American Journal of Epidemiology

Vol. 182, No. 8
DOI: 10.1093/aje/kwv115
Advance Access publication:
September 26, 2015

Practice of Epidemiology

Estimating the Distribution of the Incubation Periods of Human Avian Influenza A(H7N9) Virus Infections

Victor Virlogeux, Ming Li, Tim K. Tsang, Luzhao Feng, Vicky J. Fang, Hui Jiang, Peng Wu, Jiandong Zheng, Eric H. Y. Lau, Yu Cao, Ying Qin, Qiaohong Liao, Hongjie Yu*, and Benjamin J. Cowling*

* Correspondence to Dr. Hongjie Yu, Division of Infectious Disease, Key Laboratory of Surveillance and Early Warning on Infectious Disease, China Center for Disease Control and Prevention, 155 Changbai Road, Beijing 102206, People's Republic of China (e-mail: yuhj@chinacdc.cn); or Prof. Benjamin J. Cowling, School of Public Health, Li Ka Shing Faculty of Medicine, University of Hong Kong, Hong Kong Special Administrative Region, People's Republic of China (e-mail: bcowling@hku.hk).

Initially submitted December 11, 2014; accepted for publication April 23, 2015.

A novel avian influenza virus, influenza A(H7N9), emerged in China in early 2013 and caused severe disease in humans, with infections occurring most frequently after recent exposure to live poultry. The distribution of A(H7N9) incubation periods is of interest to epidemiologists and public health officials, but estimation of the distribution is complicated by interval censoring of exposures. Imputation of the midpoint of intervals was used in some early studies, resulting in estimated mean incubation times of approximately 5 days. In this study, we estimated the incubation period distribution of human influenza A(H7N9) infections using exposure data available for 229 patients with laboratory-confirmed A(H7N9) infection from mainland China. A nonparametric model (Turnbull) and several parametric models accounting for the interval censoring in some exposures were fitted to the data. For the best-fitting parametric model (Weibull), the mean incubation period was 3.4 days (95% confidence interval: 3.0, 3.7) and the variance was 2.9 days; results were very similar for the nonparametric Turnbull estimate. Under the Weibull model, the 95th percentile of the incubation period distribution was 6.5 days (95% confidence interval: 5.9, 7.1). The midpoint approximation for interval-censored exposures led to overestimation of the mean incubation period. Public health observation of potentially exposed persons for 7 days after exposure would be appropriate.

incubation period; influenza; influenza A(H7N9); influenza A virus

Abbreviations: AIC, Akaike's Information Criterion; CI, confidence interval.

The incubation period of a viral infectious disease is defined as the delay from viral infection to the onset of illness (1). In early 2013, a novel avian influenza virus, influenza A(H7N9) (hereafter called H7N9), emerged in China and caused human infections, some of which were associated with severe disease and death (2). In the majority of laboratory-confirmed human cases of H7N9 infection, patients reported recent exposure to live poultry, typically in the setting of live poultry markets in urban areas (3). These defined occasions for exposure have permitted estimation of the distribution of H7N9 incubation periods. The incubation period is particularly important for defining the period of public health observation of exposed contacts of confirmed H7N9 cases, with the upper 95th percentile of the estimated incubation period distribution being considered a reasonable threshold for the duration of such observation, while even higher percentiles of the distribution might be chosen in some circumstances. Various estimates of the incubation period distribution for human infections with H7N9 virus have been published (4–9). Our objective in the current study was to describe alternative approaches for estimation of the incubation period and to identify reasons for discrepancies between different published estimates.

METHODS

Sources of data

During the 2013–2014 outbreak, all laboratory-confirmed human cases of H7N9 virus infection were reported to the Chinese Center for Disease Control and Prevention, and relevant clinical and epidemiologic data were recorded in an electronic database (4). Data extracted for this study included age, sex, geographical location, and dates of exposure, illness onset, and hospital admission. In the majority of cases, the information on exposure was recorded as intervals of 2 or more days during which infection was thought to have occurred rather than exact dates of presumed infection.

