

SPC Applications in Syndromic Surveillance

Ron Fricker

with A. Dunfee, B. Hegler, C. Hu, and M. Knitt

**Quality and Productivity Conference
June 6, 2007**

The New Status Quo?

"All the News That's Fit to Print"

The New York Times

National Edition
 South: Mostly cloudy and warm with scattered showers and storms, except partial sunshine near the Gulf coast and also in much of Georgia. Weather map and details are on Page C14.

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Smallpox Vaccinations Are Urged and Prairie Dogs Are Banned to Halt Monkeypox

By LAWRENCE K. ALTMAN
 The federal government recommended smallpox vaccinations yesterday for all those exposed to monkeypox, including pregnant women and children. It also banned the sale and distribution of prairie dogs in the nation and prohibited the importation of all rodents from Africa.

The Centers for Disease Control and Prevention also issued a list of signs and symptoms to determine which patients had monkeypox and to help in the agency's investigation of this potentially fatal viral disease. The actions seek to control the first outbreak of monkeypox in the Americas and to prevent importing it and other diseases endemic elsewhere in the world. Imported rodents are believed to have brought monkeypox to the United States from West and Central Africa, where it is endemic.

Yesterday, there were 54 cases of monkeypox under investigation in four states. Laboratory tests have confirmed monkeypox in 23 patients. Of the 54, Indiana reported 21 cases. Wisconsin reported 10 cases. Jersey reported 1 case.

Monkeypox is fatal in up to 10 percent of cases, much lower than the 30 percent figure for smallpox before it was eradicated worldwide in 1980. The government stopped routine smallpox vaccinations in 1979. The Bush administration began vaccinating health care workers this year in a program to protect against the infection after exposure.

The vaccine is given in two doses, one at the time of exposure and a second one 28 days later. The Centers for Disease Control and Prevention said the vaccine is 85 percent effective in preventing monkeypox. The disease centers said the vaccination was most effective during the first four days after exposure to an infected animal and to a lesser extent during the 12 to 14 days after exposure.

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Of 54 suspected cases, four states and countless questions.

Dogs and importing rodents from Africa took effect immediately and will remain in effect until health officials can determine the safety of such importations.

Senators James M. Jeffords, independent of Vermont, and John Ensign, Republican of Nevada, yesterday called for an Environment and Public Works Committee hearing on regulations on importing exotic pets.

ing sick animals after they had been checked by a veterinarian. Federal health workers are tracking shipments of potentially infected animals to help prevent the spread of monkeypox and to reduce the chances of the disease gaining a permanent foothold. The disease centers included these signs and symptoms for monkeypox: a rash consisting of raised bumps

Mystery outbreak's global reach grows

By M.A.J. McKENNA
 cases of the illness was taken plane in Frankfurt his pregnant wife er after he develo- tions. On Monday, said the wife was

Anthrax Found in NBC News Aide

Suspicious Letter Is Tested at Times — Wide Anxiety

By DAVID BARSTOW
 An assistant to the NBC anchor Tom Brokaw has tested positive for anthrax infection more than two weeks after she opened a threatening letter addressed to Mr. Brokaw that contained a white powder, officials said yesterday.

Even as law enforcement officials were cordoning off Rockefeller Center, the newsroom at The New York Times was evacuated when a reporter opened an envelope that also contained a white powder.

The substance was still being tested last night, as investigators explored potential links between the two incidents. Both letters were mailed from St. Petersburg, Fla., and had similar handwriting, according to law enforcement officials.

The reports of possible bioterrorism caused widespread anxiety in New York and across the country. People depleted supplies of antibiotics at drugstores and besieged their doctors. Offices were evacuated after a spate of threats, and companies made emergency adjustments to the way they received mail. (Page B9)

The NBC case marked the second time an American has been stricken with a form of anthrax since the Sept. 11 terror attacks.

In the other case, a man died after he contracted an inhaled form of the disease at a newspaper office in Boca Raton, Fla. Two other people at the office were exposed to anthrax



Mayor Rudolph W. Giuliani at a news conference yesterday at NBC, where he tried to calm new fears that were raised by an anthrax case.



Travelers wear masks to ward off Asia's mystery illness at Hong Kong's Chek Lap Kok airport on Monday.

Internationally, tensions eased slightly after the government of China said it will provide information to the global health agency about a pneumonia outbreak four months ago. A12

Please see ILLNESS, A12

WEST NILE CASES RAISING QUESTIONS OVER TRANSPLANTS

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INSIDE

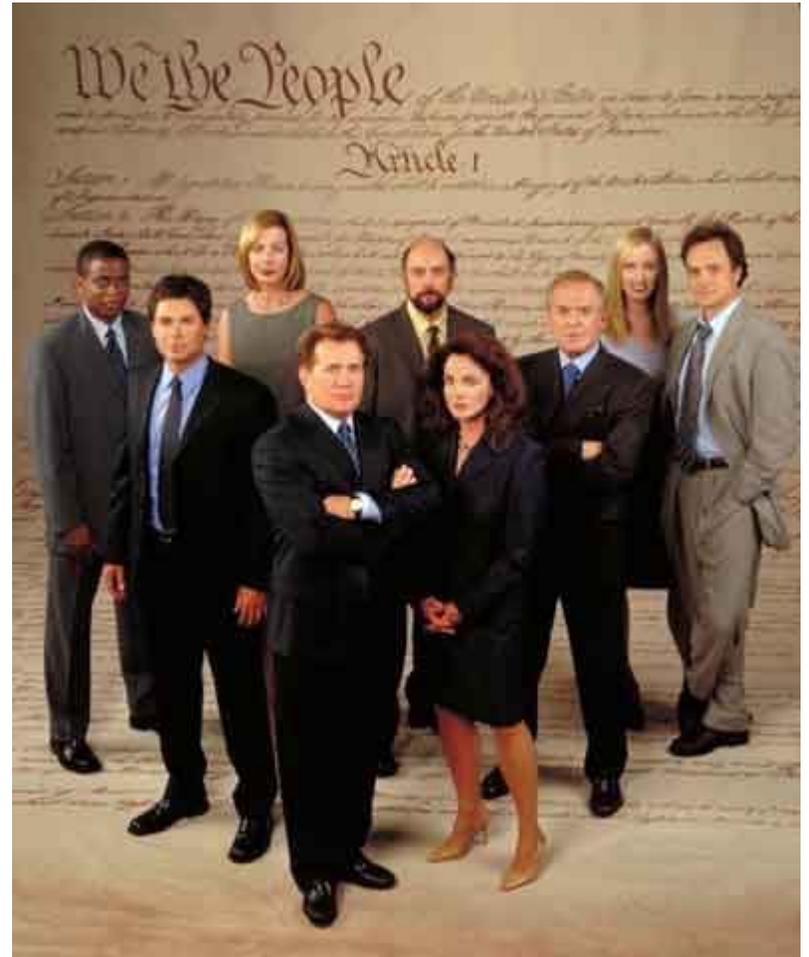
Chinese government asks the World Health Organization to help identify the cause of a pneumonia outbreak four months ago. A12

Even in Popular Culture...

