Incidence of Influenza A(H1N1) pdm09 Infection, United Kingdom, 2009–2011

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We conducted a longitudinal community cohort study of healthy adults in the UK. We found significantly higher incidence of influenza A(H1N1)pdm09 infection in 2010–11 than in 2009–10, a substantial proportion of subclinical infection, and higher risk for infection during 2010–11 among persons with lower preinfection antibody titers.

The epidemiology of A(H1N1)pdm09 in the United Kingdom during 2009–2011 was characterized by 3 distinct waves: first wave, April–August 2009; second wave, September 2009–April 2010; and third wave, August 2010–April 2011. We report results from a community-based longitudinal cohort study that compared the epidemiology of influenza A(H1N1)pdm09 infection over the second and third waves. The North West London Research Ethics Committee approved this study (reference 09/H0724/27).

case-based population-level surveillance and cross-sectional serologic surveys to estimate incidence and patterns of influenza infection are limited by the lack of accurate denominator data, inability to account for subclinical infections, difficulties in distinguishing between antibodies induced by natural infection and vaccination, and use of samples from high-risk groups. For these reasons, community-based longitudinal studies are ideal to estimate the incidence of infection and spectrum of illness. However, studies of this design describing the 2009 pandemic of influenza A(H1N1)pdm09, reported only from Hong Kong, Singapore, and Vietnam, examine only the 2009–10 season (1–3).

The incidence of A(H1N1)pdm09 virus HI titers >32 (prevalence rates for England (4)). Incident infection was defined as antibody seroconversion (4-fold rise in HI titer) in paired serum samples collected at the start and end of a wave among unvaccinated persons (because HI assay cannot differentiate infection from vaccination) or detection of A(H1N1)pdm09 virus in nasal swabs. The incidence of infection was estimated for the second and third waves as the proportion of incident infections among unvaccinated participants.

Development of any symptoms was recorded on a Web-based questionnaire emailed to participants every 3 weeks. The average response rate was 75%. Illness episodes were categorized as acute respiratory infection (episode with any symptoms), influenza-like illness ([ILI] episode with fever plus cough or sore throat), and fever (recorded temperature ≥38°C) alone. Visits to primary care or hospital during illness were also recorded. Data were analyzed using Stata version 9.0 (StataCorp, College Station, TX, USA) with the χ2 test to compare proportions and t test to compare means after checking for normal distribution by assessing for kurtosis, skewness, and the Shapiro-Wilk test. Hosmer-Lemeshow test was used to estimate goodness-of-fit for each logistic regression.

At recruitment, after the first pandemic wave, A(H1N1) pdm09 seroprevalence was 26% (95% CI 21.4–31.2), with seroprevalence significantly higher in participants 18–25 years of age than in older age groups (Table 1). Participants with ILI in the preceding 3 months corresponding to the first wave had significantly higher (p<0.001) mean A(H1N1) pdm09 virus HI titers, which in conjunction with the age distribution, suggests first-wave infection rather than cross-reactive antibodies (5). Overall cumulative incidence

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The Study

A total of 342 healthy adult staff and students of Imperial College London (London, UK) were recruited during September–November 2009 and followed for 2 consecutive influenza seasons: 2009–10 and 2010–11 (Figure 1). Participants’ median age was 28 years (interquartile range 20–36 years); 83% were <40 years of age. At each time point, collected serum samples were tested for antibodies to A(H1N1)pdm09 virus (A/England/195/09 strain) by the hemagglutination-inhibition (HI) assay (4). Participants were asked to record temperature, self-sample, and return nasal swabs when experiencing influenza-like symptoms. Swabs were tested for respiratory viruses with standardized real-time reverse transcription PCR. Influenza seroprevalence rates were defined as the proportion of persons with HI titers ≥32 (4).

Because our study began at the end of the first pandemic wave, cumulative incidence of A(H1N1)pdm09 infection over the first wave was estimated as the difference between age-specific seroprevalence rates at recruitment (T0 in Figure 1) and published prepandemic (2008) seroprevalence rates for England (4). Incident infection was defined as antibody seroconversion (4-fold rise in HI titer) in paired serum samples collected at the start and end of a wave among unvaccinated persons (because HI assay cannot differentiate infection from vaccination) or detection of A(H1N1)pdm09 virus in nasal swabs. The incidence of infection was estimated for the second and third waves as the proportion of incident infections among unvaccinated participants.

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Incidence of Influenza A(H1N1)pdm09 infection during the first wave was 12.7% (95% CI 7.1%–18.4%) and 26.6% (95% CI 15.3%–37.8%) among participants 18–25 years of age with no increase in older age groups (online Technical Appendix Table 1, wwwnc.cdc.gov/EID/articlepdfs/19/11/13-0295-Techapp1.pdf).

The incidence of infection over the third pandemic wave was significantly higher (p = 0.02) than over the second wave (Figure 1). Among participants with prewave titers <8, the incidence of infection was significantly higher over the third wave than over the second wave (p<0.001); incidence did not differ for participants with prewave titers >8 (Table 2, Appendix, wwwnc.cdc.gov/EID/article/19/11/13-0293-T2.htm). Age-specific incidence was significantly higher (p = 0.01) over the third wave than the second wave among participants 26–40 years of age (third wave: 25.4% [95% CI 15.2–35.5]; second wave: 10.9% [95% CI 5.1–16.7]) but not the other age groups (Table 2, Appendix). For 11 infected participants with paired serum samples and virus detected in nasal swabs, 2 (18%) did not show antibody seroconversion (online Technical Appendix Table 2).

During an illness episode, 20% of infected participants reported fever or ILI, 17% visited their general practitioner, and none visited a hospital (Figure 2). Because predictions...
of a small third pandemic wave were disproved (4), the reasons for this large wave remained unclear. Multivariate logistic regression was undertaken with infection as the dependent variable and age, sex, and prewave titers as independent variables. Each doubling increase in prewave HI titers, after adjustment for age and sex, was associated with increased risk for A(H1N1)pdm09 infection associated with protection against symptomatic illness (7). Although these nonseroconverters might have antibodies detectable by microneutralization assay, such nonseroconverters, undetectable by serosurveys using the standard HI assay, further highlight the possibility of underestimating community infection rates when cross-sectional serosurveys alone are used.

Despite our intensive symptom ascertainment, 4 participants with influenza reported no symptoms. Cross-reactive cellular immune responses that are highly prevalent in the population (13) have recently been shown to be associated with protection against symptomatic illness (14).

Our analysis of pandemic influenza in a community cohort over successive seasons offers insight into...
Figure 2. Proportion of influenza A(H1N1)pdm09–infected persons who had symptoms during their illness episode during the second wave (September 2009–April 2010), third wave (August 2010–April 2011), and entire study period, United Kingdom. Proportion of persons with reported symptoms over the study period is combined from the second and third waves. Symptoms were recorded by a Web-based symptom questionnaire emailed to participants every 3 weeks. Symptoms associated with illness episode were acute respiratory infection (ARI; illness episode with any symptoms), influenza-like illness (ILI; episode with fever plus cough or sore throat), fever (recorded temperature ≥38°C) alone, or visit to a general practitioner (GP). The graph depicts the average with 95% CIs calculated by using binomial distribution.

Contributors of the unexpectedly larger third pandemic wave. Our analysis also highlights the necessity of using cohorts to complement routine case-based surveillance to estimate influenza burden.

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References


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