Statistical analyses

For each case i, if infection occurs at time X_i and symptom onset occurs at time Z_i, the incubation period is defined as $T_i = Z_i - X_i$. However, estimation of the incubation period is often complicated because infection events cannot be directly observed. If patient i reports that infection most likely occurred during a period of exposure between times L_i and U_i, where $L_i \leq X_i \leq U_i$, the incubation time is bounded by the interval $(Z - U_i,\ Z - L_i)$. These data are a special type of survival data, and a natural approach would be to "reverse" the time axis, setting Z as the origin and X as the outcome time. "Reversing" the time axis is valid only when the density function for infection is uniform in chronological time (10–12). This condition should be reasonable here in the setting of H7N9, with each exposure interval being relatively short. Moreover, in order to allow for the coarseness of exposure data reported on a daily basis, we added 0.5 to each upper bound and subtracted 0.5 from each lower bound (13).

A subset of cases reported single dates of exposure of 7, 8, 9, or 10 days prior to symptom onset. On further investigation of the original case notification forms or the medical records, it was found that an exact date of exposure at 7 days actually indicated exposure at some uncertain time in the previous week—that is, an incubation period between 0 and 7 days. To account for the possibility that these longer single exposure times were inaccurate, we explored the sensitivity of estimated incubation period distributions by extending the potential period of infection from 0 days to 3 days after the single-exposure date.

The most basic approach to dealing with interval-exposure data is to impute the infection date as the midpoint of any exposure interval, which then permits empirical estimation (13). However, this approach may lead to overestimation of the incubation period distribution, which tends to be right-skewed (14). The "gold standard" approach for nonparametric estimation of a distribution based on interval-censored data is the generalized nonparametric maximum likelihood estimator extension of the Kaplan-Meier estimator developed by Turnbull (15), which simplifies to the empirical distribution function if all exposure times are exactly observed. The incubation period can often be appropriately characterized by a parametric model, which can easily accommodate interval-censored data. The gamma (16), Weibull (4), lognormal (10), exponential (17), and log-logistic (18) distributions have previously been used to describe incubation period distributions. Comparison between models may be made qualitatively through visual comparison with a nonparametric estimate and quantitatively by means of a metric such as Akaike's Information Criterion (AIC) (19).

Table 1. Alternative Parametric Estimates of the Distribution of Influenza A(H7N9) Incubation Periods Based on All Available Exposure Data ($n = 229$) for Influenza A(H7N9) Cases Reported in Mainland China From February 2013 Through August 2014

Model	Incubation Period, days						AIC
	Mean		95th Percentile		99th Percentile		
	Estimate	95% CI[a]	Estimate	95% CI[a]	Estimate	95% CI[a]	
Modified data[b]							
Weibull	3.4	3.0, 3.7	6.5	5.9, 7.1	8.0	7.3, 8.8	326
Gamma	3.3	2.6, 5.9	8.8	7.0, 15.1	12.8	10.4, 21.7	328
Lognormal	3.2	2.9, 3.6	7.2	6.4, 7.9	10.8	9.5, 11.9	336
Log-logistic	3.4	3.0, 3.9	7.7	6.8, 8.5	13.4	11.6, 15.3	347
Exponential	3.2	3.0, 3.5	9.6	8.9, 10.3	14.8	13.7, 15.8	410
Original data							
Weibull	4.4	4.0, 4.9	8.9	8.3, 9.5	11.2	10.3, 12.0	537
Gamma	4.5	2.8, 16.2	11.0	7.2, 37.0	15.6	10.4, 51.1	535
Lognormal	4.2	3.8, 4.7	10.2	9.2, 11.1	16.0	14.1, 17.7	561
Log-logistic	4.7	4.2, 5.2	11.2	10.0, 12.4	20.9	17.8, 24.0	571
Exponential	4.1	3.8, 4.4	12.2	11.3, 13.1	18.7	17.3, 20.2	617

Abbreviations: AIC, Akaike's Information Criterion; CI, confidence interval.
[a] 95% CIs were calculated by means of bootstrapping with 10,000 repetitions.
[b] Modified data were the data for which exact reported exposures of 7, 8, 9, or 10 days prior to symptom onset were modified to exposure during the intervals 0–10, 0–11, 0–12, or 0–13 days prior to symptom onset, respectively.

