THE LANCET Respiratory Medicine

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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Supplemental Appendix

The incidence of medically attended influenza during pandemic and post-pandemic seasons through the Influenza Incidence Surveillance Project, 2009 – 2013

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IISP WORKING GROUP

The IISP Working Group consists of epidemiologists and laboratorians contributing substantially to study design, data collection and/or laboratory diagnostic testing, and data analysis and interpretation.

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DATA COLLECTION METHODS

Recruitment of Health Care Providers and Clinics
Participating IISP sites recruited ≥5 health care providers or clinics for surveillance. Ideally, all providers within a clinic would participate; however, individual clinicians were allowed to be recruited if they could identify their patient population and did not send acute care (unscheduled) visits to a provider not participating. Provider/clinic characteristics and capabilities required for inclusion in IISP:

- Acute care visits: providers or clinics that triaged acutely ill patients to non-participating clinicians or urgent care clinics, or providers that generally did not see acutely ill patients were not recruited.
- Small to moderate practice size: individual providers were required to have an approximate weekly patient volume of 100-150 patients. Larger clinics were permitted after demonstrating the ability to maintain methodology across multiple staff.
- Enumerated patient population size: providers or clinics were required to be able to enumerate or estimate the patient panel by age group. The provider could report the total number of registered patients or the average number

of unique persons who have been seen by the provider in a given year (3 years of data desired for making this estimation). This is NOT the same as the number of patient visits each year, since in any given year people may come more than once or they may not have a visit. This served as an approximation of a population for incidence calculation.

- Respiratory specimen collection: clinical staff had to be able to collect respiratory specimens from patients and submit to the public health laboratory (PHL) within 72 hours.
- Age representation: for each site, the combination of all clinics/providers participating had to represent all age groups.

Surveillance Methods

1. Aggregate Data Reporting
    a. Providers report the total number of ILI patient visits and all-cause patient visits by age group each week.
    b. Age Groups (years): <1, >1 - <2, >2 - <5, >5 - <18, >18 - <25, >25 - <50, >50 - <65, ≥65
2. Patient Data Collection

    Demographic and clinical data was collected on sampled patients. A data dictionary was provided including data formats required for reporting. Demographic data included a minimum of non-personally identifiable variables with previously established associations with respiratory illness or health care seeking, including: age, race, ethnicity, and gender. Clinical data included a minimum of non-identifiable variables with established associations with respiratory illness or health care seeking is included. There were questions for the patient and questions for the clinician; however, some providers or clinics may obtain vaccination history through medical chart review in lieu of patient self-report.

    - Patient questions: date of illness onset, reported symptoms since illness onset, and use of antipyretics in the past 6 hours (only needed if clinician measuring temperature). Vaccination history: all patients should be asked about influenza vaccination receipt for the current season; 2014-15 vaccine until 2015-16 vaccine is available. Type of vaccine is optional, but asked to distinguish LAIV from injected. There is no expectation of differentiating types of injected vaccines.
    - Clinician questions: type of specimen collected, measured temperature, influenza antiviral prescribing, patient diagnosis, severity of illness, referral to hospital, and rapid testing conducted.
3. Specimen Collection

    Providers collected a respiratory specimen from the first ILI patients attended each week until a count of 10 was reached. While this was not a random sample, it is systematic and designed for ease of implementation. Persons meeting the case definition were asked to undergo a nasal, nasopharyngeal (NP), oropharyngeal (OP), or dual NP/OP swab as part of routine standard of care for acutely ill patients with respiratory symptoms. Patient refusal was expected, thus specimen collection continued until the specimens from 10 ILI patients had been collected. Providers were not to select patients based on suspicion of influenza. Swabs were immediately placed into 1-3mL viral transport media and maintained at 4°C for a maximum of 72 hours or frozen at -70°C.

