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Surveillance for outbreaks of influenza-like illness in the institutionalized elderly

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SUMMARY

Respiratory outbreaks are common in aged-care facilities (ACFs), are both underreported and frequently identified late, and are often associated with considerable burden of illness and death. There is emerging evidence that active surveillance coupled with early and systematic intervention can reduce this burden. Active surveillance for influenza-like illness and rapid diagnosis of influenza were established in 16 ACFs in Sydney, Australia, prior to the winter of 2006. A point-of-care influenza test and laboratory direct immunofluorescence tests for common respiratory viruses were used for diagnosis. We achieved early identification of seven respiratory disease outbreaks, two of which were caused by influenza. For the influenza outbreaks, antiviral treatment and prophylaxis were initiated 4–6 days from symptom onset in the primary case. A simple active surveillance system for influenza was successfully implemented and resulted in early detection of influenza and other respiratory disease outbreaks. This enabled earlier implementation of prevention and control measures and increased the potential effectiveness of anti-influenza chemoprophylaxis.

Key words: Control, infectious disease epidemiology, influenza, public health, surveillance system.

INTRODUCTION

The age and frailty of residents, the extent of their co-morbidities and the closeness of living arrangements contribute to aged-care facilities (ACFs) being the setting for outbreaks of influenza and other respiratory illnesses [1–3]. Influenza epidemics are common [4] and often result in high attack rates in residents [3–6], despite the majority being vaccinated. Staff members are often implicated in the introduction and transmission of influenza [2, 7], which is to be expected in a setting where residents lack mobility and may be infrequently visited by family members. Influenza vaccination is the cornerstone of influenza control and coverage of healthcare workers is an important

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predictor of the impact of influenza outbreaks [8–10]. Outbreaks involving the institutionalized elderly often occur out of season [6, 7], highlighting the need for year-round detection systems to be in place.

There is emerging evidence that active surveillance for influenza outbreaks coupled with early and systematic intervention can reduce the burden of disease in the institutionalized elderly [1, 11–13]. However, such practice is not yet commonly adopted in ACFs or by public health authorities [14]. Consequently, the early identification [13] and reporting [15] of influenza and other respiratory disease outbreaks is often not achieved. This in turn limits the timeliness and effectiveness of recommended control measures such as isolation, rigorous hand washing and the administration of antivirals.

The early identification of influenza outbreaks relies on two components: prompt clinical identification that a respiratory disease outbreak is occurring and rapid and accurate diagnosis of the causative agent. For a surveillance system with an objective of detecting influenza outbreaks, including those out of season, a highly sensitive clinical case-definition is desirable. Improvements in sensitivity can be further achieved through the introduction of laboratory testing, although the choice of assay will affect the accuracy of virological diagnosis and as a consequence the sensitivity of the clinical case-definition [16]. Although less sensitive than traditional laboratory tests such as direct immunofluorescence (DIF) and nucleic acid tests such as polymerase chain reaction (PCR) methods, rapid antigen or point-of-care (POC) tests have demonstrated their usefulness in providing a prompt diagnosis of influenza [17–20], particularly when performed on specimens from the first few cases of influenza-like illness (ILI) in a cluster [21, 22].

There is little published evidence on the assessment of surveillance systems to identify respiratory virus outbreaks in ACFs. In addition to exploring the epidemiology of influenza and other respiratory pathogens over a winter season, we sought to provide insight into the practicalities of surveillance system implementation in ACFs, the timeliness of outbreak identification and the impact of active surveillance and POC testing on subsequent prevention and control measures.

METHODS

A cluster-randomized controlled trial seeking to identify optimal use of the neuraminidase inhibitor, oseltamivir, in the management of influenza outbreaks in ACFs commenced prior to the 2006 Southern Hemisphere winter. A partnership was formed between the researchers and a private health provider interested in the public health benefits of the study. The details of 16 ACFs run by the provider in the greater Sydney metropolitan area, Central Coast and Newcastle regions of New South Wales, Australia, were provided to the study team by the provider for recruitment purposes. ACFs were invited by researchers to participate in an active surveillance system for early identification of respiratory illness outbreaks. This research was conducted in accordance with protocols approved by institutional review boards for human subjects' research at the University of Sydney and The Children's Hospital at Westmead.

