Original article

Influenza testing trends in sentinel surveillance general practices in Victoria 2007 to 2014

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Abstract

The Victorian Sentinel Practice Influenza Network conducts syndromic surveillance for influenza-like illness (ILI), with testing for laboratory confirmation of a proportion of cases at the discretion of general practitioners. The aim of this study was to evaluate the consistency of sentinel general practitioners' swabbing practice within and between influenza seasons. Aggregated, weekly, non-identified data for May to October each year from 2007 to 2014 were used to calculate the proportion of patients presenting with ILI (defined as cough, fever and fatigue), proportion of ILI patients swabbed and proportion of swabs positive for influenza. Data on the proportion of consultations for ILI and the proportion of ILI patients swabbed were aggregated into time-period quintiles for each year. Analysis of variance was used to compare ILI patients swabbed for each aggregated time-period quintile over all 8 years. Spearman's correlation and Bland-Altman analyses were used to measure association and agreement respectively between ILI proportions of consultations and swabs positive for influenza in time period quintiles within each year. Data were aggregated by year for the rest of the analyses. Between 2007 and 2014 there was a slight decrease in the proportion of positive tests and the proportion of ILI patients was generally a good proxy for influenza test positivity. There was consistency in testing within and between seasons, despite an overall testing increase between 2007 and 2014. There was no evidence for temporal sampling bias in these data despite testing not being performed on a systematic basis. This sampling regimen could also be considered in other similar surveillance systems. *Commun Dis Intell* 2017;41(1):E4–E9.

Keywords: influenza, influenza-like illness, sentinel surveillance, primary health care, Australia

Introduction

A range of influenza surveillance methods and settings are used both internationally and within Australia in order to assess the onset, magnitude and duration of influenza seasons.[1–3] These include syndromic surveillance of influenza-like illness (ILI) that serves as a proxy for influenza activity. This is simple to operate, relatively cheap as no testing is required (there can be reluctance to test children), can be delivered online, is generally consistent over time and is not subject to biases in testing practices. However, the positive predictive value of ILI for influenza can vary due to the use of different case definitions across systems, differing application of definitions, incidence of influenza and other respiratory viruses during the season and the surveillance setting (e.g. primary health care, hospital outpatients, emergency departments or hospital admissions).[4–6] Syndromic surveillance is therefore usually combined with laboratory testing using modern diagnostic techniques such as real-time polymerase chain reaction (PCR)[7] enabling more accurate case ascertainment, a better understanding of circulating types, subtypes and strains, and to inform the formulation of vaccines.[8]

The Victorian Government Department of Health and Human Services funds the Victorian Sentinel Practice Influenza Network (VicSPIN), operated by the Epidemiology Unit at the Victorian Infectious Diseases Reference Laboratory. The Network is comprised of approximately 100 participating general practitioners (GPs), and aims for representation of approximately 1 GP per 200,000 population in metropolitan areas and 1 per 50 to 100,000 in rural areas.[9,10] It operates each year between May and October. This system conducts syndromic and laboratory surveillance of ILI and influenza among general practice patients to assess the onset, magnitude and duration of each influenza season, circulating strains and vaccine effectiveness. Each week, GPs are requested to report their total number of consultations and the number that met the ILI case definition.[2] Nose and/or throat swabbing of ILI patients within 4 days of symptom onset for PCR testing is done at the discretion of the general practitioner rather than systematically,[8] which has the potential to introduce selection bias.[11] Whom GPs select to swab and the frequency at which they do it may vary throughout the season due to many factors such as individual GPs' preferences, the patient's

vaccination status[12] and influenza incidence or perception of it,[13] which may in turn be influenced by media reporting.[14] Swabbing of ILI patients by VicSPIN GPs over the whole season has ranged from 39% in 2005[10] to 69% in 2013.[12]

The aim of this study was to evaluate whether the percentage of patients swabbed by sentinel GPs has changed within and between influenza seasons.