In this study, the incubation period distributions were first estimated using the interval-censored data and compared between the different parametric models suggested above and the Turnbull model (16). For the parametric models, 95% confidence intervals for mean incubation times and 95th percentiles of the incubation distribution were estimated using a parametric bootstrap with 10,000 resamples (20). Secondly, the incubation period distribution was also estimated using the modified data accounting for the uncertainty about long exposure intervals of 7, 8, 9, or 10 days. We also explored the precision of estimates of the mean and 95th percentile of the incubation period distribution based on cumulative data available at various calendar times. All analyses were conducted using R, version 3.1.1 (R Foundation for Statistical Computing, Vienna, Austria) and the "interval" and "survival" packages in R.

RESULTS

As of August 5, 2014, a total of 438 laboratory-confirmed cases of H7N9 were reported in mainland China. Of these cases, 229 patients had available data on exposure dates. The median age of the 229 patients was 58 years; 68% were male, and 57% lived in urban areas, which was similar to the demographic characteristics of all 438 confirmed cases. The data on exposure intervals are shown in Web Figure 1 (available at http://aje.oxfordjournals.org/). Forty-five percent (104/229) of the patients had single-date exposure data, while the remainder reported exposure intervals of 2 days or longer. Among the 104 cases with single exposure dates, 31 reported single exposures at 7, 8, 9, or 10 days prior to symptom onset.

First, we estimated the incubation period distribution for the crude original data without accounting for the problem of exact exposure dates (Table 1). Using the gamma parametric model (best AIC value), the estimated mean incubation period was 4.5 days, the variance was 11.1 days, and the 95th percentile was 11.0 days. Under the midpoint approximation for interval-censored exposures using the original data, the mean was 5.5 days and the 95th percentile was 8 days.

We then estimated the incubation period distribution using the modified data. Figure 1A compares the various fitted parametric models for the incubation period distribution with the nonparametric maximum likelihood estimator. Visual inspection of the parametric curves in comparison with the Turnbull estimate in Figure 1A confirmed that all of the 2-parameter distributions provided reasonable fits in comparison with the nonparametric estimate of the incubation period distribution, while the exponential distribution was slightly inferior. According to the AIC value (Table 1), the best-fitting parametric distribution was the Weibull distribution (AIC = 326), while the gamma distribution had a very similar fit (AIC = 328), followed by the lognormal (AIC = 336) and log-logistic (AIC = 347) distributions. For the nonparametric Turnbull estimate, the mean incubation period was 3.4 days (95% confidence interval (CI): 1.5, 6.7), the variance was 2.9 days, and the 95th percentile was 6.2 days. For the fitted Weibull distribution (Figure 1C), the mean and variance were 3.4 days (95% CI: 3.0, 3.7) and 2.9 days, respectively, and the 95th percentile was 6.5 days.

In Figure 1B, the midpoint approximation clearly led to overestimation of the incubation period distribution compared with the nonparametric Turnbull estimate and the Weibull model, and the mean of the empirical distribution under the midpoint approximation was 5.5 days, with a 95th percentile of 6.0 days.

