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ORIGINAL ARTICLE

Rapid mapping of the spatial and temporal intensity of influenza

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Abstract

Surveillance of influenza epidemics is a priority for risk assessment and pandemic preparedness, yet representation of their spatiotemporal intensity remains limited. Using the epidemic of influenza type A in 2016 in Australia, we demonstrated a simple but statistically sound adaptive method of mapping epidemic evolution over space and time. Weekly counts of persons with laboratory confirmed influenza type A infections in Australia in 2016 were analysed by official national statistical region. Weekly standardised epidemic intensity was represented by a standard score (z-score) calculated using the standard deviation of below-median counts in the previous 52 weeks. A geographic information system (GIS) was used to present the epidemic progression. There were 79,628 notifications of influenza A infections included. Of these, 79,218 (99.5%) were allocated to a geographical area. The GIS maps indicated areas of elevated epidemic intensity across Australia by week and area that were consistent with the observed start, peak and decline of the epidemic when compared with counts aggregated at the state and territory level. This simple, adaptable approach could improve local level epidemic intelligence in a variety of settings and for other diseases. It may also facilitate increased understanding of geographic epidemic dynamics.

Keywords Epidemics · Pandemics · Influenza, human · Geographic information systems · Australia · Laboratories · Risk assessment · Epidemic intelligence

Introduction

Surveillance of influenza is a global priority, to inform risk assessment, control and response. Key questions are whether the infection is spreading, how fast it is spreading and where has it spread [1]? More geographically refined epidemic intelligence is desired by epidemic response stakeholders such as local public health controllers and epidemiologists, to facilitate situational awareness and to motivate and inform local response activities in a timely manner [2]. Yet, surprisingly few examples exist of systems or algorithms for rapidly generating spatial representations of changing influenza intensity over time using systematically collected surveillance data.

Official influenza activity maps reported by the USA and Australian health authorities have limited geographic resolution, showing levels only for whole states or territories. The quantity mapped is based on epidemiologists' qualitative interpretation of local data and thus may be subjective or biased by anecdotal information. Intensity in each region is categorised into 'Sporadic', 'Localised', 'Regional' or 'Widespread', based on interpretation of local surveillance information [3, 4]. Other approaches use syndromic proxies of influenza activity that can be represented with proportions or population denominators. For example, the 'moving epidemic method' is used in Europe to compare syndromic proxies of influenza activity by country [5]. It can be applied to various observations of influenza activity, including population rates and consultation proportions of influenza-like illness (ILI) or acute respiratory infections [5]. It has also been applied at a within-country regional level [6]. Another European

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example using syndromic data only aimed at signalling the start of an epidemic by region. The method aims to determine an epidemic threshold and an intensity scale using data from a training period of 5 to 10 years [7]. The USA uses the proportion of outpatient visits with ILI to represent influenza intensity each week in each state [3].

Australia is unusual in that all influenza infections confirmed by a microbiology laboratory are notifiable to regional or state health jurisdictions and are collated nationally on a daily basis [8]. The number of specimens tested is not reported, so the proportion of specimens positive for influenza is not available. Thus, only raw counts can be monitored. The degree of ascertainment of influenza infections through notifications is uncertain and is likely to vary from region to region and may be biased towards hospitalised patients [9]. Like the USA [3], Australia has no national protocol or recommendation for who is tested for influenza; the number of tests done can reflect the size of the population at risk, local, organisational or individual medical care provider testing preferences, as well as the actual population incidence of infection. In Australia, the number of confirmed influenza infections has grown year on year, faster than population growth. This may be due to greater availability of, and interest in, influenza testing [10].

The problem of detecting changes in intensity of a public health surveillance time series has been developed in the context of statistical process control charts [11]. Statistical process control grew from industrial quality control systems for monitoring the quality of products made by machines or other industrial processes. This has also been applied in health care quality control monitoring [12, 13]. When the industrial process is producing quality products, it can be described as being 'in-control'. When the industrial process starts to fail, it becomes 'out of control'. The out of control state is reached when the process produces products which have some quality or measurement that exceeds an acceptable limit or threshold. When considering epidemiological time series, non-epidemic periods can be considered in-control and epidemic periods can be considered out of control.

