Poultry Market Closures and Human Infection with Influenza A(H7N9) Virus, China, 2013–14


Closure of live poultry markets was implemented in areas affected by the influenza virus A(H7N9) outbreak in China during winter, 2013–14. Our analysis showed that closing live poultry markets in the most affected cities of Guangdong and Zhejiang provinces was highly effective in reducing the risk for H7N9 infection in humans.

A novel avian influenza A(H7N9) virus was first identified in China during March 2013, and by March 25, 2014, it had caused 390 laboratory-confirmed human cases in mainland China. The majority of patients with laboratory-confirmed cases reported recent exposure to live poultry markets (LPMs) in urban areas (1, 2), and the H7N9 virus has been identified in LPMs in affected areas (3–6). Temporary closure of LPMs in Shanghai, Nangjing, Hangzhou, and Huzhou during the 2013 spring outbreak of influenza was associated with immediate and substantial reductions in incidence of confirmed H7N9 infection in those cities (7).

Although few confirmed human H7N9 infections were identified in the summer and autumn of 2013, the virus reemerged during the winter of 2013–14, and 251 confirmed cases were reported during December 1, 2013–March 25, 2014, mostly from cities in Guangdong Province in southeastern China and cities in Zhejiang Province in eastern China. In response to the identification of H7N9 in humans, poultry, or the environment, local authorities of affected cities implemented various control measures, the highest profile of which was closure of LPMs. The objective of our study was to estimate the effect of closure of LPMs in reducing incidence of human infections with H7N9 in the most affected cities of Guangdong and Zhejiang provinces during the 2013–14 winter outbreak.

The Study

During December 1–March 25, 2014, a total of 93 and 89 confirmed human H7N9 cases were reported in Guangdong and Zhejiang provinces, respectively. In response to local cases, many urban areas introduced LPM closures for varying durations. To estimate the effect of these interventions, we used the same methods applied to estimate the effect of LPM closures in cities in eastern China in April 2013 (7). We selected 9 specific areas where LPMs were closed for ≥7 consecutive days, ≥3 H7N9 cases were reported in that local urban area during the study period of December 1, 2013–March 7, 2014, and ≥1 case was confirmed before the local LPM closure (Table). The dates of these interventions in relation to the dates of onset of illness of the 69 confirmed human cases in these 9 areas are shown in Figure 1 (http://wwwnc.cdc.gov/EID/article/20/11/14-0556-F1.htm).

In our analysis we assumed the following: 1) the incidence rate of human infection with H7N9 was constant for the 2 weeks before the implementation of LPM closure in each area; 2) the incidence rate of human infection with H7N9 during the LPM closure period had a different rate from the pre-closure period and was also constant, so the ratio of incidence rates during closure versus before closure indicates the effect of LPM closure, and an incidence rate <1 indicated a reduction in incidence; and 3) illness onset in each human case-patient occurred after an incubation period based on a stochastic incubation period distribution. We further assumed that the incubation periods of cases among humans in all cities followed the same lognormal distribution. The start date of the study time horizon for a given area was either 14 days before the start date of LPM closure or the onset date of the first confirmed local

Author affiliations: School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong Special Administrative Region, China (P. Wu, J.T. Wu, L. Wei, B. Yang, V.J. Fang, T.K. Tsang, E.H.Y. Lau, G.M. Leung, B.J. Cowling); Division of Infectious Disease, Key Laboratory of Surveillance and Early-warning on Infectious Disease, Chinese Center for Disease Control and Prevention, Beijing, China (H. Jiang, H. Zhou, J. Yang, Y. Qin, M. Li, J. Zheng, Y. Cao, Z. Li, L. Feng, H. Yu); Zhejiang Provincial Centre for Disease Control and Prevention, Hangzhou, China (E. Chen, C. Chai); Guangdong Provincial Centre for Disease Control and Prevention, Guangzhou, China (J. He, H. Zhong); CAS Key Laboratory of Pathogenic Microbiology and Immunology, Institute of Microbiology, Chinese Academy of Sciences, Beijing (G.F. Gao); and Office of Director-General, Chinese Center for Disease Control and Prevention, Beijing (G.F. Gao)

DOI: http://dx.doi.org/10.3201/eid2011.140556

These authors are joint first authors.

These authors are joint senior authors.
H7N9 case in 2014, whichever was later. The end date of the study time horizon was either the last day of local LPM closure or March 7, 2014, whichever was earlier, to allow for a possible delay of case notification for 2–3 weeks.

