

Optimizing Syndromic Classification in Biosurveillance Systems

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The BioSense Initiative to Improve Early Event Detection

- 3 year CDC/BioSense funded project (R01 PH000038-0)
- Collaborative effort between RTI International (PI: Scott Wetterhall, MD, MPH) and the Carolina Center for Health Informatics within the UNC Department of Emergency Medicine
- Overarching objective: to define, test, validate, and standardize methodology for optimizing syndrome definitions designed for the early detection of disease outbreaks of public health importance

The BioSense Initiative to Improve Early Event Detection

- Specific Aim (Task 1/5): To define and apply a method for establishing a gold standard set of emergency department visits to use in evaluating sensitivity and specificity of syndrome definitions.

Defining and Applying a Method for Improving the Sensitivity and Specificity of an Emergency Department Early Event Detection System

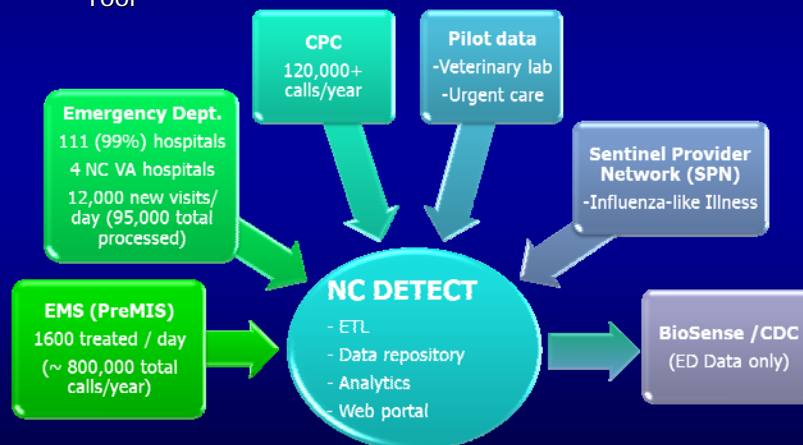
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Biosurveillance in North Carolina

- NC DETECT
 - North Carolina Disease Event Tracking & Epidemiologic Collection Tool

