SPC Applications in Syndromic Surveillance

Ron Fricker

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

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The New Status Quo?

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
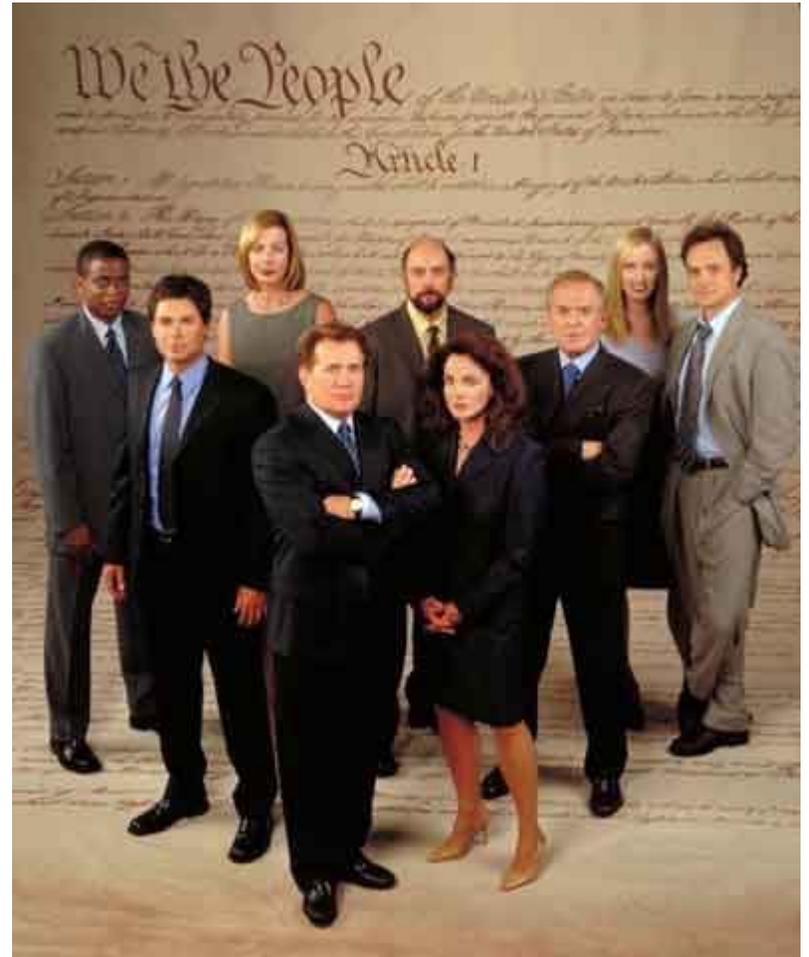
BioSense and Other Syndromic Systems Already Operational
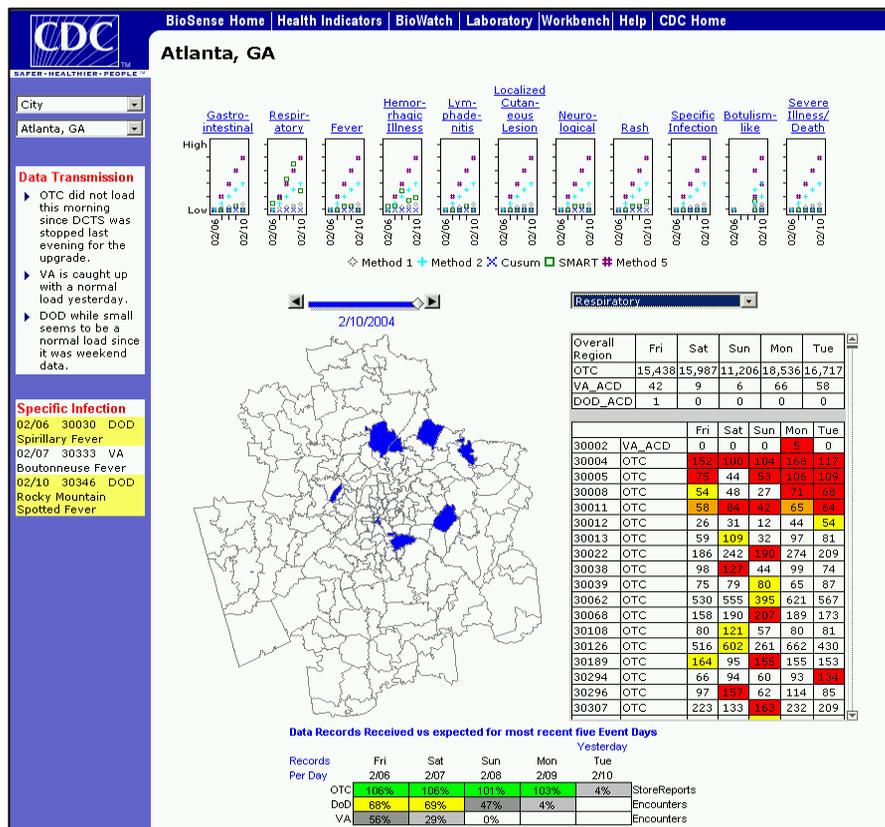
Implementation survey (Gibson et al., 2004):

- 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 <u>health-related data</u> that <u>precede diagnosis</u> and signal a <u>sufficient probability of a case</u> or an outbreak to <u>warrant further public health response</u>." [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
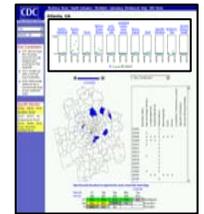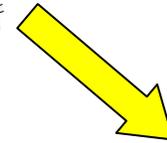
Other Early Detection Data

Syndromic Surveillance System
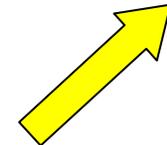
Idea of Syndromic Surveillance

