Effectiveness of Live Poultry Market Interventions on Human Infection with Avian Influenza A(H7N9) Virus, China

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Various interventions for live poultry markets (LPMs) have emerged to control outbreaks of avian influenza A(H7N9) virus in mainland China since March 2013. We assessed the effectiveness of various LPM interventions in reducing transmission of H7N9 virus across 5 annual waves during 2013–2018, especially in the final wave. With the exception of waves 1 and 4, various LPM interventions reduced daily incidence rates significantly across waves. Four LPM interventions led to a mean reduction of 34%–98% in the daily number of infections in wave 5. Of these, permanent closure provided the most effective reduction in human infection with H7N9 virus, followed by long-period, short-period, and recursive closures in wave 5. The effectiveness of various LPM interventions changed with the type of intervention across epidemics. Permanent LPM closure should be considered to maintain sufficient effectiveness of interventions and prevent the recurrence of H7N9 epidemics.

Human infections with avian influenza A(H7N9) virus were laboratory confirmed in China in the spring of 2013 (*1*). Since then, 1,567 human cases and 615 fatal cases have been officially reported in 5 epidemic waves (February–September 2013, October 2013–September 2014, October 2014–September 2015, October 2015–September 2016, and October 2016–September 2017) as of March 2, 2018 (*2*). Compared with the previous 4 epidemic waves, the 2016–17 fifth wave raised global concerns because of several characteristics. First, a surge in laboratory-confirmed cases of H7N9 virus infection was observed in wave 5, along with some clusters of limited human-to-human transmission (*3*,*4*). Second, a highly pathogenic avian influenza H7N9 virus infection was confirmed in Guangdong Province and has caused further human infections in 3 provinces (*5*,*6*). The genetic divergence of H7N9 virus, its geographic spread (*7*), and a much longer epidemic duration raised concerns about an enhanced potential pandemic threat in 2016–17.

Live poultry markets (LPMs) are a major source of human infections with H7N9 virus; the maintenance, amplification, and dissemination of H7N9 viruses have occurred in LPMs (*8*,*9*). Most human patients were exposed to H7N9 viruses through direct exposure to infected poultry or indirect exposure in contaminated environments, which increased the risk of H7N9 infections (*9*). Closure of LPMs is thus considered to play a key role in reducing the risk of animal-to-human transmission of H7N9. Different levels of LPM interventions were implemented in different geographic areas during 2013–2018. Permanent and temporary LPM closures were the main measures used to reduce the exposures of human population to H7N9 virus and reduce transmission (*10*,*11*). In some counties, alternative practices to complete bans of LPMs have also been put in place, such as bans on overnight poultry storage combined with regular cleaning and disinfection or market rest days (*12*).

So far, the effectiveness of LPMs interventions in controlling H7N9 epidemics has been discussed in several studies. In comparison with the previous 4

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epidemic waves, a quantitative effectiveness assessment of LPM closure on the fifth H7N9 epidemic wave has not yet been conducted. Moreover, previous studies investigated the effect of the occurrence of LPM closure on controlling the H7N9 epidemic only by directly comparing the detection and isolation rates of H7N9 virus in the environment (*13*,*14*), investigating the number of H7N9 cases (*10*,*15*), or evaluating the posterior estimates of H7N9 incidence using transmission models before and after LPM closure (*16*–*18*). Although such modeling studies have quantified the effectiveness of LPM closure, inaccurate estimates of the effectiveness may have arisen because they did not account for the full characteristics of the LPM interventions (e.g., the type, start date, and duration of the interventions) and the underlying natural transmission dynamics of H7N9. In particular, neglecting the natural transmission dynamics of H7N9 may have led to underestimates or overestimates of the effectiveness of LPM closure if the interventions were implemented before or after the epidemic peak. Given the limitations of previous studies and variations in the implementation of LPM interventions in different geographic areas, there is a need to consider the potential effects of the characteristics of various interventions on the control of H7N9 epidemics.

