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EXECUTIVE SUMMARY – PART II

This is the follow up to Part I of a study to evaluate an early warning system for infectious disease outbreak that was implemented in the Seattle Fire Department. Part I covered prior research, elements of what a successful early warning system (Sit Found) should include and a description of the system that was implemented in Seattle. A major component of the early warning system was the monitoring and alerting service provide by FirstWatch ©.

This study does not attempt to prove that the Sit Found symptom data can predict or forecast influenza-like illness (ILI) or predict the outcome of laboratory virus tests. Information about when data is collected (timing) is not precise enough to determine if the symptom data was captured before a hospital visit or lab test. A predictive model would require knowing precisely when hospital visits occurred and when tests were conducted and would require matching patient information across all three data sources. Therefore the best that the study can do is give some evidence that the SFD Sit Found program provides useful information in detecting an unexpected outbreak of some infectious disease.

Findings:

1. The Situation Found and FirstWatch systems were able to track and generate alerts associated with the outbreak of the H1N1 virus in 2009. Reports of symptoms in the field were highly correlated with University of Washington Virology laboratory results and emergency department (ED) patients who had influenza-like illness (ILI) during the outbreak periods.

    a. The Sit Found early warning system may have predictive value for unexpected outbreaks such as the 2009 H1N1 outbreak. The statistical analysis showed that 80%-90% of ILI at emergency departments and 70%-80% of laboratory confirmed virus cases during the H1N1 outbreaks were highly associated with the early warning data.

    b. The FirstWatch program accurately generated alerts before and during about the H1N1 outbreak, and during regular flu seasons. This supports the conclusion that the FirstWatch program is valuable in alerting public health officials about novel infectious diseases that rise to the epidemic or pandemic level.

2. The Situation Found symptoms were broadly defined and did not correlate very well in the months/years outside of the H1N1 outbreak. In other words the real-time symptom data did not match a particular clinical case definition and picked up a lot of “noise” during the regular flu seasons. For example, in early 2010 there was a high volume of RSV and Rhinovirus detected by laboratory results which may explain why the SFD Sit Found program recorded much higher percentages of flu symptoms than ILI cases or influenza lab cases.

    a. The Situation Found data showed an increase in influenza-like symptoms at and during the regular flu season cycles although the increase did not trigger a significant number of alerts from the FirstWatch program.

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3. The Situation Found program is not particularly useful in identifying occupational illnesses in firefighters who came in contact with patients with influenza-like symptoms. Essentially, the level of contacts per firefighter was too small and there are too many other factors that could result in a firefighter illness.

4. As indicated in Part I, the Situation Found program is useful in helping EMS and public health agencies identify when to start escalating prophylactic measures and taking steps to handle potential surges at emergency departments.

A. SYMPTOM DATA USED IN THE EVALUATION

As described in the Part I of the study combinations of influenza-like symptoms were collected in the field – e. g., Fever, Cough-Fever, Cough-Fever-Respiratory, etc. Early in the analysis it appeared that certain combinations of symptoms were more closely associated with ILI than the total number of cases with any influenza-like symptom. For example, *Fever* by itself - or in combination with any other symptom - varied consistently with the typical flu seasons as measured by ILI patients and lab test results. Fever and fever combinations was also highly associated with the H1N1 outbreak and more so than the aggregate of all cases with flu-like symptoms. Any combination of symptoms that include *Fever or Cough or Respiratory* - or any one of those three in combination with another symptom - varied consistently with the flu season and was more highly associated with the H1N1 outbreak than the aggregate of all cases with flu-like symptoms. Finally, *specific* combinations of symptoms – e. g, Fever-Respiratory, Cough-Fever, Gastro-Respiratory, etc., varied closely with the flu season and had the highest association with the initial H1N1 outbreak in the Spring of 2009. However these specific combinations did not show significant associations with lab test results or ILI cases during the second H1N1 outbreak in the Fall of 2009. (There are several possible explanations, discussed below.)

The statistical association with ILI diagnosis or lab tests is addressed in the next section. From the charts, below the SFD Sit Found program appears to have captured symptoms that varied consistently with the regular flu season and with the H1N1 outbreaks in 2009.

The charts are based on data from July 7, 2007 through September 7, 2011. Key periods and date ranges used in the analysis are:

2007-2008 Flu Season:	September 22, 2007 to April 26, 2008
1st H1N1 Outbreak:	March 28, 2009 to July 18, 2009
2nd H1N1 Outbreak:	September 5 to December 12, 2009
2010-2011 Flu Season:	September 4, 2010 to April 30, 2011

These dates are not precise in that there is no real “start” and “end” date for influenza seasons and instances of H1N1 in the community appeared at different times and clinical confirmation of the H1N1 virus occurred days or weeks after its presence in the community. For purposes of the statistical analysis some specific date ranges are necessary.