SUPPLEMENTARY ANALYSIS AND RESULTS

Evaluation of Sampling Strategy

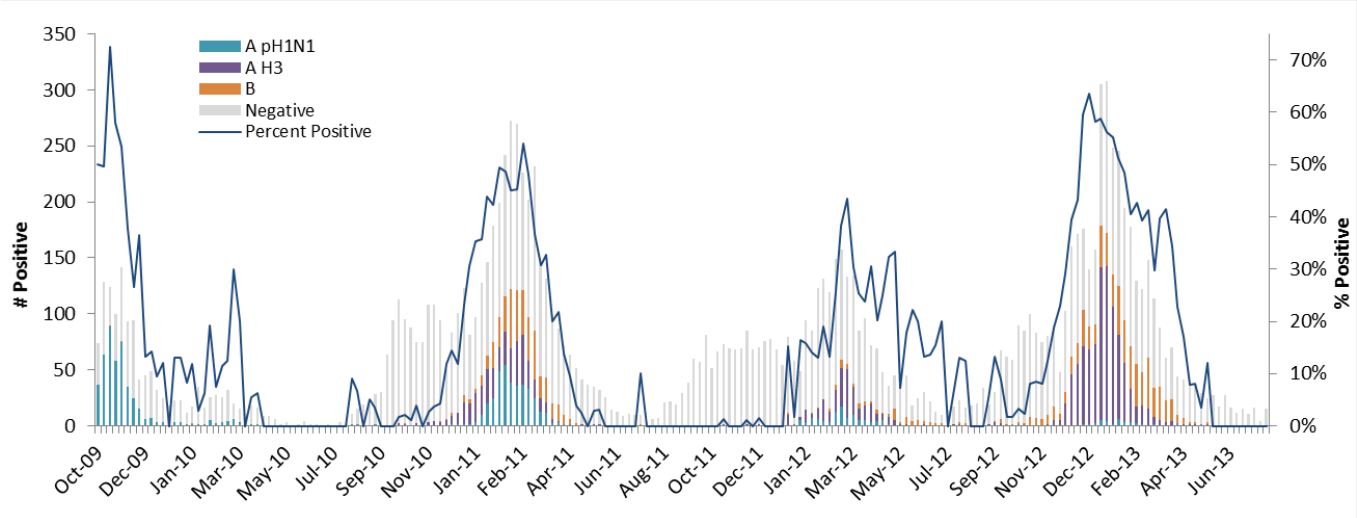
To minimize costs and clinic burden, a systematic sampling strategy was used for specimen collection. The systematic sampling strategy was chosen due to the impracticality of implementing a randomized sampling strategy in busy clinics that are only nominally incentivized to conduct surveillance. However, the selection of 10 ILI patients for sampling was chosen to ensure that for the small clinic size required for participation in IISP would ensure that a large portion, if not all, ILI patients attended in a given week are sampled. Overall, 57% of all ILI patients who presented during the year were sampled. Of all clinics, only 6 total had a median weekly number of ILI patients >10, and only 64 clinics experienced weeks with >10 ILI patients and represented only 7% of all clinic-weeks combined. An evaluation of using a sampling weight for each patient tested according to the number of ILI patients reported in a given week, stratified by state and age group was used to calculate the weekly weighted average number of ILI patients positive for influenza, adjusted for clustering of patients by clinic. The result demonstrated no difference in incidence point estimates, but slightly wider confidence limits. It is noteworthy that we have examined the proportion of patients who tested influenza positive if sampled on a Monday compared with the rest of the week, and found an overall 2·4% higher rate of positivity (p=0·012); however, further investigation demonstrated that the difference was only significant during the 2009-2010 season. When the 2009-10 season was excluded, Monday patients had a 1·8% higher influenza positivity rate, but not statistically significant. In summary, we conclude that Monday patients are more likely to test positive for influenza; however, the surveillance design ensures that all days of the week are represented by the program.

Evaluation of Population Estimation
We evaluate these reported numbers in three ways. First, as referenced in our initial 2009-10 report, we compared our reported population by age group with that of the US Census reported population and found them to be comparable. We conduct this analysis annually and by state to ensure comparability with the US and state populations. Second, as referenced in the current manuscript, we assessed the plausibility range of the proportion of the population represented by the total patient visits for each provider before allowing their data to be used in the combined incidence calculation. Third, to evaluate if there was a difference between the incidence estimates for providers reporting population based on an established registry vs. the number of unique individuals, we conduct a regression analysis using the log transformed ILI incidence as the outcome and population type as the predictor. Both in the null model and after controlling for several potential influential variables, no difference has been detected in the incidence by the provider's method of population estimation.

Predictors for the Log of Cumulative ILI Rate	**Coefficient (% Effect)**	**SE**	**P value**
Denominator Type	-0·12554	0·13993	0·3707
Provider Population Size	-0·000024	0·00000914	<0·01
Percent Pediatric	0·01446	0·00229	<0·01
Report Frequency*	0·102	0·046	0·03
Region (REF = West)			
Midwest	0·34911	0·19164	0·07
East	0·18673	0·18505	0·3141
Southeast	0·08107	0·2594	0·755
Year (REF = 2012)			
2009	0·00424	0·21588	0·9844
2010	-0·24687	0·18433	0·182
2011	-0·68677	0·17628	<0·01
Intercept	2·4136	0·22362	<0·01

SUPPLEMENTARY TABLE AND FIGURE

Supplemental Figure. The national weekly number and percent of medically attended influenza-like illness patients with RT-PCR confirmed influenza infection from October 2009 – July 2013.



Self-Reported Vaccination Rates by Year

	Pediatric ILI Patients				Adult ILI Patients		
	Vaccinated	**N**	**%**		**Vaccinated**	**N**	**%**
2009-10	235	882	26.64		150	602	24.92
2010-11	652	2003	32.55		218	1138	19.16
2011-12	653	1771	36.87		278	1077	25.81
2012-13	636	2291	27.76		467	1695	27.55