Our study aimed to assess the differences in the effectiveness of various LPM interventions across 5 epidemic waves, especially during the 2016–17 epidemic wave. Specifically, we compared 4 LPM interventions: permanent, long-period, short-period, and recursive closures. We compared the daily incidence rates of H7N9 for different types and closing levels of LPM closure across 5 epidemic waves and quantified the effect of 4 LPM interventions on H7N9 transmission in the 2016–17 epidemic wave.

Materials and Methods

Data Sources

We compiled a database recording the characteristics (e.g., the type, start date, and end date) of LPM closure (Appendix, https://wwwnc.cdc.gov/EID/article/26/5/19-0390-App1.pdf). We initially identified 32 types of LPM closure in cities with ≥1 H7N9 case (Appendix Table 1, Figure 1) and classified them based on the duration of LPM closure and the proportion of closing days. The duration of LPM closure refers to the total number of closing days; the proportion of closing days is equal to the duration of LPM closure divided by the duration of each epidemic wave. Given variations in duration, start dates, and end dates of the 5 H7N9 epidemic waves, it was not reasonable to use similar start and end dates for all epidemic waves to estimate daily incidence rates (DIRs). To give more comparable estimates of DIRs, we set the duration of each epidemic as the period separating the 5th from the 95th percentiles of the days of onset of illness in each wave. First, taking the duration of closure into consideration, we classified LPM closure measures into 4 categories: permanent closure, whereby LPMs were permanently closed within the epidemic wave or for the entire epidemic wave duration; long-period closure (≥14 days within the epidemic wave [*10*,*17*]); short-period closure (<14 days within the epidemic wave); and recursive closure, whereby LPMs were closed for 1 or 2 day with a repetition of the closing over time (the closing might be implemented weekly, biweekly, or monthly). Second, we classified LPM closures according to the proportion of days of closing out of the total epidemic wave duration, using a quantile classification method (i.e., <25%, 25%–75%, and >75% of epidemic wave duration) because of abnormal distributions of the proportions of closing days in waves 1–5 (Appendix Figure 2). We collected the onset date and information on residence for all laboratory-confirmed H7N9 human cases during March 2013–September 2017 from the World Health Organization (https://www.who.int/csr/don/17-january-2017-ah7n9-china), Monthly Risk Assessment Summary reports (https://www.who.int/influenza/human_animal_interface/avian_influenza/archive), websites of the national and provincial Health and Family Planning Commission of China (http://www.nhc.gov.cn), FluTrackers (http://www.flutrackers.com), HealthMap (https://healthmap.com.au), and avian influenza reports from the Centre of Health Protection of Hong Kong (https://www.chp.gov.hk/tc/index.html).

Statistical Analyses

Assessment of Type of LPM Closure on H7N9 DIR

We first assessed the effect of 4 types of LPM closures (recursive, short-period, long-period, and permanent closures) on H7N9 DIRs. We calculated DIR estimates only for counties where >1 H7N9 case was reported in 2013–2017 (Appendix). In addition to looking at the type of the intervention, we also explored the influence of the closing levels of LPM closure (<25%, 25%–75%, and >75% of epidemic wave duration) on DIRs. We used a generalized linear mixed effect model (GLMM) followed by a multiple comparison procedure (Tukey test) to compare DIRs by contrasting counties with no measures to counties with different

