Short reports

Timing of influenza vaccination in an Australian community-based surveillance system, 2010–2014

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In Australia, the National Immunisation Program provides influenza vaccine free to people at high-risk of severe influenza including the elderly, anyone with an underlying medical condition, pregnant women, Indigenous Australians and nursing homes residents. This program aims to deliver the seasonal influenza vaccine to these groups before the onset of the influenza season, typically between March and May of each year. The timing of vaccination is important for a number of reasons.

For individual protection, the vaccine needs to be given before the influenza virus is circulating. Based on recent European research, some high-risk groups might be better vaccinated late in the pre-season because immunity may wane over the course of a single season.[1–3]

For estimates of influenza vaccine effectiveness (VE) derived from health facility-based surveillance data (using the test-negative study design), knowing when someone was vaccinated is important for determining whether they can be expected to have developed immunity as a result of vaccination. Such estimates typically exclude or consider unvaccinated those people vaccinated within 10 to 14 days of attendance at the health facility because vaccine-induced immunity takes this long to develop.[4] Avoiding this potential misascertainment of immunisation status is challenging in recruitment sites that are different from where people receive the vaccine, such as hospital-based studies, as the vaccination date may not be easily verified.[4–9]

The whole-of-life vaccine registry[10] could provide data on the timing of vaccination for adult groups targeted by the Australian National Immunisation Program. However, full implementation may take several years. We aimed to assess whether adults (≥18 years of age) were vaccinated before the onset of the influenza season and whether misclassification bias was likely to be a concern for estimating VE in Australia by using data from 2 existing national influenza surveillance systems for 2010 to 2014.

We plotted the onset of illness for patients with influenza admitted to hospitals participating in the Influenza Complications Alert Network (FluCAN),[11] an Australia-wide hospital-based sentinel surveillance system, against the uptake of influenza vaccine throughout each season among participants of Flutracking,[12] an online national community influenza-like illness (ILI) surveillance system.

Flutracking participants were recruited by a combination of emailed invitations via organisation email networks, government and commercial workplaces, promotional activities in the media, and increasingly through participants inviting friends over recent years.[13] The cumulative proportion of vaccinated participants who reported being vaccinated was plotted by week for each season to document vaccine uptake. Vaccinated participants needed to have responded to at least 1 weekly online survey by the end of the influenza season defined as a period of 24 to 26 weeks between April and October in each year.

In hospitals participating in FluCAN, data are collected on hospitalised patients with confirmed influenza including the date of their illness onset and their vaccination status. The number of vaccinated hospitalised patients with confirmed influenza by week of onset of illness in each season was plotted as a measure of severe influenza activity.

We separately graphed those aged 18–64 years and those aged 65 years or over as the provision of free vaccine to the elderly may influence the timing of vaccination. Except for Indigenous status, Flutracking does not collect data on other medical and demographic factors that influence eligibility for free government supplied vaccine. Although the group of patients aged 18–64 years is expected to be mostly made of people ineligible for free vaccine, it may include those who are eligible such as the few Indigenous participants as well as pregnant women or those with underlying medical conditions.

Ethical approval for Flutracking was obtained from the Hunter New England Human Research Ethics Committee. Ethics committees of the Australian National University and all participating hospitals approved FluCAN.

The number of Flutracking participants who reported being vaccinated has almost doubled since 2010 for those aged 18–64 years and increased by more than 3 and a half times for those aged 65 years or over (Table 1). By the beginning of June (week 22; Figure 1; Table 2), the majority of Flutracking respondents aged 65 years or over who received the influenza vaccine at any time during the season had already been vaccinated (range 70% to 91%). In 3 of the 5 seasons, slightly less of the younger age group (Figure 2; Table 2) had been vaccinated at this point (range 67% to 86%). Between 2% and 11% of patients admitted to hospital for a severe respiratory illness during each season had developed an ILI by the start of June. In 2012, a higher proportion of patients were admitted earlier in the season compared with other years.

From the beginning of May (week 18–19) to the beginning of June (week 22), vaccine uptake among those aged 65 years or over increased from 46% to 70% in 2010, from 60% to 86% in 2011, 60% to 84% in 2012, 77% to 91% in 2013, and 63% to 89% in 2014.