In statistics, the 'standard score', or more commonly, 'z-score', can be used as a measure of difference from a reference value. It is measured in units of standard deviations. The reference value is usually estimated as the mean (average) of previous observations that are known to be in control. Standard deviations are a conventional statistical estimate of the variability of real data. When dealing with in-control counts of infectious disease notifications in an area, the Poisson statistical distribution provides a means of estimating expected variability in data.

In statistical process control terms, a graph of z-scores based on in-control (non-epidemic) counts that follow a Poisson distribution is called a 'u-chart' [12]. The z-score is an appealing statistical quantity because its magnitude reflects not only the size of the departure from the expected reference level but is also standardised in a unitless measure, the standard deviation. This standardisation makes it widely applicable to many diseases.

Using the u-chart process control principle applied to influenza infections reported in residents of Australian statistical regions during the 2016 influenza season, we demonstrated an adaptive approach to representing epidemic intensity when only surveillance counts are available and no suitable denominator is available. This may provide an alternative automated means of providing more local-level epidemic intelligence for health protection officials.

Methods

We requested non-identified records of notified laboratory-confirmed influenza cases from the National Notifiable Diseases Surveillance System (NNDSS) [8]. The provided records included influenza type, were date-stamped to allow weekly aggregation and were geo-tagged. The date allocated was based on the laboratory specimen collection date. The week ending date was allocated to the date of the Friday at the end of the 7-day period containing the specimen collection date. Geo-tagging was done by allocating the residential postal code of the influenza patient to a national official statistical region classification called 'Statistical Area Level 4' (SA4) of the 2011 Australian Statistical Geography Standard (ASGS). SA4s are the largest sub-state geographical areas in the ASGS, and each has a population consisting of approximately 100,000–500,000 persons. The SA4 boundaries reflect regional employment zones [14]. Postal codes straddling > 1 SA4 were assigned to the SA4 containing the largest areal proportion of the postcode. NNDSS data were not provided for the Australian Capital Territory (~ 400,000 persons, < 2% of the Australian population). We excluded records without an assigned SA4. To reduce confusion caused by epidemic patterns of distinct virus types, we restricted our analysis to influenza type A, which dominated the 2016 influenza season (89% of notifications).

Statistical analysis

We aggregated influenza type A notifications into weekly counts for 2015 and 2016, with 2015 providing the baseline period. For each SA4, and for each week of 2016, we computed a standard score (commonly known as a z-score) using a 52-week moving window of the time series of weekly counts as follows:

Step 1: Compute the median of the weekly counts for the past 52 weeks.

Step 2: Compute the mean and estimated standard deviation of all weekly counts in the past

52 weeks that were less than or equal to the median.

Step 3: Estimate the z-score by subtracting the mean from the current week's observed count and divide the result by the standard deviation.

The equation for the z-score is $z = \frac{(n_0 - \bar{x})}{\sigma}$ where n_0 is the count in the most recent week, week *0*, and the standard deviation, σ, was estimated as $\sigma = \sqrt{\bar{x}}$ where $\bar{x}$ is the mean of counts less than or equal to the median in the prior 52 weeks, that is,

$$\bar{x} = mean(x_{-1}, \ldots, x_{-52}) \text{ where } x_i$$

$$= \begin{cases} missing, & n_i > median(n_{-1}, \ldots, n_{-52}) \\ n_i, & n_i \leq median(n_{-1}, \ldots, n_{-52}). \end{cases}$$

where n_i is the count in week *i* relative to week *0*. Missing values of x_i were not included in the calculation of $\bar{x}$.

By using the lowest 26 weekly counts in the past 52 weeks, the mean and standard deviation provide expected counts when influenza is diagnosed sporadically, assuming epidemic influenza occurs in fewer than 6 months of the year. In calculating the standard deviation, we assumed that the below-median counts followed a Poisson distribution for counts, in which the variance is equal to the mean. Thus, we estimated the standard deviation as simply the square root of the mean. If the baseline mean was zero, then the standard deviation was zero and the z-score was inestimable.

The z-scores were categorised into six intensity levels in intervals of 10 (0- < 10, 10- < 20, ... 40- < 50, > 50). This provided good discrimination of intensity levels during 2016.

Choropleth maps are maps with each region colour-shaded according to a value range in which the estimated statistic lies. We generated choropleth maps for each week based on the categorised z-scores. Colour shades ranged from light yellow (low intensity) to dark reddish brown (high intensity). SA4s with inestimable z-scores were shown in grey.

