state level from the NNDSS. The residuals from one-step-ahead forecasts were suggested for surveillance. In VanBrackle and Williamson (1999) this idea was further investigated and the average run length was investigated applying the Shewart, the moving average method and the EWMA method to these residuals for 4 different types of shifts. Other examples of time series modeling can be found in Healy (1983),Ngo et al. (1996), Simonsen et al. (1997), Quenel and Dab (1998) and Cardinal et al. (1999). Reviews of different inferential approaches to the surveillance of processes with autocorrelation or with regression on time or on other variables are found in Frisén (1999).

Other medical problems include kidney failures with various possible changes studied in Smith and West (1983) in a Bayesian framework. Representing the problem as a state space model, the multiprocess Kalman filter was used to calculate on-line posterior probabilities for the different states. Some discussion of how to construct alarm systems based on these probabilities was included. Further reading can be found in Smith et al. (1983) and Gordon and Smith (1990). In Whittaker and Fruhwirth-Schnatter (1994), the same approach was used for detecting the onset of growth in bacteriological infections. An alarm was triggered if the posterior probability of a change exceeded a fix constant. The use of a Shewart-Cusum chart applied to recursive residuals from a continuous time first-order autoregressive, CAR(1), model, where the parameters of the model was continuously updated using a Kalman filter can be found in Schlain et al. (1992). In this case the method was applied to a tumour biomarker. Another examples of this approach can be found in Schlain et al. (1993) and Stroup and Thacker (1993).

4 DETECTION OF A CHANGE IN A SPATIAL STRUCTURE

In most public health surveillance programs, measurements are made at various locations both in space and in time, not only in time. For example, the cases of disease reported to the CDC through the NNDSS are collected at various places all over the US. The data on birth malformations reported by the ICBDMS consists of data from 35 different countries as of 1 January 2000. This leads to a multivariate situation, with possible spatial dependence between the locations of observation. To deal with this multivariate situation, methods of multivariate surveillance must be used. A multivariate version of the Sets method, using data of malformations from multiple sources, has been proposed (Chen, 1978 and Chen et al., 1982). In this case, fixed time periods was used contrary to the univariate one which uses the time between events. Here the number and size of terminated sets within the time period is used. In Stroup et al. (1988) the possibility of using multiple time series for detection of excess deaths from pneumonia and influenza was discussed. Here, one-step-ahead forecasts were used.

In many cases the methods used to analyse data from surveillance systems prospectively ignores the spatial structure of the data. All of the surveillance methods discussed so far are examples of this. One of the main purposes of the surveillance systems in use is to detect changes in the data observed. If the spatial structure of the data is ignored, this will lead to insufficient and sub-optimal surveillance methods due to loss of information of the observed process. The spatial component in infectious diseases, such as influenza, is clear. An example is the joint collaboration of different European countries during the winter of 1993-1994 (Fleming and Cohen, 1996) where the epidemic started in Scotland and spread south to the rest of the countries via England and France. A considerable time lag in influenza peeks was evident, which could be used for preventive actions.

In many cases the key issue of the public health surveillance itself includes detection of changes in spatial patterns, not only average changes in the case when the data collected are spatially correlated An example of this is various forms of clustering of diseases of which the case of child leukaemia has been the topic in many retrospective studies. In Dolk (1999) the role of assessing spatial variation and clustering of birth defects is treated. As in the area of detection of increased incidence rates, the area of cluster detection is dominated by different type of retrospective analysis methods, not designed for surveillance (Knox, 1964; Stone, 1988; Besag and Newell, 1991; Lawson, 1993; Waller and Turnbull, 1993; Waller and Lawson, 1995; Tango, 1995; Kulldorff and Nagarwalla, 1995 and Kulldorff, 1997). Papers on the detection of elevated risk due to possible putative sources include Diggle and Rowlingson (1994) and Lawson et al. (1999). However, in many of these situations there would have been an interest also in studying the development prospectively.

To construct surveillance methods for spatial processes is a complicated problem. In previous sections, which only included the time domain, we considered different assumptions of the observed process and different ways of observing and modelling this process. In the spatial domain the same questions are raised. General theory of statistics for spatial data can be found in Cressie (1993). In Lawson (2001) a discussion of how to generalize various kinds of spatio-temporal models to allow for prospective surveillance is given. In the case of spatial surveillance, a change in a parameter of the distribution of the observations can have a clear spatial interpretation, for example, a stronger tendency of clustering.

When confronted with a problem involving both spatial as well as temporal components, which is the case in surveillance of spatial structures, different approaches can be used. One example is the surveillance, in time, of a purely spatial statistic, which describes the spatial pattern for each time-point. This is the case when using a univariate test statistic designed for a retrospective test and following it through time using some surveillance method. This approach was used in Rogerson (1997), where a modification of the retrospective test suggested in Tango (1995) both for general and focused clustering was used prospectively and sequentially with a CUSUM method. The proposed system was evaluated using the ARL and the median run length. The same approach was used in Rogerson (2000) based on the Knox statistic suggested in Knox (1964).

In Raubertas (1989), the spatial structure of the reporting units is taken into consideration, leading to a multivariate surveillance situation. It is argued by the author that when the incidence of a disease is positively correlated between neighbouring reporting units, the sensitivity of the Poisson CUSUM method may be improved by pooling within neighbourhood observations, using closeness as weights. For each reporting unit a Poisson CUSUM is used. For the whole system an alarm is triggered as soon as any of the individual CUSUM schemes signals an alarm. ARL^0 and ARL^1 are suggested as measures of performance.