Site visits to participating homes were conducted by members of the study team during which time education sessions were conducted with staff. Information on the identification, reporting, impact and control of influenza outbreaks in ACFs as well as information on the function and purpose of active surveillance of ILI and antivirals was provided. In addition to presenting new information to staff, the sessions were a useful opportunity for the researchers to gather information on available resources, attitudes and practices in the facilities which served to orient the design of the active surveillance system. In each facility, members of the nursing staff were nominated as the routine surveillance contacts for liaison with members of the study team. POC tests to detect influenza A or B (Quidel QuickVue™ test, Quidel Corporation, USA) and training in their use were provided to ACFs.

In our study, ILI was defined as acute onset of fever $\geqslant 38\ ^{\circ}C$, with acute cough or any other respiratory sign or symptom. An influenza outbreak was defined as two cases of ILI in staff or residents over a 3-day period, with at least one testing positive for influenza; or, three cases of ILI in staff or residents over a 7-day period, with at least one testing positive for influenza. Under these conditions, one positive result to confirm an outbreak could be achieved by POC, DIF, PCR (or serological testing if other tests were negative at time of onset). Once an influenza outbreak was identified, any resident or staff member with any respiratory symptoms during the outbreak period were regarded as a possible case. Clustering of multiple cases of ILI not meeting the temperature criteria for fever also triggered laboratory investigation.

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Table 1. *Structure and function of the influenza-like illness active surveillance system implemented in 16 aged-care facilities (ACFs) in the Sydney area, June to November, 2006*

	Description of surveillance and laboratory testing activities		
Level of alert	ACF	Study team	Laboratory
Level 1 (no ILI)	Nursing staff actively looking for ILI	Study team calls ACF 3 times/week (Mon./Wed./Fri.)	
Level 2 (1 case of ILI)	Nursing staff report case of ILI to study team	Daily calls to ACF	
Level 3 Respiratory outbreak (2 cases of ILI in 3 days) (3 cases of ILI in 7 days)	Nursing staff report cases of ILI POC and laboratory testing	Daily calls to ACF Daily calls to laboratory Investigation on site POC and laboratory testing	Daily contact with study team
Level 4 Influenza outbreak	Nursing staff report cases of ILI to study team	Daily investigation on site Laboratory testing Daily calls to laboratory	Daily contact with study team

ILI, Influenza-like illness; POC, point of care.

Active surveillance, consisting of thrice-weekly telephone calls commenced in June 2006, the beginning of the Australian winter. These calls were performed by trained members of the study team: a doctor, research nurse or epidemiologist. Clinical and demographic information was collected at the time of the call and included: staff or resident status, age, sex, location or main work area within the ACF, onset date, a measured temperature (if available), presence of respiratory signs and symptoms (including cough, sore throat, wheeze, running nose, sneeze, sputum production, respiratory distress, rapid breathing), hospitalization details, deaths, General Practitioner (GP) visits and whether any specimens were collected. The person-hours required to conduct surveillance were estimates gathered from informal study team discussions. If the surveillance detected a respiratory outbreak, active surveillance calls or on-site visits would be undertaken on a daily basis until 8 days after the last new case was reported. Table 1 gives details of the surveillance system.