To verify the face validity of our results for each state and territory, we estimated the epidemic start, peak and end dates based on weekly counts of notifications. The epidemic start date was the ending date of the first week of a sequence of 6 weeks in which counts increased monotonically. Epidemic end was the ending date of the first week that was below the count in the epidemic start week.

Statistical computation was done in MATLAB version R2016a and maps were generated using ArcMap 10.3.1.

Ethics approval

This study was approved as negligible risk research by the UNSW Human Research Ethics Committee.

Results and discussion

In 2016, there were 79,628 notifications of influenza A infections in Australia, excluding the Australian Capital Territory (ACT) for which data were not provided. Of these, 79,218 (99.5%) were able to be allocated to an SA4. Of the 19% of notifications in which subtypes were reported, 64% were A(H3N2), with the remaining being A(H1N1). Of the 87 Australian mainland and Tasmanian SA4s, we had influenza notifications for 86, since data were unavailable for the single SA4 in the Australian Capital Territory. Tables 1 and 2 show the distribution of counts and z-scores across all 4472 weekly counts for the 52 weeks in 2016 and 86 SA4s. Queensland had the highest median count (10) and highest median z-score, while Tasmania had the lowest median count (0) and the Northern Territory had the lowest median z-score (0.96). South Australia had the most frequent high counts and z-scores with upper quartiles of 27 and 17.68, respectively. Tasmania had the highest frequency of low counts, with an upper quartile of 4, and the Northern Territory had the highest frequency of low z-scores with an upper quartile of 3.59. The most populous state, New South Wales (NSW), had the third highest median count (6) and the second highest median z-score (2.22) of all states and territories. It also had the second highest upper quartile z-score (9.90), after South Australia (17.68).

Complete maps of influenza intensity z-scores in 2016, by week, and a video presentation of the evolving epidemic, are available in the Supplementary material. There were brief periods of elevated intensity (z-score > 10) outside of the capital, Brisbane, in various parts of eastern Queensland during March 2016. The early June epidemic start date in Western Australia (Table 3) was not evident in the maps at that time. In late June, a rural SA4 in northern NSW showed elevated activity which persisted for several weeks. This coincided with the epidemic start date estimated for the state (Table 3). The maps showed a brief increase in part of urban Melbourne in late June, prior to the epidemic start date for Victoria in early July (Table 3).

Sustained, continuous elevated intensity appeared on the weekly maps in Australia from early July (Supplementary material), 1 month after the estimated epidemic start date for Australia (Table 3). Figure 1 shows the intensity maps for 4 weeks starting with the week ending 8 July 2016. In that week, moderate intensity (20 < z-score < 50) was evident in parts of NSW and its capital Sydney. This is consistent with the earlier epidemic start in NSW (Table 3). In the week ending 15 July, Brisbane, the capital of Queensland started to show moderate intensity, while elevated intensity started in part of Melbourne, the capital of Victoria. This is consistent with the later epidemic start date in Queensland and then 1 week later in Victoria (Table 3). By 22 July, parts of Sydney were experiencing more intense activity, while lower level activity was spreading through regional Queensland in

Table 1 Descriptive summary of all weekly counts of influenza A notifications for all Level 4 Statistical Areas (SA4s) (N = 4472), by state or territory, Australia[a], 2016

State or territory	Population[b]	No. SA4s	Mean	Median	Max	Quartile 1	Quartile 3
New South Wales	7,739,274	28	21	6	342	2	17
Victoria	6,179,249	17	13	5	155	1	12
Queensland	4,848,877	19	21	10	192	5	22
South Australia	1,713,054	7	19	7	126	2	27
Western Australia	2,558,951	9	12	5	120	2	11
Tasmania	517,588	4	5	1	100	0	4
Northern Territory	245,740	2	6	3	39	1	6
Australia*	24,210,809	86	17	6	342	0	9

[a] Excluding the Australian Capital Territory for which data were not available.

[b] Source of population data: Australian Bureau of Statistics, 3101.0 Australian Demographic Statistics, Sep 2017.

the north-east and Victoria in the south-east of Australia. By 29 July, intensity was elevated in Adelaide (the capital of South Australia) and Perth (the capital of Western Australia). These increases were later than the estimated epidemic start dates for these states (Table 3). Throughout July, there was no increased intensity evident in the Northern Territory (capital Darwin), or in Tasmania (capital Hobart), which is broadly consistent with their later epidemic start dates (Table 3).