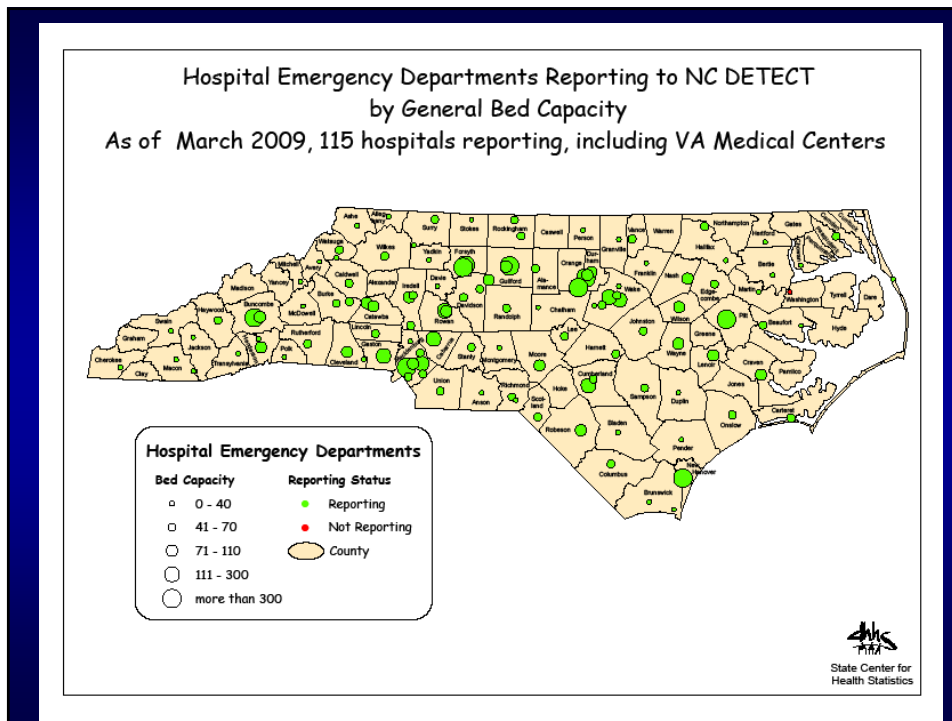


NC DETECT ED Syndrome Definitions

- Operationalize clinical case definitions derived from the CDC's text-based case definitions for bioterrorism syndromes*
- Search free text data in the chief complaint and triage note data elements for the presence of terms which represent disease specific clinical concepts
- Generally require both a constitutional (e.g. fever, aches) and a syndrome specific search term (e.g. cough, dyspnea)
- ED records are updated twice daily and queried by public health officials through the NC DETECT web portal
- Monitor 9 syndromes routinely

* Centers for Disease Control and Prevention. Syndrome definitions for diseases associated with critical bioterrorism-associated agents. October 23, 2003.

<http://www.bt.cdc.gov/surveillance/syndromedef/index.asp>



Syndrome Definition Development

- **Ongoing development** is overseen by the NC DETECT Syndrome Definition Workgroup and is based on the experience of workgroup members and guided by end-user feedback
- There is a **lack of a standard methodology** for syndrome development and agreement as to the choice of the gold standard against which to measure their validity
- This makes it difficult to assess the benefit of definition modifications and to **compare the sensitivity and specificity of definitions** across systems
- Using NC DETECT data we developed an expert-reviewed **gold standard dataset** for the evaluation of the sensitivity and specificity of our respiratory syndrome then made a revised syndrome with greater sensitivity available to end-users for feedback

Gold Standard Development

- Create an expert-reviewed gold standard (GS) data set which can be used to calculate the sensitivity and specificity of syndrome definitions
 - Static database of 956 thousand ED visits from NC DETECT
 - Only 2.6% matched the NC DETECT respiratory syndrome definition
 - A stratified sampling method with optimal sample allocation achieves acceptable statistical accuracy compared with a simple random sample but requires individual review of far fewer records
 - Minimum sample size and optimal allocation was determined using an algorithm developed by Chromy* and applied based on estimates of the proportions of respiratory syndrome cases in each strata from an earlier pilot study

* Chromy JR. Design optimization with multiple objectives, In Proceedings of the Survey Research Methods Section, American Statistical Association, 1987; 194-199.

Record Selection for Expert Review

Records were stratified by:

1. Less stringent respiratory definition with no constitutional requirement
2. Presence of triage note

3,699 records allocated into four strata were reviewed for gold standard classification.

	Less Stringent Respiratory Definition Positive	Less Stringent Respiratory Definition Negative
Triage Note Present	503	418
Triage Note Absent	585	2193

NC DETECT Respiratory Definition

Respiratory Clinical Concepts

cough, cyanosis/hypoxia, dyspnea, hemoptysis
tachypnea, pleural effusion, pleurisy, pneumonia, stridor

AND

Constitutional Clinical Concepts

achy, anorexia, diaphoresis, fever/chills
fussy infant, lightheaded, malaise, myalgias
documented temperature $\geq 38^{\circ}\text{C}$

- Requires BOTH a respiratory and a constitutional term
- Searches BOTH Chief Complaint and Triage Note fields for key words representing clinical concepts
- Weighted Sensitivity and Specificity based on GS dataset are 23.1% and 98.6%, respectively

Sensitivity and Specificity

The sensitivity and specificity of syndrome definitions directly impact system performance

- ↑ Sensitivity
 - Identifies more syndromic cases (↓FN)
 - Decreases the likelihood of missing an event
 - Trade-off is an increased number of false alarms which may result in more demand on personnel
- ↑ Specificity
 - Decreases the number of false positive (↓FP) cases resulting in fewer false alarms and less demand on personnel
 - Trade-off is higher likelihood of missing an event

Sensitivity and Specificity

The appropriate balance between these statistical parameters is a function of both the early event detection system under consideration and the event or syndrome being monitored

- ↑ Sensitivity is better for:
 - Events or diseases of greatest concern to public health
 - Systems with the capacity to investigate multiple signals
 - Electronic "reach back" capability
 - Traditional outbreak investigation methods
- ↑ Specificity is better for:
 - Less serious or extremely rare disease entities
 - Case finding for known outbreaks
 - Systems with fewer resources for outbreak investigation

