Absence of Influenza A(H1N1) During Seasonal and Pandemic Seasons in a Sentinel Nursing Home Surveillance Network in the Netherlands

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Absence of Influenza A(H1N1) During Seasonal and Pandemic Seasons in a Sentinel Nursing Home Surveillance Network in the Netherlands

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OBJECTIVES: To describe the epidemiological, virological, and institutional characteristics of influenza-like illness (ILI) in nursing homes (NHs).

DESIGN: Continuous clinical surveillance of ILI and virological surveillance of ILI and other acute respiratory infections (ARIs) during four influenza seasons.

SETTING: National sentinel NH surveillance network.

PARTICIPANTS: National sentinel residents.

MEASUREMENTS: Weekly registration of ILI cases (influenza seasons 2008/09–2009/10), influenza virus detection (influenza seasons 2006/07–2009/10), and collection of institutional characteristics of NHs at start of participation.

RESULTS: During the 2008/09 influenza season, ILI incidence started to rise in Week 49 of 2008, peaked in Week 3 of 2009 (158 cases per 10,000 resident weeks), and flattened out by Week 16 of 2009 (mean ILI incidence during epidemic: 73 cases per 10,000 resident weeks). During the 2009/10 influenza pandemic, there was no epidemic peak. Influenza virus type and subtype varied throughout virological surveillance but was limited to influenza A(H3N2) and B viruses. Higher staff vaccination coverage (>15%) was associated with lower ILI-incidence in the 2008/09 influenza season in a univariate negative binomial regression analysis (incidence rate ratio = 0.3, 95% confidence interval = 0.1–0.8)).

CONCLUSION: Neither seasonal nor pandemic influenza A(H1N1) viruses were detected in the network, despite widespread community transmission of seasonal and influenza A(H1N1) virus. ILI incidence trends corresponded to virological trends. Sentinel surveillance of ILI combining clinical and virological data in NHs increases understanding of transmission risks in this specific vulnerable population. **J Am Geriatr Soc 59:2301–2305, 2011.**

Key words: nursing home; influenza-like illness; influenza; surveillance

Residents of long-term care facilities, particularly nursing homes (NHs), are among the most vulnerable to influenza because of the high prevalence of underlying chronic illnesses,[1] age-related immunosenescence,[2–4] the closed environment typical for this population, suboptimal antiviral strategies,[5] suboptimal vaccination responses,[6] and transmission of the virus through their caregivers.[7,8] As a result, influenza morbidity and mortality in NH residents is substantial, and case-fatality rates often exceed 5%.[9,10]

Epidemiological and virological surveillance of influenza-like illness (ILI) in the general Dutch population has been operational since 1970 in a network of general practitioners (GP network).[11] This GP network collects clinical, virological, and epidemiological data on ILI, among other clinical diseases. GP-based surveillance excludes NHs, for which elderly care physicians are responsible in the Netherlands.

NH prevention and control guidelines on influenza are often based on surveillance systems monitoring general

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populations,[12,13] influenza outbreaks,[14] or small and short ILI surveillance initiatives.[15]Given the dynamics of the NH population, influenza transmission may well differ from and occur regardless of influenza activity in the general community [16–18] or NH influenza outbreak status. Epidemiological, clinical, and virological characteristics of ILI trends need to be determined in the NH population, independent of influenza outbreak status or general population influenza activity, to help optimize NH strategies for prevention and control of influenza.

Since 2006, in addition to a European network of Healthcare-Associated Infections in European Long Term Care Facilities (HALT),[19] the Sentinel Surveillance Network on Infectious diseases in nursing homes (SNIV) is responsible for ILI surveillance. This study describes the epidemiological, virological, and institutional characteristics associated with ILI in Dutch NHs during four influenza seasons (2006/07–2009/10). It includes three seasonal epidemics and the A(H1N1) 2009/10 pandemic season.

METHODS

Setting

NHs were recruited through academic networks for training of elderly care physicians, through publications in Dutch geriatric and infectious disease journals, and through prior participation in a national study.[20] NHs were selected based on geographic distribution and size (>50 beds). Feasibility of respiratory specimen collection and accompanying clinical diagnostics was piloted from January 2007 to December 2008. The network became officially operational on January 1, 2009, with 18 participating NHs. It aimed to recruit 30 NHs in the surveillance network.