These data suggest that the majority of people are vaccinated before the onset of the influenza season, at least for these 5 seasons that exhibit the typical winter period of transmission. In turn, this suggests that misascertainment bias is unlikely to be a major concern for hospital-based vaccine effectiveness studies in Australia[14–18] and that unusually early season onset (or delayed vaccine availability) would be needed to compromise the current tim-

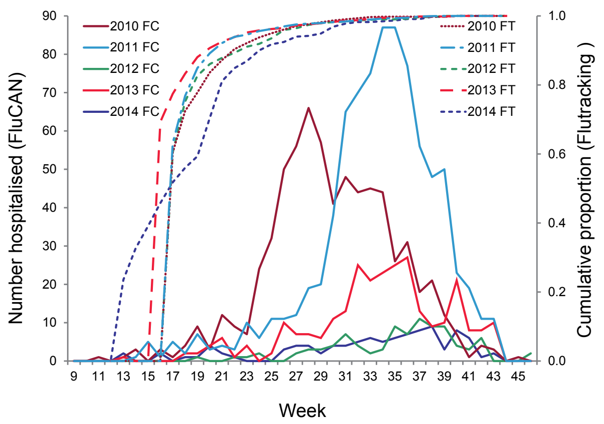
Table 1: Number of vaccinated Flutracking respondents who completed at least one online survey during the year and patients admitted to FluCAN-participating hospitals with an influenza-like illness, 2010 to 2014, by age group and year

Year	Vaccinated Flutracking respondents		Vaccinated patients admitted to hospitals participating in FluCAN	
	18–64 years	≥65 years	18–64 years	≥65 years
2010	5,716	450	122	100
2011	6,334	617	90	93
2012	7,272	915	329	684
2013	9,032	1,290	193	276
2014	9,786	1,617	490	837

Table 2: Proportion of vaccinated Flutracking respondents who reported being vaccinated by week 22 in each season, 2010 to 2014, by age group

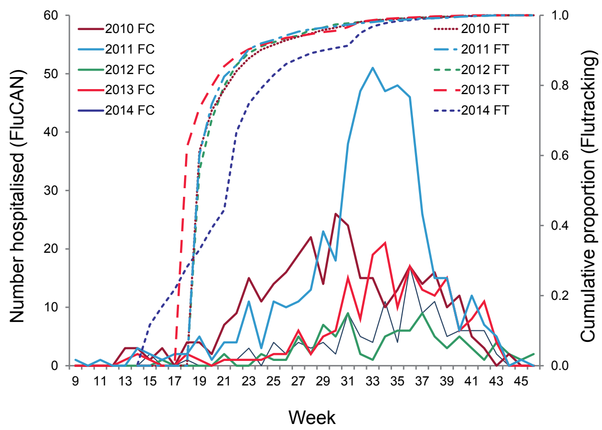
Year	Age group	
	18–64 years %	≥65 years %
2010	67	70
2011	86	86
2012	84	84
2013	88	91
2014	86	89

Figure 1: The onset of illness for hospitalised patients aged ≥65 years with confirmed influenza and cumulative proportion of vaccinated Flutracking respondents aged ≥65 years who reported being vaccinated, 2010 to 2014, by week



FC = FluCAN; FT = Flutracking

Figure 2: The onset of illness for hospitalised patients aged 18–64 years with confirmed influenza and cumulative proportion of vaccinated Flutracking respondents aged 18–64 years who reported being vaccinated, 2010 to 2014, by week



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ing of the delivery of the vaccine program for most recipients. In Australia, the influenza vaccine usually becomes available in March, and we note that a significant proportion of the Flutracking sample had received vaccine by April–May, when Flutracking surveillance typically commences. It is possible that Flutracking participants may receive influenza vaccination earlier than the general population given that the weekly online survey reminds them about the vaccine by asking them if they have been vaccinated in the prior week. However, the uptake of vaccine among Flutracking participants who were vaccinated is consistent with an earlier Australian study that found that vaccine coverage estimated from pre-season pneumonia cases (in whom influenza was an unlikely cause) were similar to mid-season test-negative controls for those aged 65 years or over, those aged less than 65 years with a medical condition and those aged less than 65 years without a medical condition.[19]