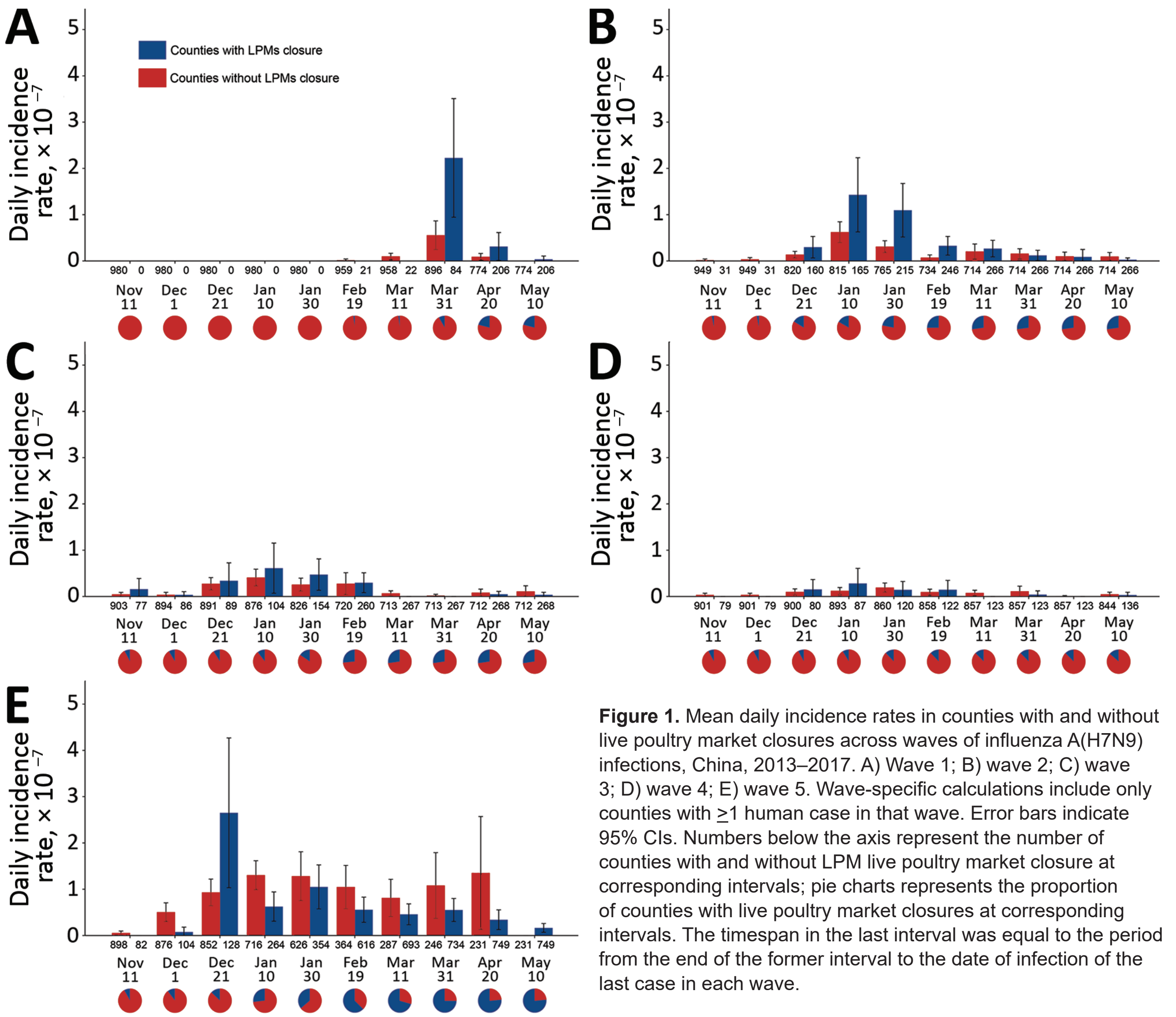

Figure 1. Mean daily incidence rates in counties with and without live poultry market closures across waves of influenza A(H7N9) infections, China, 2013–2017. A) Wave 1; B) wave 2; C) wave 3; D) wave 4; E) wave 5. Wave-specific calculations include only counties with ≥1 human case in that wave. Error bars indicate 95% CIs. Numbers below the axis represent the number of counties with and without LPM live poultry market closure at corresponding intervals; pie charts represents the proportion of counties with live poultry market closures at corresponding intervals. The timespan in the last interval was equal to the period from the end of the former interval to the date of infection of the last case in each wave.

types and closing levels of LPM closure before and after these measures were taken.

Assessment of LPM Interventions on Risk for Animal-to-Human and Human-to-Human Transmission in the 2016–17 Epidemic Wave

To further assess the effect of the type of LPM closure on reduction in H7N9 transmission risk in each site, we constructed an H7N9 transmission model similar to that developed by Yu et al. (*16*) and Virlogeux et al. (*18*) using data from the 2016–17 epidemic wave (Appendix). We included 17 sites (60 districts/counties) with ≥5 urban and semiurban cases in wave 5 (Appendix Figure 3). We compared the reduction in the number of animal-to-human infections before and after closure among 4 LPM interventions using Welch's analysis of variance and multiple comparison (Tamhane's T2 test).

