UNIVERSITY INFLUENZA SURVEILLANCE PROJECT: 2003–2004

BACKGROUND

Each year, respiratory illnesses such as influenza cause considerable morbidity and mortality. From 1990–1999, epidemics of influenza across the US have been responsible for an average of 36,000 deaths annually [1]. Since complications from influenza are especially detrimental to the elderly, the mortality rate due this disease is expected to continue to rise as our population ages [1]. Across all ages, influenza is believed to affect 10–20% of the population each year [2]. Thus, in a county as large as Los Angeles with an estimated population of almost 10 million [3], even a minor influenza season can account for over 1 million ill residents. In light of our already beleaguered healthcare system, this level of illness can debilitate hospitals and emergency rooms [4].

Influenza surveillance presents a unique challenge since most people affected by influenza do not seek medical care. Influenza cases that are properly diagnosed are not reportable to most local health departments and thus go uncounted each season. As such, there is no gold standard for influenza surveillance in the world today. For that reason, many health departments worldwide are looking for new methods of surveillance for respiratory illness as a proxy for influenza.

University settings may provide a unique opportunity for routine influenza surveillance due to the defining characteristics of college students. College students are a population that is particularly vulnerable to infection with unique respiratory illnesses since they frequently travel to or have arrived from areas that would likely expose them to novel viral strains (e.g., China, Southeast Asia). In addition, students typically live in close contact with numerous other students (i.e., in dormitories, sororities, fraternities, and apartments), conditions that can facilitate the spread of respiratory illness. Lastly, unlike the broader community, university students often seek medical care at a single health center located at their university. Accordingly, universities are often considering methods of enhancing their surveillance of respiratory illnesses in order to mitigate the effects of respiratory disease on their student population.

In order to assess the usefulness of universities as potential sites for influenza surveillance, a pilot program was developed by the ACDC. The objectives of the study were to: 1) describe the characteristics of respiratory illness in university students, 2) evaluate the feasibility of university student health centers as sentinel sites for influenza surveillance, 3) facilitate the identification of common and novel respiratory viruses in circulation, and 4) compare student viral surveillance with other respiratory illness surveillance systems.

METHODS

University student health centers in Los Angeles County (LAC) were contacted and asked to participate in the project. The project underwent review and approval by the LAC Department of Health Services (DHS) Institutional Review Board (IRB). Universities that expressed interest in participating in the project obtained additional IRB approval from their respective university IRB committees.

Participating health centers received influenza test supplies to perform nasopharyngeal (NP) swabs on students presenting to their facility with a respiratory illness meeting the project case definition. An in-service was provided to the medical staff of participating health centers to review the biology and pathology of the influenza virus, explain the project background and protocol, and provide refresher training on how to perform an NP swab test.

On one day each week, participating sites were asked to identify students presenting to their health center with a respiratory illness meeting the project case definition. For inclusion in the study, the test subject needed to: 1) be ≥18 years of age, 2) be a student at the university where the testing was being performed, 3) have a fever >100.1 at the time of the office visit, 4) have an illness onset day <4 days

before the office visit, 5) have at least one other respiratory symptom (e.g., cough), and 6) be able to provide informed consent. Students that met the project inclusion criteria were asked to read and sign a project consent form and complete a symptom survey. The symptom survey asked for basic demographic and symptom as well as other relevant illness information (e.g., recent travel and vaccination status). The signed consent form remained at the testing site and the symptom survey was faxed to ACDC for data entry and analysis. An NP swab culture was performed on the student and sent to the LAC Public Health Laboratory (PHL) for testing. Health centers were asked to submit no more than three specimens per week for testing.

In order to maintain student anonymity, the symptom survey and NP swab were coded with the last four digits of the student identification number. The primary project liaison at each health center maintained a list of the participant code numbers and corresponding student names. This allowed the health center liaison to add the test results to the student's permanent medical record and contact the student for additional treatment if necessary.

In addition to specimen testing, each site was asked to report the number of upper respiratory infection (URI) and influenza visits and the total number of primary care visits recorded at their facility each week. The data was collected from each facility's coded billing records and included URI, Influenza/Flu and ENT diagnosis codes. These numbers were used to calculate the percentage of primary care visits due to acute respiratory complaints by week for each health center. The mean number of acute respiratory and primary care visits reported from each university during the project was used to calculate the average weekly percentage of respiratory visits at each site. The university data was compared to state- and nationwide influenza-like illness (ILI) data for the 2003–04 influenza season. For these surveillance systems, an ILI visit is defined as fever >100 °F and either cough or sore throat.

Weekly reports were sent via email to each health center liaison summarizing the specimens submitted from their site and the current status of each specimen. Monthly reports provided an overview of data collected from each health center individually and aggregate data for all project sites combined.

A rapid enzyme immunoassay (EIA) test* and a complete viral culture** were performed on each NP secretion specimen. In January 2004, the rapid EIA test was replaced with the more sensitive rapid culture test (Diagnostics Hybrid Inc.'s Mixed FreshCells™: R-Mix). The test identifies the same viruses as the complete viral culture, but results are available much sooner. Positive results for the rapid tests were communicated from ACDC immediately back to the student health center via phone. Final viral culture results were faxed to the student health centers as they became available.