Flutracking data for those aged 65 years or over are also consistent with periodic nationally representative vaccination coverage surveys by the Australian Institute of Health and Welfare (AIHW) in 2002, 2003, 2004, and 2009, which found that between 70% and 78% of the elderly were vaccinated by the end of April and 86% to 92% by the end of May.[20–23] A minority of Flutracking participants aged 65 years or over were vaccinated between the beginning of May and the start of June, indicating that most are vaccinated earlier in the season. Exactly how early is not known as Flutracking surveillance only commences in April. As noted, this is important for the elderly who may benefit from receiving the vaccine closer to the onset of the influenza season because of possible waning immunity.

AIHW vaccination coverage estimates for younger age groups tend to be lower than recorded by Flutracking, presumably related to selection biases associated with Flutracking such as much higher education levels of participants compared with the general population.[24] The Flutracking subset for those aged 18–64 years may also be biased by over-representation of groups eligible or ineligible for free government vaccine.

The consistency of Flutracking data with representative studies does suggest that it might be able to provide general information on when influenza vaccines are being given and an indication of the magnitude of misacertainment of immunisation status for hospital-based studies of influenza vaccine effectiveness. Early vaccine coverage estimates, whether through community or hospital-based systems, may be useful for identifying community concerns about vaccine safety and for triggering public health investigations to explore decreases in coverage. For instance, negative public reaction to vaccination after the 2009 H1N1 influenza pandemic[25] led to slow uptake of the seasonal trivalent influenza vaccine in the following year (as suggested by the uptake of the vaccine in 2010 in Figures 1 and 2). Until an adult vaccine registry is established, these two surveillance systems can provide data on vaccine uptake that is not currently available from any other source. However, these data must be carefully appraised each season given the increasing but non-random community participation in Flutracking and the biases inherent to each system: FluCAN mostly relies on patient recall for the date of vaccination and Flutracking is a sample of online volunteers that have different socio-demographic features to the general Australian population.

Conflicts of interest

None

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Contribution of authors

BC designed the study and, with AC, performed the analysis and drafted the manuscript. SC provided Flutracking data. All authors provided input into the analysis and interpretation of results.