When an influenza outbreak was identified, nose and throat swabs and blood were collected from consenting staff and residents who were either symptomatic or eligible to receive prophylaxis due to their exposure to cases. Exposure was defined as working or residing in a wing of the ACF where an outbreak has been declared, or in a wing where subsequent infection had been confirmed, at and since the time of onset in the index case in that wing. POC testing was used to first confirm influenza outbreaks, with DIF used to confirm positive influenza A or B POC tests or to detect adenovirus, parainfluenza viruses types 1–3 (PIVs) and respiratory syncytial virus (RSV) if cases were identified between 24 h and 48 h of symptom onset. Nucleic acid testing (NAT) for influenza A and B, RSV, PIVs, adenovirus, coronaviruses and human metapneumovirus was performed wherever possible. Acute blood samples were obtained from consenting participants, and oseltamivir therapy was started as indicated. Treatment was given for 5 days, prophylaxis for at least 10 days, or until 8 days after symptom onset of the last case in the wing, whichever duration was longer. Four to six weeks later convalescent sera were collected and examined in parallel, with a serological diagnosis made if there was a minimum fourfold rise in complement-fixing antibody titres to influenza A and B.

Respiratory tract specimens were transported to the laboratory at 4 °C in viral transport medium. For influenza virus diagnosis, DIF was performed on acetone-fixed smears of deposits from nose and throat swabs and stained with fluorescein-conjugated monoclonal antibodies (Chemicon International, USA) against influenza A and B nucleoprotein. RNA was extracted from the remaining original clinical samples using the High Pure viral RNA kit (Roche Diagnostics GmbH, Germany) according to the manufacturer's instructions. A nested reverse transcriptase–polymerase chain reaction (RT–PCR) was performed to detect influenza A and B using a published method [23]. Results from POC testing were expected within 10 min, results from DIF testing were expected within 24 h, while results for NAT were subject to the

laboratory schedule and reagent availability. Serological diagnoses were available 4–6 weeks after outbreaks were identified.

Residents were recorded as vaccinated against influenza in 2006 if vaccine vial stickers for that season were identified or vaccination was documented in the medical notes by their attending GP. Staff were recorded as being vaccinated according to documentation collected when consent to participate was given.

Outbreaks were investigated by the study team, comprising a public health physician, nurses and epidemiologists. Active and retrospective case-finding were conducted, recent deaths and hospitalizations were ascertained and enhanced infection control measures (improved compliance with hand washing, minimization of movement of residents and group activities, closure of facilities to new admissions, restricted visiting, cohort nursing and enhanced surface cleaning) were recommended and appeared to be well adhered to. Attack rates for residents was calculated by dividing cases in each group by the number of potentially exposed residents in the facility on the day the outbreak was declared and converting this to a percentage. The number of symptomatic staff and the total number of staff were used to calculate the staff attack rate.

RESULTS

A total of seven outbreaks of respiratory disease were identified in the 16 ACFs participating in the surveillance system during a 6-month period in 2006. In four outbreaks a single aetiological agent was identified, including two outbreaks caused by influenza A and one each due to PIV-1 and RSV. In the remaining outbreaks no viral respiratory pathogen was identified, despite collecting respiratory samples within 3 days of onset. In these outbreaks, there were 56 symptomatic people out of a total of 377 residents in the three facilities. Respiratory samples were collected for 14 people, of whom 12 had a negative DIF (seven of these also had a negative POC test) and another two had a negative POC test (DIF not done). Twenty POC tests were used during the reported surveillance period. The total number of staff reported with new respiratory signs or symptoms during the outbreaks was 10 compared with 93 for residents. The average age of residents reported during outbreaks was 84·7 years, while the average staff age was 47·5 years. About 4·5 person-hours per week were required to conduct the active surveillance by telephone.

Table 2 shows the outbreaks identified during surveillance. The median time from onset of illness in the primary case to the first diagnostic test used for outbreak identification was 4 days (range 1–11 days). This range includes residents who might be retrospectively identified after declaration of the outbreak because they either did not meet the case-definition or had not been identified by staff. There were five hospitalizations and three deaths reported during the outbreaks, including four hospitalizations occurring during an influenza outbreak. For those outbreaks caused by influenza, the time from onset of illness in the primary case to the first diagnostic test was 4 and 6 days, respectively.