Figure 2 shows the intensity levels for four time points spanning the entire season. These were the first week of each month from July through October. In early July, only one SA4, in rural northern NSW, showed elevated activity. By early August, there was intense activity (z-score > 50) on the east coast of NSW and in Sydney, slightly less intensity in Brisbane. There was elevated intensity along much of the east and south-east coast, including Melbourne, Hobart and Adelaide, and regional Western Australia. By early September, there was intense activity in at least some SA4s in all capitals except Darwin. This coincides with Australia's estimated epidemic peak (Table 3). There was also intense activity in most of regional NSW and parts of Queensland and Victoria. There was moderate intensity in much of regional Western Australia. By early October, there was elevated intensity across most of Australia, including Darwin and the Northern Territory. Activity had returned to background levels in urban Sydney and parts of regional NSW and Victoria.

Consistent with the later epidemic peak and continuing epidemic activity in South Australia to the end of 2016 (Table 3), elevated intensity continued in and around Adelaide throughout December 2016 (Supplementary material). The Northern Territory's epidemic peak at the end of September (Table 3) coincided with the highest intensity shown for the territory in the maps (Supplementary material).

Table 2 Descriptive summary of all weekly influenza A intensity values (z-scores) for all Level 4 Statistical Areas (SA4s) (N = 4472)[a], influenza A, by state or territory, Australia[b], 2016

State or territory	Mean	Median	Max	Quartile 1	Quartile 3
New South Wales	12.59	2.22	205.59	0.17	9.90
Victoria	7.94	2.10	73.12	− 0.11	9.09
Queensland	7.81	2.24	99.43	0.12	8.60
South Australia	9.77	1.58	71.23	− 0.79	17.68
Western Australia	5.10	1.02	52.18	− 0.33	5.17
Tasmania	5.84	1.12	102.67	− 0.27	4.51
Northern Territory	3.01	0.96	35.33	− 0.40	3.59
Australia[b]	9.09	1.83	205.59	− 0.04	8.60

[a] Ninety-one of 4472 (2.0%) inestimable z-scores were excluded from the calculations in the Table. Z-scores were inestimable if the denominator was zero.

[b] Excluding the Australian Capital Territory for which data were not available.

Table 3 Estimated seasonal influenza A epidemic start, peak and end dates, by state and territory, Australia[a], 2016

State or territory	Epidemic start	Peak week	Epidemic end
New South Wales	24 Jun 2016	2 Sep 2016	11 Nov 2016
Victoria	8 Jul 2016	2 Sep 2016	18 Nov 2016
Queensland[†]	1 Jul 2016	9 Sep 2016	18 Nov 2016
South Australia	1 Jul 2016	16 Sep 2016	–
Western Australia	10 Jun 2016	2 Sep 2016	11 Nov 2016
Tasmania	22 Jul 2016[c]	9 Sep 2016	4 Nov 2016
Northern Territory	15 Jul 2016	30 Sep 2016	–
Australia[a,b]	3 Jun 2016	2 Sep 2016	30 Dec 2016

Epidemic start was the ending date of the first week of a sequence of 6 weeks in which counts increased monotonically. Epidemic end was the ending date of the first week that was below the count in the epidemic start week. An epidemic end shown as '–' means the count did not decline below that of the epidemic start before the end of 2016

[a] Excluding the Australian Capital Territory for which data were not available.

[b] Queensland and Australia had one additional period of 6 weeks of sustained counts starting at the end of January 2016 but which subsequently declined prior to the main epidemic period starting at the beginning of July.

[c] Tasmania did not have a period of 6 weeks of continuous increase in counts, so the epidemic start was based on a 5-week period of increase.