Potential strategies for early detection
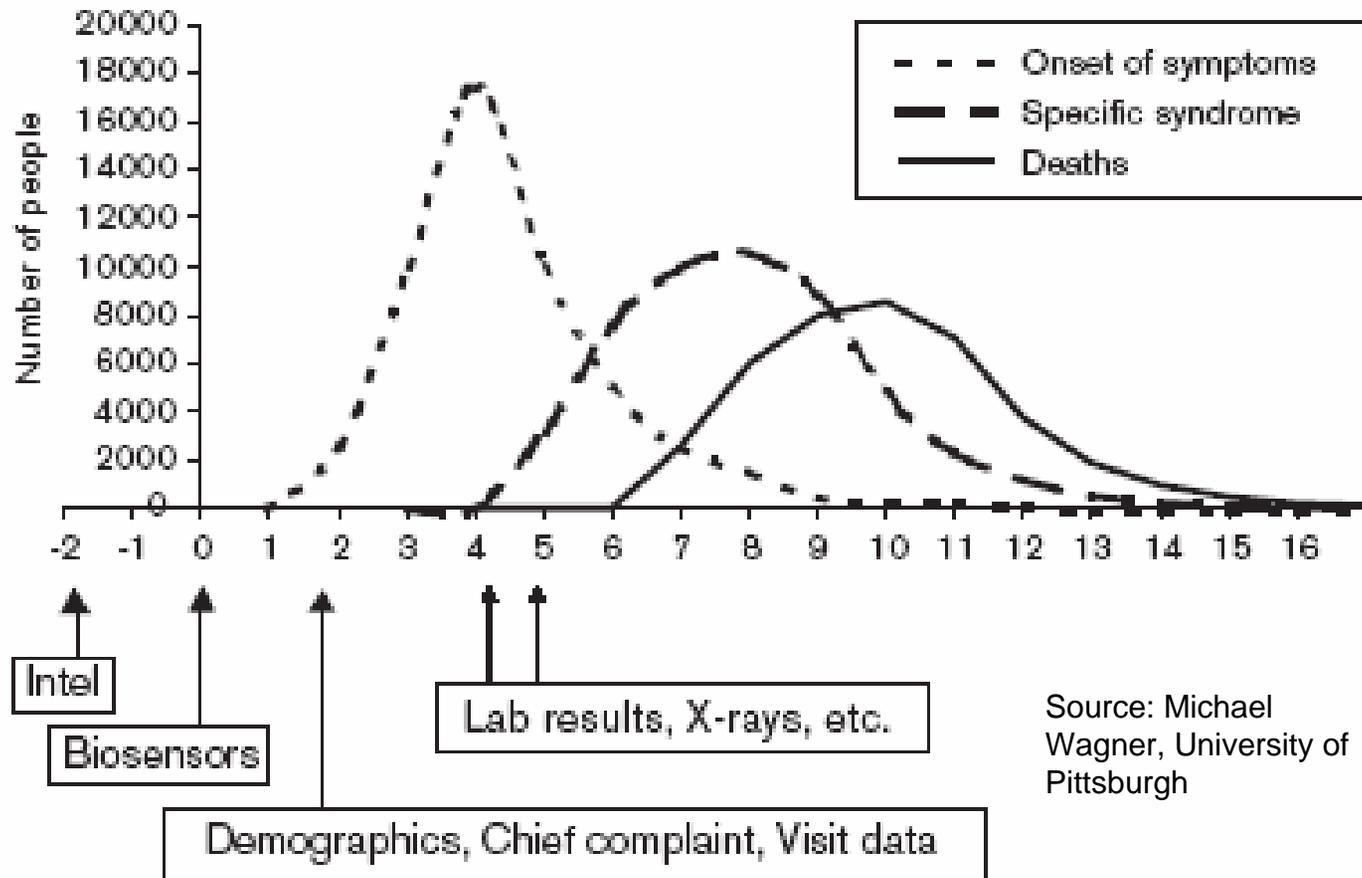
Source: Michael Wagner, University of Pittsburgh

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"
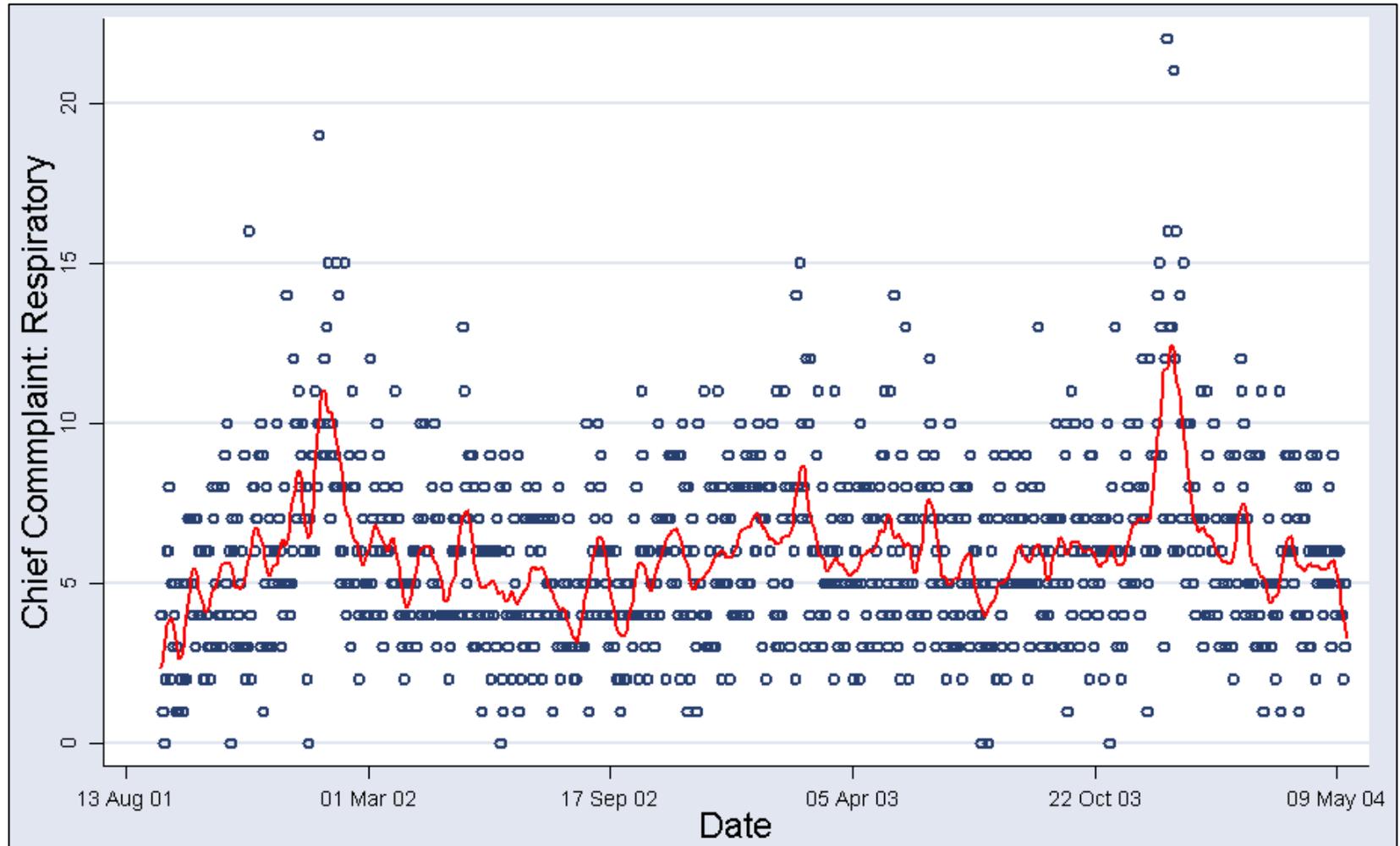
Hospital C: Different Syndromes over Time