Data Collection

An influenza season is typically defined as the period from Week 40 of 1 year to Week 20 of the next year. The period between influenza seasons is defined as the interseasonal period. During the 2009/10 pandemic season, influenza surveillance continued according to official World Health Organization guidelines to monitor the pandemic.[21]

Epidemiological surveillance of ILI was performed from Week 40 of 2008 (n = 8 NHs) to Week 20 of 2010 (n = 25 NHs). In each NH, facility-based elderly care physicians and nurse practitioners were instructed to report ILI according to the following case definition: acute or sudden (prodromal stage <4 days) onset of symptoms with at least one systemic symptom (fever or febrile feeling, malaise, headache, myalgia) and one respiratory symptom (cough, sore throat, shortness of breath).[12] Using a Web-based registration tool, physicians registered the number of residents meeting this ILI definition weekly, in addition to outbreak status and antiviral medication use.

Virological surveillance was performed from Week 1 of 2007 (n = 8 NHs) to Week 20 of 2010 (n = 25 NHs) and was organized similar to the GP sentinel surveillance to ensure comparability.[22] Elderly care physicians and nurse practitioners were asked to take respiratory specimens (a nose swab and a throat swab) from two ILI cases per week or, when two cases did not present, from two residents with other acute respiratory infections (ARIs) and to send these to the Laboratory for Infectious Diseases and Perinatal Screening at the Dutch National Institute for Public Health and the Environment using standard sampling packages. They were also asked to report on the specimen form, clinical diagnosis, symptoms, antiviral medication, and vaccination status. Respiratory specimens were shipped at ambient temperature directly or with 1 day delay by regular mail to the Dutch National Institute for Public Health and the Environment according to shipping protocol.

Respiratory specimens were analyzed identically according to international validated (sub)typing reverse transcriptase polymerase chain reaction protocols.[23]

Information on characteristics of 18 NHs was collected at the start of each NH's participation in the network from January 1, 2009, using a questionnaire. These facility-level data were not available for earlier years of clinical and virological surveillance of ILI. The questionnaire included questions about, among others, the institution (number of beds, percentage of vaccine coverage of residents and healthcare workers), wards (type, number of residents, exchange of healthcare workers between wards), and room characteristics (occupancy, toilet and shower facilities).

Statistics

Weekly ILI incidence per 10,000 resident weeks was calculated as the number of residents with ILI divided by the number of resident weeks times 10,000. In addition, the number of reported ILI cases per week were calculated after adjusting the weekly ILI incidence curve using a 3-week unweighted moving average.[21] Resident numbers were estimated using bed capacity per home because occupancy was always close or equal to 100%.

Associations between five institutional characteristics (healthcare worker vaccination coverage, NH size, healthcare worker exchange between wards, percentage of residents living on psychogeriatric wards, percentage of individual rooms) and ILI incidence were calculated using uni- and multivariate analyses (adjusted for all institutional characteristics documented) using negative binomial regression for the 2008/09 influenza season. Cutoff values for institutional characteristics were based on the mean value of the characteristic or the dichotomous question related to the characteristic. Statistical analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, NC).

RESULTS

Epidemiological Surveillance of ILI

Although no institutional influenza outbreaks were reported in the network during the ILI surveillance period, ILI was frequently diagnosed. In the 2008/09 influenza season, ILI incidence started to increase in Week 49 of 2008; peaked in Week 3 of 2009, with 158 cases per 10,000 resident weeks; and leveled off by Week 16 of 2009. During the 2009/10 pandemic influenza season, NH ILI incidence

was consistently below 30 cases per 10,000 resident weeks, despite widespread community transmission of influenza A(H1N1) during that season [24] (Figures 1 and 2A and B).