The H7N9 epidemics in 2013–2017 followed a seasonal pattern, with peaks in the winter months and sporadic cases in the summer months. Thus, we considered the reductions in number of infections, together with LPM interventions, to be correlated with the seasonal pattern of the H7N9 epidemics. We incorporated absolute humidity, the most dominant contributor to the H7N9 epidemic, into transmission models to modulate the seasonal pattern of H7N9 epidemic in a sensitivity analysis (Appendix) (*19*,*20*). We assumed the transmissibility of H7N9 virus to be higher at lower absolute humidity in accordance with previous studies (*19*,*20*) and an observed pattern of H7N9 epidemic in the 17 study sites (Appendix Figure 4). In addition, we separated the effect of LPM closure from the natural transmission dynamics of H7N9 viruses by comparing the differences in

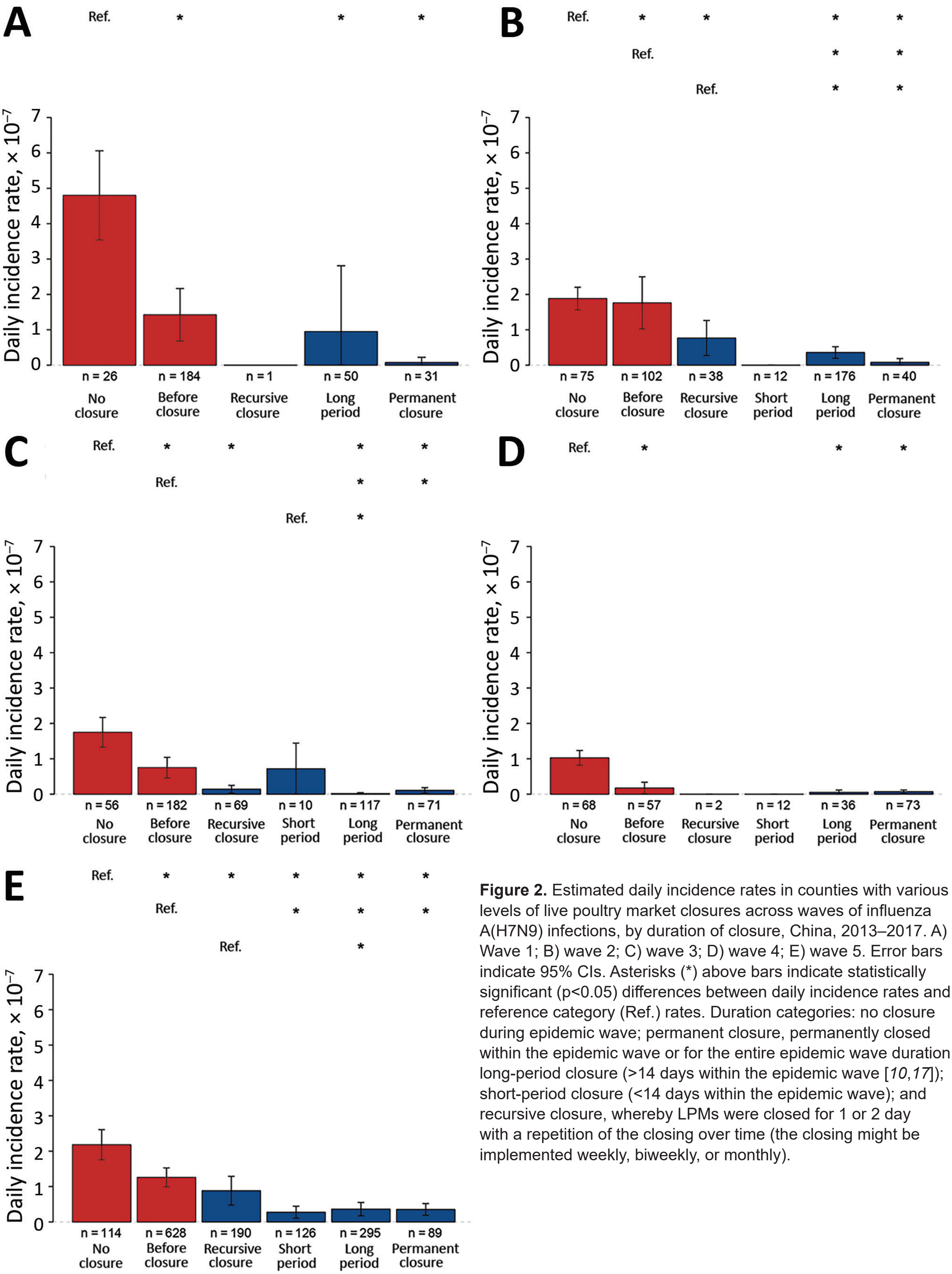

Figure 2. Estimated daily incidence rates in counties with various levels of live poultry market closures across waves of influenza A(H7N9) infections, by duration of closure, China, 2013–2017. A) Wave 1; B) wave 2; C) wave 3; D) wave 4; E) wave 5. Error bars indicate 95% CIs. Asterisks (*) above bars indicate statistically significant ($p<0.05$) differences between daily incidence rates and reference category (Ref.) rates. Duration categories: no closure during epidemic wave; permanent closure, permanently closed within the epidemic wave or for the entire epidemic wave duration; long-period closure (>14 days within the epidemic wave [*10*,*17*]); short-period closure (<14 days within the epidemic wave); and recursive closure, whereby LPMs were closed for 1 or 2 day with a repetition of the closing over time (the closing might be implemented weekly, biweekly, or monthly).

the reductions in the number of infections between 2 sites (1 with and 1 without LPM closure) where a similar season pattern of human H7N9 infections had been observed. We created hypothetical start and end dates of LPM closures in sites without such closures and assumed them to be consistent with those in sites with closures. We used the Mann-Whitney U test to compare the differences of the reductions in the number of infections between the 2 sites.

Results