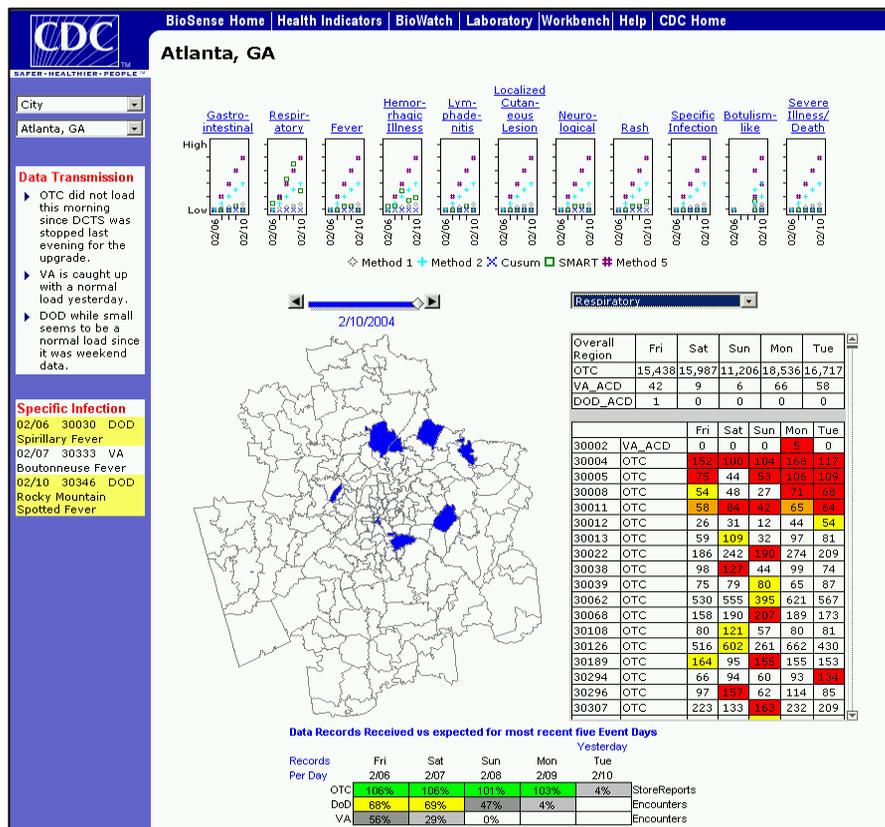
“That’s how it’s gonna be, a little test tube with a-a rubber cap that’s deteriorating... A guy steps out of Times Square Station. Pshht... Smashes it on the sidewalk... There is a world war right there.”

“Josh”

West Wing, 1999



BioSense and Other Syndromic Systems Already Operational



Implementation survey (Gibson et al., 2004):

- Survey of ~100 states and major cities; 40 responses
- >50% have syndromic surveillance in place
- ~90% have a system or are planning one

(One) Definition of Syndromic Surveillance

- “...surveillance using health-related data that precede diagnosis and signal a sufficient probability of a case or an outbreak to warrant further public health response.” [1]
- On-going discussion in public health community about use of syndromic surveillance for “early event detection” vs. “situational awareness”

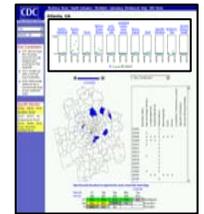
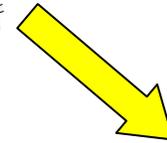
[1] CDC (www.cdc.gov/epo/dphsi/syndromic.htm, accessed 5/29/07)

Leveraging Secondary Health Data

- Ideal is automatic or near real-time data analysis
- Use data, methods to allow for identification of subtle trends not visible to individual MD's
- Provide indicators to trigger detection, investigation, quantification, localization, and outbreak management