(Smoothed) Numbers of Cases

Red = Resp, Orange = Gastro, Green = Unspecified Infection, Blue = Neuro, Purple = Rash
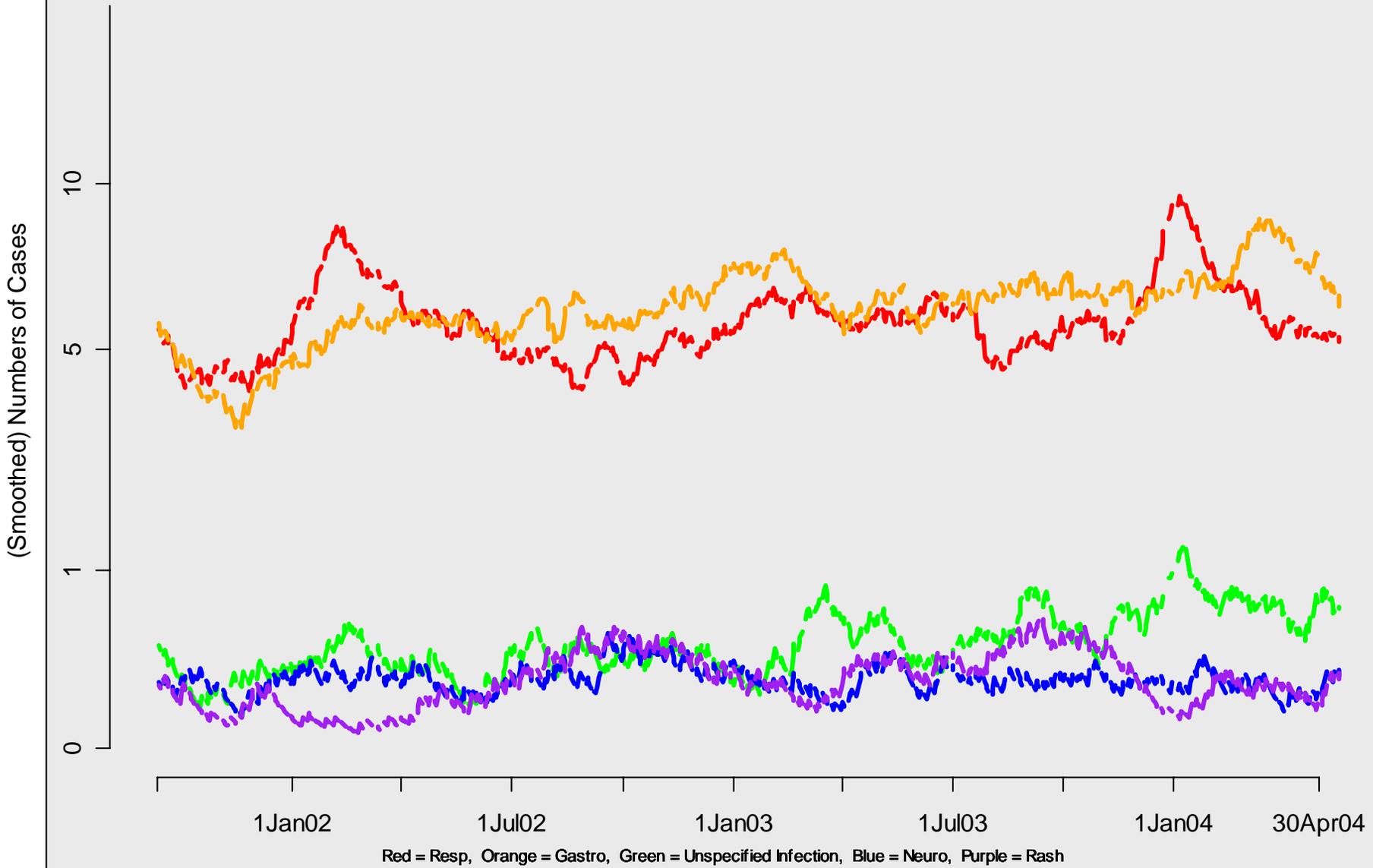
Gastro Cases at Different Hospitals over Time