The comparison over time of DIRs between counties with and without LPM closures (Figure 1) showed that counties with measures had higher DIRs than counties free of closures during 2013–2017. In wave 5, DIRs decreased over time in counties with closures, whereas DIRs for counties without measures remained fairly high. Comparisons of DIRs for counties with different types (Figure 2) and levels (Figure 3) of LPM closure showed that, with the exception of wave 1 and wave 4, showed that DIRs were significantly lower in counties after closure than before ($p<0.001$) (Appendix Table 2). The DIRs in counties after LPM closure were also significantly lower than those estimated for counties without closures ($p<0.001$) (Appendix Table 2). We observed no statistically significant difference between counties with recursive, short-period, long-period, or permanent closures except for counties with recursive, long-period, and permanent closures in wave 2; for counties with short-period and long-period closures in wave 3; and for counties with recursive and long-period closures in wave 5. No DIRs were significantly different among counties with different levels of closing days, but the difference was significant in 25%–75% versus >75% of epidemic wave duration in wave 2.

To further quantify the effectiveness of LPM intervention in each site in wave 5, we compared the reduction in number of daily infections before and after closure among counties with 4 LPM interventions. A total of 142 laboratory-confirmed cases were located in 17 sites in wave 5 (Table 1), which is much higher than the total number of H7N9 cases in these sites in waves 1–4 ($n = 116$). A compilation of the onset dates of illness for these cases (Appendix Figure 5) shows that, with the exception of 4 study sites where human H7N9 epidemics ended before closing LPMs (study sites 8, 10–11, and 14), there was an observable drop in the number of H7N9 cases after LPM intervention in each site. After LPM closure, Gusu District in Suzhou, with permanent closure, had a higher reduction (97.0%, 95% CI 94.0%–100.0%) than other sites. The mean posterior estimates of the reductions ranged from 48% to 98% in sites with long-period closure. Guangzhou implemented recursive measures at the beginning of the epidemic but had a much lower reduction (34.0%, 95% CI 15.0%–70.0%). Compared with Guangzhou, which had short-period closures in the second intervention (73.0%, 95% CI 53.0%–77.0%), Foshan (96%) and Fuzhou (95%) showed larger relative reductions in the daily number of infections. Overall, the mean reduction in daily number of infections increased successively among sites with recursive, short-period, long-period, and permanent closures ($p<0.001$) (Appendix Table 3).