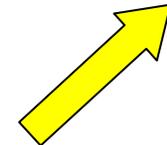
**Clinical
Data and
Lab Results**



**Syndromic
Surveillance
System**

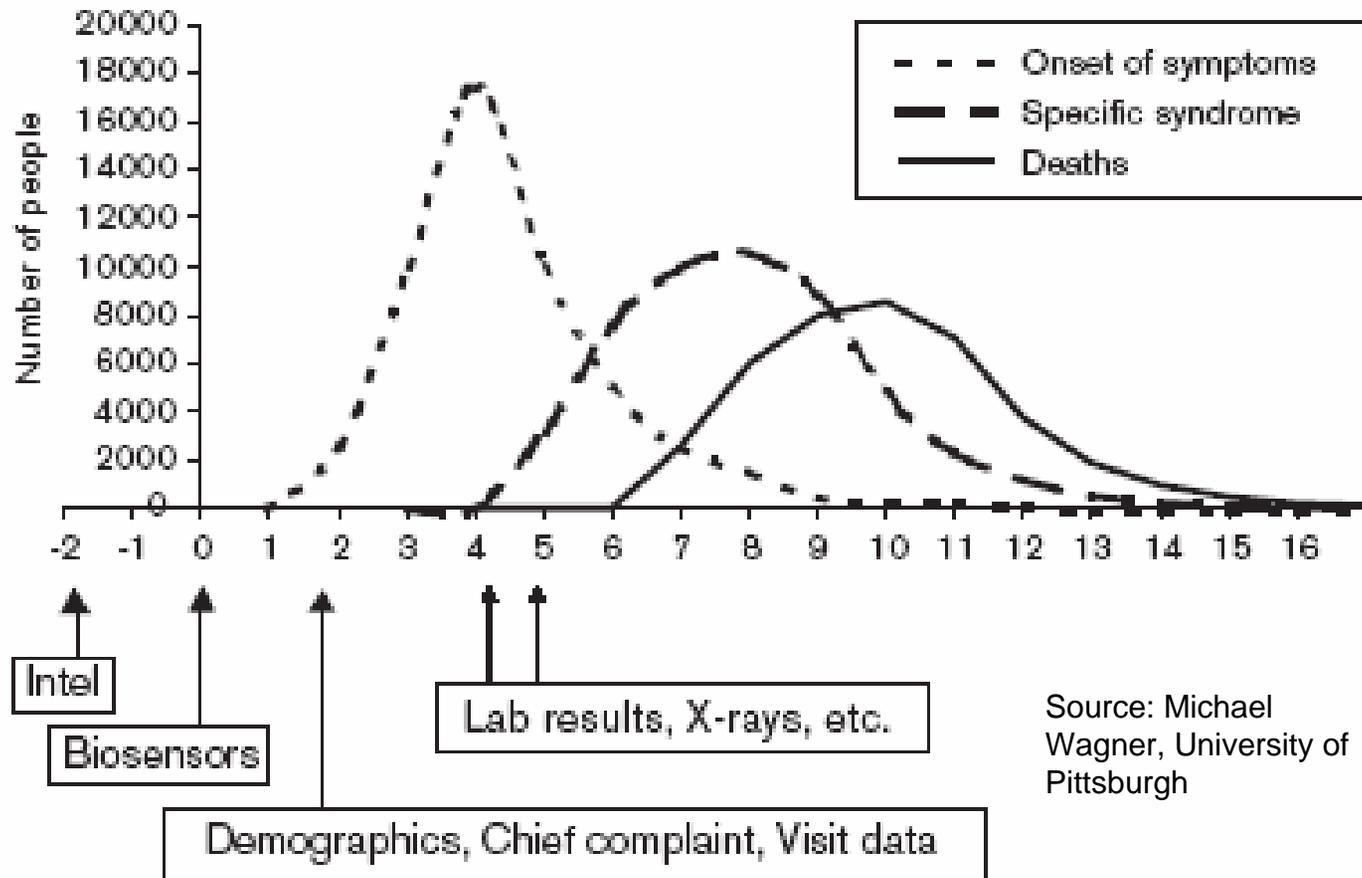


**Other Early
Detection Data**



Idea of Syndromic Surveillance

Potential strategies for early detection



Source: Michael Wagner, University of Pittsburgh

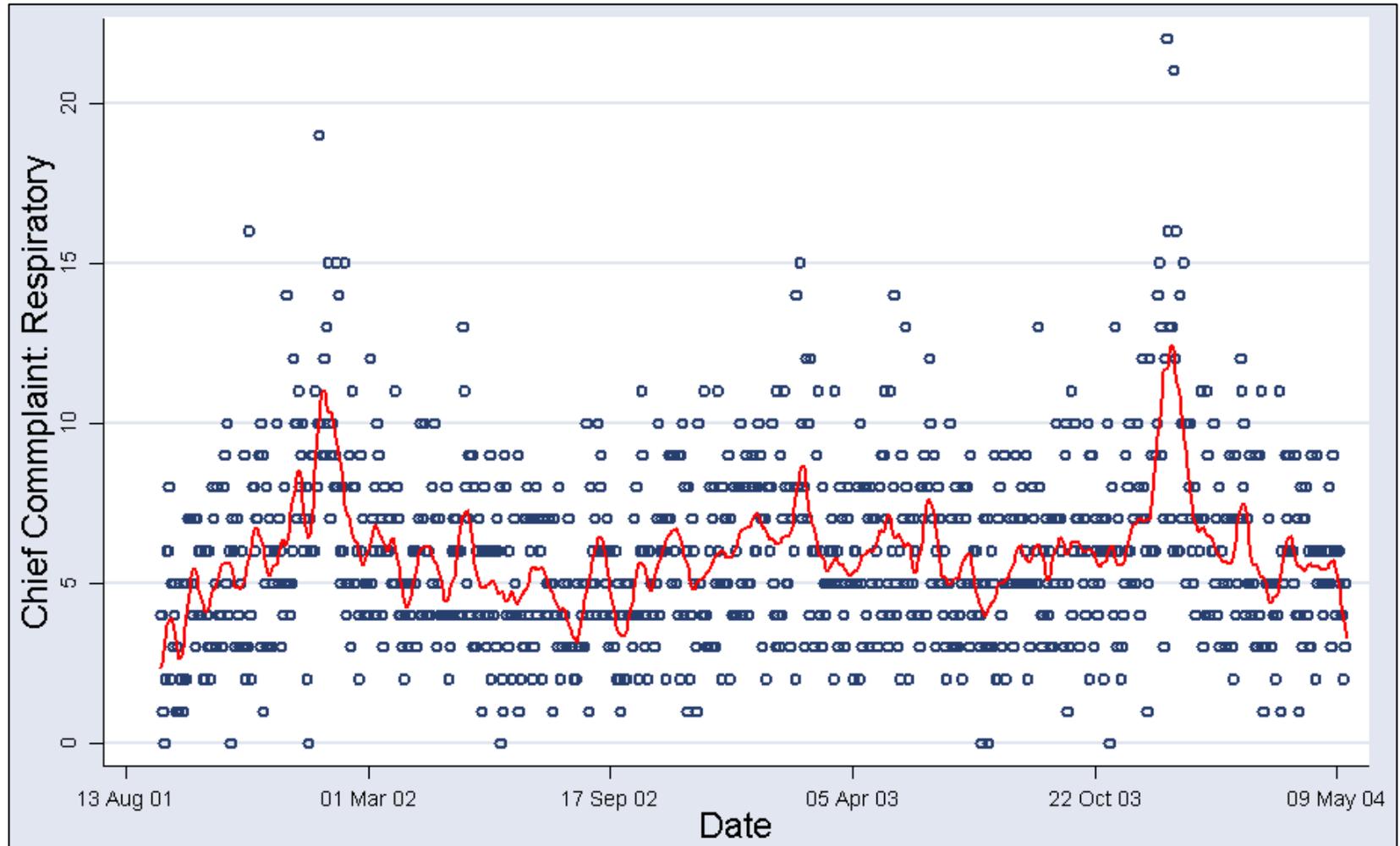
Statistical Process Control (SPC) for Syndromic Surveillance

- In manufacturing setting, SPC used to monitor production and test for a change level of quality
 - Sequential hypothesis test for distributional parameter(s) of quality characteristic (often the mean)
- In syndromic surveillance, goal is to monitor whether a pathogen has been released
 - Test whether distribution of leading indicators has shifted in some meaningful (i.e., worrisome) way
 - Focus needs to be on nonspecific—but relevant—symptoms
 - If symptoms are obvious and specific, then observation by clinician is likely sufficient