The median time from onset of illness in staff to their being tested for respiratory viruses was 4·5 days, compared with a median duration of only 2 days for residents. For both of the influenza outbreaks, the outbreak definition was first met following identification of two cases of ILI where symptom onset occurred within a 3-day period. In the first influenza outbreak, there were four residents and one staff member who had subsequent confirmation of infection with influenza at the time the outbreak was declared. Overall, 7/10 symptomatic residents who were available for testing were confirmed cases (by POC test, DIF, RT–PCR and/or seroconversion), two of four suspected cases in staff were confirmed, and one asymptomatic resident who received oseltamivir prophylaxis seroconverted. The resident influenza immunization coverage prior to the 2006 winter was 84% (75/89); the coverage in consenting staff was 27% (6/22). In the second influenza outbreak, only the index case, a staff member, tested positive for influenza (by all laboratory methods), while 0/8 other symptomatic staff and 31 asymptomatic staff or residents who received oseltamivir chemoprophylaxis had any laboratory evidence of influenza infection, despite conducting respiratory sampling within the first 1·6 days of illness (range 0–4 days). We were unable to gather the resident influenza immunization coverage prior to the 2006 winter; however, prior to the 2007 winter it was 66% in residents (41/62 with 10 unknown) at this ACF, the coverage for consenting staff was 44% (8/18 with 39 unknown).

For the influenza outbreaks, prevention and control measures, including oseltamivir treatment and prophylaxis, were commenced on days 4 and 6 after the onset of illness in the primary cases in each of the outbreaks. At the time control measures were commenced in the first influenza outbreak, there

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Table 2. *Summary of respiratory disease outbreaks identified by active surveillance in participating aged-care facilities (ACFs) in the Sydney area, June–November, 2006*

Respiratory illness													
Out-break	Time to testing (days from onset in 1st case to first POC test performed)	No. of residents with confirmed influenza when respiratory outbreak identified	Time to commencement of antivirals (days from onset in 1st case to commencement of antivirals)	Outbreak duration (Days from onset in case 1 to last case onset)	Resident cases§/ total residents	Resident attack rate	Staff cases§/ total staff	Staff attack rate	Total cases§	Total attack rate	Number hospitalized	No. of deaths	Aetiology
A	11	n.a.	n.a.	17	18/74	24%	1/83	1%	19	12%	0	0	Unknown – not influenza
B*	4	n.a.	n.a.	20	10/159	6%	0/150	0%	10	3%	0	0	Unknown – not influenza
C*	4	n.a.	n.a.	19	28/114	25%	0/100	0%	28	13%	0	0	Unknown – not influenza
D	2	n.a.	n.a.	10	11/78	14%	1/85	1%	12	7%	0	1	Parainfluenza 1
E†‡	11	n.a.	n.a.	18	13/145	9%	3/120	3%	16	6%	1	2	RSV
F*	2	4	6	19	13/92	14%	4/79	5%	17	10%	4	0	Influenza A
G	3	0	4	7	0/160	0%	9/150	6%	9	3%	0	0	Influenza A

Other illness

- There were 5 outbreaks of gastroenteritis: 4 in July and 1 in October, two of which occurred in facilities that also reported respiratory disease outbreaks.
- The facility that reported outbreaks of RSV and gastroenteritis also reported an outbreak of conjunctivitis.

n.a., Not applicable; POC, point of care; RSV, respiratory syncytial virus.

* Outbreak occurred in two phases at different geographical sections within the ACF.

† Outbreak of conjunctivitis.

‡ Facility experienced an outbreak of gastroenteritis.

§ Suspected and confirmed.

were six residents and one staff member suffering with ILI.

DISCUSSION

Historically, influenza outbreak notification to public health authorities has not been timely [6, 7, 24]. As a consequence, prevention and control measures are only instigated after many preventable infections have already occurred. Given that a single influenza case has public health significance due to the potential for rapid propagation of the infection, it highlights the need for early identification in order to optimize therapy and interrupt transmission. Lessons learned from settings like ACFs may become of great use in management of seasonal influenza in other closed environments (e.g. boarding schools, prisons) and also in the ongoing revision of plans for pandemic influenza.