When we examined potential for human-to-human transmission, we found that the estimated effective reproduction number was 0.147 (95% CI 0.034–0.285) (Table 2; Appendix Figure 6). The slightly higher daily number of infections estimated by the model incorporating animal-to-human and human-to-human transmission (Appendix Figure 5) also suggests the potential for human-to-human transmission when compared with those estimates in an animal-to-human transmission model (Appendix Figure 7). Sensitivity analyses examined the influence of mean serial interval and of the proportion of unreported cases on the effective reproduction number. A decrease in the effective reproduction number was observed when the mean serial interval increased (Appendix Table 4). After accounting for the seasonality of H7N9 affected by absolute humidity, estimates of the reduction in number of daily infections changed slightly in some sites (Appendix Table 5), which should not be surprising, because the season pattern of H7N9 epidemics may well vary from one site to another (Appendix Figure 4). After we adjusted for the potential effect of the natural transmission dynamics of H7N9 virus, the net effect of LPM closure varied in study sites with long-period (range 0.5%–52.0%) and permanent (45.0%, 95% CI 32.0%–88.0%) closures in wave 5 (Table 3). In all study sites except 1, the differences in reductions in number of infections among sites with and without closures were statistically significant ($p<0.001$).

Discussion

LPM closing measures have often been implemented reactively, after the occurrence of human H7N9 cases in a given county (Appendix Figure 8); it is thus not surprising to find generally high DIRs in counties that undertook such measures (Figure 1). However, what matters most is what happened to the DIR and mean daily number of illnesses after these closing measures were taken. Both DIRs and mean daily number of illness onsets decreased in counties or sites following