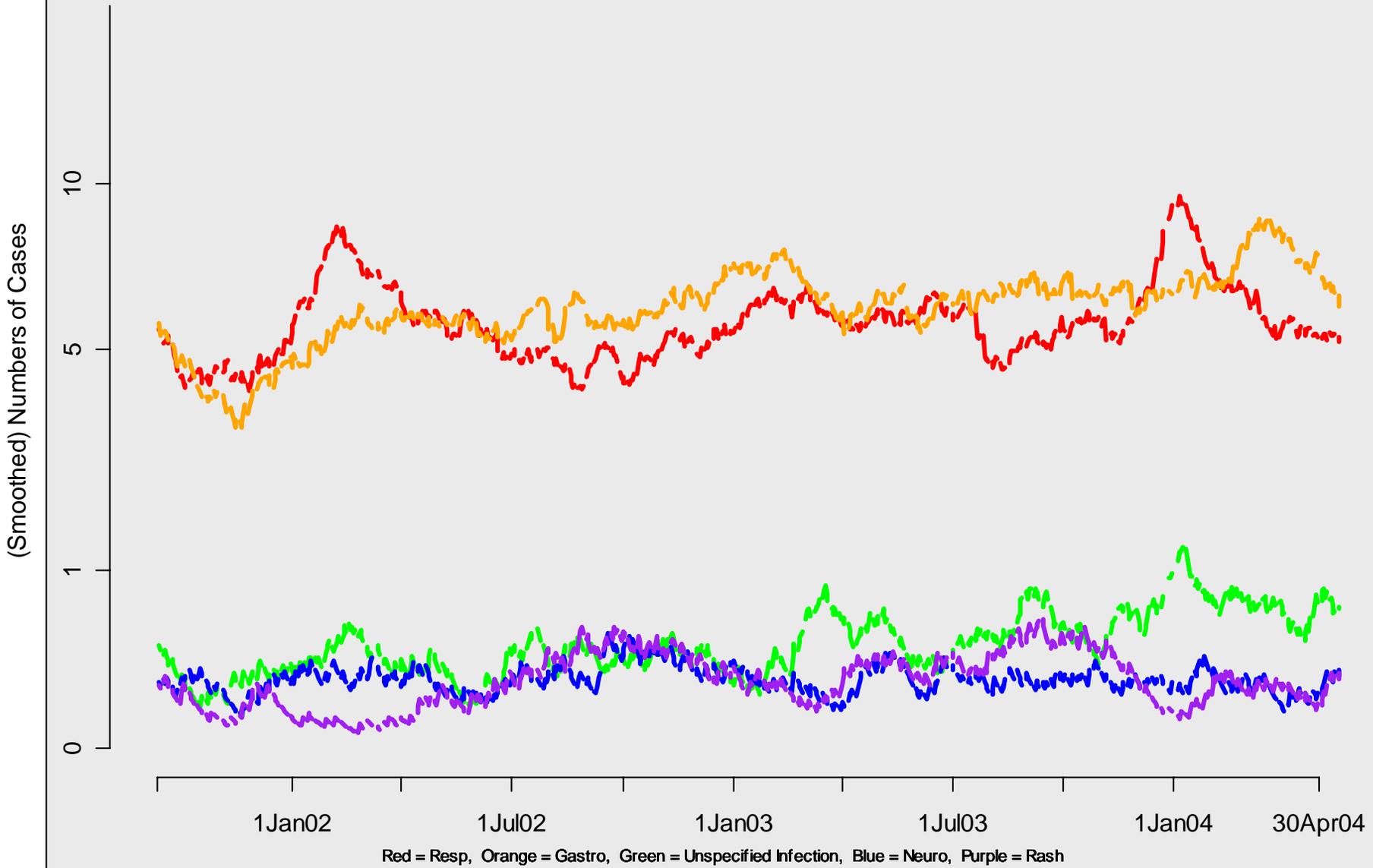
Challenges in Developing Statistical Methods for Syndromic Surveillance

- Nonstationary data
 - No control over “in-control” distribution
- Systematic effects
 - Seasonal, day-of-the-week and other effects in data
- Transient “out-of-control” conditions
 - Outbreaks/attacks begin, peak, and subside
- Vague alternative hypotheses
 - Detect only bioterrorism or natural diseases too?
 - Which diseases and/or outbreak manifestations?

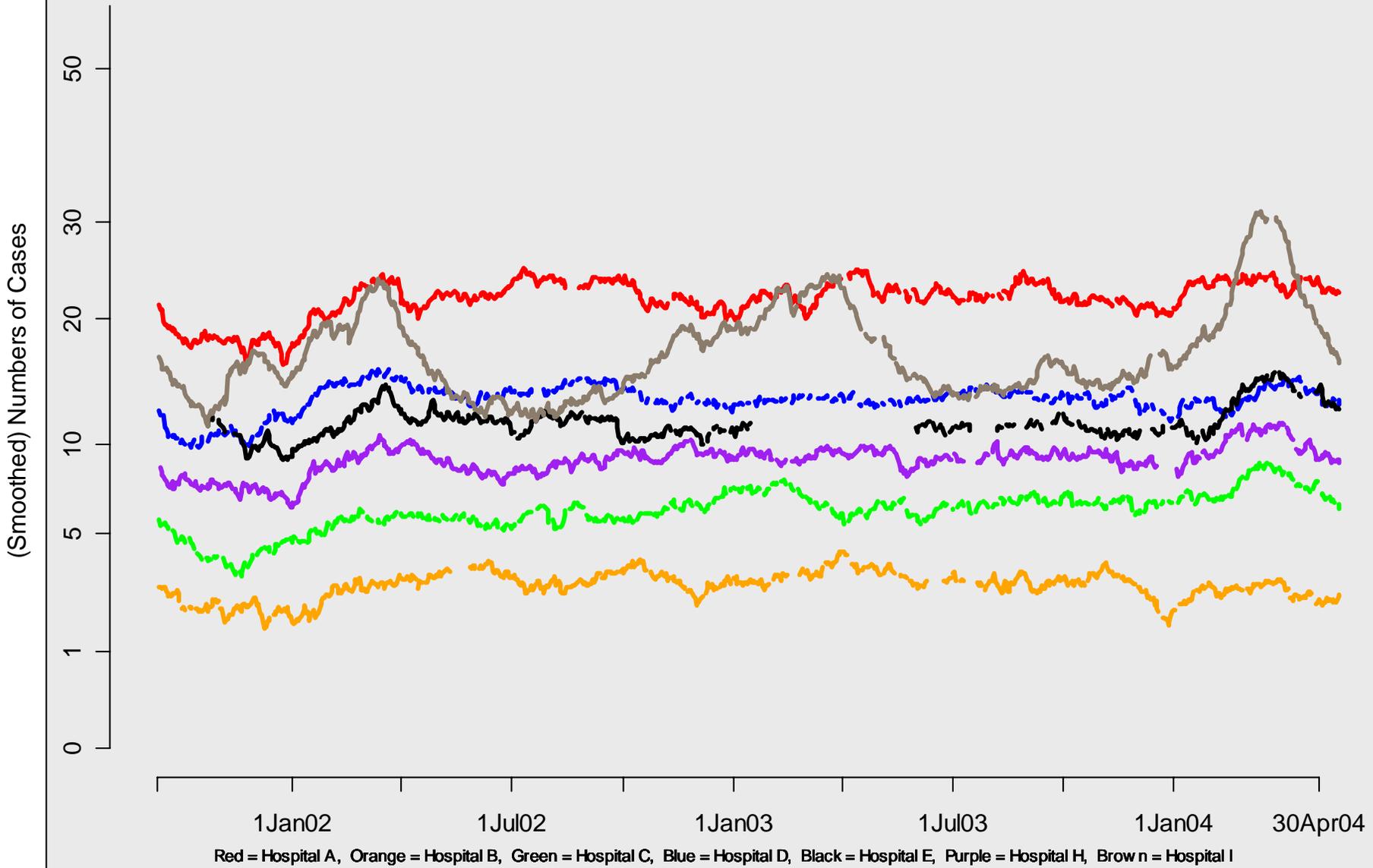
Respiratory Data From “Hospital C”



Hospital C: Different Syndromes over Time



Gastro Cases at Different Hospitals over Time



Evaluating Performance of Early Aberration Reporting System Methods

- Early Aberration Reporting System (EARS) designed to be a “drop-in” surveillance system
 - Often little historical information available
 - But increasingly being used as standard health surveillance system
- Implemented in SAS
- See www.bt.cdc.gov/surveillance/ears
- Uses Shewhart-like methods
 - Though originally motivated by CUSUM