Methods

Aggregated, weekly, non-identified data obtained from VicSPIN practices were obtained for the surveillance periods of May to October each year from 2007 to 2014, to calculate the proportion of patients in GP consultations presenting with ILI (defined as cough, fever and fatigue),[8,15] the proportion of ILI patients swabbed and proportion of swabs positive for influenza. Weekly data on the proportion of consultations that were for ILI and the proportion of ILI patients swabbed were aggregated into time-period quintiles for each year. Analysis of variance (ANOVA) was used to compare the proportion of ILI patients swabbed during the same time period quintile over all 8 years as well as quintiles within each season, with Bonferroni correction for multiple comparisons applied when the initial result was significant. Spearman's rank correlation was used to measure the strength of association and Bland-Altman analyses to measure agreement between the proportions of consultations for ILI and swabs positive for influenza within each year.

Data were aggregated by year for the rest of the analyses. Rates of ILI consultations, ILI patients swabbed and swabs positive for influenza were analysed using Pearson's chi-square for strength of association and the chi-square test for trend.

Weeks where the number of patients swabbed exceeded the number of ILI patients were excluded. Where time-period quintiles were used, weeks at the beginning (weeks 18 to 21) and end (weeks 42 to 43) of the season were excluded as the small numbers during these periods caused large fluctuations in proportions calculated.

Statistical calculations including ANOVA, Pearson correlation and Bland Altman analyses were performed in Microsoft Excel, with *P*-values and chi-square analyses computed using DanielSoper.com Statistics Calculators version 3.0 beta.[16] Other online epidemiological calculators used were Social Science Statistics[17] for Spearman's rank correlation tests and AusVet[18] for chi-square analyses.

Data in this study were collected, used and reported under the legislative authorisation of the Victorian Public Health and Wellbeing Regulations 2009. Monash University granted the study exemption from ethical review (project number CF15/1277 – 2015000606).
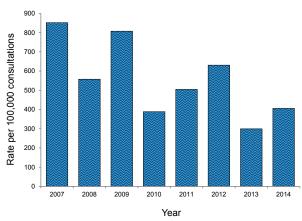
Results

Over the 208 weeks of data collection between 2007 and 2014, sentinel GPs reported 1,384,141 patient consultations. The reported number of patients swabbed exceeded the reported number of ILI consultations in 7 weeks, resulting in the exclusion of 126 (1.7%) swabbed patients and 100 (1.3%) ILI patients. A further 747 ILI patients including 436 swabbed patients were excluded from the beginning and end of seasons for the time period quintile analyses.

Influenza-like illness consultations by year

Between 2007 and 2014, 7,421 patients presented with ILI, with a median of 889 patients per year; the minimum of 481 was in 2013 and the maximum of 1,567 was in the pandemic year of 2009. This corresponded to 299 and 807 ILI patients per 100,000 consultations respectively (Figure 1). The annual variation in ILI consultation rates was statistically significant ($\chi^2 = 800.96$, df = 7, $P < 0.01$).

Figure 1: Rate of influenza-like illness patients per 100,000 consultations, VicSPIN, 2007 to 2014, by year
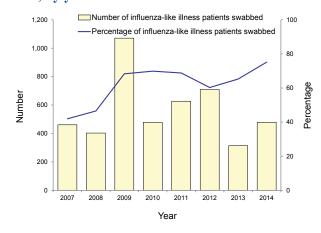

Influenza-like illness swabbed by year

There were 4,542 ILI patients swabbed between 2007 and 2014, with a median of 479 patients (67%) per year. The minimum and maximum number of patients was 314 in 2013 and 1,071 in 2009 respectively. The percentage of ILI patients swabbed per year increased from a low of 42% in 2007 to a high of 75% in 2014. The difference between the annual

percentage of ILI patients swabbed during this period was statistically significant ($\chi^2 = 384.07$, df = 7, $P < 0.001$). However, the trend was non-linear ($\chi^2 = 198.97$, df = 6, $P < 0.001$). The percentage of ILI patients swabbed from 2007 to 2008 was significantly lower than from 2009 to 2014 ($\chi^2 = 333.38$, df = 1, $P < 0.01$). The percentage of swabbed ILI patients varied between 60% and 75% between 2009 and 2014 (Figure 2).