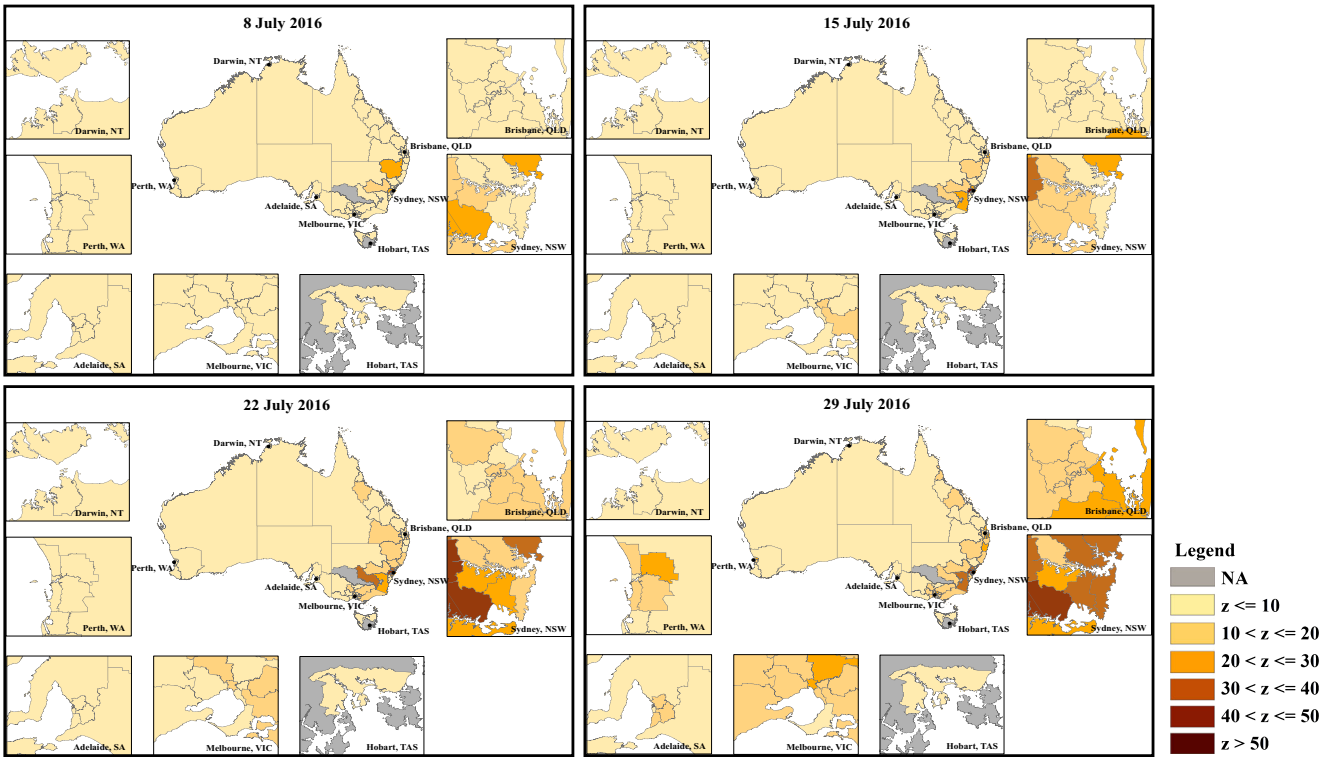

Fig. 1 Early influenza A epidemic intensity (z-score) weeks ending 8 July through 29 July 2016, by Level 4 Statistical Area, Australia. (1) Statistical areas in which the z-score was inestimable in that week are shown in grey; (2) data were not available for the Australian Capital Territory, which is shown in grey

