

A space-time criterion for early detection of epidemics of influenza-like-illness

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Abstract. *Objectives:* To develop a method based on a space-time criterion for early detection of epidemics of influenza-like-illness in France. *Methods:* Since 1984, the French Communicable Diseases computer Network (FCDN) routinely detects epidemics of influenza-like-illness when the national incidence rate is, for 2 consecutive weeks, above a threshold computed by a periodic regression model. It appears that some areas reported early increases in incidence sev-

eral weeks before the national epidemic. An optimised space-time criterion allows an early detection of the epidemic periods. *Results:* Applying this space-time criterion to the last 11 epidemics (from 1986), the sensitivity was 0.82 and the specificity was 0.99. *Conclusion:* This simple procedure can be used as an additional tool for early detection of an epidemic taking into account the distribution of new cases in space and time.

Key words: Alert, Epidemiologic method, Influenza, Population surveillance, Sensitivity and specificity

Introduction

Since 1984, the French Communicable Diseases computer Network (FCDN) has provided weekly morbidity data on 8 diseases including influenza-like-illness (ILI) [1]. It involves about 1% of the total number of French general practitioners throughout continental France. These 'sentinel general practitioners' (SGP) are electronically connected to an information system and send, in real time, the morbidity data they collect. In return they receive information via the same system.

Each winter, a large increase in reports of influenza-like-illness is observed in France, corresponding to an epidemic period [2]. The FCDN has previously demonstrated its usefulness in detecting epidemics in France e.g. ILI [3], acute gastroenteritis [4] and chickenpox. Currently, a method developed by Serfling [5] is used in France and in the USA, but it is limited by a lack of consideration of any spatial dimension. This method aggregates local data to a national level and therefore lacks the sensitivity required to detect the local start of an epidemic. The use of spatial information may, therefore, enhance the sensitivity of the detection system.

We have developed a system which detects a new epidemic when, in a given number of French districts, the weekly incidence of reported cases exceeds a given value. An algorithm determines the optimum val-

ues for these two parameters (number of districts and incidence level) from data collected over the last 10 years.

Materials and methods

Definition of the space-time criterion

The criterion was defined by two exhaustive and mutually exclusive decision rules: detection and absence of detection. Epidemic detection was positive when in a given number of French districts the weekly incidence of cases exceeded a given value. The threshold for detection of epidemics according to this criterion was dependent on two parameters: (i) the number of districts N , and (ii) the minimum weekly incidence value S in cases per SGP per week. The absence of detection is defined by all other situations.

Data

For this study, we used the time-series dataset of influenza-like-illness. The first two years of the Sentinel surveillance were not included in the analysis because the starting points of epidemics occurring during the 1984–1985 and 1985–1986 seasons could not be defined precisely.

Table 1. Characteristics of the space-time criterion. Epidemic detection is defined as positive when more than 7 districts exceed the threshold value of 4.2 reported cases per SGP. Absence of detection is defined by all other situations. For these parameters (7 districts, 4.2 reported cases), the sensitivity (Se) was 0.82, the specificity (Sp) 0.99, the positive predictive value (PPV) was 0.82, and the negative predictive value (NPV) 0.99

	Pre-epidemic windows	Normal windows	
Epidemic detection	9	2	$PPV = 0.82$
Absence of detection	2	180	$NPV = 0.99$
	$Se = 0.82$	$Sp = 0.99$	

External reference

The Serfling method [5] is the criterion routinely used to detect epidemics. An epidemic is said to have commenced if the observed value of incidence is above the upper 95% confidence interval limit of the non-epidemic periodic regression model during two consecutive weeks. The new criterion was assessed according to whether it was able to detect epidemics at least one week earlier than the Serfling method, but no more than 3 weeks earlier.