Percentage of swabs positive by year

There were 1,624 swabs positive for influenza over the 8 years of data collection with a median of 182 positive swabs per year or 37% of swabs taken. The minimum percentage positive was 22% in 2013 and the maximum was 47% in 2007. There was a slight, but statistically significant ($\chi^2 = 10.63$, df = 1, $P < 0.01$), non-linear downward trend in the percentage of ILI patients with influenza-positive swabs during the study (Figure 3).
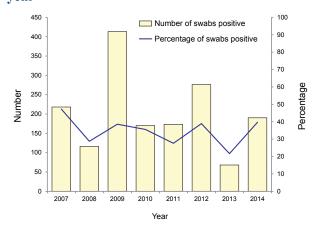
Figure 2: Percentage and number of influenza-like illness patients swabbed, VicSPIN, 2007 to 2014, by year
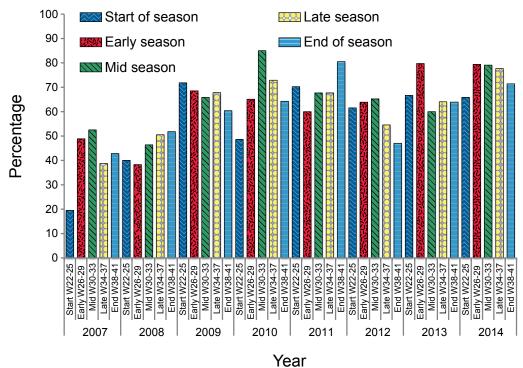

Figure 3: Percentage and number of swabs positive for influenza, VicSPIN, 2007 to 2014, by year

Figure 4: Percentage of influenza-like illness patients swabbed, VicSPIN, 2007 to 2014, by time period quintile

W = Weeks

Influenza-like illness patients swabbed during seasons

The percentage of ILI patients swabbed for every year, divided into seasonal quintiles, is shown in Figure 4.

The percentage of ILI patients swabbed did not significantly differ between time-period quintiles during each annual influenza season (Table 1). Similarly, no significant differences were observed when the same time-period quintiles over all 8 seasons were compared ($F = 0.87$, $F_{critical} = 2.64$, $df = 4$, $P = 0.49$).

Table 1: ANOVA F test values for the proportion of influenza-like illness patients swabbed for influenza, VicSPIN, 2007 to 2014, (degrees of freedom = 4)

Year	n	F	$F_{critical}$	*P* value
2007	440	2.37	3.06	0.10
2008	364	2.33	3.06	0.10
2009	977	0.13	3.06	0.97
2010*	436	4.35	3.06	0.02*
2011	574	0.96	3.11	0.46
2012	639	2.78	3.06	0.07
2013	290	1.43	3.18	0.28
2014	447	0.77	3.11	0.56

* Not significant after Bonferroni correction

Correlation and agreement of influenza-like illness patients with swabs positive for influenza

When compared by time period quintiles, the proportion of patients with ILI correlated positively with the proportion of swabs positive for influenza in every year; and was statistically significant in all but 2008 and 2011 (Table 2). All years when the incidence of influenza was assumed to be high, that is, when the percentages of swabs positive for influenza was greater than the median for 2007 to 2014, were statistically significant.

Bland Altman analyses by time quintiles in each year showed that the fixed differences between the proportion of patients presenting with ILI and the proportion of swabs positive for influenza shown by the intercepts, were not significant. However, in addition to the fixed differences, in all years there were significant increasing differences between the 2 proportional measures as their magnitude increased, as indicated by the slope.

Discussion

The lack of variation in swabbing practice with time-period quintiles indicates that swabbing practice by VicSPIN GPs was generally consistent within and between influenza seasons from 2007 to 2014, despite the overall increase in testing since 2009. Consequently, although VicSPIN GPs do not systematically sample ILI patients for influenza testing, no temporal sampling bias was apparent.[19]

There was an increase in testing from 2009 among sentinel GPs, although laboratory testing, without explicit caps, has always been available to them.