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Chart A – Percentage of SFD Patients with Flu Symptoms 2007-2011

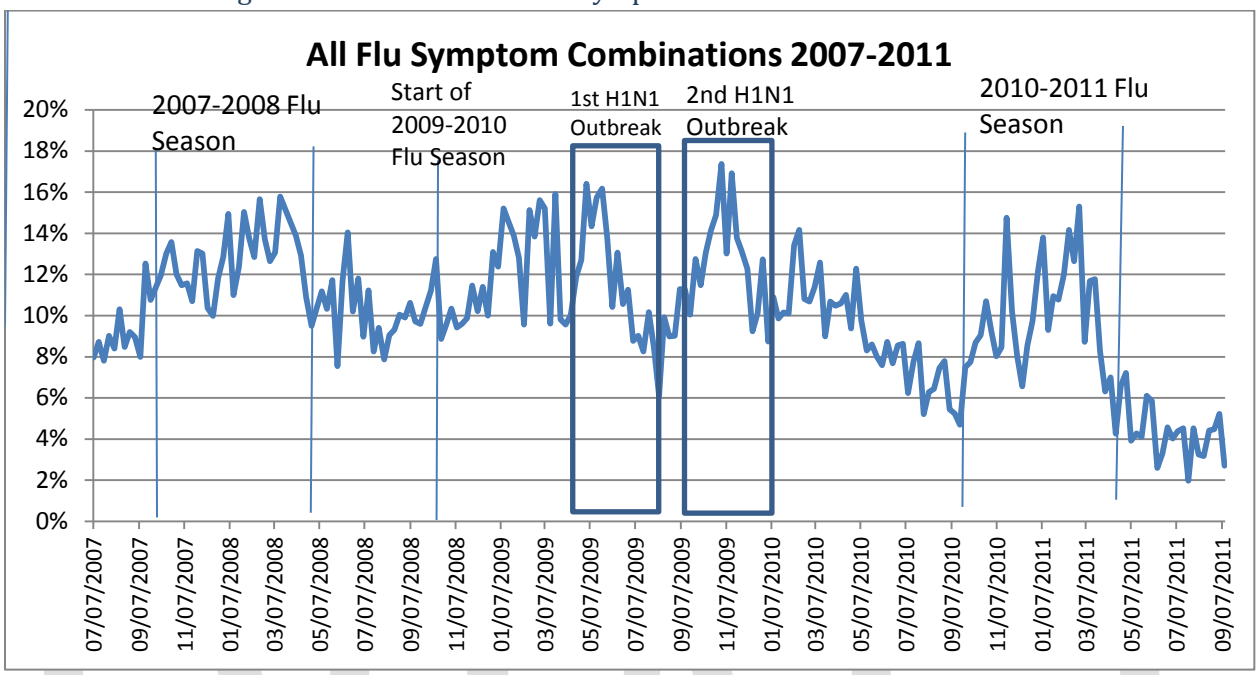


Chart B – Percentage of SFD Patients with Fever, Cough, Respiratory Symptom Combinations 2007-2011

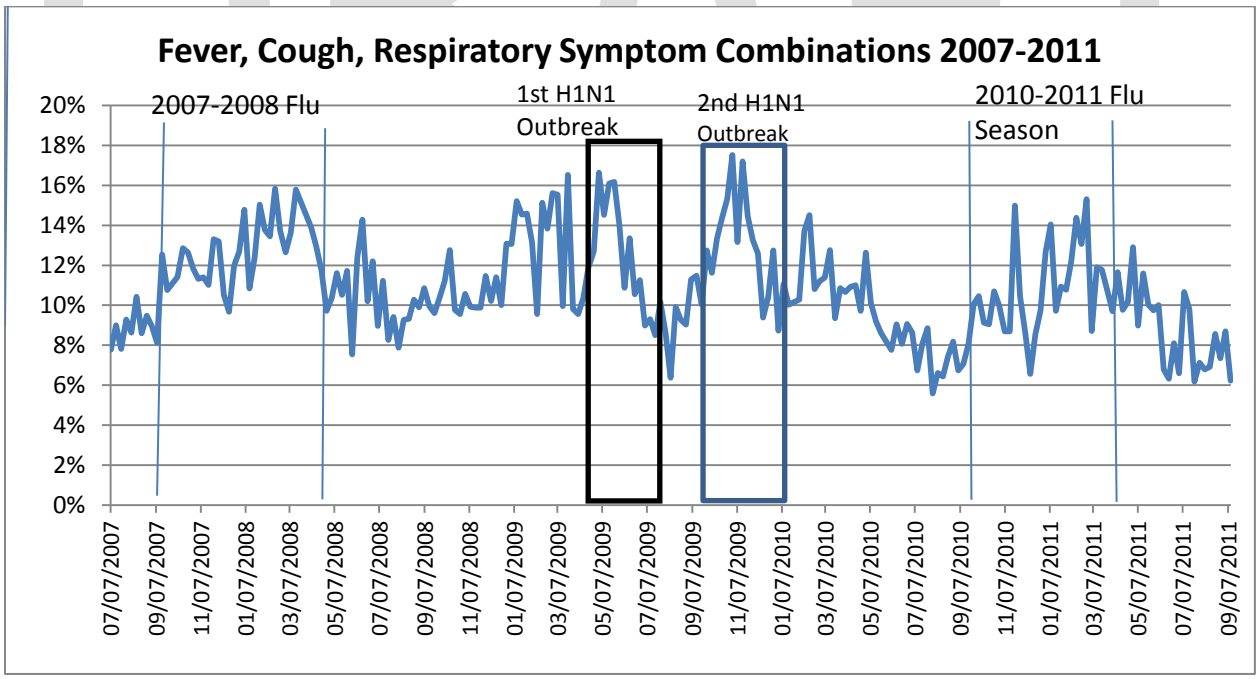
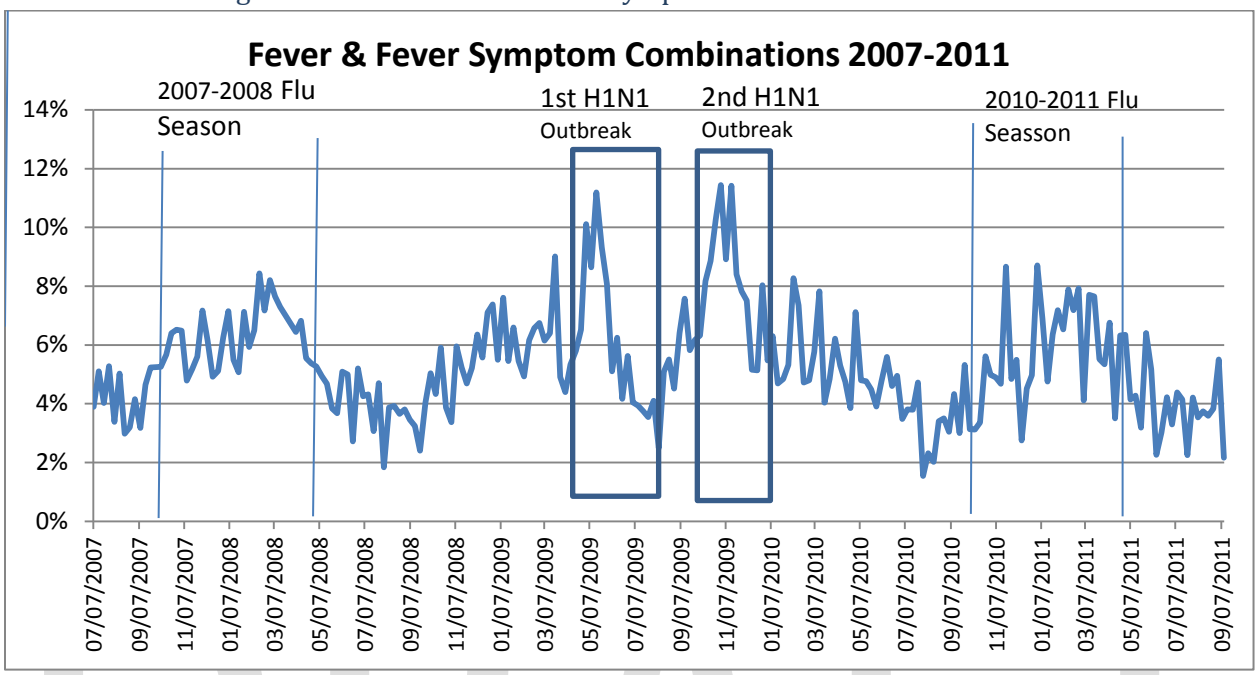