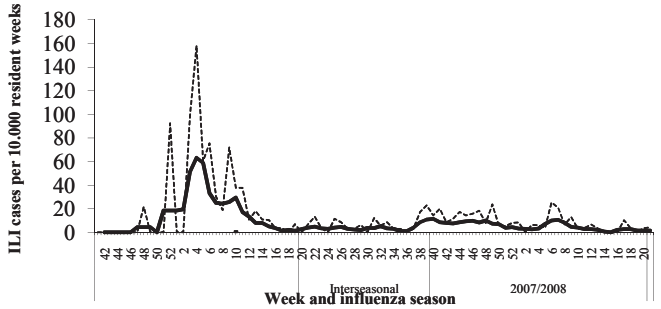

Figure 1. Epidemiological sentinel surveillance of influenza-like illness (ILI) in the Sentinel Surveillance Network on Infectious diseases in nursing homes: weekly (gray) and 3-week centered moving average (black) incidence of ILI per 10,000 resident weeks during the 2008/09 and 2009/10 (pandemic) influenza seasons.

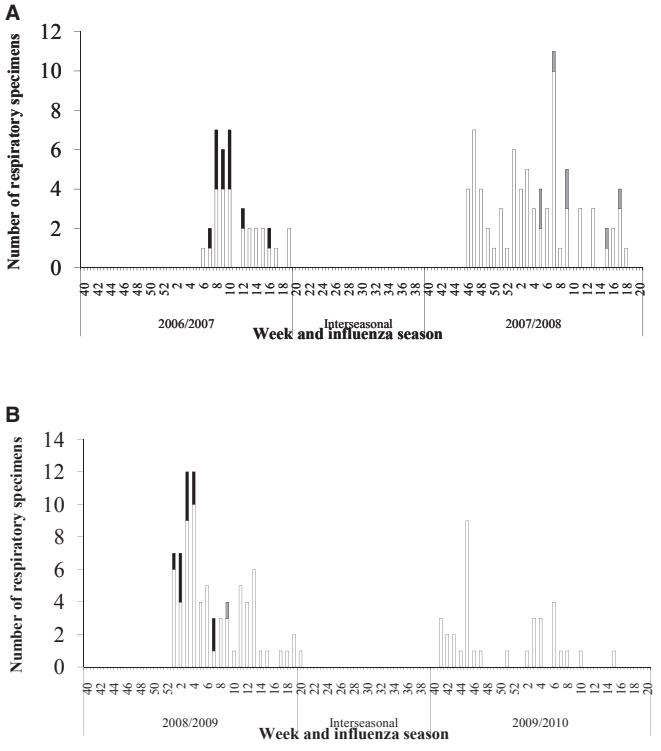

Figure 2. Virological sentinel surveillance of influenza-like illness (ILI) and acute respiratory infection (ARI) in the Sentinel Surveillance Network on Infectious diseases in nursing homes: weekly number of ILI and acute respiratory illnesses (ARIs) per influenza virus type and subtype during the (**A**) 2006/07 and 2007/08 and (**B**) 2008/09 and 2009/10 (pandemic) influenza seasons. Black: influenza A(H3N2) virus. Gray: influenza B virus (2007/2008: Weeks 5, 7, 9, 15, and 17; 2008/2009: Week 9). White: no influenza virus detected.

Virological Surveillance of ILI

From Week 1 of 2007 until Week 20 of 2010, 25 of the 28 NHs took a total of 255 respiratory specimens from residents diagnosed with ILI or ARI (range 1–42 specimens). Overall adherence to virological surveillance was 56%. Adherence was calculated as the number of respiratory specimens sent in for virological surveillance divided by the theoretical maximum number of respiratory specimens that could have been sent in based on the study protocol. Residents from psychogeriatric and geriatric wards were equally represented in this subset of 255 residents, with 79% of residents being aged 75 and older. The most common systemic and respiratory symptoms were malaise (84%) and coughing (91%). No antiviral therapy or prophylaxis was documented. Eighty-nine percent of residents received seasonal influenza vaccination. There was a mean 2-day delay between onset of symptoms and laboratory analysis. Of all respiratory specimens received, 12% were positive for influenza virus type A or B. Prevalence of influenza virus type and subtype varied between influenza seasons. Influenza A(H3N2) and B viruses were detected during influenza seasons 2006/07 (37 specimens), 2007/08 (82 specimens), and 2008/09 (81 specimens). No influenza viruses were detected during the 2009/10 season (54 specimens). No seasonal or pandemic influenza A(H1N1) viruses were detected in any of the influenza seasons. The increase and decrease in the number of influenza virus detections corresponded to the ILI incidence dynamics measured during the 2008/09 and 2009/10 influenza seasons, respectively (Figures 1 and 2A and B).