Red = Hospital A,   Orange = Hospital B,   Green = Hospital C,   Blue = Hospital D,   Black = Hospital E,   Purple = Hospital H,   Brown = Hospital I
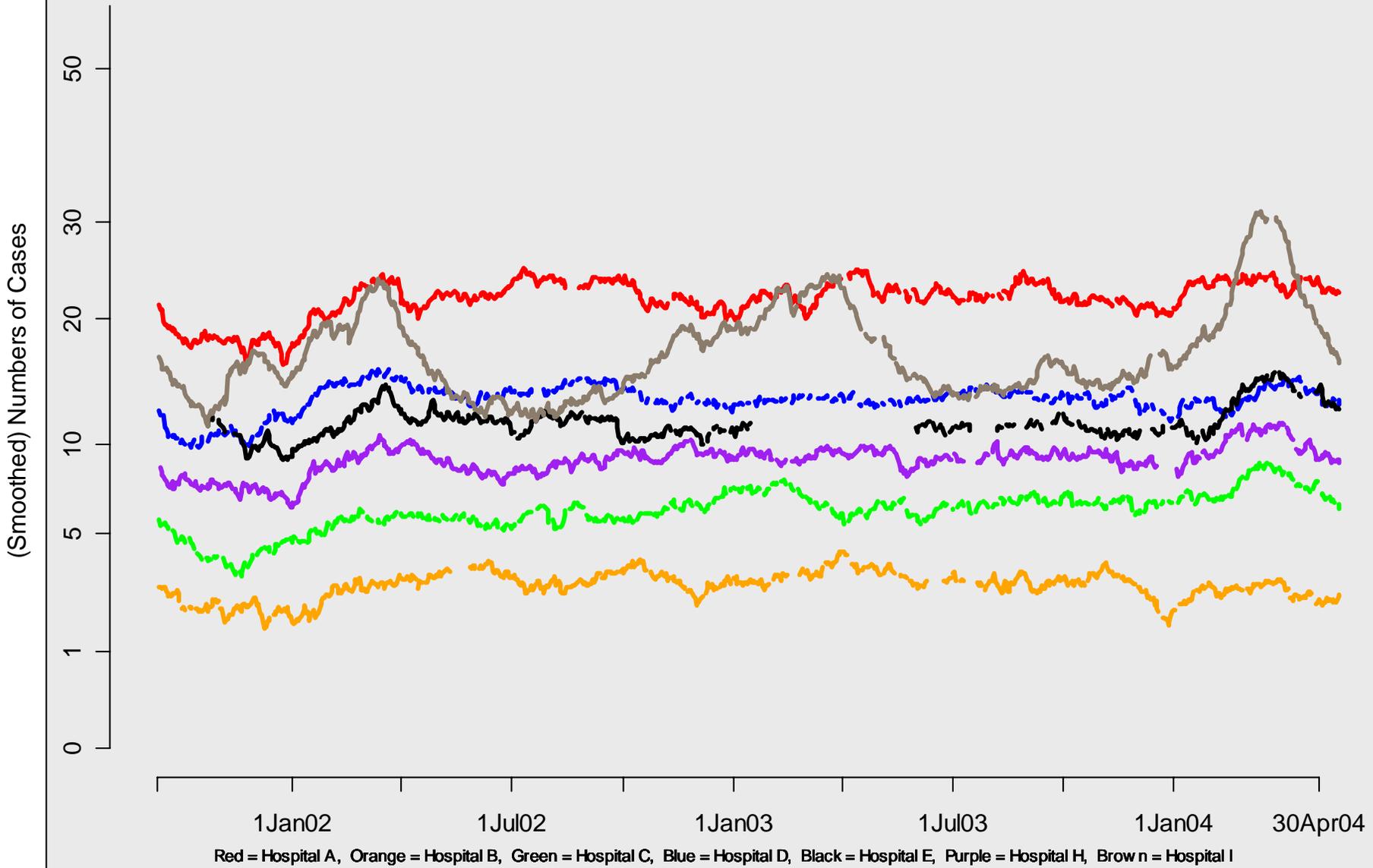
Evaluating Performance of Early Aberration Reporting System Methods

- 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

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

- 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 $Y(t-1),...,Y(t-n)$ on $n,...,1$

- 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:

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

Large count: c=90

	None	Small	Large
A	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

- $D = 3, 4, \ldots, 15$ days

- M in 3 levels:
  - "small"
  - "medium"
  - "large"