EARS' Methods: C1, C2, and C3

$$C_1(t) = \frac{Y(t) - \bar{Y}_1(t)}{s_1(t)}$$

- Sample statistics calculated from previous 7 days' data
- Stop when statistic > 3

$$C_2(t) = \frac{Y(t) - \bar{Y}_3(t)}{s_3(t)}$$

- Sample statistics calculated from 7 days' of data prior to 2 day lag
- Stop when statistic > 3

$$C_3(t) = \sum_{i=t}^{t-2} \max[0, C_2(i) - 1]$$

- Stop when statistic > 2

Alternative: CUSUM on Residuals from “Adaptive Regression”

- Adaptive regression: regress a sliding baseline of observations on time relative to current observation
 - I.e. regress $Y(t-1), \dots, Y(t-n)$ on $n, \dots, 1$
- Calculate standardized residuals from one day ahead forecast, $X(t) = R(t) / \sigma_Y$, where

$$R(t) = Y(t) - \left[\hat{\beta}_0 + \hat{\beta}_1 \times (n+1) + \hat{\beta}_j \right]$$

- CUSUM:

$$S(t) = \max \left[0, S(t-1) + X(t) - k \right]$$

with

$$k = \frac{1}{2} \sqrt{\frac{(n+2)(n+1)}{n(n-1)}}$$

Comparison Methodology

- Generate synthetic data:

$$Y(t) = \max \left(0, \lceil c + s(t) + d(t) + Z(t) + o(t) \rceil \right)$$

- Fix thresholds to achieve ATFS = 100 days
- Compare across various scenarios using ATFOS and percent of outbreaks missed
- Scenarios:

	<i>None</i>	<i>Small</i>	<i>Large</i>
<i>A</i>	0	20	80
σ	n/a	10	30

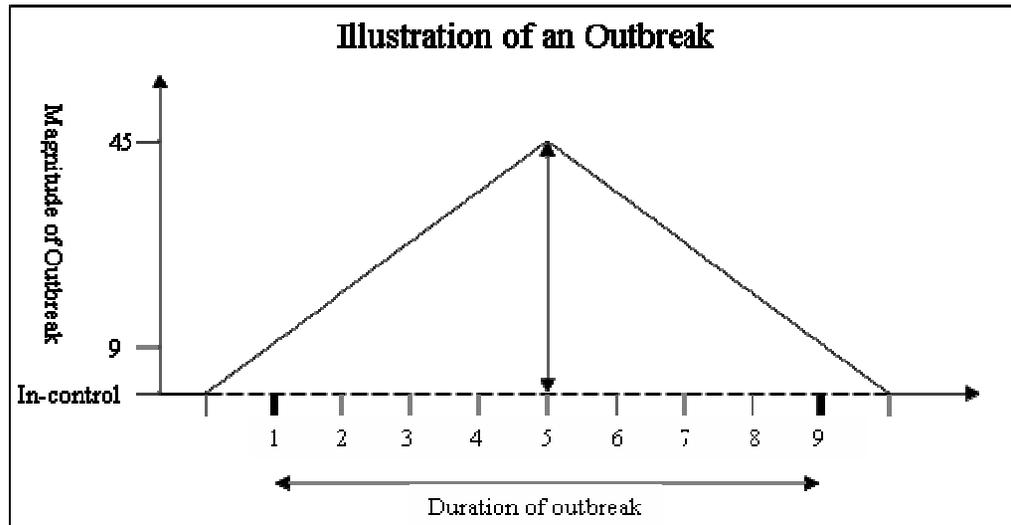
Large count: c=90

	<i>None</i>	<i>Small</i>	<i>Large</i>
<i>A</i>	0	2	6
μ, σ	n/a	1.0, 0.5	1.0, 0.7

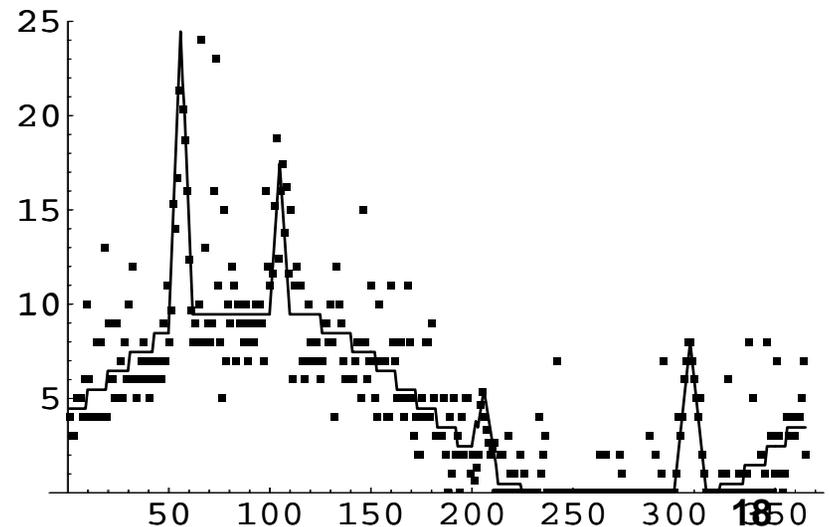
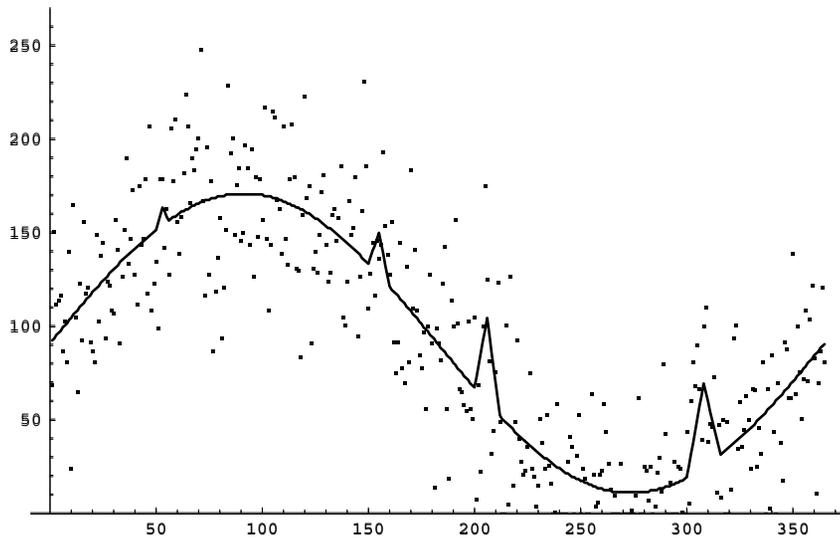
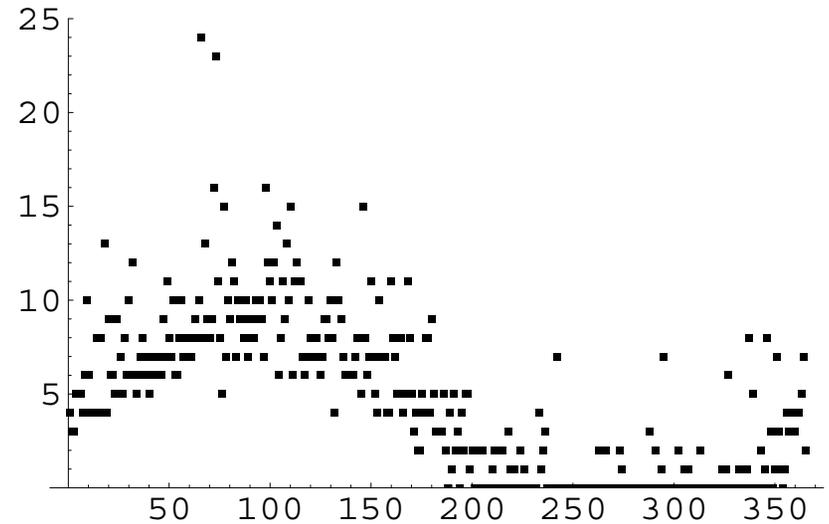
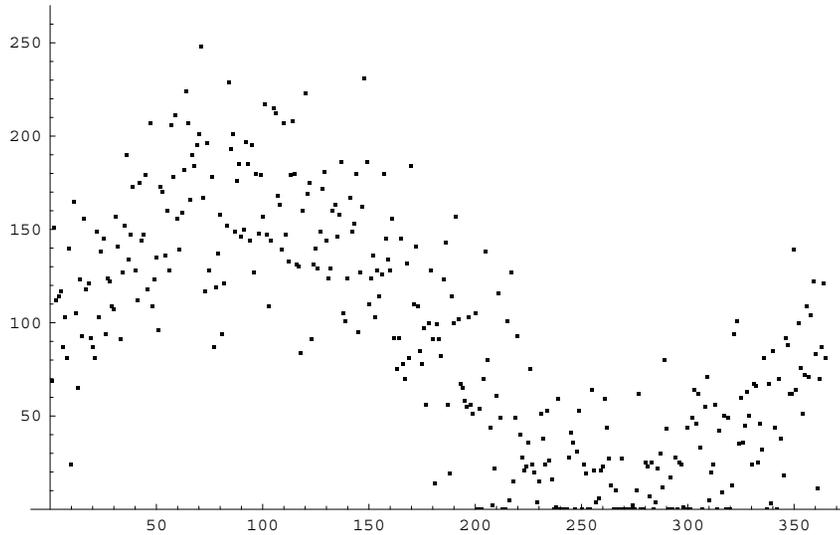
Small count: c=0