Validating the new epidemic detection criterion

Validation of the criterion is based on the method used for diagnostic procedure, i.e. in terms of sensitivity, specificity and prediction values. To calculate these characteristics, we chose the Serfling method to define a reference for the beginning of each epidemic. This external standard is used to define time-periods corresponding to 'pre-epidemic windows' and non-epidemic periods named 'normal windows' (Table 1). We divided the 1986–1997 time series of influenza-like-illness surveillance (i.e. 579 weeks) into periods of 3 consecutive weeks called 'windows'. The period of 3 consecutive weeks immediately before the beginning of an epidemic is defined as the 'pre-epidemic window'. To be considered as relevant, the new crite-

ri-
on should therefore be able to detect a start of epidemic during the associated 'pre-epidemic window'. The 8 windows before, and the 8 windows after the 'pre-epidemic window' are defined as 'normal windows'. If the new criterion detects the beginning of an epidemic during the associated 'normal windows', this detection is considered as false alert. This procedure is used to build a table where detections (positive or negative) and absence of detection (justified or not) are counted (Table 1). Sensitivity (Se), specificity (Sp) and predictive values are calculated [6, 7] from this table.

Optimisation of criterion parameters

An algorithm for estimating parameter values has been developed by using the two following nested parameter values: (i) 1 to 10 districts, and (ii) 1 to 10 cases per SGP and per week in a given district. For each set of parameters, positive detection and absence of detection were classified in the appropriate windows (pre-epidemic or normal). For each pair of parameter values N , S , Se , Sp and predictive values were calculated. Sensitivity was calculated as the number of positive detections, according to the space-time criterion, divided by 11 (total number of influenza epidemics between 1986 and 1997). Specificity was calculated as the

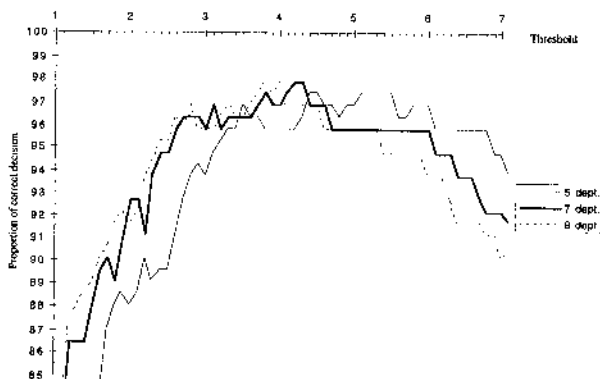


Figure 1. Optimisation of criterion parameters by maximisation of the value of the proportion of correct decisions (E). This figure shows the evolution of the proportion of correct decisions as a function of the threshold. Each curve corresponds to the value of the number N of districts ($N = 5$, $N = 7$, $N = 9$) which exceed the corresponding threshold value.

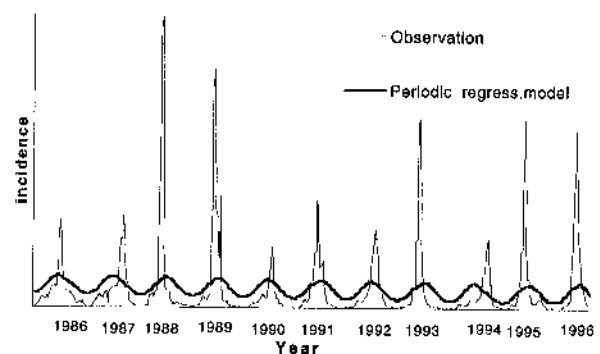


Figure 2. Influenza-like-illness incidence and the space-time criterion detection system. For an 11-year period of surveillance of influenza-like-illness the following information is plotted: (i) the weekly incidence as a function of time, (ii) the upper limit of the confidence interval of a periodic regression model used as the external reference for epidemic detection.