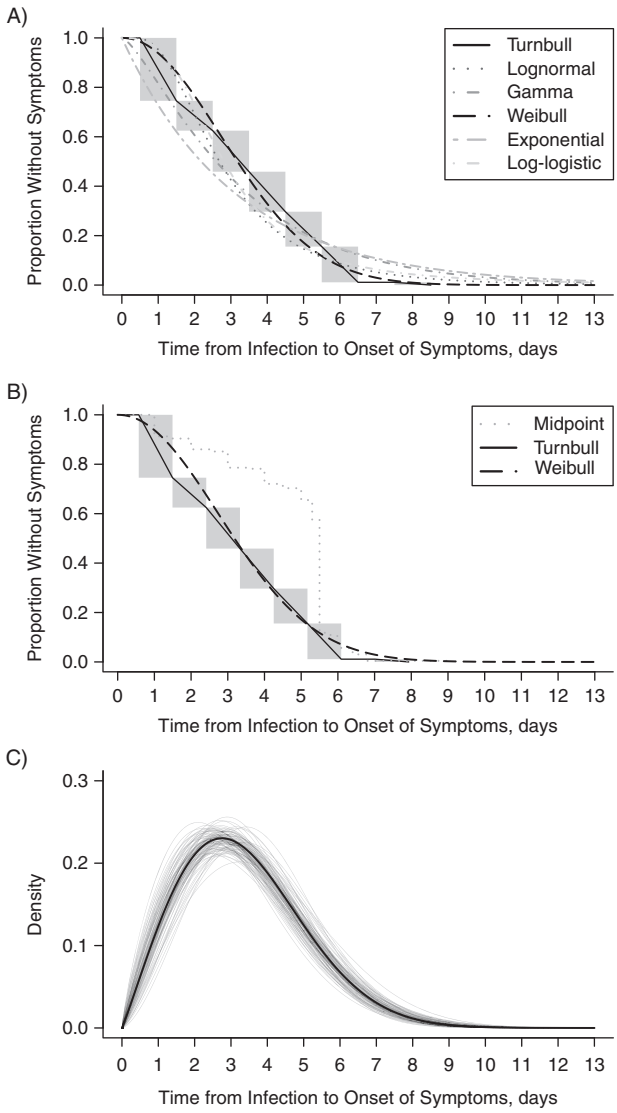

Figure 1. Parametric and nonparametric estimates of the distribution of incubation periods for human avian influenza A(H7N9) virus infections, based on 229 laboratory-confirmed cases with available data on exposure times, China, 2013–2014. A) Comparison of alternative parametric models (lognormal, gamma, Weibull, exponential, and log-logistic) with the nonparametric maximum likelihood estimator (Turnbull). For the nonparametric estimate (Turnbull), gray rectangles show intervals where the estimate was not unique. B) Comparison of the nonparametric maximum likelihood estimator (Turnbull) and the best-fitting parametric model (Weibull) with the empirical distribution using a midpoint approximation for interval-censored exposures (midpoint). C) Probability density function of the Weibull distribution used to estimate the distribution of incubation periods for the 229 cases. The solid black line represents the fitted Weibull distribution, and the gray lines represent the uncertainty range, estimated by bootstrapping with 1,000 resamples.

Table 2. Published Estimates of the Incubation Periods of Human Avian Influenza A(H7N9) Virus Infections, 2013–2014

First Author, Year (Reference No.)	No. of Patients Analyzed	Method	Incubation Period, days			
			Mean	95% CI	Median	Range
Current study	229	Parametric	3.4	3.3, 3.6		
Wu, 2014 (21)	NA[a]	Parametric	3.4	2.2, 5.0		
Yu, 2014 (3)	NA[a]	Parametric	3.3	1.4, 5.7		
Cowling, 2013 (4)	32	Parametric	3.1	2.6, 3.6		
Gao, 2013 (9)	62	Midpoint			5.0	2–8
Gong, 2014 (7)	30	Midpoint			2.0	
Sun, 2014 (8)	16[b]	Midpoint			2.5[b]	
	30[c]				4.0[c]	
Li, 2014 (5)	23	Midpoint			6.0	1–10
Huang, 2014 (6)	22	Midpoint			7.5	2–12.5

Abbreviations: CI, confidence interval; NA, not applicable.

[a] The Yu et al. (3) and Wu et al. (21) studies estimated the incubation period distributions indirectly, via the delay in the impact of live poultry market closures on incidence of human infections in urban areas during the first wave of the epidemic in 2013 and the second wave in 2013–2014, respectively. These studies did not include any data on exposure dates for individual cases.

[b] Rural H7N9 cases.

[c] Urban H7N9 cases.