References

1. Castilla J, Martinez-Baz I, Martinez-Artola V, Reina G, Pozo F, Garcia Cenoz M, et al. Decline in influenza vaccine effectiveness with time after vaccination, Navarre, Spain, season 2011/12. *Euro Surveill* 2013;18(5).
2. Pebody R, Andrews N, McMenamin J, Durnall H, Ellis J, Thompson CI, et al. Vaccine effectiveness of 2011/12 trivalent seasonal influenza vaccine in preventing laboratory-confirmed influenza in primary care in the United Kingdom: evidence of waning intra-seasonal protection. *Euro Surveill* 2013;18(5): pii: 20388.
3. Kissling E, Valenciano M, Larrauri A, Oroszi B, Cohen JM, Nunes B, et al. Low and decreasing vaccine effectiveness against influenza A(H3) in 2011/12 among vaccination target groups in Europe: results from the I-MOVE multicentre case-control study. *Euro Surveill* 2013;18(5): pii: 20390.
4. Sullivan SG, Feng S, Cowling BJ. Potential of the test-negative design for measuring influenza vaccine effectiveness: a systematic review. *Expert Rev Vaccines* 2014;13(12):1571–1591.
5. Cheng AC, Holmes M, Irving LB, Brown SG, Waterer GW, Korman TM, et al. Influenza vaccine effectiveness against hospitalisation with confirmed influenza in the 2010-11 seasons: A test-negative observational study. *PLoS One* 2013;8(7):e68760.
6. Cheng AC, Kotsimbos T, Kelly HA, Irving LB, Bowler SD, Brown SG, et al. Effectiveness of H1N1/09 monovalent and trivalent influenza vaccines against hospitalization with laboratory-confirmed H1N1/09 influenza in Australia: a test-negative case control study. *Vaccine* 2011;29(43):7320–7325.
7. Seyler T, Rondy M, Valenciano M, Moren A. Protocol for hospital-based case control studies to measure seasonal influenza vaccine effectiveness against laboratory confirmed influenza hospitalisations across the European Union and European Economic Area Member States; 2014.
8. Australian Government Department of Health and Ageing. *The Australian Immunisation Handbook,* 10th edn 2013: Commonwealth of Australia; 2013.
9. European Centre for Disease Prevention and Control. Influenza vaccination. 2015. Available from: http://ecdc.europa.eu/en/healthtopics/seasonal_influenza/vaccines/Pages/influenza_vaccination.aspx
10. National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases. Adult vaccination: Vaccines for Australian adults: NCIRS Fact sheet: August 2015.
11. Kelly PM, Kotsimbos T, Reynolds A, Wood-Baker R, Hancox B, Brown SG, et al. FluCAN 2009: initial results from sentinel surveillance for adult influenza and pneumonia in eight Australian hospitals. *Med J Aust* 2011;194(4):169–174.
12. Dalton C, Durrheim D, Fejsa J, Francis L, Carlson S, d'Espaignet ET, et al. Flutracking: a weekly Australian community online survey of influenza-like illness in 2006, 2007 and 2008. *Commun Dis Intell* 2009;33(3):316–322.
13. Dalton CB, Carlson SJ, McCallum L, Butler MT, Fejsa J, Elvidge E, et al. Flutracking weekly online community survey of influenza-like illness: 2013 and 2014. *Commun Dis Intel* 2015;39(3):E361–E368.
14. Fielding JE, Grant KA, Papadakis G, Kelly HA. Estimation of type- and subtype-specific influenza vaccine effectiveness in Victoria, Australia using a test negative case control method, 2007–2008. *BMC Infect Dis* 2011;11:170.
15. Janjua NZ, Skowronski DM, De Serres G, Dickinson J, Crowcroft NS, Taylor M, et al. Estimates of influenza vaccine effectiveness for 2007–2008 from Canada's sentinel surveillance system: cross-protection against major and minor variants. *J Infect Dis* 2012;205(12):1858–1868.
16. Kwong JC, Campitelli MA, Gubbay JB, Peci A, Winter AL, Olsha R, et al. Vaccine effectiveness against laboratory-confirmed influenza hospitalizations among elderly adults during the 2010-2011 season. *Clin Infect Dis* 2013;57(6):820–827.
17. Skowronski DM, Janjua NZ, De Serres G, Winter AL, Dickinson JA, Gardy JL, et al. A sentinel platform to evaluate influenza vaccine effectiveness and new variant circulation, Canada 2010–2011 season. *Clin Infect Dis* 2012;55(3):332–342.
18. Talbot HK, Griffin MR, Chen Q, Zhu Y, Williams JV, Edwards KM. Effectiveness of seasonal vaccine in preventing confirmed influenza-associated hospitalizations in community dwelling older adults. *J Infect Dis* 2011;203(4):500–508.
19. Cheng AC, Brown S, Waterer G, Holmes M, Senenayake S, Friedman ND, et al. Influenza epidemiology, vaccine coverage and vaccine effectiveness in sentinel Australian hospitals in 2012: the Influenza Complications Alert Network (FluCAN). *Commun Dis Intell* 2013;37(3):E246–E252.
20. Australian Institute of Health and Welfare. 2002 Influenza Vaccine Survey: Summary results. Canberra: AIHW; 2003.
21. Australian Institute of Health and Welfare. 2003 Influenza vaccine survey: summary results. Canberra: AIHW; 2004.
22. Australian Institute of Health and Welfare. 2004 Adult Vaccination Survey: summary results. Canberra: AIHW; 2005.
23. Australian Institute of Health and Welfare. 2009 Adult Vaccination Survey: summary results. Canberra: AIHW; 2011.
24. Carlson SJ, Dalton CB, Butler MT, Fejsa J, Elvidge E, Durrheim DN. Flutracking weekly online community survey of influenza-like illness annual report 2011 and 2012. *Commun Dis Intell* 2013;37(4):E398–E406.
25. Taylor MR, Stevens GJ, Agho KE, Kable SA, Raphael B. Crying wolf? Impact of the H1N1 2009 influenza pandemic on anticipated public response to a future pandemic. *Med J Aust* 2012;197(10):561–564.