Chief Complaint and Triage Note

- Compound syndrome definition: requirement for more than one term to satisfy the query
 - In this case, a respiratory and a constitutional term
 - More difficult to satisfy due to inherent limitations of Emergency Department data
 - Only 20-25% of chief complaints contain more than one clinical concept
 - Only 19% of visits in this dataset contributed TN data
 - Triage notes contain pertinent negatives which may cause false positive results if negation is not recognized
- Removing the requirement for a constitutional symptom or eliminating the triage note field from the free text search would be expected to affect syndrome performance

Effect of Syndrome Modification on Sensitivity and Specificity

Query	Sn* (%)	Sp* (%)	PPV* (%)	NPV* (%)
Standard Respiratory Query • CC and TN • + Constitutional	23.1	98.6	57.8	94.0
Revised Respiratory Query #1 • Search CC Only • + Constitutional Requirement	9.5	99.8	76.2	93.1
Revised Respiratory Query #2 • Search both CC and TN • - Constitutional Requirement	53.3	92.8	37.6	96.1

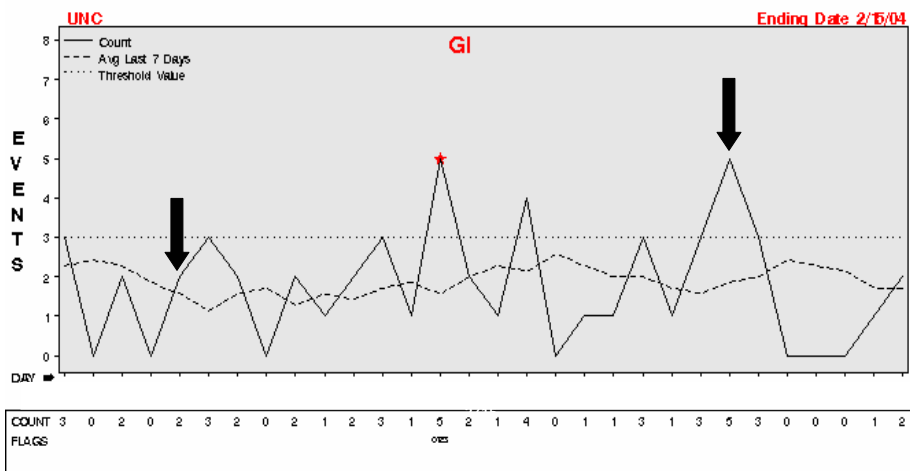
* Weighted values which represent expert reviewed records (n=3,699) weighted for the total database excluding injury visits (n=956,015)

End-user Feedback

The revised respiratory syndrome was made available on the NC DETECT web portal and end-user feedback was solicited

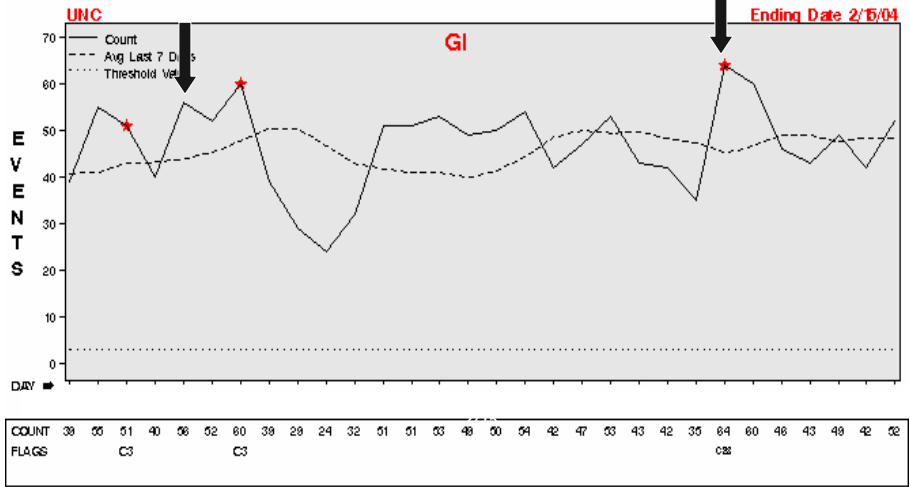
- After several months:
 - “Overlaps with ILI and standard respiratory”
 - “Have not found it to be useful”
 - “Not providing additional information”
 - It was felt, however, that having the more sensitive syndrome might be useful as a confirmatory tool when an aberration was detected in the standard respiratory syndrome
- After another year:
 - “I don't like it”
 - “Take it down”
 - “Too many false positives”
 - “I like higher specificity of the standard respiratory syndrome”