We reviewed published estimates of the incubation period distribution and found generally higher estimates from studies that used the midpoint approximation (Table 2). Early estimates based on restricted sample size data and median method estimation provided the longest incubation times (5, 6), compared with other studies also based on restricted sample sizes but with single exposure data (7, 8). Our results estimated with interval-censored data were consistent with estimates derived from larger-sample-size studies, with a shorter incubation time (3, 4, 21), while Gao et al. (9) estimated a higher median incubation time based on cases with single exposures.

We estimated the mean and 95th percentile of the incubation period distribution at various times since the beginning of the epidemic using the Weibull distribution (Figure 2). Both estimates were steady over time, with similar point estimates after late April 2013 and increasing precision as sample size increased. This analysis did not account for delays from illness onset to notification, which were approximately 1–3 weeks.

To examine the sensitivity of our results to inclusion of adjustments for patients with single-exposure data, we fitted the different distributions to the data using a different correction for exact exposure dates by extending the potential period of infection from 0 days to 3 days after and before the single-exposure date. We observed similar results (Web Table 1).

DISCUSSION

Using all available data on exposures from 229 patients with laboratory-confirmed H7N9 virus infection, we estimated that the mean incubation period was approximately 3.4 days, and 95% of infections led to symptoms within 6.5 days. This latest estimate of the incubation period distribution is consistent with some previous estimates based on exposure data (mean of 3.1 days (4), median of 2.0 days (7), and medians of 2.5 days (rural) and 4.0 days (urban) (8)) but somewhat shorter than some other estimates (median of 6.0 days (5), median of 7.5 days (6), and median of 5.0 days (9)) (Table 2). These studies with longer incubation periods led the public health authorities to extend the period of medical surveillance or quarantine for close contacts of confirmed cases from 7 days initially to 10 days (22, 23). These discrepancies in estimates could be due to differences in estimation methods and handling of raw data. The midpoint method used in some studies was shown to overestimate the incubation period distribution (Figure 1B), while cleaning the raw data on longer exposures (Web Figure 1) also led to shorter estimates.

Our estimates are concordant with smaller-sample-size studies based on parametric methods with interval exposure data (4), as well as on inference from ecological data, based on the impact of live poultry market closures in reducing the incidence of human infection (3, 21). Moreover, we showed that our estimates were steady over time, and reasonable estimates were available based on data from 50 cases (Figure 2). Our results suggest that incubation periods of 8–10 days are unlikely, while medical surveillance for exposed persons would be appropriate for no more than 7 or 8 days, since 97% and 99% of cases, respectively, would show symptoms within those periods. The Chinese Center for Disease Control and Prevention and the World Health Organization now recommend a 7-day observation period for exposed persons (24, 25), although some other organizations continue to recommend 10 days (22, 23).

Similar observations between midpoint imputation and parametric estimates were previously observed in the case of influenza A(H5N1). Despite the small number of available data, Huai et al. (26) reported in 2008 an overall median incubation period of 5 days (range, 2–9.5 days) for a cohort of 24 patients using midpoint imputation, whereas Cowling