Institutional Characteristics and Associations with ILI

Institutional data were available from 18 NHs (Table 1). Univariate analysis, but not multivariate analysis, of NH characteristics showed that NHs with vaccination coverage of healthcare workers of 15% or greater (10 NHs) had a statistically lower incidence of ILI during the 2008/09 influenza season (incidence rate ratio = 0.3, 95% confidence interval = 0.1–0.8) than NHs with less than 15% coverage (8 NHs). Resident vaccination coverage was not included in the logistic regression analysis because there was insufficient distinction in vaccination rates of residents (mean vaccination coverage 91%, range 70–99%).

DISCUSSION

In contrast to the 2008/09 influenza season, ILI incidence remained at low levels in NHs throughout the 2009/10 pandemic influenza season, despite widespread community circulation of pandemic influenza A(H1N1) at that time.[22] Virological surveillance corresponded with this observation, with the 2009/10 season characterized by a smaller number of collected specimens than in three previous influenza seasons, despite a higher number of participating NHs. Influenza A(H1N1) viruses (seasonal or pandemic) were not detected in any of the respiratory specimens collected during virological surveillance. This was remarkable because significant (co)circulation of seasonal influenza A (H1N1) was detected in the general population during the 2007/08 and 2009/10 seasons.[11] Epidemiological surveillance

Table 1. Uni- and Multivariate Negative Binomial Regression Analyses of Nursing Home Characteristics and Associations with Incidence of Influenza-Like Illness for the 2008/09 Influenza Season

	Incidence Rate Ratio (95% Confidence Interval)	
Institutional Characteristic	**Univariate**	**Multivariate***
Vaccination coverage staff <15%	0.3 (0.1–0.8)	0.3 (0.1–1.2)
Psychogeriatric residents <50%	0.6 (0.2–1.9)	0.6 (0.2–2.1)
Healthcare worker exchange, no	0.7 (0.2–2.8)	1.0 (0.2–4.3)
Number of beds<158	2.4 (0.7–8.0)	0.9 (0.2–3.6)
Individual rooms, part	0.2 (0.0–1.4)	0.6 (0.1–4.0)

* Corrected for percentage vaccination coverage of healthcare workers (cutoff 15%), percentage of residents from psychogeriatric wards (cutoff 50%), healthcare worker exchange (yes vs no), number of beds (cutoff 158), and individual rooms (part vs all).

data were not available for NHs during the 2006/07 and 2007/08 influenza seasons.

Although not entirely absent,[25] the apparent limited circulation and low resident attack rate of influenza A (H1N1) in NHs is remarkable. It is unlikely that better general hygiene management had played a role because norovirus outbreaks were still frequently recorded in the SNIV network during the pandemic season and are also related to hygiene management.[26] It is likely that residents have had a certain degree of cross-protection from previous exposure to influenza A(H1N1), in particular the strains circulating before 1957.[27]

Despite the fact that the characteristics analyzed were NH based rather than resident based, a protective effect of a high uptake of healthcare worker vaccination on lower ILI incidence in NH residents was found. This is consistent with previous data in larger settings,[28,29] suggesting that vaccination of healthcare workers might have direct or indirect benefits for residents and healthcare workers, even though influenza virus could only be confirmed in 12% of the episodes. Current effectiveness of promotional campaigns for vaccination of healthcare workers vary and suggest marginal effects based on the low vaccination coverage in the Netherlands and Europe (25%) and that further research into more-effective campaigns is warranted.[30]

There was only a short delay between onset of ILI and ARI symptoms and laboratory analysis, indicating feasibility of virological surveillance. A limitation might be that, although NHs were asked to send a respiratory specimen of two ILI and ARI cases per week, this was not implemented uniformly, with some NHs showing higher adherence rates than others. The importance of virological surveillance and the registration of ILI cases will continue to be emphasized to the participating NHs. Despite this possible limitation, major concerns about representativeness are likely to be unfounded. Epidemiological trends corresponded with virological trends during the surveillance period. Furthermore, other studies, although not performed in NHs, reported absence of ILI in healthy older adults during the pandemic.[24]

Specific epidemiological and virological trends of ILI can be distinguished in the NH population. The integrated virological and epidemiological surveillance system for ILI should be the basis for NH prevention and control strategies in addition to already successfully established (ILI) surveillance systems in general populations [12,13] and influenza outbreak surveillance [14] in NHs. These will provide further insight into specific dynamics and interactions between the NH population and general population.