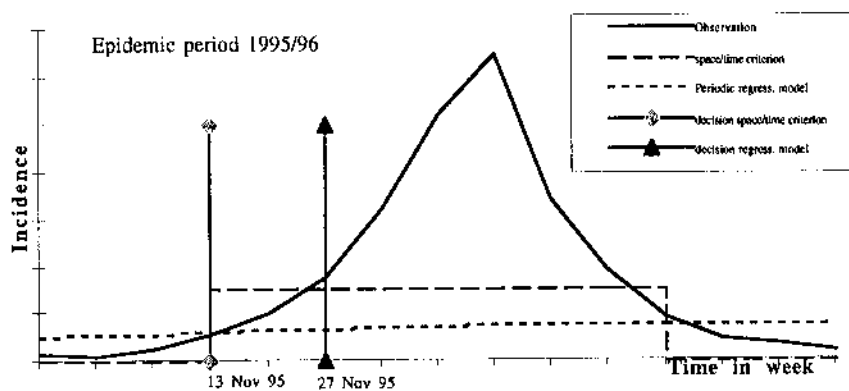


Fig. 3a

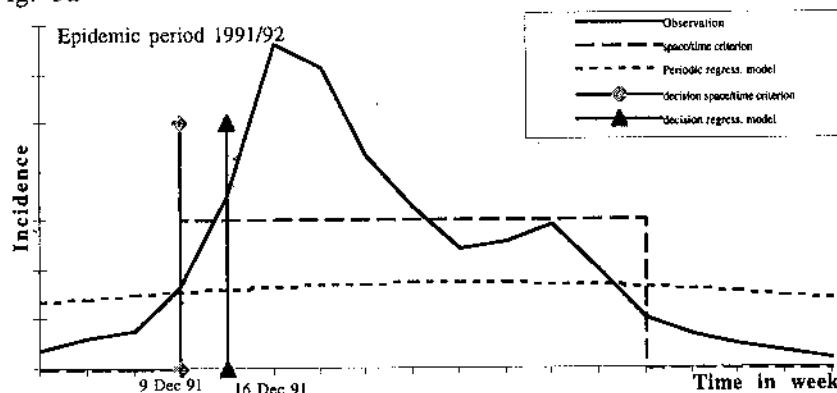


Fig. 3b

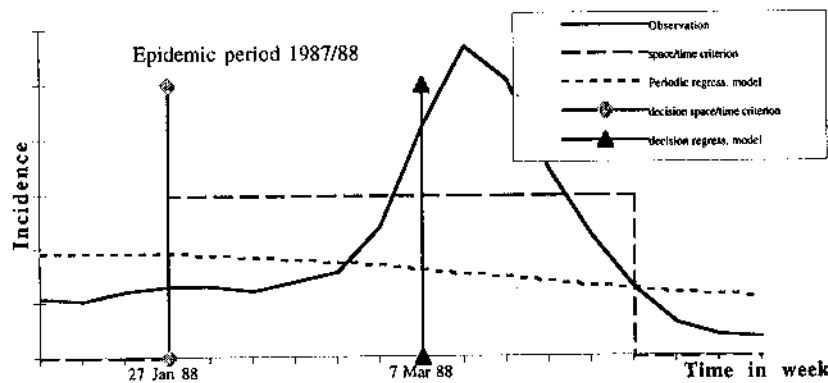


Fig. 3c

Figure 3. Detection of ILI epidemic with the space-time criterion (e.g. 7 districts with incidence ≥ 4.2 cases per SGP). (a) A positive detection occurred on 13 November 1995, i.e. two weeks before the reference method. (b) Only one week before the reference method. (c) Six weeks before the reference method. Each figure shows the following: (1) the weekly incidence as a function of time, (2) the space-time criterion, (3) the upper limit of the confidence interval of a periodic regression model used as the external reference for epidemic detection, (4) detection with the space-time criterion (dot), and (5) detection with periodic regression model (triangle).

number of absences of detection, according to the space-time criterion, divided by 182 time slots (total number of non-epidemic 3 week-periods between 1986 and 1997). The proportion of correct decisions (E), according to the proportion P of epidemics ($n = 11$) out of the total number of time slots ($n = 193$) was calculated as follows:

$$E = ((1 - P) \times Sp + P \times Se)$$

Maximisation of E was used as a criterion for parameter estimation.