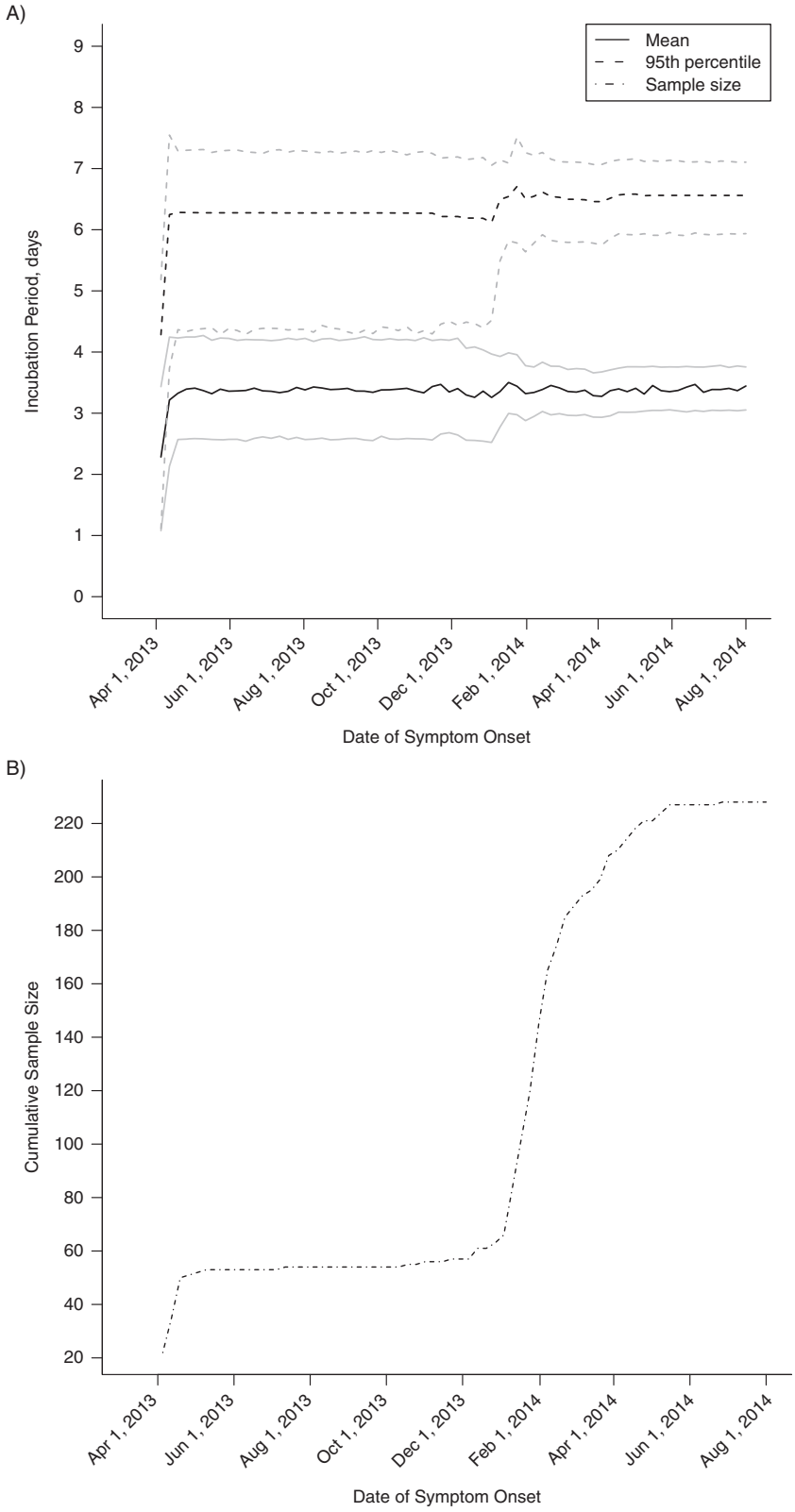

Figure 2. Estimated mean incubation time and 95th percentile of incubation times for human avian influenza A(H7N9) virus infections (estimated on the basis of cumulative data available at different times during the epidemic), by date of symptom onset (A), and cumulative sample size by date of symptom onset (B), China, 2013–2014. In part A, the black solid line shows the mean incubation period over time, and the black dashed line shows the 95th percentile of the incubation period distribution, while the gray solid and dashed lines show the corresponding 95% confidence intervals. Part B shows the cumulative number of cases with available data on exposure.

et al. (4) more recently reported a mean incubation period of 3.3 days (95% CI: 2.7, 3.9) for a cohort of 41 patients after accounting for interval censoring. Although midpoint imputation can provide practical estimates during the early stages of an emerging epidemic with potentially scarce data, the consequent bias in estimates that we identified in this approach shows the advantage of assessing the incubation period distribution with appropriate techniques.

Our study had some limitations, as only a subset of the patients registered in the Chinese Center for Disease Control and Prevention database had available data on potential exposures (229/438; 52%). Moreover, a substantial number of patients reported wide exposure intervals (Web Figure 1). With a very small sample size, it would be difficult to use parametric or nonparametric methods to estimate the incubation period distribution with accuracy and precision, and one of the priorities with an emerging infection is comprehensive investigation of the early cases to define the epidemiologic parameters.