Chart C – Percentage of SFD Patients with Fever Symptom Combinations 2007-2011



B. COMPARISON TO OTHER SURVEILLANCE SYSTEMS

Sources of data include: Weekly emergency department (ED) from August 11, 2007 through August 14, 2010, weekly UW Virology Laboratory data from July 7, 2007 through September, 2011, and weekly flu symptom data from the SFD Infectious Disease Monitoring program from July 7, 2007 through September, 2011. (A more detailed description of the data sources and limitations on the data is contained in the Phase I report.)

Attachment A and B contain the regression analysis showing the relationship between the influenza-like symptom data collected by SFD and the visits to ED and laboratory results.

The ED visit data covered the period of from August 11, 2007 through August 14, 2010 and reflects the count of visitors with influenza-like illness and the percentage of ED visitors with influenza-like illness. The UW laboratory data covered the period from July 7, 2007 through September 10, 2011. Both sets of data cover regular "flu season" periods, non-flu season periods and the two outbreaks of H1N1.

Charts D through F compare Sit Found symptoms with ED patients and laboratory tests. As indicated the percentage of SFD patients with flu symptoms fairly matches ILI patients and laboratory results over the regular flu seasons and H1N1 outbreaks. However, there is substantially more volatility in the flu symptom data which is reflected in the statistical analysis.

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Chart D – % of ED Patients with ILI and SFD Patients with Symptoms