Early Aberration Reporting System (EARS-NH)



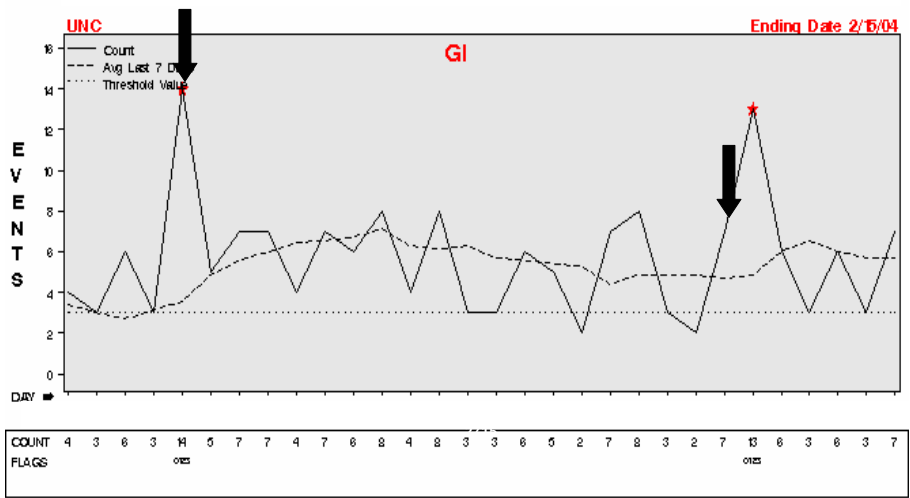
GI Syndrome: Weighted Sensitivity 28.0%, Weighted Specificity 97.4%

Early Aberration Reporting System (EARS-NH)



C1=Mild Sensitivity C2=Moderate Sensitivity C3=Ultra Sensitivity

Early Aberration Reporting System (EARS-NH)



C1=Mild Sensitivity C2=Moderate Sensitivity C3=Ultra Sensitivity

Conclusions

- When dealing with large datasets, stratified sampling allows for the creation of an expert reviewed reference standard while limiting resource utilization.
- Empirically derived syndrome definitions used in NC DETECT tend to have relatively low sensitivity and high specificity.
- Increasing sensitivity translates into improved case detection, but at the cost of decreased specificity requiring the review of additional false positive records.
- Input from system end-users is essential in understanding the impact of such approaches on these users' workload.
- Additional processing such as age stratification, especially during a known outbreak, may create more manageable query results.

Limitations

- Although the methodology for their creation can be reproduced, individual gold standard datasets cannot be shared across syndromic surveillance systems
- Sensitivity and specificity are also affected by the search terms, searching method (deterministic vs. probabilistic) and aberration detection algorithm used by each system
- Positive predictive value is directly proportional to the prevalence of the disease - the optimal statistical parameters for a given syndrome may change depending on the disease prevalence in a population or at different points in a given investigation