In conclusion, for emerging infectious diseases, accurate and precise estimates of the distribution of incubation times are necessary to inform public health policy and to specify case definitions. Robust inference accounting for interval censoring of exposures is recommended when estimating the incubation period distribution (10).

ACKNOWLEDGMENTS

Author affiliations: Department of Biology, Ecole Normale Supérieure de Lyon, Lyon, France (Victor Virlogeux); School of Public Health, Li Ka Shing Faculty of Medicine, University of Hong Kong, Hong Kong Special Administrative Region, China (Victor Virlogeux, Tim K. Tsang, Vicky J. Fang, Peng Wu, Eric H. Y. Lau, Benjamin J. Cowling); and Division of Infectious Disease, Key Laboratory of Surveillance and Early Warning on Infectious Disease, Chinese Center for Disease Control and Prevention, Beijing, China (Ming Li, Luzhao Feng, Hui Jiang, Jiandong Zheng, Yu Cao, Ying Qin, Qiaohong Liao, Hongjie Yu).

Victor Virlogeux and Ming Li are joint first authors.

This study was funded by the Harvard Center for Communicable Disease Dynamics (grant U54 GM088558 from the US National Institute of General Medical Sciences), a commissioned grant from the Health and Medical Research Fund of the Health, Welfare and Food Bureau of the Hong Kong SAR Government, the Area of Excellence Scheme of the Hong Kong University Grants Committee (grant AoE/M-12/06), the US National Institutes of Health (Comprehensive International Program for Research on AIDS grant U19 AI51915), and the Chinese Ministry of Science and Technology (grant 2012 ZX10004-201).

We thank staff members of the Bureau of Disease Control and Prevention and Health Emergency Response Office of the National Health and Family Planning Commission and provincial and local departments of health for providing assistance with administration and data collection. We also thank staff members at the county-, prefecture-, and provincial-level Center for Disease Control and Prevention offices in the provinces where human influenza A(H7N9) cases occurred for providing assistance with field investigation, administration, and data collection.

The funding bodies played no role in the study design, data collection and analysis, the preparation of the manuscript, or the decision to publish. The views expressed are those of the authors and do not necessarily represent the policy of the Chinese Center for Disease Control and Prevention.

B.J.C. has received research funding from MedImmune Inc. (Gaithersburg, Maryland) and Sanofi Pasteur (Lyon, France) and consults for Crucell N.V. (Leiden, the Netherlands).

REFERENCES

1. Vynnycky E, Fine PE. Lifetime risks, incubation period, and serial interval of tuberculosis. *Am J Epidemiol*. 2000;152(3):247–263.
2. Gao R, Cao B, Hu Y, et al. Human infection with a novel avian-origin influenza A (H7N9) virus. *N Engl J Med*. 2013;368(20):1888–1897.
3. Yu H, Wu JT, Cowling BJ, et al. Effect of closure of live poultry markets on poultry-to-person transmission of avian influenza A H7N9 virus: an ecological study. *Lancet*. 2014;383(9916):541–548.
4. Cowling BJ, Jin L, Lau EHY, et al. Comparative epidemiology of human infections with avian influenza A H7N9 and H5N1 viruses in China: a population-based study of laboratory-confirmed cases. *Lancet*. 2013;382(9887):129–137.
5. Li Q, Zhou L, Zhou M, et al. Epidemiology of human infections with avian influenza A(H7N9) virus in China. *N Engl J Med*. 2014;370(6):520–532.
6. Huang Y, Xu K, Ren DF, et al. Probable longer incubation period for human infection with avian influenza A(H7N9) virus in Jiangsu Province, China, 2013. *Epidemiol Infect*. 2014;142(12):2647–2653.
7. Gong Z, Lv H, Ding H, et al. Epidemiology of the avian influenza A (H7N9) outbreak in Zhejiang Province, China. *BMC Infect Dis*. 2014;14:244.
8. Sun J, Gong Z, Lv H, et al. Comparison of characteristics between patients with H7N9 living in rural and urban areas of Zhejiang Province, China: a preliminary report. *PLoS One*. 2014;9(4):e93775.
9. Gao H-N, Lu H-Z, Cao B, et al. Clinical findings in 111 cases of influenza A (H7N9) virus infection. *N Engl J Med*. 2013;368(24):2277–2285.
10. Cowling BJ, Muller MP, Wong IO, et al. Alternative methods of estimating an incubation distribution: examples from severe acute respiratory syndrome. *Epidemiology*. 2007;18(2):253–259.
11. Lindsey JC, Ryan LM. Tutorial in biostatistics methods for interval-censored data. *Stat Med*. 1998;17(2):219–238.
12. De Gruttola V, Lagakos SW. Analysis of doubly-censored survival data, with application to AIDS. *Biometrics*. 1989;45(1):1–11.
13. Farewell VT, Herzberg AM, James KW, et al. SARS incubation and quarantine times: when is an exposed individual known to be disease free? *Stat Med*. 2005;24(22):3431–3445.
14. Sartwell PE. The distribution of incubation periods of infectious disease. *Am J Hyg*. 1950;51(3):310–318.
15. Turnbull BW. The empirical distribution function with arbitrarily grouped, censored and truncated data. *J R Stat Soc Series B Methodol*. 1976;38(3):290–295.