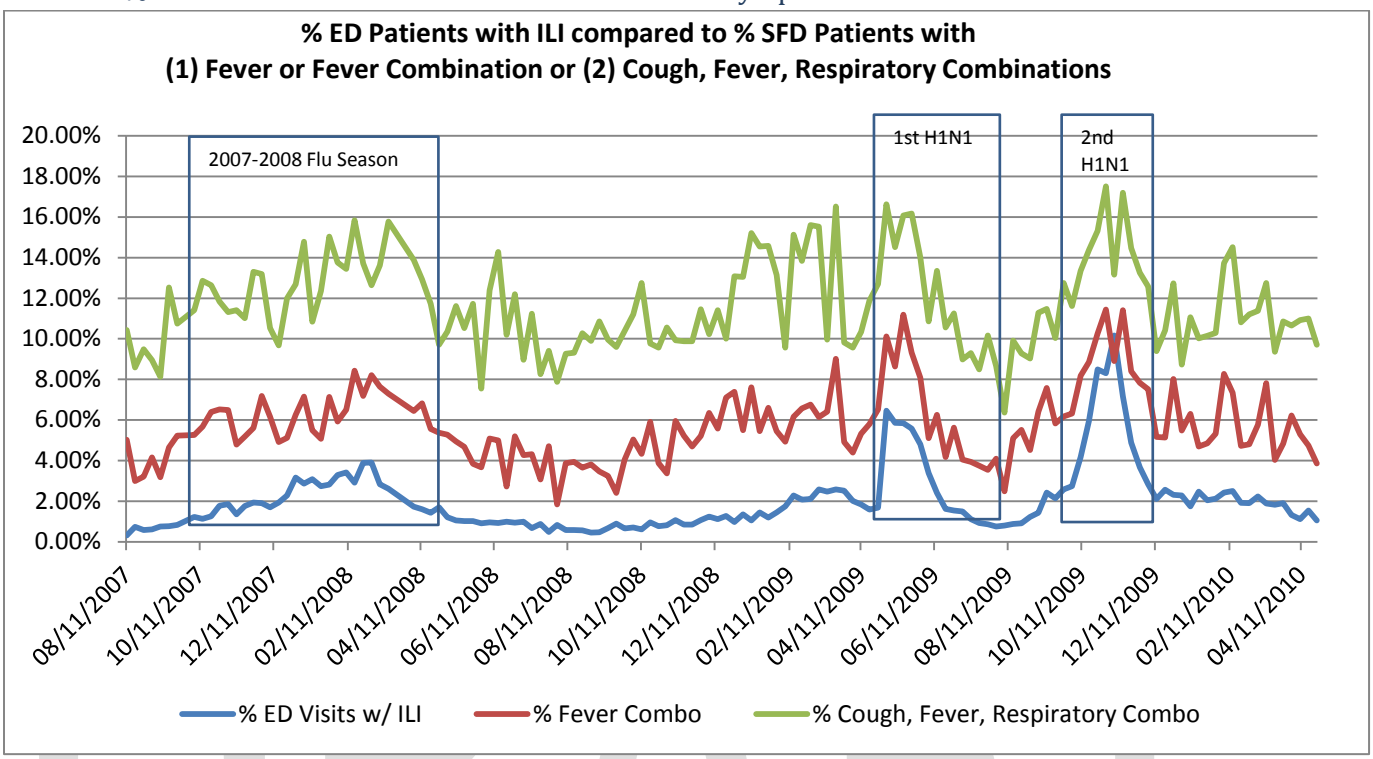


Chart E – Lab Virus Count and Symptom Combinations

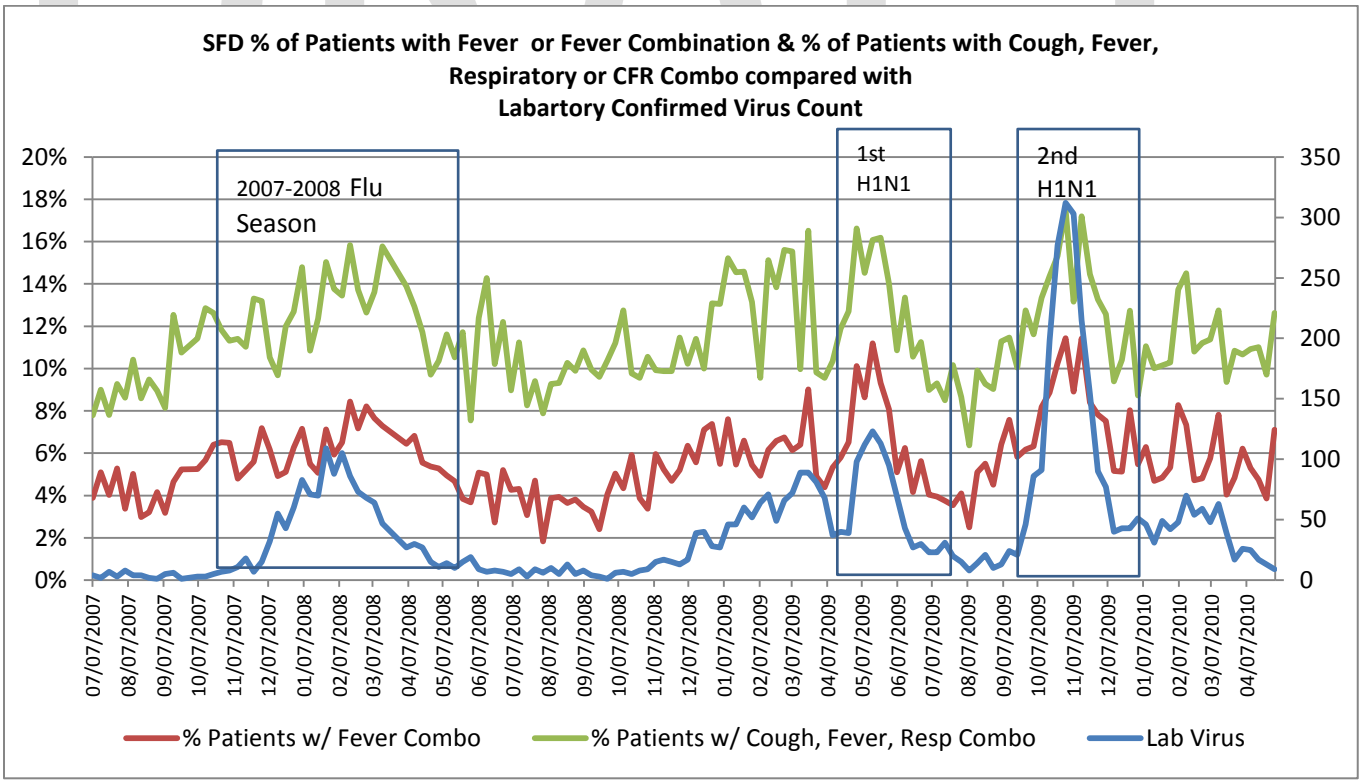
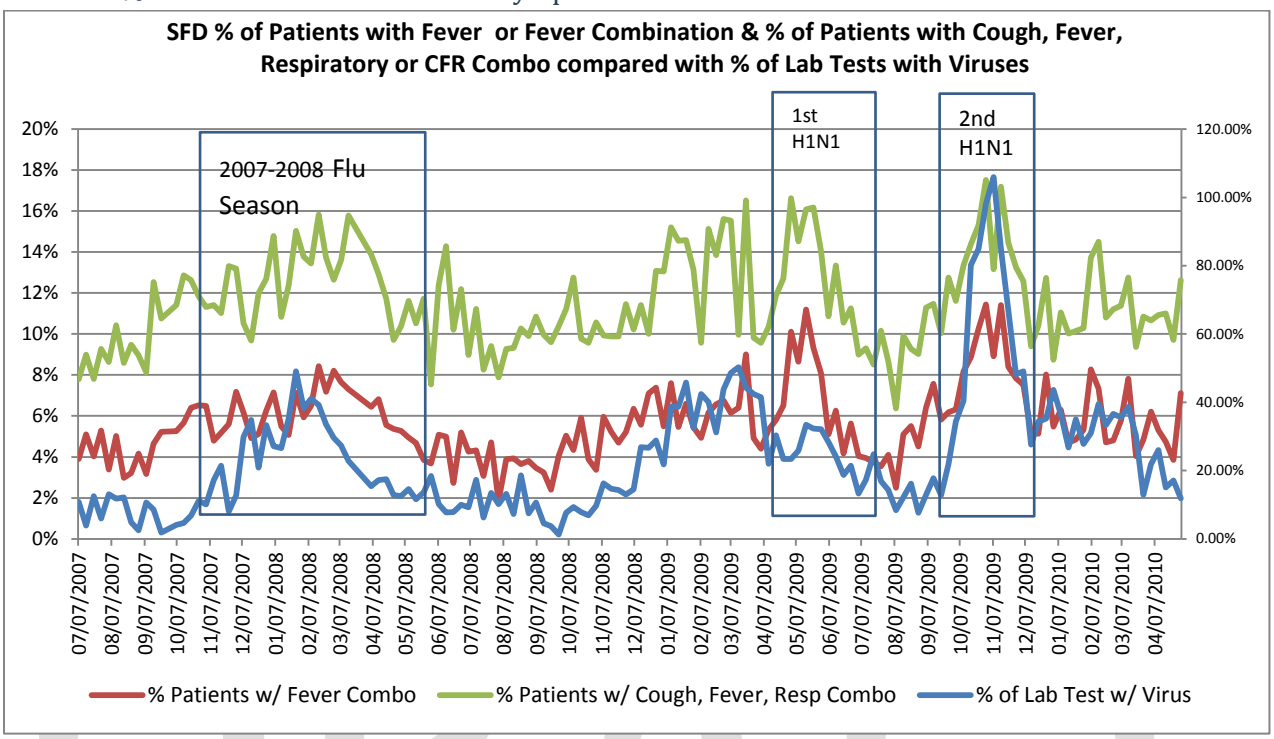


Chart F – % of Lab Tests with Virus and Symptom Combinations



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1. Sample Periods and Patient Profile

The analysis focuses on regular flu season periods (2007-2008, 2008-2009, and 2010-2011), the H1N1 outbreak periods and non-flu season periods. The 2009-2010 regular flu season was not analyzed because it included the 2nd H1N1 outbreak so the data is not comparable to other regular flu seasons.

During the flu seasons there were more viruses detected, more ED patients had ILI and more SFD patients had influenza-like symptoms (ILS) than during the non-flu season periods. The 1st H1N1 outbreak started at the end of the normal flu season and the second H1N1 outbreak started at the beginning of the next flu season (2009-2010).

As expected, the percentage of ED patients with ILI, percent of laboratory tests detecting viruses and percentage of SFD patients with ILS were higher during the second H1N1 outbreak probably because of the additional infectious diseases in the community.

Table 1 – ED, Lab, Sit Found Data During H1N1 Outbreaks

	1st H1N1 Period	Average Per Week	% of Patients or Tests	2nd H1N1 Period	Average Per Week	% of Patients or Tests
ED patients	85,797	5,047		72,048	4,803	
ED patients with ILI	2,622	154	3.06%	3,372	225	4.68%
Lab Tests	3,825	225		3,234	216	
Lab Detected Viruses	1,052	62	27.5%	1,947	130	60%
SFD Patients	6,542	385		9,541	636	
SFD Patients with ILS	1,096	64	17%	1,727	115	18%

2. Correlation Analysis

Correlation analysis indicates whether the variation (up and down) between two variables is associated and whether one variable "explains" the variation in the other. The measure of association is the represented by the Correlation Coefficient [R] and the explanatory value is measured by the Coefficient of Determination [R^2]

Explaining variation [R^2] can be used to conclude that one variable (X) has value in ***predicting*** the value of the other variable (Y). In this study these coefficients are used to identify which set of symptoms – if any – are strongly associated with ILI and viruses detected in the lab. As mentioned previously, a prediction of Y from X in this study is not possible. The timing of data capture is not known and patient records cannot be matched across the three data sources is not possible. However, the correlation analysis (and subsequent regression analysis) is useful in determining whether the SFD Sit Found program is valuable in detecting the unexpected outbreak infectious disease.