RTI-UNC BioSense Research Team



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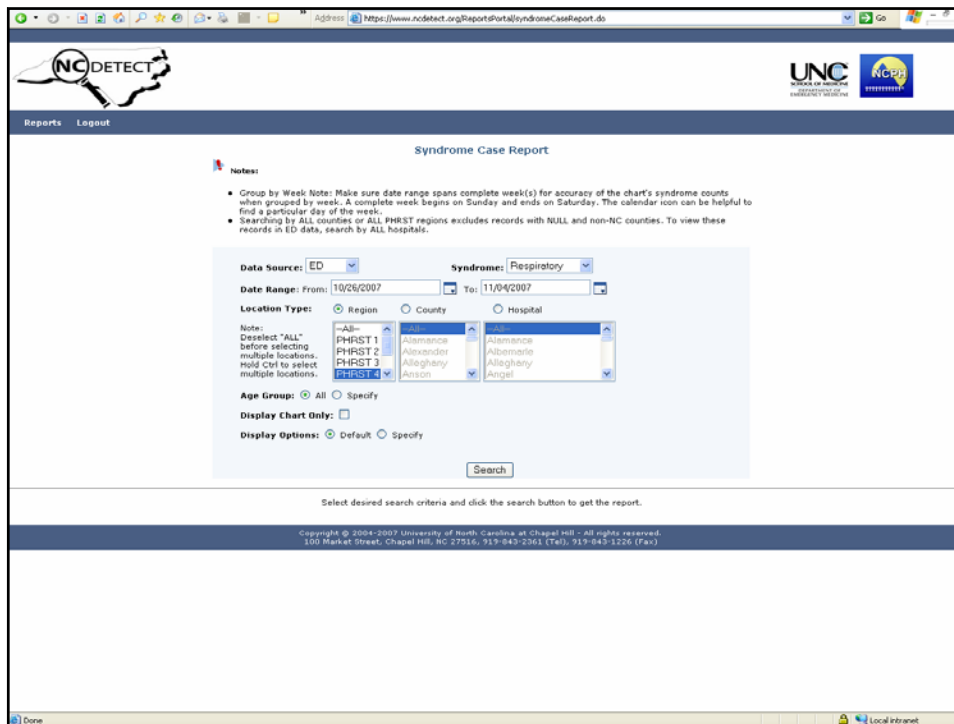
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www.simpsonizeme.com

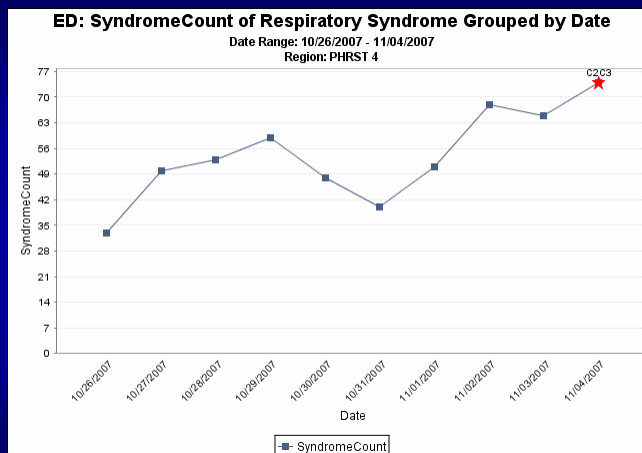


Gold Standard Development

- Goal: to create an expert-reviewed gold standard (GS) data set which can be used to calculate the sensitivity and specificity of syndrome definitions
 - Static database of 1.1 million ED visits from NC DETECT
 - October 1, 2004 through Sep 30, 2005
 - Injury visits were excluded based on primary ICD-9-CM code resulting in 956 thousand remaining visits
 - Only 2.6% matched the NC DETECT respiratory syndrome definition
 - Manual review of nearly 1 million individual records to create the gold standard data set would have been too labor intensive

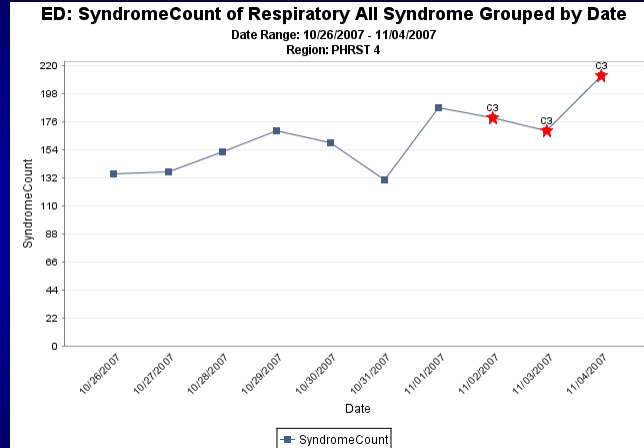


Standard NC DETECT Respiratory Definition



- Constitutional requirement, high specificity
- 541 total cases, 30-70 visits/day

Revised NC DETECT Respiratory Definition



- No constitutional requirement, higher sensitivity
- 1629 total cases, 130-200 visits/day