Another approach is to focus on the spatial model assumed for the observations and to make a sufficient reduction of the spatial structure at each time-point. In this case no information about the spatial structure will be lost. This approach was used in Järpe (1999) in the case of surveillance of clustering in a spatial log-linear model with a fixed lattice. Here the sufficient reduction resulted in the surveillance of a univariate statistic involving the sufficient spatial components for each time. A complete separation of the spatial and the temporal components was possible. The expected delay of an alarm for a fixed false alarm probability was examined for some examples. In Järpe (2000), a shift process spreading spatially as time increased was considered. Here a likelihood ratio statistic was suggested, including a sufficient reduction of the spatial structure. In this case, though, a complete separation of the spatial and temporal components was not possible due to the nature of the problem. Different ways of treating the multivariate structure in the spatial surveillance situation was discussed. As an application, the problem of an increased rate of radiation was investigated. Some evaluation and comparison with the system currently in use in Sweden, which is based on a moving window was made. The situation with a spreading shift process would correspond well to the surveillance of influenza, where the disease spread across Europe from Scotland (Fleming and Cohen, 1996).

As pointed out also in Lawson (2001), the possibility of development within this area is bright since there are a number of possible applications of statistical surveillance in a spatial context.

5 DISCUSSION AND CONCLUDING REMARKS

The usefulness of properly designed statistical surveillance methods cannot be exaggerated and many authors point out the need for such a system in various public health settings. Except for several practical issues such as the collection of data and the epidemiological investigations to follow an alarm, a surveillance system also raises a number of statistical challenges. Due to the nature of such a system with respect to the sequential type of decision situation, the common retrospective analysis methods are not useful. Many papers have addressed the problem of on-line surveillance but the mistake of not noting the sequential type of decision situation is quite common. In many of the papers, which deal with the inferential aspects correctly, lack of proper statistical evaluation of the suggested methods is evident. Usually, the only measures considered are the ARL^0 and ARL^1. However, in public health surveillance the event to be detected is not probable to occur at the same time as the surveillance starts. This means that the ARL^1 is not a suitable measure of evaluation. Instead other types of measures should be used, which takes into account also possible later shifts, since the performance of a surveillance method depends on the time of the change.

When constructing a surveillance method theoretically, often the intention is the fulfillment of some optimality criteria. The minimization of the $ARL^1$for a fixed value of ARL^0 is the common criteria. The logical drawbacks of this criterion and the advantages of other ones, such as the minimal expected delay for a fixed value of the probability of a false alarm, are discussed in Frisén (1999) and Frisén and Sonesson (2000). In many applications, including public health surveillance, only one measure of performance is not enough. Therefore one should aim at a complete and thorough evaluation of proposed systems. We suggest using measures such as the conditional expected delay, the expected delay, the probability of successful detection and the predictive value.

In practice, data is collected from many different sources, for example in the National Notifiable Diseases Surveillance System. This means that the observed process is multivariate. When discussing the coordination of disease data in different databases, this is a recognized fact (Levy, 1996 and Thacker et al., 1996). However, the proposed surveillance methods in public health, mainly treats the problem as a univariate one. In that way, the dependence between the different observations is not taken into account, which leads to loss of information. Instead, the surveillance situation should be handled as a multivariate one (Wessman, 1998a; Wessman, 1998b and Järpe, 2000).

It is our hope that research within this area is continued since there remains numerous problems to be solved and prospects for development are bright, which will be of great importance for society. In the case of a Poison process, the properties of the proposed likelihood ratio method and Shiryaev-Roberts method have to be examined properly.

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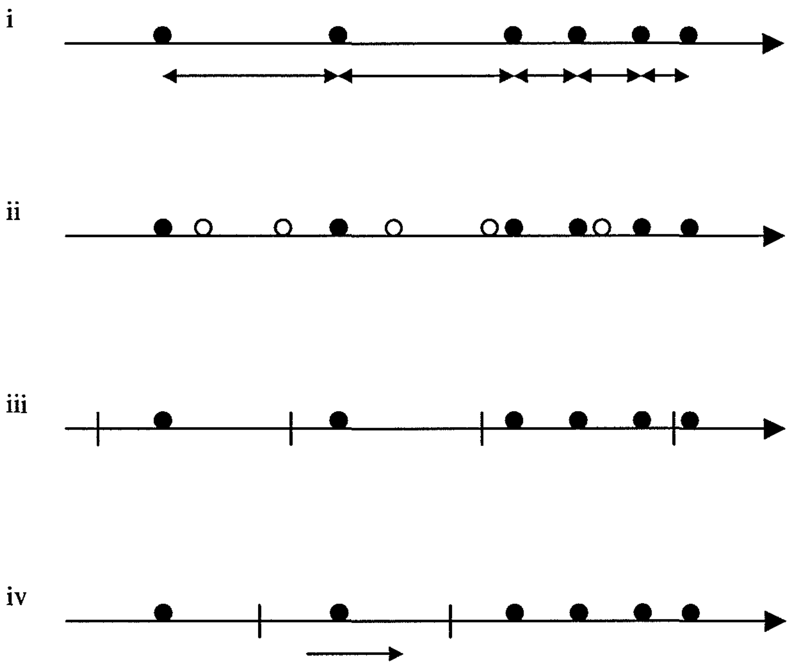

FIGURE 1:

Different ways of measuring the events of a Poisson process will be of great importance for the possibility of detecting an increased incidence rate. In the figure, a coloured dot represents an adverse event and a white dot represents an acceptable event.

i: Time intervals between adverse events measured in continuous time, as in the Exponential CUSUM.

ii: Time intervals between adverse events measured by the number of acceptable events, as in the Sets method.

iii: Using instead the number of events in fixed time intervals gives raise to the Poisson CUSUM.

iv: Observing the process using a moving window is another proposed approach.

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