Illustration of an Outbreak

Magnitude of Outbreak

45

9

In-control

1 2 3 4 5 6 7 8 9

Duration of outbreak
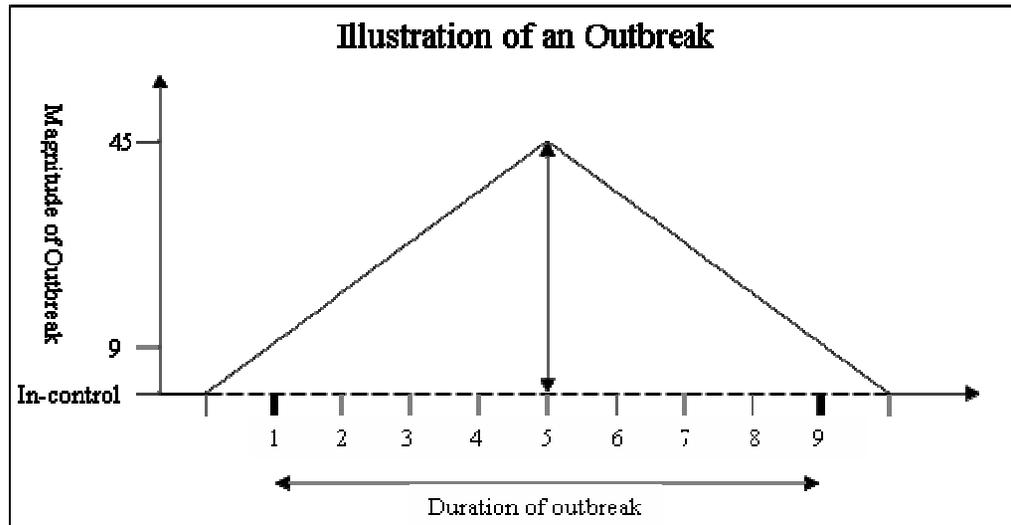
What does *Y*(t) Look Like?
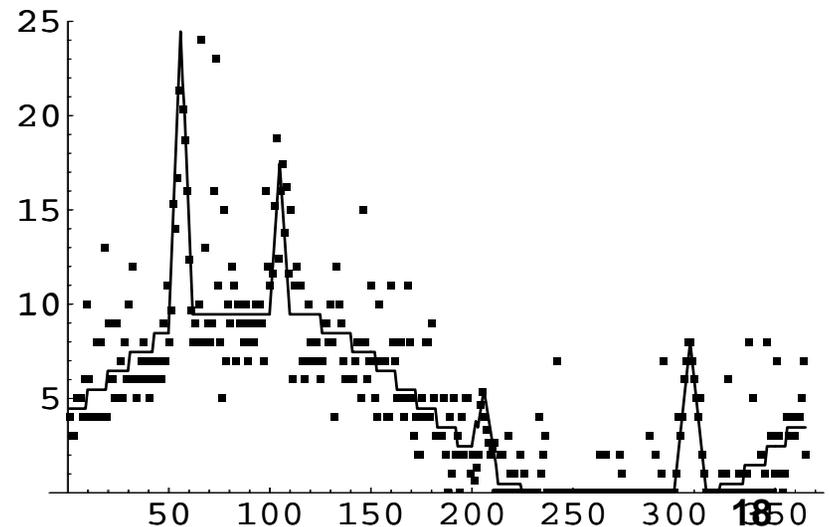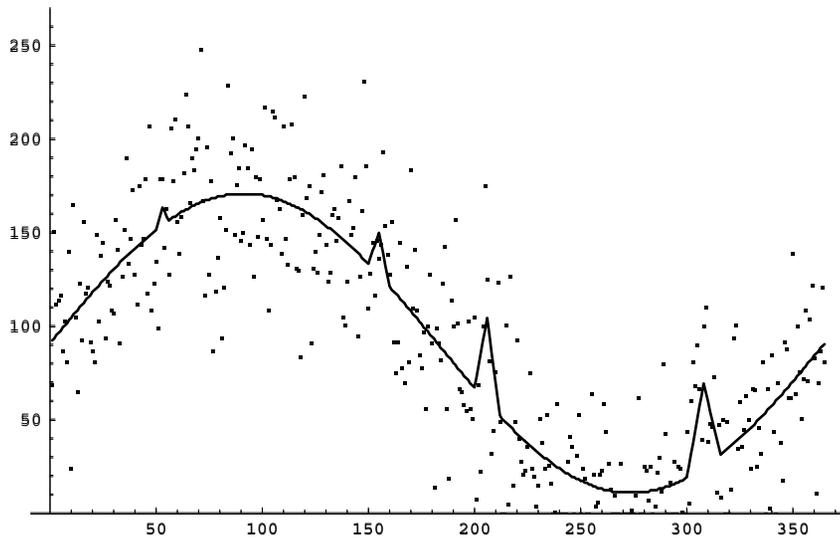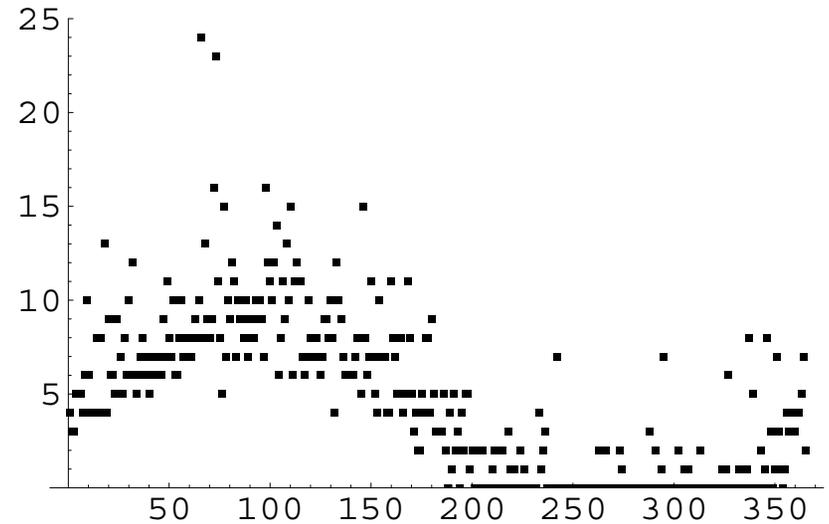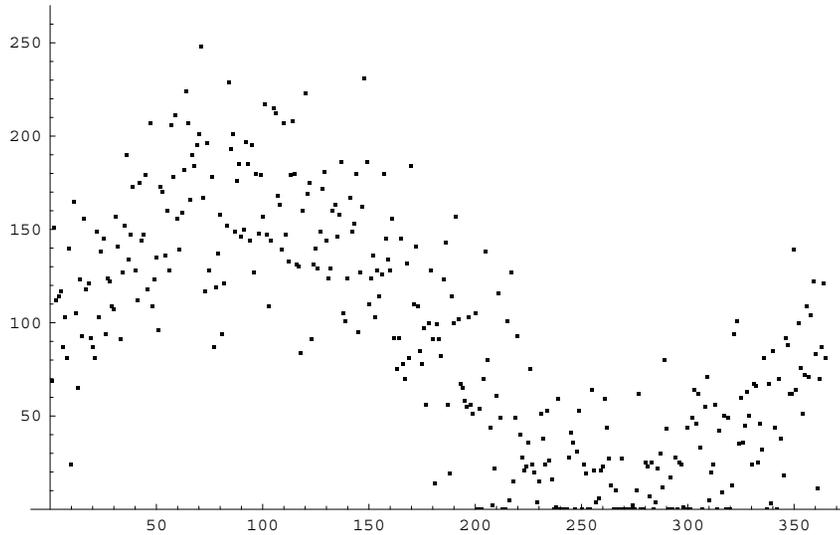