There was no significant correlation [R or R^2] of the SFD flu symptom data with either the ED or laboratory data for *non-flu seasons and flu seasons outside of the H1N1 outbreak*. There was some consistency in the variation of the SFD symptom data with the other sources but the correlations were relatively low (R under 0.7 and R^2 under 0.5) and none of the calculations were statistically significant.

Tables 2 and 3 show the correlation coefficients [R] and coefficient of determinations [R^2] between the dependent or estimated variable (ILI or lab results) and independent variable (symptom). The information is only for H1N1 outbreak periods. The table only includes R^2 values that are statistically significant at the 0.05 level of confidence. There were a number of other high R and R^2 values calculated for ILI and laboratory results but these were not statistically significant. For example, Laboratory Viruses Detected and Percent of SFD patients with Cough-Fever-Respiratory Symptoms Combinations had an R = 0.799 and R^2 = 0.639. Both are reasonable high but the R^2 was not statistically significant.

The coefficient values identify which variables might produce useful regression models that explain the variation in ILI and laboratory results – i. e., those with high R^2 values are most likely to have valid regression models that will also have high R^2 values. Furthermore, the highlighted rows in Table 1 and 2 show variables with significant relationships in both H1N1 outbreak periods.

Given the differences between the two periods (reflected in Table 1) it is not surprising that the relationships between the variables (as measured by the correlation coefficients) would not be the same for those periods. If the sample data could be matched at the patient level or captured on a daily basis (versus weekly) the correlation between SFD symptom data and the laboratory and ED data might be more consistent between the two periods. For purposes of this study there appears to be a sufficient level of association between the symptom data and other sources to move forward with a more rigorous statistical analysis.

Table 2 – Correlation Coefficients for 1st H1N1 Outbreak

H1N1 - MAR 28 - JULY 18 2009	R	R^2
ED Visit Comparison		
%ED w/ ILI with %Flu Symptoms	0.886	0.784

%ED w/ ILI with %Cough, Fever, Respiratory	0.884	0.781
%ED w/ ILI with %Fever Combination	0.916	0.839
%ED w/ ILI with %Symptom Categories	0.872	0.761
%ED w/ ILI with % Fever, CoughFever, FeverGasResp	0.820	0.672
Laboratory Comparison		
Lab-Viruses Detected & % Flu Symptoms	0.853	0.727
Lab-Viruses Detected & % Fever Combination	0.842	0.709
Lab-Viruses Detected & % Fever, CoughFever, FeverGasResp	0.807	0.652
Lab-InfluA & InfluB & % Fever, CoughFever, FeverGasResp	0.793	0.628

The % symbol in the rows above means the percentage of ED patients with ILI or percentage of SFD patients with Sit Found flu symptom(s)

Table 3 – Correlation Coefficients for 2nd H1N1 Outbreak

H1N1 – SEP 5 – DEC 12 2009	R	R^2
ED Visit Comparision		
%ED w/ ILI with %Fever Combination	0.839	0.705
Laboratory Comparison		
Lab-Viruses Detected with % Fever Combination	0.856	0.732
Lab-Viruses Detected with % CoughFeverResp, CoughFevrGastroResp	0.838	0.702
Lab- % of Test w/ Virus with % Cough, Fever, Respiratory Combo	0.803	0.644
Lab- % of Test w/ Virus with % Fever Combinations	0.853	0.728
Lab-InfluA & InfluB with % Fever Combinations	0856	0.732
Lab-InfluA & InfluB with % CoughFevResp, CoughFevGastroResp	0.829	0.687

3. Regression Analysis

Attachment A and B contains linear and polynomial regression analysis for emergency department (ED) data, laboratory test data and various combinations of SFD Sit Found symptom data. The periods for which the data was collected go "up and down" and do not really follow a linear pattern. Although the linear regression produces useful results and allows *multiple* dependent variables ($X_1 \ldots X_n$) to be included in the formula the analysis also includes a third-order polynomial equation. The polynomial equation only allows one independent (X) variable but as shown in the Attachments the polynomial frequently produces better results.

The regression calculations included a wide range of variable combinations – those that are significant and many that are not. From the correlation analysis attention should be focused on the Percent of SFD patients with Fever (and other symptoms combined with Fever). Table 4 shows those results:

Table 4 – Regression with Percent of Patients with Fever & Fever Combinations

% Fever Combination (X) with:	1st H1N1 Period		2nd H1N1 Period	
	Linear	Polynomial	Linear	Polynomial
	Adjusted R^2	Adjusted R^2	Adjusted R^2	Adjusted R^2
% of ED Patients with ILI	0.828	0.894	0.682	0.781
Viruses Detect by Lab Tests	0.696	0.656	0.712	0.783

The p-values for R2 are well below 0.05 and residuals are fairly normally distributed. The charts in Attachments A and B indicate that the residual distributions for both the linear and polynomial models show some departure from "normalcy". Ideally the standardized residual points would evenly distributed

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above and below the horizontal lines with few points above 1.0 (and none above 2.0). As indicated by the histograms the residuals are skewed to right or left and do not reflect a perfect bell curve. Despite these discrepancies the models appear to be sufficient in concluding that there is a very strong association between the Fever Combination symptom and ILI and lab test data.