Results

The proportion of correct decisions was plotted against the incidence of reported cases per SGP (threshold value) for different numbers of districts. The highest proportion of correct decisions with the lowest threshold value (4.2 or more reported cases per

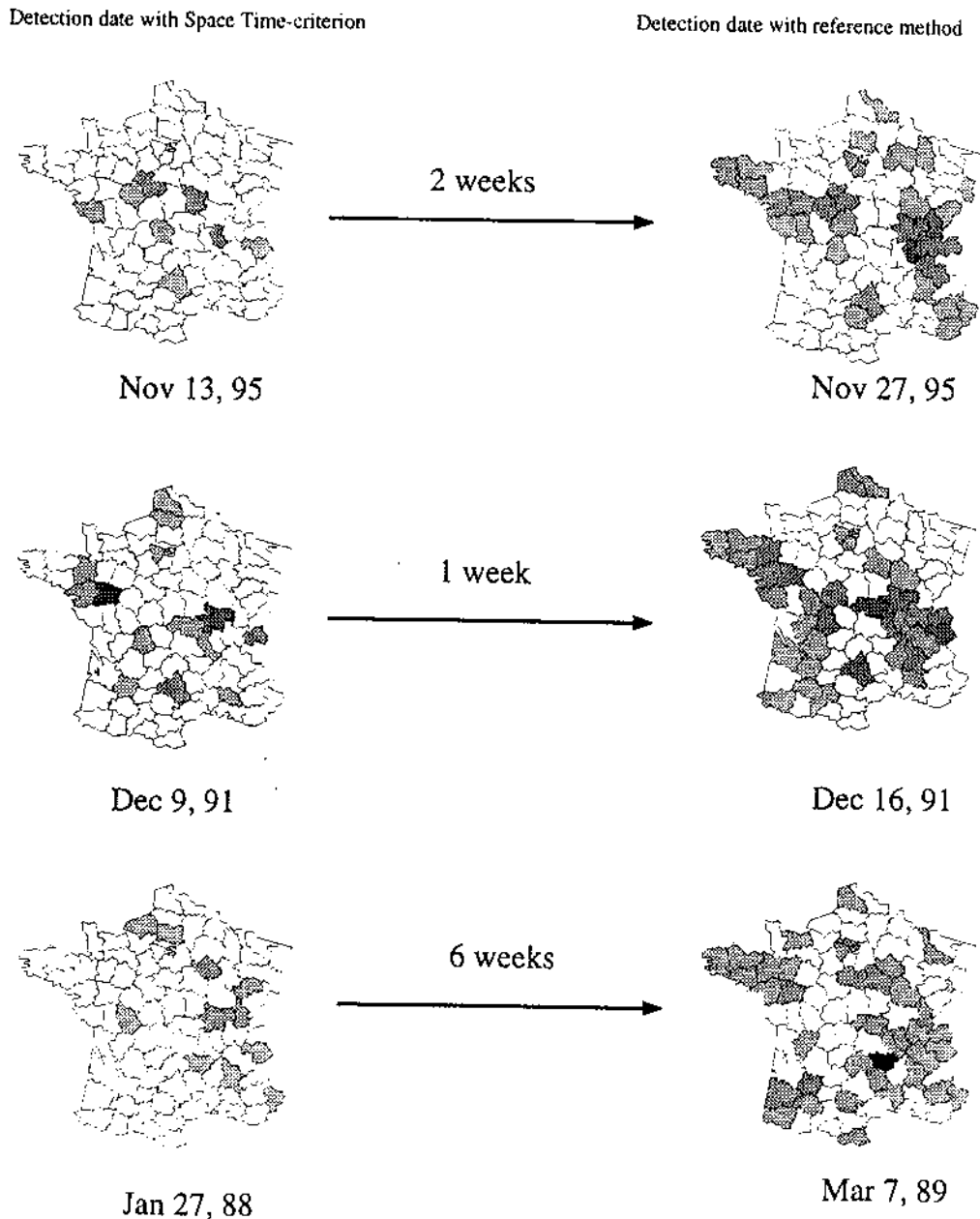


Figure 4. Spatial representations of the space-time criterion detection. Incidence maps for the weeks in which the new criterion predicted epidemics were compared with incidence maps for weeks in which epidemics were predicted by the reference method. We can see on these maps the reduced number of districts crossing an incidence threshold (in dark) of 4.2 cases per physician per week that allows a detection of an epidemic period compared with the higher ones of the classical method.