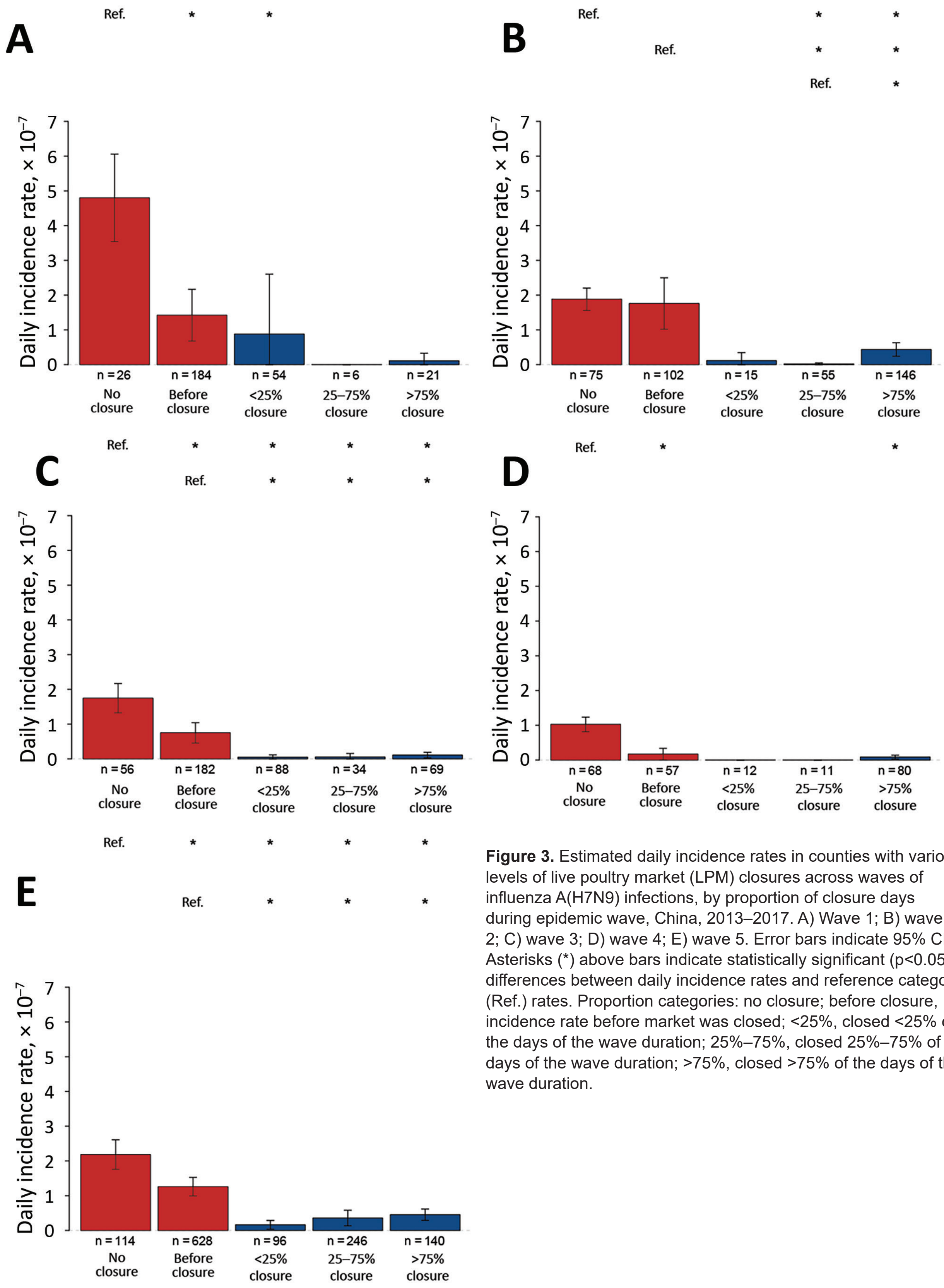

Figure 3. Estimated daily incidence rates in counties with various levels of live poultry market (LPM) closures across waves of influenza A(H7N9) infections, by proportion of closure days during epidemic wave, China, 2013–2017. A) Wave 1; B) wave 2; C) wave 3; D) wave 4; E) wave 5. Error bars indicate 95% CIs. Asterisks (*) above bars indicate statistically significant ($p<0.05$) differences between daily incidence rates and reference category (Ref.) rates. Proportion categories: no closure; before closure, incidence rate before market was closed; <25%, closed <25% of the days of the wave duration; 25%–75%, closed 25%–75% of the days of the wave duration; >75%, closed >75% of the days of the wave duration.

LPM interventions, but the effect varied depending on the type of intervention and epidemic wave.

In general, permanent, long-period, and short-period closures provided comparable estimates in terms of DIR reduction. However, the association between the type and closing levels of LPM measures and DIRs showed different results across waves. For example, the difference in DIRs in counties with dif-

Table 1. Characteristics of study sites in the 2016–17 epidemic wave of influenza A(H7N9), China.

Province	City	District/county, n = 60	Site no., n = 17	No. cases		Type of LPM closure	LPM closures	
				Urban	Semiurban		Start date	End date
Jiangsu	Suzhou	Gusu District	1	19	1	Permanent	2016 Dec 31	Unreported
		Huqiu District, Wujiang District, Wuzhong District, Xiangcheng District	2	12	6	Long-period	2016 Dec 27	Unreported
		Kunshan City	3	5	1	Long-period	2016 Dec 19	Unreported
	Wuxi	Xishan District, Binhu District, Huishan District, Liangxi District (Chongan District, Nanchang District, Beitang District), Xinwu District, Jiangyin City	4	9	8	Long-period	2016 Dec 29	2017 Apr 27
	Changzhou	Zhonglou District, Tianning District, Wujin District, Xinbei District, Jintan City, Liyang City	5	8	4	Long-period	2016 Dec 30	2017 Apr 30
	Nantong	Chongchuan District	6	5	0	Long-period	2017 Feb 25	Unreported
Guangdong	Guangzhou	Haizhu District, Tianhe District, Panyu District, Baiyun District	7 7	5	3	Recursive Short-period	2017 Jan 1 2017 Feb 16	2017 Feb 15 2017 Feb 28
	Foshan	Nanhai District, Shunde District	8	1	4	Short-period	2017 Jan 16	2017 Jan 25
Zhejiang	Ningbo	Yuyao City, Cixi City, Fenghua City, Ninghai County	9	1	8	Long-period	2017 Feb 11	Unreported
	Hangzhou	Yuhang District, Xiaoshan District, Linan City, Fuyang City, Chunan County	10	2	5	Long-period	2017 Feb 11	Unreported
	Wenzhou	Dongtou District, Yueqing City, Ruian County, Cangnan County	11	1	4	Long-period	2017 Feb 11	Unreported
	Lishui	Suichang County, Jingning County, Jinyun County, Qingyuan County	12	0	5	Long-period	2017 Feb 11	Unreported
Hunan	Xiangtan	Yuetang District, Yuhu District, Xiangtan County	13	3	2	Long-period	2017 Jan 24	Unreported
Anhui	Suzhou City	Yongqiao District	14	5	0	Long-period	2017 Feb 15	2017 Apr 30
Fujian	Fuzhou	Jinan District, Gulou District, Taijiang District	15	5	0	Short-period	2017 Feb 7	2017 Feb 17
Sichuan	Aba	Jinchuan County, Ruoergai County, Xiaojin County	16	0	5	Recursive	2017 May 10	Unreported
Shanghai	Shanghai	Chongming District, Fengxian District, Jiading District, Jingan District, Jinshan District	17	2	3	Long-period	2017 Jan 28	2017 Apr 30