Our model therefore included these parameters: the incidence rates before and after closure in each city and the parameters of the incubation period distribution. We estimated these parameters using Markov chain Monte Carlo method (online Technical Appendix, http://wwwnc.cdc.gov/EID/article/20/11/14-0556-Techapp1.pdf), using flat priors for the logarithms of the incidence rate before closure and the incidence rate ratio, a lognormal distribution with mean of 3.3 days and 97.5th percentile 5.7 days for the incubation period, and a lognormal distribution with mean of 0.76 and 97.5th percentile 5.2 for the coefficient of variation of the incubation period corresponding to the posterior distribution from our previous analysis (7). After estimating separate effects of LPM closure in each urban area, we fitted an overall model, assuming the incubation period remained constant across all areas.

Point estimates of the effectiveness of LPM closure varied from 61% to 89% in the 4 areas in Guangdong Province, and from 70% to 89% in the 5 areas in Zhejiang Province with generally wide CIs, and the effectiveness was estimated to be 97% (95% CI 89%–100%) in the overall model, assuming the same incidence rate ratio associated with LPM closure in each area (Figure 2). In the latter model, the incubation period distribution had a mean of 3.4 days (95% CI 2.2–5.0) and 95th percentile of 4.8 days.

As in our previous analysis of LPM closures in April 2013 (7), here we found that LPM closures were effective in reducing human risk for H7N9 infection in cities in Guangdong and Zhejiang provinces during the 2013–14 winter outbreak. The relatively short closure periods and the small number of cases in each city prohibited area-specific estimates of effectiveness that had narrow credibility intervals (Figure 2). In addition, the effect of LPM closure estimated here may incorporate other contemporaneous interventions as well as potential reductions in poultry consumption and population exposure to live poultry associated with the H7N9 outbreak (8), seasonal variation of avian influenza cases as observed in H5N1 infections, decl ine in media coverage, decline in seeking of health care by possible patients, and decreased laboratory testing output related to staff fatigue during the second wave of the epidemic.

Although our results support the effectiveness of LPM closure in protecting human health, closure of LPMs is a temporary and drastic measure that may be associated with substantial costs to society and the poultry industry (9). More sustainable interventions are needed. In the special administrative region of Hong Kong, LPM rest days, on which stalls are cleared of unsold poultry and disinfected, have been used since 2001 to reduce the amplification of avian influenza viruses in LPMs (10,11). Ideally, improved surveillance of avian viruses in poultry would enhance identification and closure of contaminated markets and un-contaminated markets could remain open.

Our findings are limited by the ecologic nature of our analysis. It is possible that the incidence rate of human infection with H7N9 in a city appeared to decline substantially at the same time LPMs were closed in that city for reasons other than the closure of LPMs or by chance. Information about the prevalence of H7N9 virus in poultry in different markets and the distribution network of poultry farms and markets would support construction of more complex models of the underlying transmission dynamics. Another limitation was that we could not include interventions used in locations where LPMs were not closed. Our analysis was designed to be self-controlled by comparing...
Poultry Market Closures and Influenza A(H7N9), China

incidence of human cases before and after market closures. Finally, we could not examine the effect of LPM closures in other locations that had few cases during winter 2013–14. In general, our findings apply to urban areas, where live poultry purchases mainly occur in LPMs.

Conclusions
Closure of live poultry markets was highly effective in reducing human risk for H7N9 infection during winter months of the 2013–14 influenza season. However, preventive actions such as enhanced surveillance of poultry and scheduling regular rest days could prevent the necessity of using this costly intervention.

Acknowledgments
We thank staff members at county-, district-, prefecture-, and provincial-level centers for disease control at Guangdong and Zhejiang provinces for providing assistance with field investigation, administration, and data collection.

This study was funded by the US National Institutes of Health (Comprehensive International Program for Research on AIDS grant U19 AI51915), the China-U.S. Collaborative Program on Emerging and Re-emerging Infectious Diseases, grants from the Ministry of Science and Technology, China (2012 ZX10004-201), the Harvard Center for Communicable Disease Dynamics from the National Institute of General Medical Sciences (grant no. U54 GM088558), and the Area of Excellence Scheme of the Hong Kong University Grants Committee (grant no. AoE/M-12/06). The funding bodies had no role in study design, data collection and analysis, preparation of the manuscript, or the decision to publish.

G.M.L. has received consulting honoraria from Janssen Pharmaceuticals. B.J.C. reports receipt of research funding from MedImmune, Inc. and Sanofi Pasteur, and consultation fees from Crucell NV.