Outbreaks

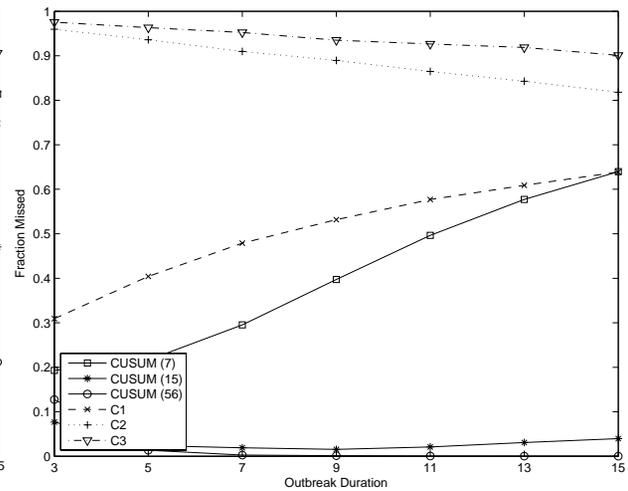
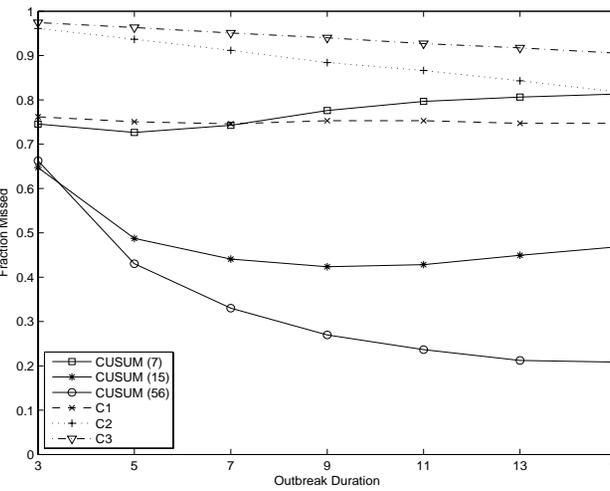
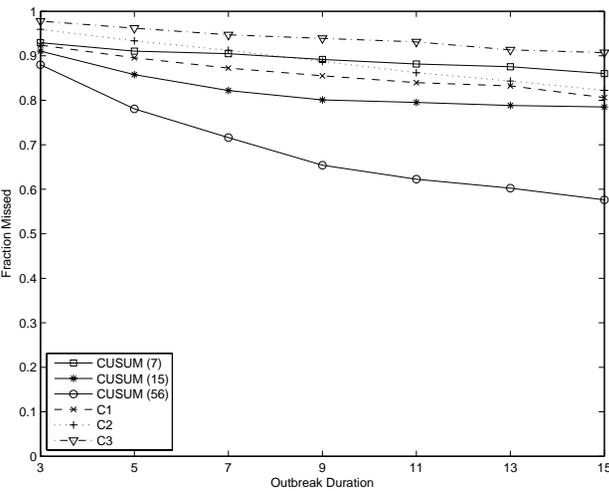
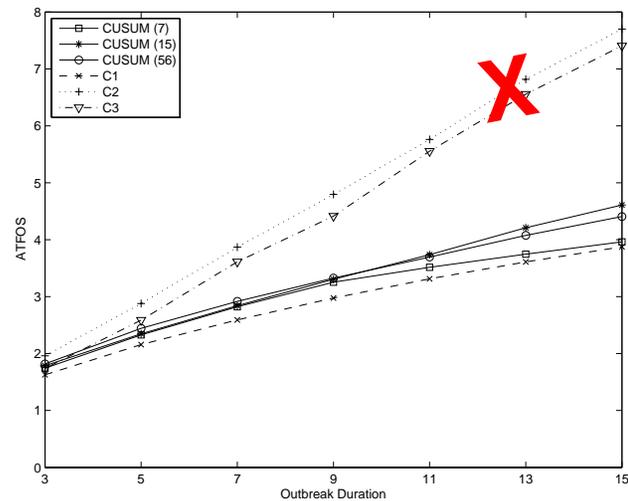
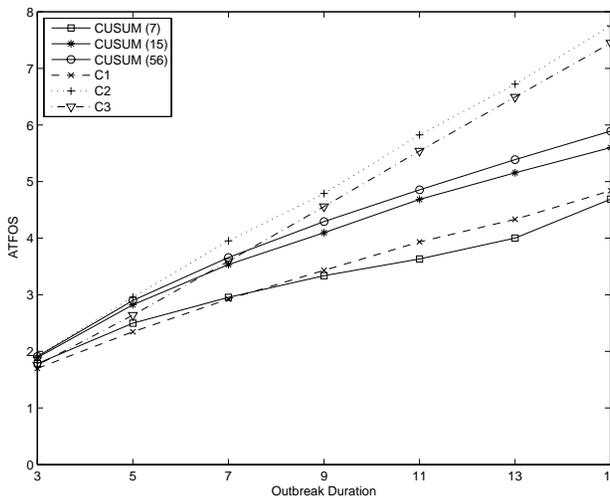
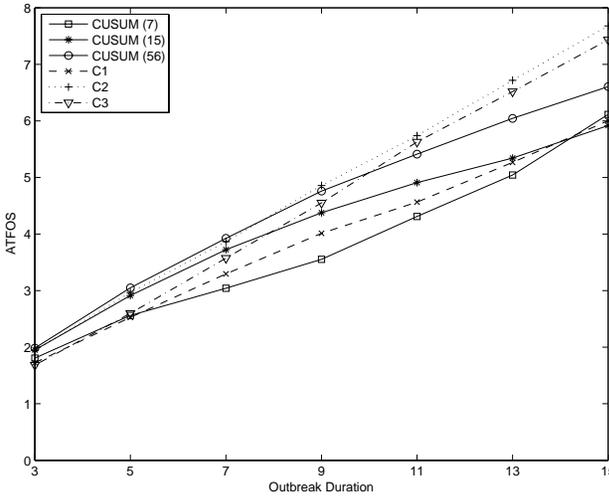
- Linear increase and decrease, characterized by magnitude M and duration D
- $D = 3, 4, \dots, 15$ days
- M in 3 levels:
 - “small”
 - “medium”
 - “large”