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Author Contribution: Veldman-Ariesen M.-J. and Haenen A.: Concept and design of the study, acquisition of institutions, and data collection. Meijer A.: Laboratory aspects of specimen collection and linked clinical data and virological analyses of the collected specimens. All authors contributed equally to data interpretation and manuscript preparation.

Sponsor's Role: None.

APPENDIX

Almere – Zorggroep Almere, Baarslag, F. Amsterdam Zuidoost – Gaasperdam, Bolle-de Vries Robles, H. Assen – Anholt, Scheper, H. Assen – Nieuw Graswijk, Scheper, H. Barneveld – Norschoten loc. Klaverweide, Jansen-Reimerink, Y.M.M. Barneveld – Norschoten loc. Kweekweg, Jansen-Reimerink, Y.M.M. Capelle Aan den Ijssel – Rijckehove, Essen, L. van den Helder – den Koogh, Vrij, P. de Deventer – St. Jozef Verpleeghuis, Douma, G. Dieren – Gelders Hof, Pluymert, M. Echt – de Egthe, Beurskens, M. Etten-Leur – het Anbarg, afd. Verpleging, Leen, M. van GOUDA Part vs all residents – Bloemendaal, Boeren, R.M. Gouda – de Riethoek, Boeren, R.M. Heeswijk Dinther – Cunera, Verwer, T. Krimpen Aan den Ijssel – Zorgcentrum Crimpenerstein, Essen, L. van Lekkerkerk – de Breeje Hendrick, Boeren, R. Maarssen – Zuwe Snavelenburg, Riet, L. van Maastricht – La Valence, Castermans, R. Naarden – Naarderheem, Beckers, A. S. Gravenhage – Lozerhof, Bos, C. S Gravenhage – Preva Verpleeghuis, Ficken, M. Sliedrecht – Waerthove, Remmert, P. Veenendaal – de Meent, Sloesen, P. Velp Gld – H.A. Lorentzhuis, Fodor, M. Velp Gld – Oosterwolde, Fodor, M. Velp Gld – t Jagthuis, Verpleeghuis, Fodor, M. Zevenaar – Verpleeghuis Zevenaar, Schaapsmeerders, F.H.M.

REFERENCES

1. Glezen WP, Greenberg SB, Atmar RL et al. Impact of respiratory virus infections on persons with chronic underlying conditions. JAMA 2000;283:499–505.
2. Remarque EJ, Cools HJ, Boere TJ et al. Functional disability and antibody response to influenza vaccine in elderly patients in a Dutch nursing home. BMJ 1996;312:1015.
3. Roos-Van Eijndhoven DG, Cools HJ, Westendorp RG et al. Randomized controlled trial of seroresponses to double dose and booster influenza vaccination in frail elderly subjects. J Med Virol 2001;63:293–298.