Table 2: Spearman's correlation and Bland Altman analyses for proportions of consultations that are influenza-like illness and proportions of swabs positive for influenza, VicSPIN, 2007 to 2014

| Year | n | Spearman's rho, df=3 | | Bland Altman agreement | | | |
		r_s	*P* value (2 tailed)	Intercept‡	*P* value intercept	Slope	*P* value slope
2007†	440	1.0	<0.001*	-0.0003	0.98	1.9103	*P*<0.001
2008	364	0.7	0.19	-0.008	0.24	1.9651	*P* <0.001
2009†	977	1.0	<0.001*	-0.002	0.67	1.887	*P* <0.001
2010	436	0.9	0.04*	-0.0032	0.37	1.9634	*P* <0.001
2011	574	0.6	0.28	-0.0054	0.16	1.9597	*P* <0.001
2012†	639	0.9	0.04*	0.0137	0.2	1.8572	*P* <0.001
2013	290	0.9	0.04*	-0.0026	0.12	1.9654	*P* <0.001
2014†	447	0.9	0.04*	0.0022	0.63	1.9405	*P* <0.001

* $P < 0.05$

† Greater than median percentage influenza positive for 2007 to 2014.

‡ Intercept = fixed difference between proportions of consultations that are influenza-like illness and proportions of swabs positive for influenza.

The pandemic year of 2009 may have simply prompted greater awareness and concern about influenza among sentinel GPs, however there have also been wider changes in attitudes to testing in primary care over that time. PCR testing with its rapid availability of results has become increasingly widely used after introduction of government reimbursement through Medicare in 2005 and funding for purchase of new PCR machines after the 2009 pandemic.[1,2,20] PCR testing has increased to the point where it is thought to be responsible for the substantial increase in statutory notifications over the 2010 to 2015 period, since syndromic surveillance has not seen similar increases in seasonal incidence.[1,21]

The slight downward trend in the proportion of swabs positive between 2007 and 2014 may be partly related to the observed increase in testing over the same period. However, this relationship is likely to be obscured by several factors, including variability in influenza incidence and other causes of ILI, and the age groups affected in a given year, for instance, GPs may be more reluctant to swab children, and nursing home resident surveillance is covered by a different part of the system in Victoria.[12,22,23]

Theoretically, swabs are more likely to be positive in years with higher incidence of influenza. There was a positive correlation between the percentage of consultations with diagnosis of ILI and percentage of swabs positive in all 8 years of data collection. This was statistically significant in all but 2 years, including those of presumed higher influenza incidence. This confirms that ILI is a reasonable proxy for interpreting the severity of influenza seasons in this dataset.

A limitation of this study is that the small sample size for the time-period quintile analyses may have underpowered the study to detect statistically significant variation in swabbing, as well as correlation and agreement of swabs positive for influenza with consultations for ILI. Furthermore, no conclusions about other sources of sampling bias such as vaccination status, age or other factors can be drawn from this study as they were not examined.

VicSPIN gives timely ILI and laboratory test data from a broadly representative sample of GPs, providing an important part of influenza surveillance in Victoria and Australia as a whole. Between 2007 and 2014 there was a slight decrease in the proportion of positive tests and the proportion of patients with ILI was generally a reasonable proxy for influenza test positivity in these primary care patients, especially in high incidence years. During the study period, GPs in the VicSPIN surveillance program did not vary their ILI testing practices by

time period quintiles, despite an overall increase in testing since 2009. This study supports the current VicSPIN practice of testing for influenza at the discretion of the GP and the confidence that can be placed in the surveillance data that are produced. Achieving systematic sampling is likely to require considerable effort and may reduce GP participation with little impact on the value of surveillance. This sampling regime could also be considered in other similar surveillance systems.

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References

1. Fielding JE, Regan AK, Dalton CB, Chilver MB, Sullivan SG. How severe was the 2015 influenza season in Australia? *Med J Aust* 2016.;204(2):60–61.

2. Kelly HA, Grant KA, Tay EL, Franklin L, Hurt AC. The significance of increased influenza notifications during spring and summer of 2010-11 in Australia. *Influenza Other Respir Viruses* 2013;7(6):1136–1141.

3. Clothier HJ, Atkin L, Turner J, Sundararajan V, Kelly HA. A comparison of data sources for the surveillance of seasonal and pandemic influenza in Victoria. *Commun Dis Intell* 2006;30(3):345–349.

4. Navarro-Mari JM, Pérez-Ruiz M, Cantudo-Muñoz P, Petit-Gancedo C, Jiménez-Valera M, et al. Influenza-like illness criteria were poorly related to laboratory-confirmed influenza in a sentinel surveillance study. *J Clin Epidemiol* 2005;58(3):275–279.