Descriptive analysis was performed on data collected from the symptom survey and the NP swab specimens. Facility-specific trends in the percentage of respiratory visits were compared between schools and against sentinel physician data reported state- and nation-wide.

RESULTS

Five universities in LAC were asked to participate in the project for the 2003–04 influenza season. Of these, four were able to complete the necessary paperwork in time to participate in the project. Three sites began the project in November 2003 and the fourth site began in early-December 2003 with all sites participating through March 2004 (Table 1). Participating universities varied on geographic location, student body size, and student characteristics.

A total of 19 specimens were submitted during the project. Of these, 11 (58%) were positive for influenza A (H3N2), 1 (5%) was positive for parainfluenza Type 1 and 7 (37%) specimens tested negative for those respiratory viruses identifiable via a complete viral culture test. Table 2 shows the breakdown of specimen results by university. Overall, 63% of the submitted specimens were positive for a respiratory virus. The

* EIA test: BD Directigen™ Flu A + B
** Viral Culture: RhMK and MRC-5 cells, identifies Flu A, Flu B, Parainfluenza Types 1-3 and Adenovirus

student health centers had a range of 40%-100% in the percent of submitted specimens testing positive for a respiratory virus.

Table 1. University Demographics*

	University A	University B	University C	University D
Student body size	> 30,000	5,000–10,000	> 30,000	< 5,000
Undergraduate	77%	71%	52%	44%
Male	40%	45%	52%	71%
International Students	5.4%	5.8%	17.4%	26.1%
Avg. # primary care visits/year	40,000	12,000	36,000	7,000
Flu vaccination	Nominal Fee	Nominal Fee	Nominal Fee	Free
Project Start Date	11/5/03	11/5/03	11/18/03	12/10/03

* Data collected from university registrars/websites and student health center self-reports.

Table 2. Summary of Collected Specimens by University

	Project Start Date	# of Weeks Participated	# Specimens Submitted	# Positive	# Negative	Percent Positive
University A	11/5/03	21	2	2	0	100%
University B	11/5/03	21	5	3	2	60%
University C	11/18/03	19	7	5	2	71%
University D	12/10/03	16	5	2	3	40%
Total			**19**	**12**	**7**	**63%**

Table 3 provides a summary of the basic demographics of the project participants. Over 90% of the students reported living in either a dorm or apartment and almost 50% reported travel outside of the university within 1 week of illness onset. Only 42% of the participants reported ever having a flu shot and only 16% reported having a flu shot for the 2003–04 influenza season.

Table 3. Participant Demographics

Gender	58% male (n=11)
Age (mean)	22 years (range: 18-31)
Place of residence	58% Dorm (n=11) 37% Apartment (n=7) 5% Home (n=1)
Temperature (mean)	101.2 °F
Days from symptom onset to clinic visit (mean)	1.7 days
Travel	47% (n=9)
Flu Shot (ever)	42% (n=8)
Flu Shot (2003-04 season)	16% (n=3)

The percent of symptoms reported by participants testing positive for influenza A versus participants testing negative are shown in Table 4. Typical influenza-associated symptoms (e.g., fever, cough, fatigue, headache, body aches, etc.) were reported by most of the participants who were positive for influenza A. In addition, runny nose and vomiting, which are not characteristic of influenza infection, were reported by 82% and 27% respectively of those testing positive for influenza A. Large differences in the percent of participants reporting cough, runny nose and vomiting were seen between those students testing positive versus negative for influenza.

Table 4. Summary of Symptoms Reported by Patients Testing Positive vs. Negative for Influenza (n=18)

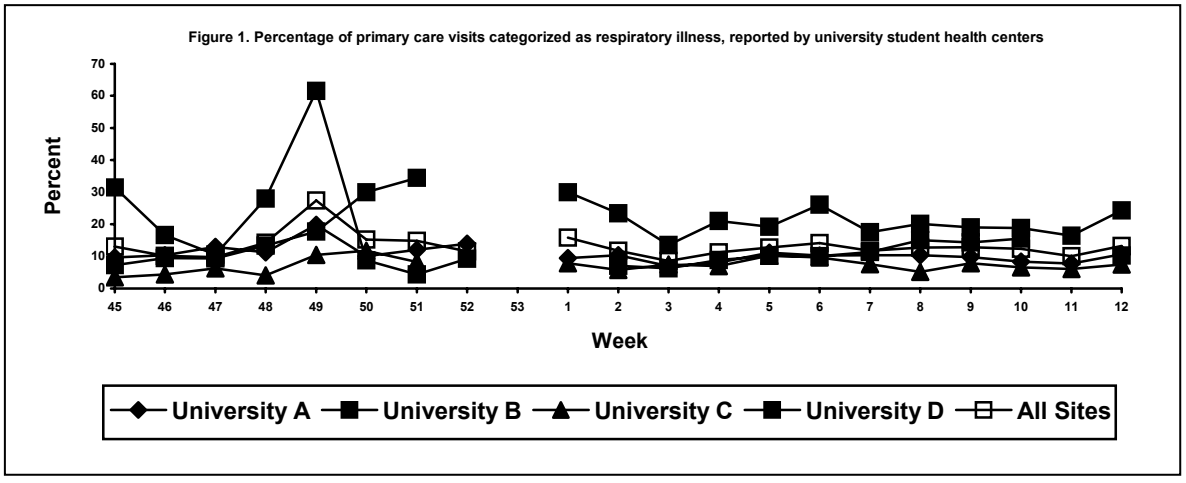
	Positive Specimens (n=11)		Negative Specimens (n=7)	
Symptoms	**n**	**Percent**	**n**	**Percent**
Cough	11	95%	3	43%
Fatigue	11	95%	6	86%
Fever	10	84%	7	100%
Headache	10	79%	6	86%
Body ache	10	79%	5	71%
Runny Nose	9	74%	3	43%
Chills	8	74%	6	86%
Congestion	8	74%	5	71%
Weakness	8	68%	6	86%
Sore Throat	7	68%	5	71%
Nausea	4	37%	3	43%
Vomiting	3	16%	0	0%