Dr Peng Wu is a postdoctoral fellow in infectious disease epidemiology at the University of Hong Kong. Her research interests include transmission dynamics of respiratory infections and the effectiveness of control measures.

References

Address for correspondence: Hongjie Yu, Division of Infectious Disease, Key Laboratory of Surveillance and Early-warning on Infectious Disease, Chinese Centre for Disease Control and Prevention, No. 155 Changbai Rd, Changping District, Beijing 102206, China; email: yuhj@chinacdc.cn
Poultry Market Closures and Human Infection with Influenza A(H7N9) Virus, China, 2013–14

Technical Appendix

Statistical Analysis of the Impact of Live Poultry Market Closures on Influenza A(H7N9) Virus Transmission to Humans

We studied the incidence rates of laboratory-confirmed human infection with influenza A(H7N9) virus in selected areas of mainland China in winter 2013-14.

In our analysis we assumed: (1) that the incidence rate of human infection with H7N9 was constant for the 2 weeks prior to the implementation of LPM closure in that area; (2) that the incidence rate of human infection with H7N9 during the LPM closure period was constant with a different rate, so that the ratio of incidence rates during versus prior to closure indicates the impact of LPM closure, with an incidence rate ratio <1 indicating a reduction in incidence; and (3) that illness onset in each human case occurred after an incubation period based on a stochastic incubation period distribution. We further assumed that the incubation periods of human cases in all cities followed the same lognormal distribution. The start date of the study time horizon for a given area was either 14 days before the start date of LPM closure or the onset date of the first confirmed local H7N9 case in 2014, whichever was later. The end date of the study time horizon was either the last day of local LPM closure or 7 March 2014, whichever was earlier, to allow for 2-3 weeks possible delay in case notification.

First, we defined the following:

\( N_i \) is the population size of area \( i \).

\( C_i \) is the date of closure of live poultry market in area \( i \).

\( S_i \) and \( T_i \) are the start and end of study time horizon for area \( i \).

\( X_{t,i} \) is the number of confirmed cases with onset on day \( t \) in area \( i \).
We assumed that the population in area $i$ was subject to a daily per capita force of infection $\pi_{\text{pre},i}/N_i$ before any live poultry market (LPM) was closed and $\pi_{\text{post},i}/N_i$ after all LPMs were closed. New infections in area $i$ occurred according to a Poisson process such that the number of infections on day $t$ was Poisson distributed with mean $\lambda_{\text{pre},i} = p_i \pi_{\text{pre},i}$ for $t \in [S_i, C_i - 1]$ and $\lambda_{\text{post},i} = p_i \pi_{\text{post},i}$ for $t \in [C_i, T]$ where $p_i$ was the ascertainment proportion associated with the confirmed cases in area $i$. We assumed that the incubation period followed the same (cumulative) probability distribution $F$ with mean $\mu$ and coefficient of variation $c$ for all areas. Under these assumptions, the number of cases with onset on day $t$ in area $i$ was Poisson distributed with mean

$$y_{i,t} = \begin{cases} \lambda_{\text{pre},i} & \text{for } S_i \leq t \leq C_i - 1 \\ \lambda_{\text{pre},i}(1 - F(t)) + \lambda_{\text{post},i}F(t) & \text{for } C_i \leq t \leq T_i \end{cases}$$

We estimated the pre- and post-LPM closure and the mean incubation time $\mu$ by fitting the model to the epidemic curve data in the nine areas using Markov Chain Monte Carlo methods (http://www.lce.hut.fi/teaching/S-114.202/k98/mcmc_prac.html). We assumed that $F$ follows a lognormal distribution. The priors of the parameters for $F$ were based on our previous study of the effect of LPM closure on H7N9 incidence (I):

The prior for $\mu$ was a lognormal distribution with mean 3.3 days and 97.5th percentile 5.7 days. The prior for $c$ was a lognormal distribution with mean 0.76 and 97.5th percentile 5.2.

We assumed non-informative flat priors for all other parameters. We implemented Monte Carlo Markov Chain (MCMC) using the Metropolis algorithm to obtain posterior distributions of the parameters. A random step size was chosen for each parameter at every iteration and the variance of the step size for each parameter was automatically adjusted such that the acceptance proportion was between 30% and 70% for each parameter. The MCMC was run for 500,000 iterations for each parameter and the posterior distributions were compiled from the final 70% of the iterations.

Reference