In the absence of interventions, influenza can spread quickly in the institutionalized elderly, with high attack rates in staff and residents occurring. The varying epidemiology of each influenza outbreak may mean the window of opportunity for effective control activities may also vary; however, the effectiveness of early intervention has been shown in several studies. In France [25], an analysis of influenza outbreaks in geriatric and rehabilitation care wards revealed attack rates in residents of 48% where prophylaxis was commenced on day 9 compared to an attack rate of 28% when prophylaxis was commenced after only 24 h. Although commencement of antivirals and enhanced infection control interventions may not always be feasible within 48 h, it would appear that control within 5 days may still be effective [26] and certainly more feasible for public health response.

An important indicator for evaluating the timeliness of an influenza outbreak identification system is the number of infected individuals (staff and residents) prior to commencement of antivirals. One study showed that passive surveillance for influenza outbreaks did not identify three out of eight influenza outbreaks in a timely manner (5, 11 and $\sim$30 days) [3]. Comparing this to the outbreaks identified in our study (4 and 6 days) brings into question the appropriateness of passive forms of surveillance for early outbreak identification. In one of the three homes where the outbreak was identified late, the resident attack rate was 23% before commencement of antivirals. In another, outbreak identification took 1 month, and there was an overall resident attack rate of 40% in the third home. In comparison, we were able to achieve early identification of respiratory outbreaks using active surveillance, and specifically influenza outbreaks only 4 and 6 days after symptom onset in the primary case.

Surveillance combined with rapid testing was highly useful for initial case detection in the influenza outbreaks. This was supported by the small numbers of confirmed influenza cases in residents at the time the outbreaks were declared. Prevention and control measures, including oseltamivir prophylaxis, were instigated within 7 days of onset of illness beginning in the primary case. The attack rate for residents in the first outbreak was only 14%, while in the second outbreak the overall attack rate was 3%, and occurred solely among staff. In comparison, the attack rates of recent influenza outbreaks reported in urban ACFs in eastern Australia (45%) [7] and elsewhere (20–40%) [27] were considerably higher.

Influenza presentations may vary depending on the individual, age, comorbid factors and medications [28]. Surveillance conducted in one 3-year study found that 83% of nursing-home residents identified with a respiratory illness during outbreaks presented with cough, 45% with coryza and 40% with a fever $>38^{\circ}$C [1]. However, this required trained staff able to recognize and record such symptoms. This is not necessarily a certainty in busy facilities largely staffed by workers with limited clinical training. We considered our case-definition for ILI and the outbreak definition to be appropriate for the early identification of influenza outbreaks, considering the context and setting. It was our intention to mobilize the outbreak response team every time the testing threshold was met. Surveillance definitions were chosen because we believed they would yield fewer false-positive results. This is an aim desired in practice by most public health units; we were even more motivated as some of the ACFs under study were at distances in excess of 100 km from the research centre.

Surveillance does not always identify cases during an influenza outbreak [1]. Due to their ongoing exposure to circulating viruses in the community and their pattern and nature of contact with residents, staff are often responsible for the introduction and transmission of influenza in ACFs [2]. When staff are not included in surveillance and testing procedures, outbreaks may be identified later and control may be less effective. Retrospectively, it was found that at the time the larger of the two influenza outbreaks was declared, there were three symptomatic individuals,

including a staff member who had not been identified by routine surveillance. However, syndromic surveillance of staff members may present greater difficulties than for residents as evidenced by the differences in median times from onset of illness to testing between residents and staff. In addition, issues relating to loss of remuneration due to forced absenteeism may lead to under-ascertainment of cases in staff. Consequently, potentially infectious staff are less likely to benefit from antiviral treatment and may remain in contact with susceptible residents. Additional efforts such as nursing staff telephoning absent colleagues to enquire about symptoms of illness may be useful, provided this is acceptable to staff.