All participating sites submitted weekly data on total visits and respiratory illness visits from November 2003 through March 2004; limited data was collected in December due to winter break. The percent of respiratory visits varied from an average of 7.2% per week to 20.7% per week (Table 5, Figure 1). Larger average percentages for respiratory visits were seen for University B and D, whose student bodies consist of fewer than 10,000 students. The mean number of respiratory visits reported weekly from each university was similar to the median number of visits in this category for all participating sites, however, differences were noted between the mean and median number of primary care visits per week from a few of the universities.

Table 5. Number and Proportion of Visits for Respiratory Illness

	Peak Week	Peak %	Average % / week	Range (%)	Respiratory Visits/Week (mean)	Primary Care Visits/Week (mean/median)
University A*	49	19.8	10.7	7.0 – 19.8	83	769/872
University B	51	34.4	13.6	6.3 – 34.4	47	342/372
University C*	50	11.7	7.2	3.5 – 11.7	66	956/904
University D	49	61.5	20.7	4.4 – 61.5	34	163/152
All Sites	**49**	**27.4**	**13.1**	**8.6 – 27.4**	**58**	**558/410**

* Student Body >30,000 students.



All participating student health centers had a peak in respiratory visits between weeks 49 and 51 with the peak percent ranging from 11.7% to 61.5%. The university respiratory data was consistent with the peaks in ILI visits reported by both California (peak in week 49) and the US (peak in week 51).

DISCUSSION

The University Influenza Surveillance Project was implemented to evaluate the feasibility of university student health centers to serve as sentinel sites for influenza surveillance. As this was a pilot project, the most important outcome of this year's project was whether this type of surveillance is feasible, which was found to be true.

The university health centers were excited about the project and eager to participate. Their excitement stemmed from the high incentives for project participation as well as simple project requirements. The health centers were able to work within the project parameters and effectively identify eligible students for participation in the project while maintaining the anonymity of all student participants. Lastly, data transmission (patient surveys, respiratory data, weekly and monthly reports, etc.) between the university health centers and ACDC was completed easily and efficiently.

Another important aspect to this project was providing refresher training to university health center medical staff on how to perform an NP swab—a test with which many clinicians may be unfamiliar. As novel respiratory viruses continue to emerge, clinicians will be asked to perform viral testing more frequently to distinguish common respiratory pathogens from emerging viral respiratory illness. Many clinicians are inexperienced performing NP swabs and thus may be hesitant to perform testing when treating a patient with a respiratory illness. Through this project, university health center medical staff members were able to perform NP swabs on participants and increase their repertoire of diagnostic tests to be used during the influenza season.

Due to the strict inclusion criteria, only 19 NP specimens were submitted for testing, which severely limited the statistical analyses that could be performed. Thus, while the information collected from the individual participants is interesting, firm conclusions cannot be drawn from this data.

All participating sites submitted weekly respiratory data from November 2003 through March 2004. The peaks in the percent of respiratory visits seen weekly matched the peaks in the percent of ILI visits reported in state- and nation-wide data even though the data collected by this study were not restricted to the national case definition for ILI. Using routinely collected medical billing data may prove to be useful in the future not only for influenza surveillance, but for other disease surveillance systems as well.

This project is ongoing for the 2004–05 influenza season—though changes will be implemented to expand the project and address problems from last year. Eight university student health centers will be asked to participate in the project in the hopes of expanding the geographic area covered by the project sites. To increase the number of submitted specimens, participants will not be required to have a fever at the time of the office visit. Instead, a documented fever *or* a self-report of fever within 4 days of illness onset will make a student eligible for project assuming the other inclusion criteria is met. Additionally, each site will be allowed to test up to 5 students on their chosen testing day. Data will also be collected on the number of eligible students on the chosen testing day that decline to participate in the project. If a large number of eligible students are found to decline participating in the study, additional changes may be implemented in the future that attempt to increase student incentives for participating in the project.

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