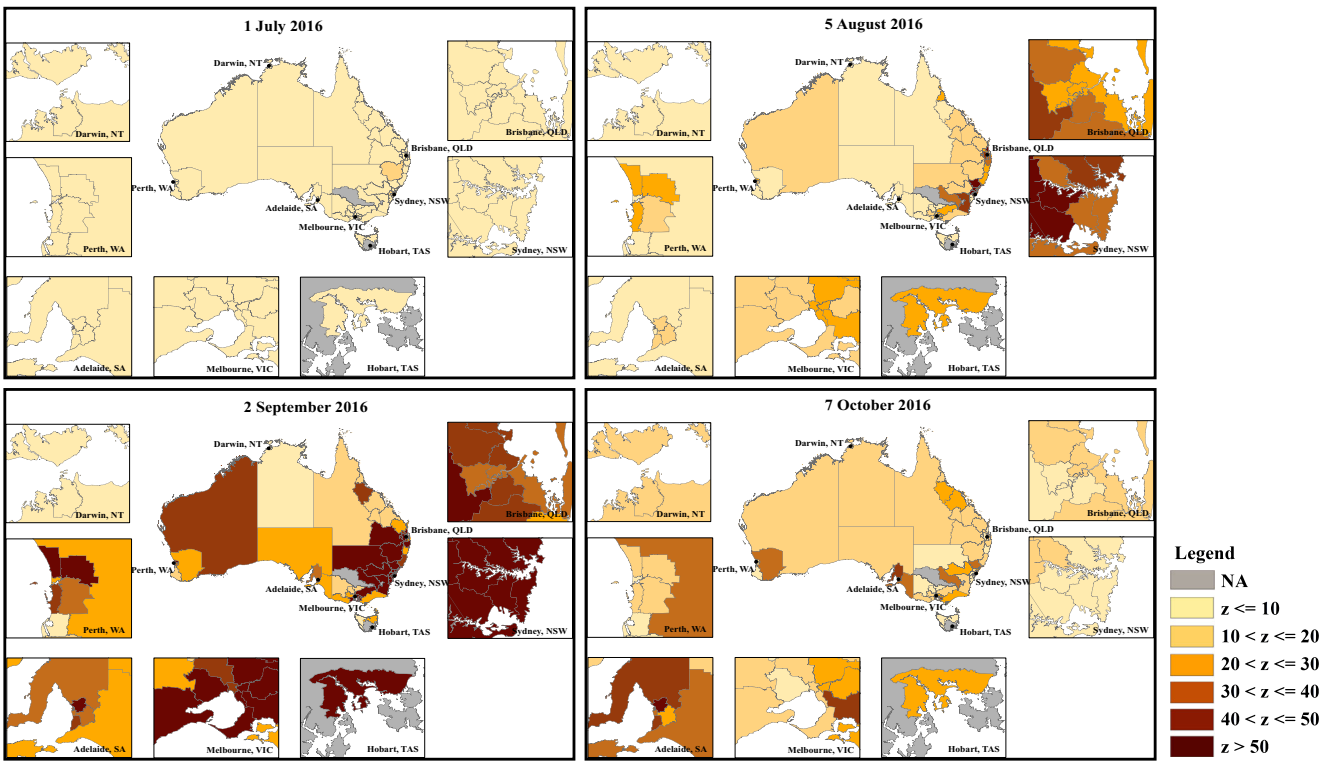

Fig. 2 Early, middle and late influenza A epidemic intensity (z-score), first week ending each month from July through October, by Level 4 Statistical Area, Australia. (1) Statistical areas in which the z-score was inestimable in that week are shown in grey; (2) data were not available for the Australian Capital Territory, which is shown in grey.

Parts of Tasmania and rural southern NSW had insufficient background activity to permit estimation of z-scores for substantial periods of time. These inestimable areas were shown as grey in the maps (Figs. 1 and 2 and Supplementary material).

The maps provided objective estimates of intensity based solely on observed data and provided plausible results consistent with trends in counts of notifications aggregated at the state and territory level. In contrast, the influenza surveillance maps published by the Australian government include varying geographic resolution by state and territory, ranging from zero to three sub-regions [4].

The United States syndromic ILI Activity Indicator Map uses a similar z-score approach to represent state level intensity of hospital outpatient attendances that present with ILI [15].

The approach developed here has some limitations. The z-score method requires at least 1 year of surveillance prior to implementation and relies on periods of sporadic disease occurrence lasting at least 6 months. These sporadic occurrences may be due to imported influenza in travellers, or due to small localised outbreaks occurring out of season, which may reduce the accuracy of the z-score. On the other hand, the out of season levels may reflect the probability of a case of influenza having confirmatory testing in that region. Apart from the sparsely populated areas of regional Tasmania and southwestern NSW, background counts were sufficient to estimate z-scores in nearly all SA4s and weeks. The scale we selected for z-scores was based on 2016 activity alone, and more years of data need to further evaluate the scale. Australia's highly urbanised and coastal population means rural statistical regions often cover large areas. The approach should be evaluated for smaller statistical region classifications.

In conclusion, we have demonstrated a promising method for easily and automatically representing spatial spread of an influenza epidemic when only continuous weekly counts of positive influenza specimens are available. Regional mapping of influenza intensity may signal rapid epidemic growth and provide valuable local level epidemic intelligence to regional officials and guide them in when to implement response measures such as establishment of ILI clinics and distribution of antiviral medication or prophylaxis.

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