4. Targonski PV, Jacobson RM, Poland GA. Immunosenescence: Role and measurement in influenza vaccine response among the elderly. Vaccine 2007;25:3066–3069.
5. van der Sande MA, Ruijs WL, Meijer A et al. Use of oseltamivir in Dutch nursing homes during the 2004–2005 influenza season. Vaccine 2006;24:6664–6669.
6. Cools HJ, Gussekloo J, Remmerswaal JE et al. Benefits of increasing the dose of influenza vaccine in residents of long-term care facilities: A randomized placebo-controlled trial. J Med Virol 2009;81:908–914.
7. van den Dool C, Bonten MJ, Hak E et al. The effects of influenza vaccination of health care workers in nursing homes: Insights from a mathematical model. PLoS Med 2008;5:1453–1460.
8. Van den Dool C, Van Strien AM, den Akker IL et al. Attitude of Dutch hospital personnel towards influenza vaccination. Vaccine 2008;26:1297–1302.
9. Meiklejohn G, Hoffman R, Graves P. Effectiveness of influenza vaccine when given during an outbreak of influenza A/H3N2 in a nursing home. J Am Geriatr Soc 1989;37:407–410.
10. Coles FB, Balzano GJ, Morse DL. An outbreak of influenza A (H3N2) in a well immunized nursing home population. J Am Geriatr Soc 1992;40:589–592.
11. Donker GA. Continuous morbidity registration at Dutch sentinel stations 2008 [Online]. Available at www.nivel.nl. Accessed October 11, 2010.
12. Dijkstra F, Donker GA, Wilbrink B et al. Long time trends in influenza-like illness and associated determinants in the Netherlands. Epidemiol Infect 2009;137:473–479.
13. Sue Huang Q, Lopez LD, McCallum L et al. Influenza surveillance and immunisation in New Zealand, 1997–2006. Influenza Other Respi Viruses 2008;2:139–145.
14. Vaux S, Poujol I, Bonmarin I et al. Surveillance of lower respiratory tract infections outbreaks in nursing homes in France. Eur J Epidemiol 2009;24:149–155.
15. Woo J, Hui E, Chan PK et al. Influenza-like illness in residential care homes: A study of the incidence, aetiological agents, natural history, and health resource utilisation. Hong Kong Med J 2009;15(Suppl 6):35–38.
16. Kohn MA, Farley TA, Sundin D et al. Three summertime outbreaks of influenza type A. J Infect Dis 1995;172:246–249.
17. Gaillat J, Dennetiere G, Raffin-Bru E et al. Summer influenza outbreak in a home for the elderly: Application of preventive measures. J Hosp Infect 2008;70:272–277.
18. Ferson MJ, Morgan K, Robertson PW et al. Concurrent summer influenza and pertussis outbreaks in a nursing home in Sydney, Australia. Infect Control Hosp Epidemiol 2004;25:962–966.
19. Jans BM, Fabbri G, Cookson B et al. Surveillance of healthcare-associated infections and related practices in European long-term care facilities (HALT). 19th European Congress of Clinical Microbiology and Infectious Diseases. Helsinki, Finland: 2009.
20. van der Steen JT, Meuleman-Peperkamp I, Ribbe MW. Trends in treatment of pneumonia among Dutch nursing home patients with dementia. J Palliat Med 2009;12:789–795.
21. World Health Organisation. WHO Regional Office for Europe Guidance for Influenza Surveillance in Humans. Brussels, Belgium, August 2009.
22. Dijkstra F, Brandsema P, van Gageldonk R et al. Jaarrapportage surveillance respiratoire infectieziekten 2009 [Online]. RIVM jaarrapportage, RIVM briefrapport 210231006. 2010; Available at www.rivm.nl. Accessed October 11, 2010.
23. Meijer A, Beerens A, Claas E et al. Preparing the outbreak assistance laboratory network in the Netherlands for the detection of the influenza virus A(H1N1) variant. J Clin Virol 2009;45:179–184.
24. van't Klooster TM, Wielders CC, Donker T et al. Surveillance of hospitalisations for 2009 pandemic influenza A(H1N1) in the Netherlands, 5 June–31 December 2009. Euro Surveill 2010;15:19461.
25. Outbreaks of 2009 pandemic influenza A (H1N1) among long-term-care facility residents – three states, 2009. MMWR Morb Mortal Wkly Rep 2010;59:74–77.
26. Veldman MJ, Haenen AA. A Surveillance of gastro enteritis, pneumonia, influenza-like illness and whooping cough measured in SNIV during 2009 [online]. Available at www.rivm.nl Accessed August 9, 2010.
27. Hancock K, Veguilla V, Lu X et al. Cross-reactive antibody responses to the 2009 pandemic H1N1 influenza virus. N Engl J Med 2009;361:1945–1952.
28. Thomas RE, Jefferson T, Lasserson TJ. Influenza vaccination for healthcare workers who work with the elderly. Cochrane Database Syst Rev 2010;16:344–356.
29. Thomas RE, Jefferson TO, Demicheli V et al. Influenza vaccination for health-care workers who work with elderly people in institutions: A systematic review. Lancet Infect Dis 2006;6:273–279.
30. Looijmans-van den Akker I, van Delden JJ, Verheij TJ et al. Which determinants should be targeted to increase influenza vaccination uptake among health care workers in nursing homes? Vaccine 2009;27:4724–4730.