Immunization of staff caring for the institutionalized elderly with an annual influenza vaccine is effective for preventing morbidity and mortality in those under care [8–10]. In the participating ACFs, influenza immunization is routinely offered free of charge to residents prior to each influenza season or may be offered to new residents by visiting GPs. Despite the evidence, this is not routinely done for staff, as reflected in the poor documentation of immunization in staff and the low coverage rates.

Influenza outbreaks in ACFs are known to occur out of season or when only low levels of virus are reported to be circulating in the community [6, 29]. One study in Canada reported there to be no seasonal pattern to respiratory outbreaks involving the institutionalized elderly [1]. The larger outbreak described here was identified when community rates of ILI, based on emergency department (ED) presentations, were low ($<2{\cdot}0$/1000 ED consultations) [30], the smaller outbreak occurred after the state health department's routine laboratory-based surveillance had ceased. If influenza vaccination of ACF residents offers some protection, this may be less at the end of season or between seasons due to immune senescence. This increases the importance of having year-round active surveillance for this highly vulnerable population [31, 32]. If active surveillance is to be established systematically and implemented widely, the use of information technology like email or standardized web-based reporting, especially zero-reporting, may require much less human resources, improve efficiency, be more acceptable and therefore more feasible. Although the limited evidence suggests that achieving sustainability of active surveillance for ILI in the long term may be challenging [33], integrating this with surveillance for other diseases of public health importance, such as gastroenteritis, may contribute to its public health utility and thus sustainability.

Both influenza outbreaks were declared following positive POC testing. Given the low sensitivity of POC testing, it is of limited usefulness for testing individual cases. Its utility may lie in pairing it with active surveillance to provide early identification of influenza in clusters of respiratory illness [21]. Although not regarded as a substitute for DIF or NAT in the confirmation of cases [34], POC tests nevertheless provide useful service. It would seem reasonable to suggest that use of rapid antigen testing as an adjunct to active surveillance appears favourable in terms of time between the onset of illness in the primary case to outbreak notification, the number of resident cases at the time public health action is taken and the total attack rate [2, 3, 5, 35, 36]. This may be of particular public health importance in outbreaks in this population, where immunization offers somewhat limited protection [31, 32, 37].

Limitations

The surveillance data presented is from a single influenza season. Case-ascertainment in the non-influenza outbreaks may have been less complete as the investigation team was less actively involved. Furthermore, the participating ACFs may not be representative of all such facilities, nor may they carry the same burden of respiratory and other illnesses. Data on influenza immunization coverage in staff was incomplete and may also be prone to entry level bias, as there were no registers documenting staff immunization and only limited numbers of staff who consented to participate in the study were included in the denominator. Using 2007 influenza vaccination coverage data as a proxy for 2006 coverage in the second outbreak is a strong limitation which may over- or under-estimate the true coverage. Maintaining active surveillance for the entire year involves a much greater commitment of resources with a lower yield over the summer months, which may influence the likelihood of this approach being adopted. There are also limitations in the accuracy of some data used in surveillance case-definitions, particularly the temperature of sick staff and residents. Temperatures were not routinely measured in cases, although efforts were made to ascertain unreported temperatures through enhanced phone surveillance. However, greater data completeness was achieved over the course of the influenza season as ACF staff and study

team members became more familiar with the system's requirements.

In the context of variable uptake and protection of influenza vaccination, and effective but time-dependent use of antivirals, the early recognition of influenza and outbreaks are essential for effective control in ACFs. Surveillance should be conducted year-round and additional assessment should be conducted for absent staff. Surveillance systems for the early identification of respiratory disease outbreaks require few resources and little training. When combined with early influenza POC testing they have the potential for early identification of influenza outbreaks in ACFs, greatly facilitating appropriate, timely public health interventions and better outbreak control using antiviral prophylaxis.

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DECLARATION OF INTEREST

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