Some Large Count Results
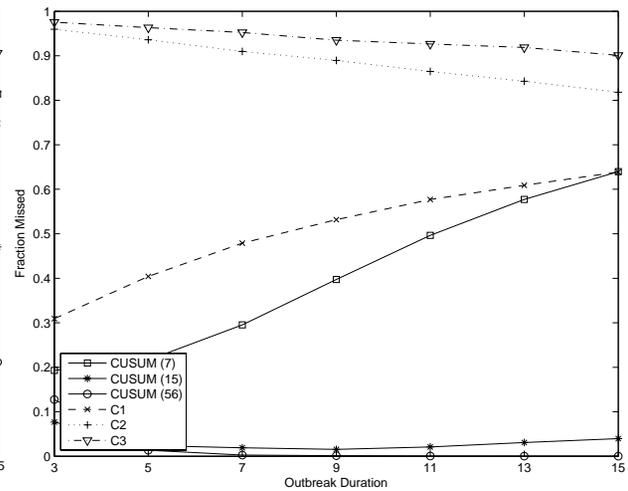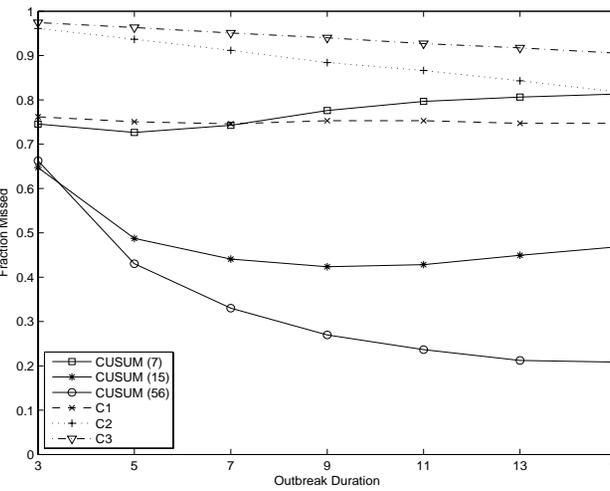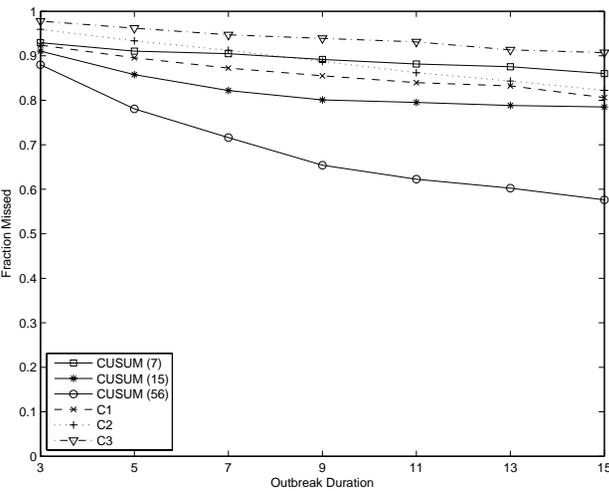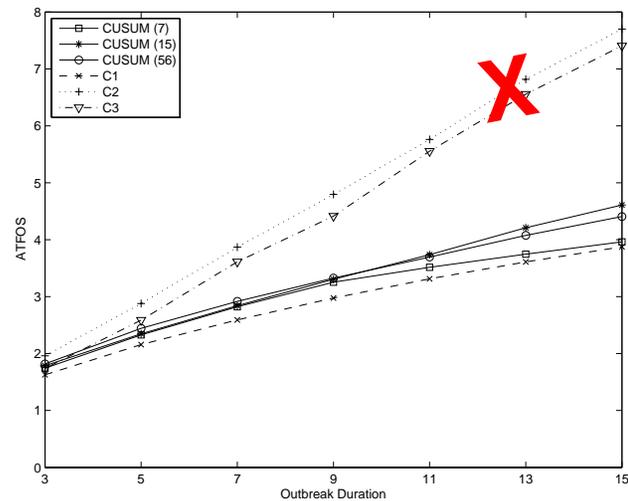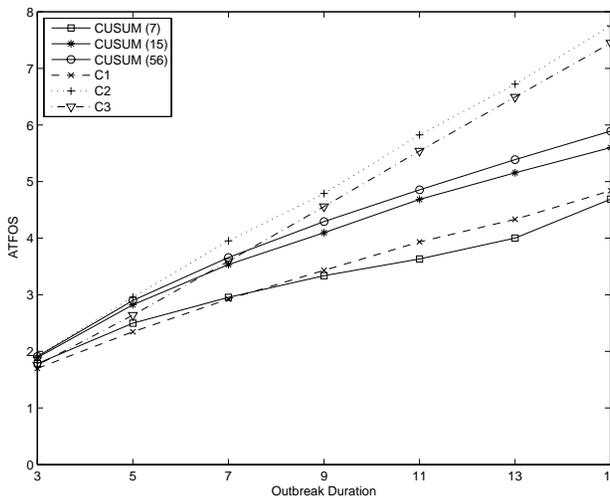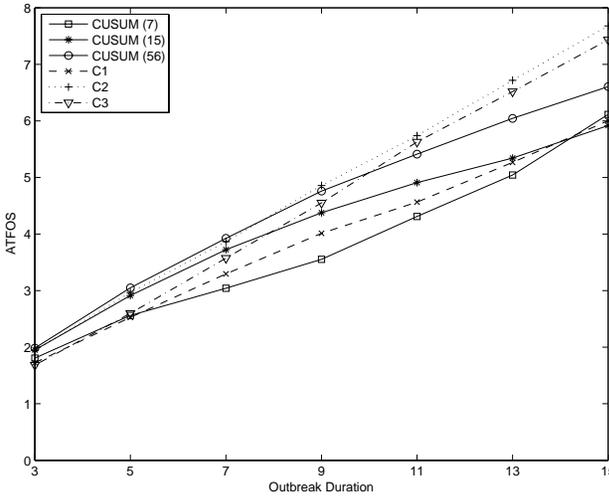
Small magnitude   Medium magnitude   Large magnitude