There is one outlier observation during the 2nd H1N1 outbreak: November 7, 2009. That week showed a significantly high volume of viruses detected and the highest number of ED patients with ILI. Excluding that one week of data would significantly change – and improve – the regression outcomes. The R^2 value for % of ED Patients with ILI would go from 0.682 to 0.868 and viruses detected in the lab would go from 0.712 to 0.814. The data for November 7th could be dropped out of the model because it is an "outlier" with a standardized residual over 2.0. However, more investigation will need to be done to determine if dropping that week's data is warranted.

There were a number of other regressions for both the 1st and 2nd H1N1 outbreak periods with high R^2 values that are statistically significant. However, these are models are not consistent for **both** periods. In particular specific combinations of SFD flu symptoms had very high R^2 values during the 1st period:

Table 5 – Regression of Specific Symptoms with Percent of ED Patients with ILI

Specific Flu Systems	Adjusted R^2
Fever, Cough-Fever, Gastro-Respiratory, Cough-Gastro-Respiratory	0.952
Fever, Fever-Respiratory, Cough-Fever, Gastro-Respiratory, Fever-Gastro-Respiratory	0.944
Fever, Cough-Respiratory, Cough-Fever-Respiratory, Cough-Fever, Cough-Fever-Gastro-Respiratory, Cough-Fever-Gastro, Fever-Gastro-Respiratory	0.920

None of these had statistically valid regression outcomes for the 2nd period. However, the results will be different if the outlier observation in the 2nd period (November 7th) is resolved.

C. OBJECTIVES OF THE PROGRAM

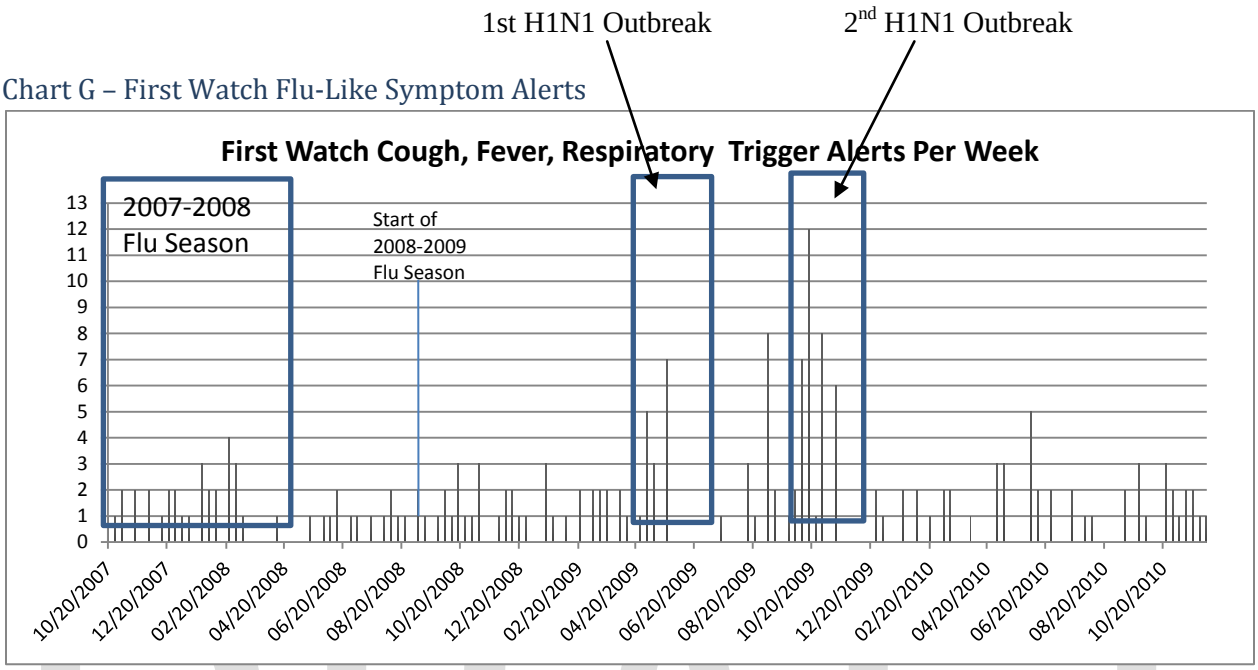
1. Outbreak Alerting – FirstWatch©

The First Watch system was configured to send alerts when flu-like symptom events exceeded thresholds (as described in Part I of this study.) As indicated in Chart G the system sent alerts consistent with the 2009 H1N1 outbreak and consistent with the 2007-2008 flu season. As widely reported, the 2009-2010 flu season had one of the highest level of confirmed flu cases in the past twenty years due mostly to the second wave of H1N1 in the Fall of 2009.[1] However, the 2010-2011 and 2011-2012 flu seasons werer extremely mild[2] and – as expected - few alerts were generated.

[1] *CDC – Seasonal Influenza (Flu) Season*: http://www.cdc.gov/flu/pastseasons/0910season.htm
CDC – Update: Influenza Activity – United States, 2009-10 Season: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5929a2.htm

[2] Influenza Mild in the US During 2011-2012 Season: CDC, *MMWR Morb Mortal Wkly Rep.* 2012;61(22):414-420. http://www.medscape.com/viewarticle/765427
Flu Season Was One of Mildest on Record, US News & World Report, June 7, 2012: http://health.usnews.com/health-news/news/articles/2012/06/07/flu-season-was-one-of-mildest-on-record-cdc-confirms

Chart G – First Watch Flu-Like Symptom Alerts



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2. Firefighter Exposures

The biggest difficulty of matching exposure to firefighter illness is that there is little information collected to tie an exposure to a firefighter illness. City policies do not allow the department to require employees to state why they are taking sick leave (disability) unless the leave is for an extended period of time and they produce documentation from a doctor supporting the absence. Even then the report of illness is vague and hard to correlate to an influenza or infectious disease.