5. Moretti ML, Sinkoc V, Cardoso LG, Camargo GJ, Bachur LF, Hofling CC, et al. Lessons from the epidemiological surveillance program, during the influenza A (H1N1) virus epidemic, in a reference university hospital of Southeastern Brazil. *Rev Soc Bras Med Trop* 2011;44(4):405–411.

6. Sreng B, Touch S, Sovann L, Heng S, Rathmony H, Huch C, et al. A description of influenza-like illness (ILI) sentinel surveillance in Cambodia, 2006–2008. *Southeast Asian J Trop Med Public Health* 2010;41(1):97–104.

7. Baumbach J, Mueller M, Smelser C, Albanese B, Sewell CM. Enhancement of influenza surveillance with aggregate rapid influenza test results: New Mexico, 2003–2007. *Am J Public Health* 2009;99 Suppl 2:S372–S377.

8. Fielding JE, Grant KA, Tran T, Kelly HA. Moderate influenza vaccine effectiveness in Victoria, Australia, 2011. *Euro Surveill* 2012;17(11). pii: 20115.

9. Fielding JE, Miller ER, Adams J, Hawking B, Grant K, Kelly HA. Influenza surveillance in Victoria, 2006. *Commun Dis Intell* 2007;31(1):100–106.

10. Turner JL, Fielding JE, Clothier HJ, Kelly HA. Influenza surveillance in Victoria, 2005. *Commun Dis Intell* 2006;30(1):137–143.

11. Thompson DL, Baumbach J, Jungk J, Sewell CM, Smelser C, Landen M. Does outpatient laboratory testing represent influenza burden and distribution in a rural state? *Influenza Other Respir Viruses* 2013;7(5):686–693.

12. Carville KS, Grant KA, Sullivan SG, Fielding JE, Lane CR, Franklin L, et al. Understanding influenza vaccine protection in the community: an assessment of the 2013 influenza season in Victoria, Australia. *Vaccine* 2015;33(2):341–345.

13. Moore K, Black J, Rowe S, Franklin L. Syndromic surveillance for influenza in two hospital emergency departments. Relationships between ICD-10 codes and notified cases, before and during a pandemic. *BMC Public Health* 2011;11:338.

14. Haddock RL, Damian YS, Duguies LA, Paulino YC. Guam's influenza epidemic(s) of 2009. *Hawaii Med J* 2010;69(6 Suppl 3):50–51.

15. Thursky K, Cordova SP, Smith D, Kelly H. Working towards a simple case definition for influenza surveillance. *J Clin Virol* 2003;27(2):170–179.

16. Soper DS. DanielSoper.com Statistics Calculators. 2016. Available from: http://www.danielsoper.com/statcalc3/default.aspx Accessed on 17 February 2016.

17. Stangroom J. Spearman's rho calculator. 2016. Available from: http://www.socscistatistics.com/tests/spearman/Default.aspx Accessed on 5 December 2016.

18. AusVet Animal Health Services. EpiTools epidemiological calculators: Chi-squared test for trend. 2016. Available from: http://epitools.ausvet.com.au/content.php?page=trend Accessed on 18 February 2016.

19. Porta MS, International Epidemiological Association. Surveillance. In: *A dictionary of epidemiology.* 5th edn. Oxford; New York: Oxford University Press: 2008. p. 239.

20. Carman WF, Wallace LA, Walker J, McIntyre S, Noone A, Christie P, et al. Rapid virological surveillance of community influenza infection in general practice. *BMJ* 2000;321(7263):736–737.

21. Kaczmarek MC, Ware RS, Lambert SB. The contribution of PCR testing to influenza and pertussis notifications in Australia. *Epidemiol Infect* 2016;144(2):306–314.

22. Kelly H, Carville K, Grant K, Jacoby P, Tran T, Barr I. Estimation of influenza vaccine effectiveness from routine surveillance data. *PLoS ONE* 2009;4(3):e5079.

23. Turner J, Kelly H. A medical locum service as a site for sentinel influenza surveillance. *Euro Surveill* 2005;10(4):96–98.