What does $Y(t)$ Look Like?



Some Large Count Results

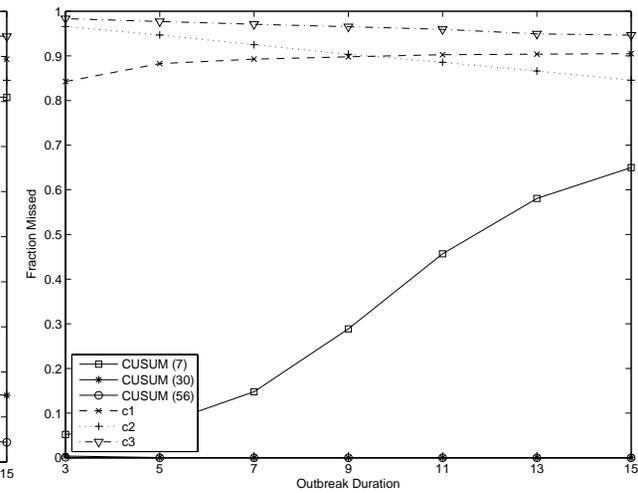
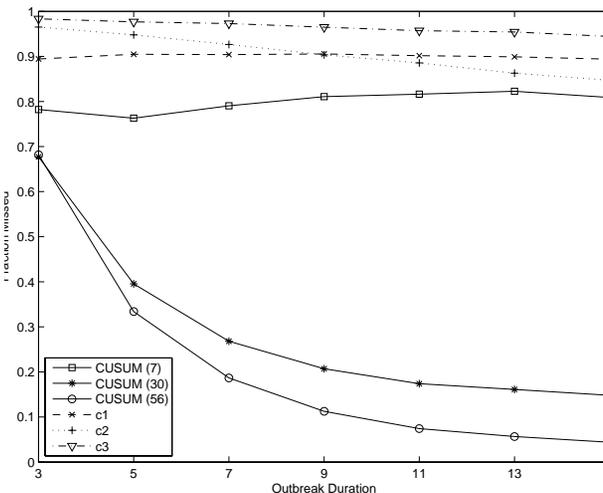
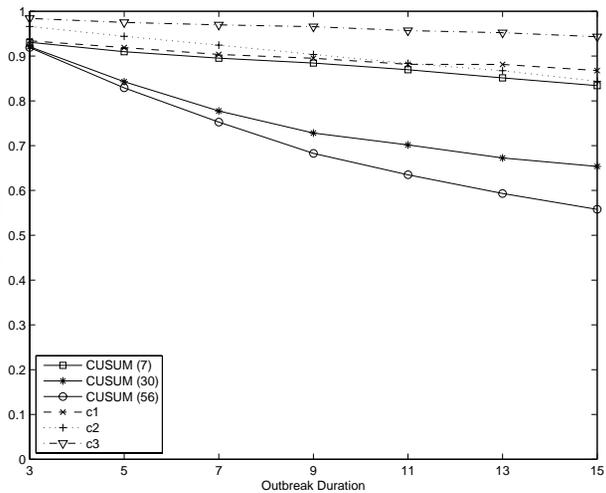
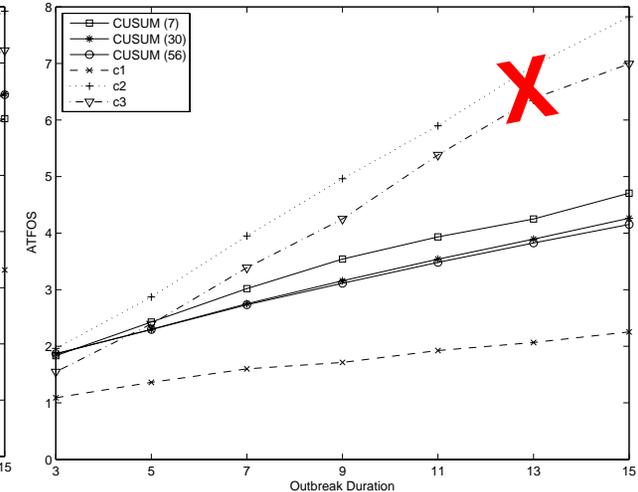
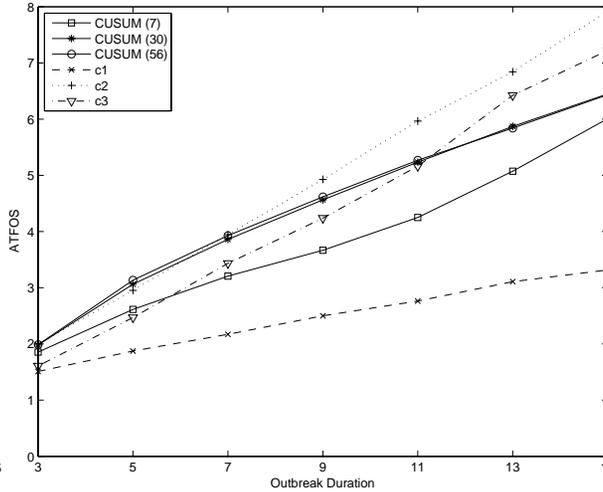
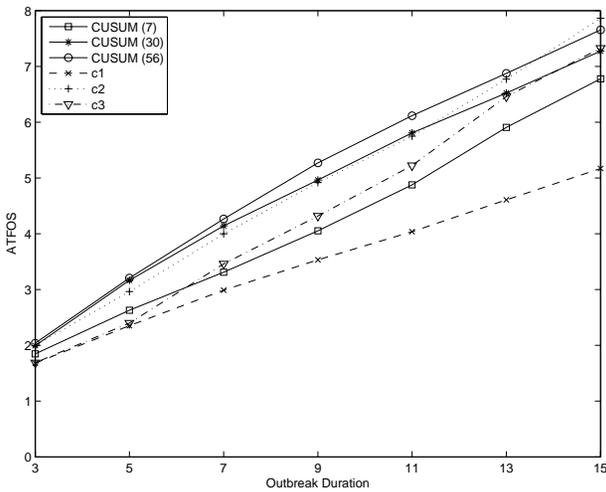