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Some Small Count Results
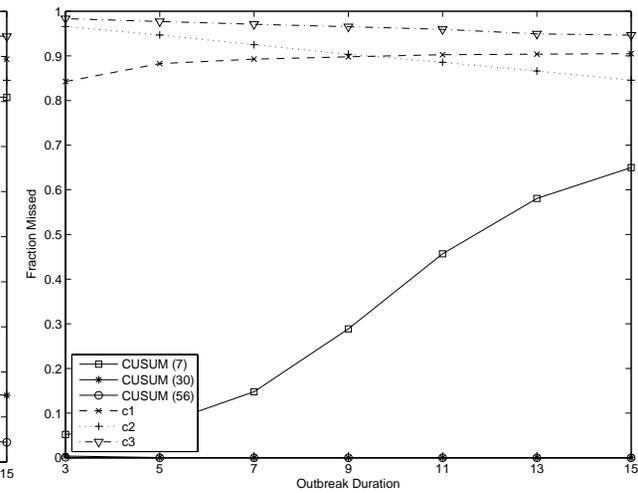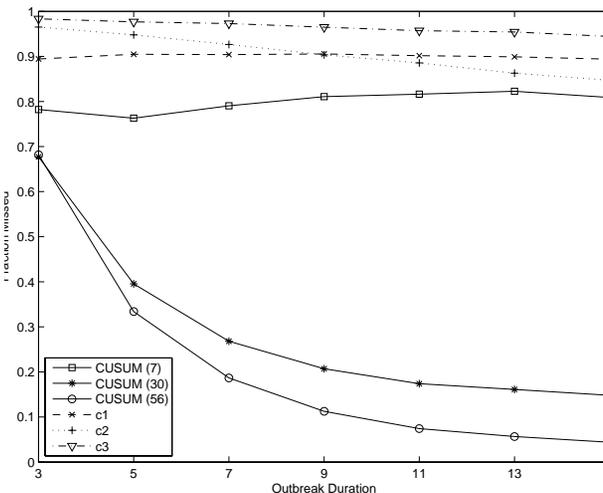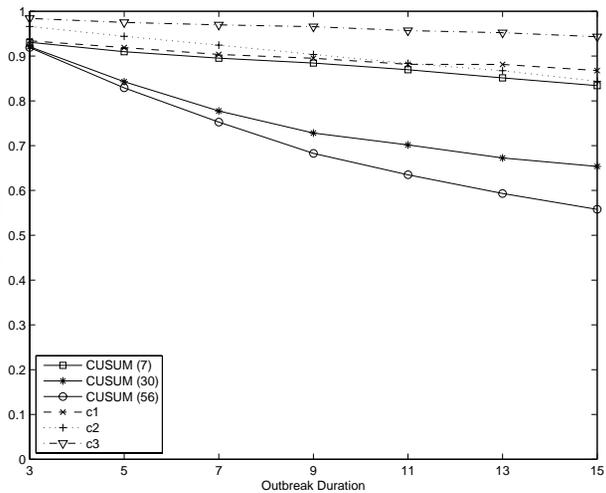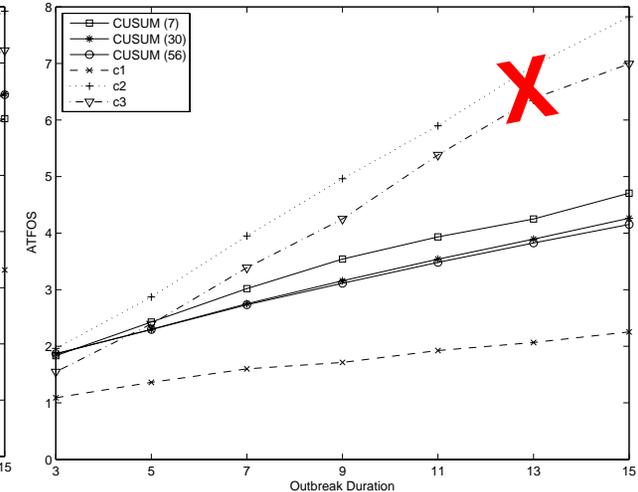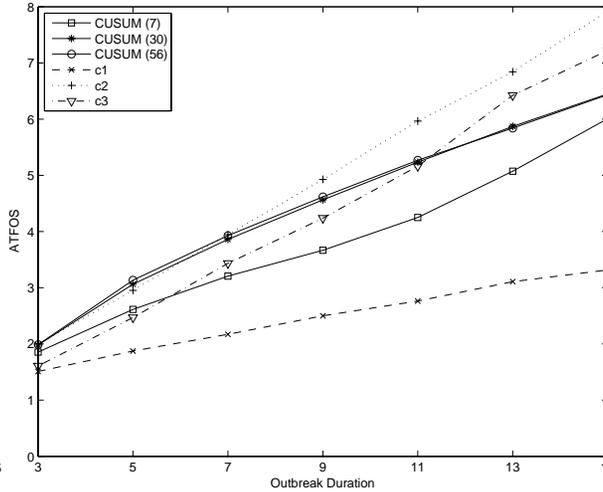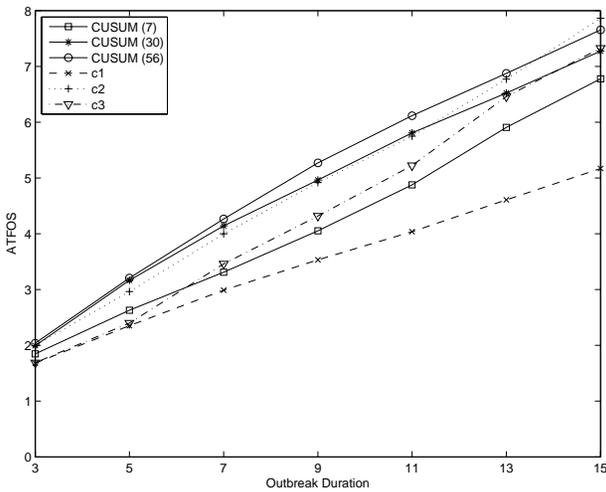
Small magnitude