SGP) occurred when 7 districts reached the threshold value (Figure 1). For these parameters, the sensitivity was 0.82, the specificity 0.99, the positive predictive value (*PPV*) 0.82, and the negative predictive value (*NPV*) 0.99 (Table 1).

Periods where 7 districts reported 4.2 or more cases per SGP were plotted over the last 11 years along with (i) the observed weekly incidences, and (ii) the upper confidence interval limit of the periodic regression model used as the external reference for epidemic detection (Figure 2). Applying the new criterion to last 11 epidemics (1986–1997), 5 of them would have been detected 2 weeks before the classical detection, and 4

epidemics 1 week before. The remaining 2 epidemics would have been detected more than 3 weeks before, and are therefore considered as false alerts.

Detailed plots of 3 epidemics are shown in Figure 3. Figure 3a illustrates a space-time criterion detection which occurred on 13 November 1995, i.e. two weeks before the reference method. Figure 3b illustrates a case where the new criterion detected an epidemic one week before the reference method. In Figure 3c the new criterion detected an epidemic six weeks before the reference method. This example was considered as a false alert (a too early detection).

Incidence maps for the weeks in which the new cri-

terion predicted epidemics were compared with incidence maps for weeks in which epidemics were predicted by the reference method (Figure 4). We can see from these maps that an epidemic is predicted with fewer cases than required for the classical method.

Discussion

The application of a new space-time criterion to historical data has demonstrated that influenza epidemics may be detected earlier than with the Serfling method [5]. This work does not intend to provide an universal criterion, but a method to derive this criterion from observed data. Our results are therefore only validated on the French dataset. It is now possible to detect an epidemic if in 7 French continental districts 4.2 cases per SGP per week or more are reported on the Sentinel system.

Although 2 out of 11 epidemics were not detected by the new criterion, a high value of sensitivity (0.82) and specificity (0.99) have been achieved. It should be emphasised that for these two epidemics, the new criterion and the reference method became positive exactly at the same time. However, following our method, the new criterion was negative during the 'pre-epidemic window' and positive outside this window.

The size of the 'pre-epidemic window' has been determined a priori but arbitrarily for practical purposes. The larger the window is, the lower the risk of error. Therefore, a 3-week period corresponds to a reasonable time lag for alerting. According to our field experience in epidemiology, it seems to be unrealistic to alert for an influenza epidemic more than 3 weeks before its detection at national level by the routine tools. However, we calculated that a timespan of 4 weeks would have produced sensitivity, specificity, *PPV* and *NPV* of 100%; this is better than with the 3 weeks 'pre-epidemic window' results, but with no improvement in its practical use.

Since we chose the criterion and validated it on the same dataset, this may have produced over-optimistic sensitivities and specificities. But it is not a static criterion defined for ever. It is devoted to be dynamically computed from data collected to the most recent periods to allow for current predictions.

It may be argued that other space units could have been chosen, such as the regions ($n = 22$ space units), or the SGP ($n = \text{approx. } 500$ space units). Moreover, this space-time criterion could have seasonal variations (as the reference method provides it). But the main goal of this work was to search for a simple, robust, and easily reproducible space- and time-based criterion, with high levels of sensitivity and specificity. Further developments may involve more refined ver-

sions taking into account our finding that the space level enhances the accuracy of epidemic detection.

This time-space criterion is clearly useful for diseases with regular patterns, which develop progressively and involve an element of spatial spread. However, this criterion needs to be validated for other patterns, e.g. outbreaks of food-borne infection. The authors intend to develop this detection tool for use with other disease under surveillance. Regarding influenza-like-illness, the space-time criterion is now routinely in use on the sentinel system.

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