Small magnitude

Medium magnitude

Large magnitude

Some Small Count Results



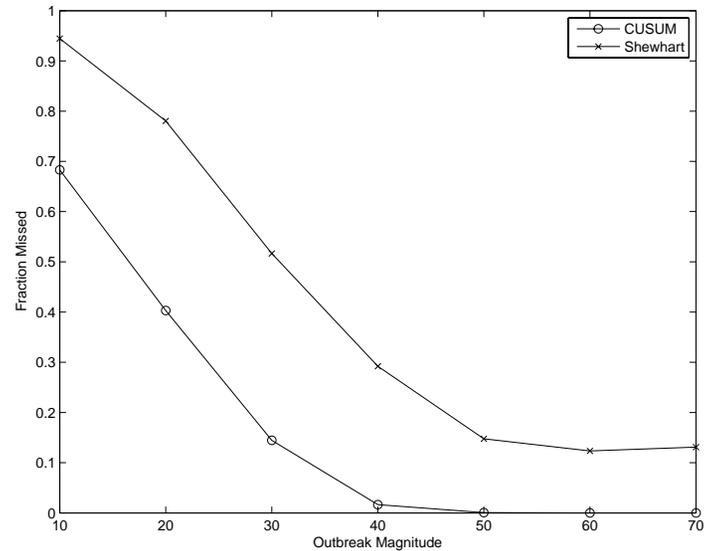
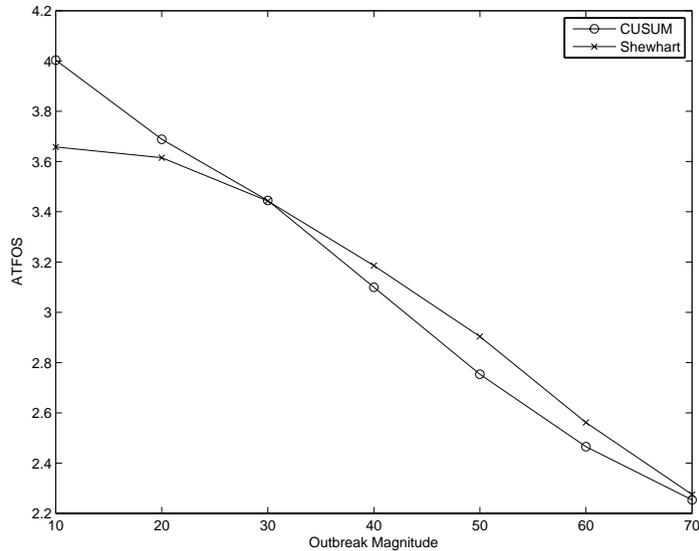
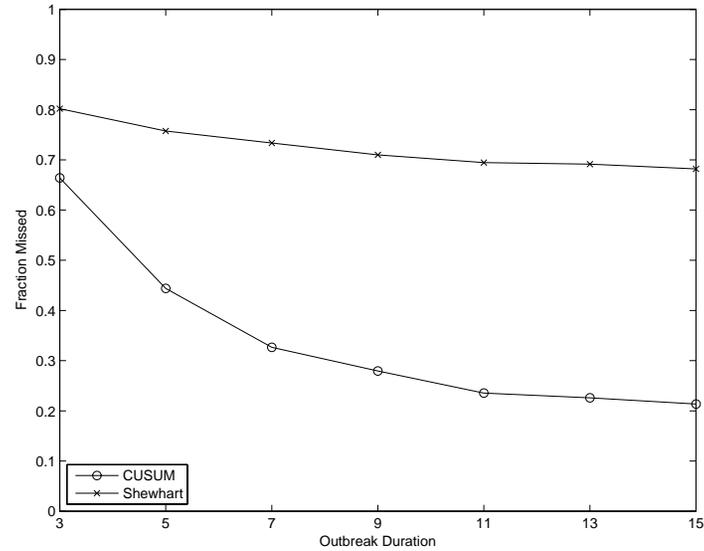
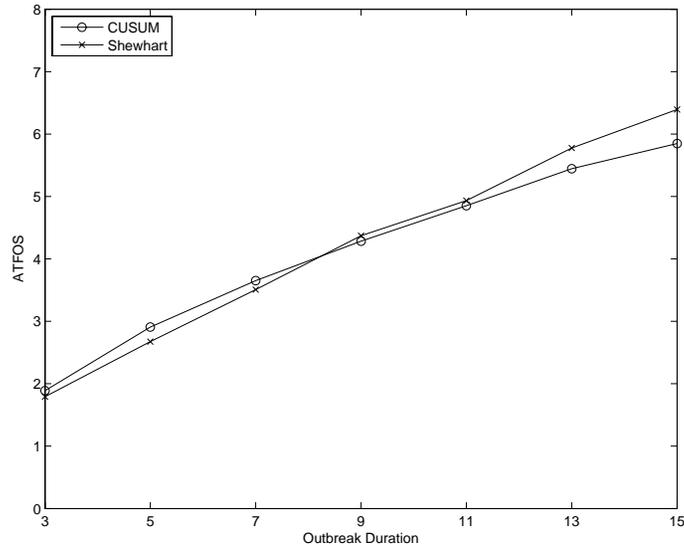
Small magnitude

Medium magnitude

Large magnitude

DRAFT

Shewhart Methods Not Suited for this Problem?



EARS Comparison Conclusions

- CUSUMs based on adaptive regression with longer baselines performed best
- CUSUMs outperformed EARS C1, C2, and C3 methods
 - Seemingly due to Shewhart design *and* additional data used in adaptive regression
- Suggests “drop in” strategy of starting with CUSUM with 7-day baseline
 - As time progresses, increase baseline until long enough to allow it to slide

Lots of Interesting Research Opportunities

- Control chart experts have a lot to offer
 - Public health community re-inventing SPC?
 - Guidance for how to compare methods
 - Determining appropriate metrics for sequential methods
- Syndromic surveillance offers challenges
 - Adapting/extending existing methods
 - Developing new spatio-temporal methods
 - Assessing multivariate vs. univariate methods
 - Managing excessive false alarm rates

Selected References

Background Information:

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Selected Research

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- Joner, M.D., Jr., Woodall, W.H., Reynolds, M.R., Jr., and R.D. Fricker, Jr., The Use of Multivariate Control Charts in Public Health Surveillance (draft).
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