16. Nishiura H. Early efforts in modeling the incubation period of infectious diseases with an acute course of illness. *Emerg Themes Epidemiol*. 2007;4:2.
17. Nishiura H, Inaba H. Estimation of the incubation period of influenza A (H1N1-2009) among imported cases: addressing censoring using outbreak data at the origin of importation. *J Theor Biol*. 2011;272(1):123–130.
18. Hien TT, Boni MF, Bryant JE, et al. Early pandemic influenza (2009 H1N1) in Ho Chi Minh City, Vietnam: a clinical virological and epidemiological analysis. *PLoS Med*. 2010; 7(5):e1000277.
19. Lindsey JK. A study of interval censoring in parametric regression models. *Lifetime Data Anal*. 1998;4(4):329–354.
20. Harrell FE Jr. *Regression Modeling Strategies with Applications to Linear Models, Logistic Regression, and Survival Analysis*. (Springer Series in Statistics). New York, NY: Springer Publishing Company; 2001.
21. Wu P, Jiang H, Wu JT, et al. Poultry market closures and human infection with influenza A(H7N9) virus, China, 2013–14. *Emerg Infect Dis*. 2014;20(11):1891–1894.
22. Centers for Disease Control and Prevention, US Public Health Service. Interim guidance on follow-up of close contacts of persons infected with novel influenza A viruses associated with severe human disease and on the use of antiviral medications for chemoprophylaxis. http://www.cdc.gov/flu/avianflu/h7n9-av-chemoprophylaxis-guidance.htm. Updated April 7, 2015. Accessed April 9, 2015.
23. Centre for Health Protection, Department of Health, Government of the Hong Kong Special Administrative Region. Update of human case of avian influenza A(H7N9). http://www.chp.gov.hk/en/view_content/37581.html. Published 2012. Updated December 28, 2014. Accessed April 9, 2015.
24. World Health Organization. Avian influenza. http://www.who.int/mediacentre/factsheets/avian_influenza/en/. Updated March 2014. Accessed March 5, 2015.
25. National Health and Family Planning Commission, People's Republic of China. National Health and Family Planning Commission notice on the issuance of human infection with H7N9 bird flu prevention and control program (third edition). https://translate.google.com/translate?sl=auto&tl=en&js=y&prev=_t&hl=en&ie=UTF-8&u=http%3A%2F%2Fwww.nhfpc.gov.cn%2Fjkj%2Fs3577%2F201401%2F8c1828375a7949cd85454a76bb84f23a.shtml&edit-text=. Updated January 29, 2014. Accessed March 9, 2015.
26. Huai Y, Xiang N, Zhou L, et al. Incubation period for human cases of avian influenza A (H5N1) infection, China. *Emerg Infect Dis*. 2008;14(11):1819–1821.