However, Department policy encourages all firefighters to document and report on any exposure to a biological and/or chemical hazard and the department maintains detailed records of those events. Review of those exposure records was not done for this study. The Department's Disability Officer indicated after a review of this study that exposure reports would not be useful. Essentially, the exposure reports filed are too few and far between to associate with exposures tracked in the Sit Found Program.

From 2009 through June 19, 2012 there were 980 firefighters exposed to patients with influenza-like symptoms. This represents almost all on-duty firefighters. However the number of exposures *per firefighter* was relatively small. For example, only two firefighters had 8 exposures per month in the 3.5 year period. The average was 1.3 exposures per month and the median was 1. Only 136 had 3 or more exposures per month. During the 5 months of the H1N1 outbreaks of 2009 the firefighters with the most exposures (top 20) were not that significant

Chart H – Firefighter Average Exposures Per Month

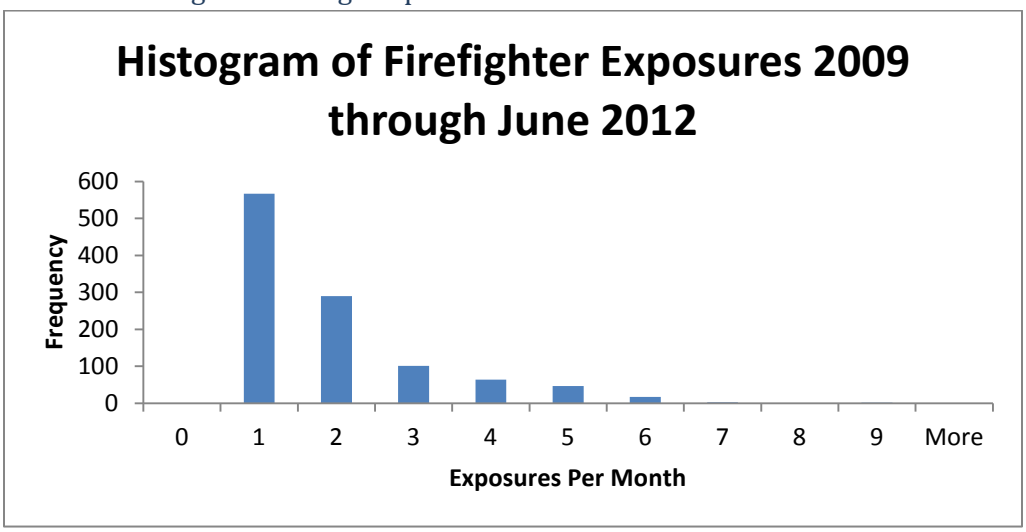

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Table 6 – Total Firefighter Exposures During H1N1 Outbreak

FF	2ndH1N1	H1N1	Avg Per Mth
FF1	33	61	12.2
FF2	37	49	9.8
FF3	35	48	9.6
FF4	16	44	8.8
FF5	27	43	8.6
FF6	25	43	8.6
FF7	26	43	8.6
FF8	27	42	8.4
FF9	23	42	8.4
FF10	19	41	8.2
FF11	27	41	8.2
FF12	22	40	8
FF13	25	40	8
FF14	22	38	7.6
FF15	23	38	7.6
FF16	21	37	7.4
FF17	0	37	7.4
FF18	21	36	7.2
FF19	20	34	6.8
FF20	21	34	6.8
FF22	17	34	6.8
FF23	20	34	6.8
FF24	16	33	6.6
FF25	16	33	6.6

3. Enhancing Prophylactic Measures

The foregoing analysis indicates that the Sit Found program can give the Fire Department and Public Health an early warning on when to start increasing prophylactic measures. For example:

- Requiring vaccinations
- Social distancing in the work place
- Increasing distance from patients at an emergency scene
- Use of goggles and gowns

Taking these measures before laboratory confirmation of an outbreak will help keep first responders and public health clinicians more available to help citizens who do become ill.

4. Assisting Public Health in Planning/Responding

The Sit Found program does not replace but augments syndromic surveillance systems. The Sit Found program allows Public Health officials to identify when surges of patients at area emergency departments might occur and what illnesses they might want to pay closer attention to during initial intake and diagnosis. This will help avoid missed opportunities at proper treatment during the initial days or weeks of an outbreak. The symptom data may also provide insight to what type of laboratory tests to apply to samples (as a means of ruling out defined diseases as well as identifying novel diseases.)

D. LESSONS LEARNED

Compliance: during the H1N1 outbreak the number of incidents that were processed through the Sit Found Program as over 70%. After two years the compliance rate dropped to 20%. A 20% sample might still be indicative of an infectious disease outbreak however more data reduces the risk of erroneous results.

Advance Research: an early warning system to detect novel diseases requires some trial-and-error to identify what data can be verified as useful. The statistical analysis conducted in the study was instrumental in refining the triggers used in the First Watch alerting system. Hopefully this study will help others construct early warning systems based on research, consultation with medical professionals and work at associating the data with multiple systems.

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