Medium magnitude

Large magnitude

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Shewhart Methods Not Suited for this Problem?
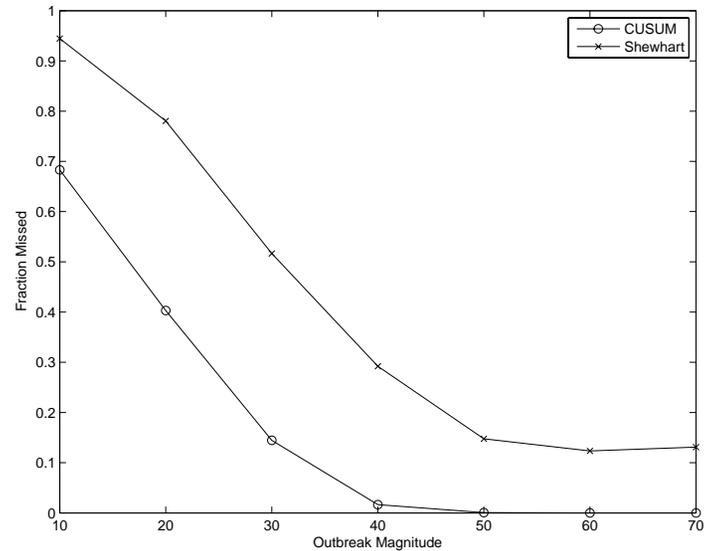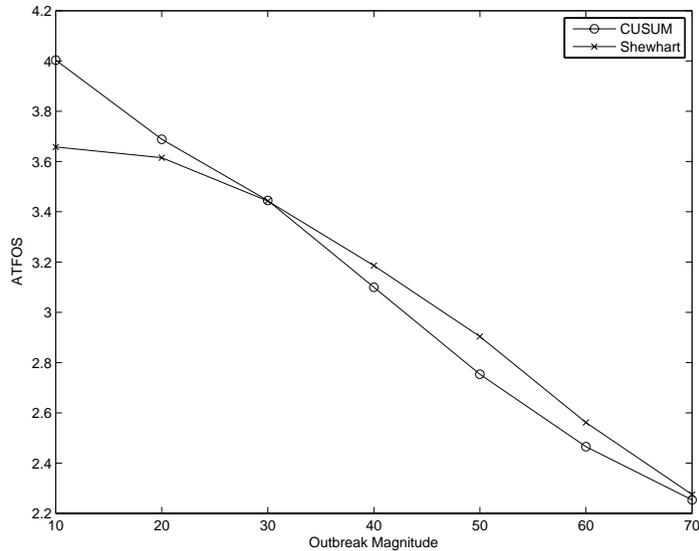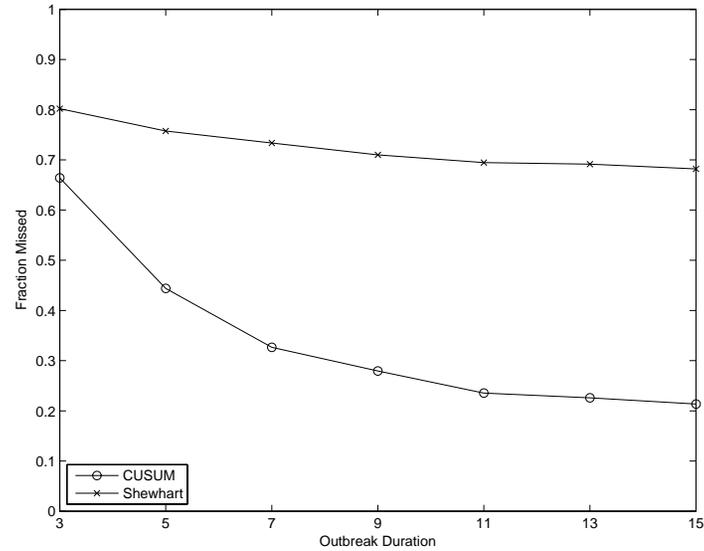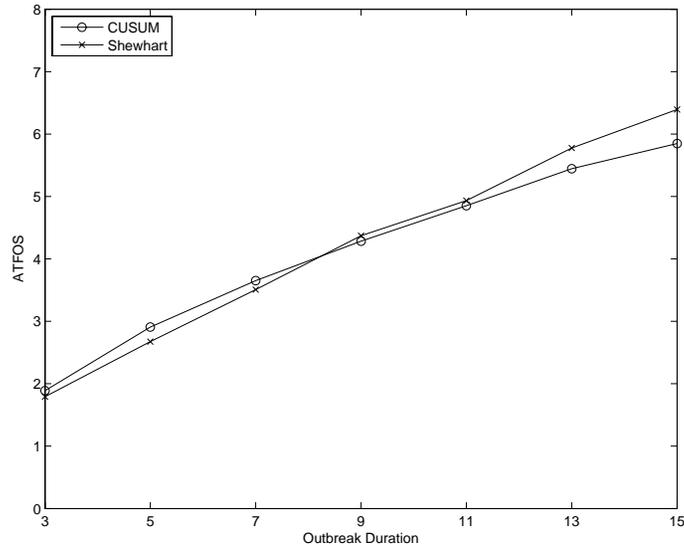
EARS Comparison Conclusions

- 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:

- Woodall, W.H., The Use of Control Charts in Health-Care and Public-Health Surveillance, *Journal of Quality Technology*, **38**, pp. 1-16, 2006.

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- Fricker, R.D., Jr., and H. Rolka, Protecting Against Biological Terrorism: Statistical Issues in Electronic Biosurveillance, *Chance*, **91**, pp. 4-13, 2006

- Shmueli, G., Statistical Challenges in Modern Biosurveillance, in submission to *Technometrics*.

Selected Research

- Fricker, R.D., Jr., Hegler, B.L., and D.A Dunfee, Assessing the Performance of the Early Aberration Reporting System (EARS) Syndromic Surveillance Algorithms, in submission to *Statistics in Medicine*.

- Fricker, R.D., Jr., Knitt, M.C., and C.X. Hu, Comparing Directionally Sensitive MCUSUM and MEWMA Procedures with Application to Biosurveillance, in submission to *Quality Engineering*.

- 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).

- Fricker, R.D., Jr., Directionally Sensitive Multivariate Statistical Process Control Methods with Application to Syndromic Surveillance, *Advances in Disease Surveillance,* **3**:1. Accessible on-line at www.isdsjournal.org.

- Stoto, M.A., et al., Evaluating Statistical Methods for Syndromic Surveillance, in *Statistical Methods in Counterterrorism: Game Theory, Modeling, Syndromic Surveillance, and Biometric Authentication*, A. Wilson, G. Wilson, and D. Olwell, eds., New York: Springer, 2006.