*Unreported indicates that the end of the LPM closure was not observed before May 31, 2017. LPM, live poultry market.

Table 2. Parameter estimation of infection rates before and after live poultry market closures in the 2016–17 influenza A(H7N9) epidemic wave, China.

Site no.	Type of closure	Expected daily no. infections (95% CI)		Reduction in no. infections after closure, % (95% CI)	Reproduction number (95% CI)
		Before closure	After closure		
1	Permanent	0.230 (0.121–0.372)	0.006 (0.000–0.023)	97.0 (94.0–100.0)	0.147 (0.034–0.285)
2	Long	0.340 (0.171–0.540)	0.034 (0.009–0.073)	90.0 (87.0–95.0)	
3	Long	0.120 (0.037–0.248)	0.010 (0.000–0.033)	92.0 (87.0–100.0)	
4	Long	0.390 (0.183–0.648)	0.018 (0.000–0.064)	95.0 (90.0–100.0)	
5	Long	0.460 (0.231–0.763)	0.008 (0.000–0.033)	98.0 (96.0–100.0)	
6	Long	0.040 (0.014–0.089)	0.022 (0.003–0.058)	48.0 (35.0–81.0)	
7	Recursive	0.162 (0.037–0.229)	0.107 (0.012–0.301)	34.0 (15.0–70.0)	
7	Short	0.107 (0.012–0.301)	0.029 (0.005–0.068)	73.0 (53.0–77.0)	
8	Short	0.190 (0.062–0.379)	0.008 (0.000–0.028)	96.0 (93.0–99.0)	
9	Long	0.120 (0.050–0.220)	0.019 (0.002–0.055)	84.0 (75.0–96.0)	
10	Long	0.090 (0.032–0.176)	0.001 (0.000–0.035)	89.0 (80.0–99.0)	
11	Long	0.110 (0.037–0.229)	0.009 (0.000–0.035)	92.0 (84.0–99.0)	
12	Long	0.090 (0.029–0.193)	0.020 (0.002–0.054)	78.0 (72.0–92.0)	
13	Long	0.220 (0.048–0.518)	0.031 (0.008–0.069)	86.0 (83.0–87.0)	
14	Long	0.190 (0.066–0.374)	0.016 (0.000–0.052)	92.0 (86.0–100.0)	
15	Short	0.350 (0.117–0.728)	0.019 (0.002–0.055)	95.0 (92.0–98.0)	
16	Recursive	0.210 (0.068–0.400)	0.060 (0.002–0.211)	71.0 (47.0–97.0)	
17	Long	0.140 (0.044–0.295)	0.022 (0.003–0.062)	84.0 (79.0–94.0)	

ferent levels of closing days was observed only in wave 2. During this wave, long-period and permanent closures represented the large majority of the measures (82.4% of the closing measures). During wave 5, short-period and recursive closures became available to authorities as potential measures and were implemented more abundantly, especially in cities with few H7N9 cases; thus, long-period and permanent closures represented only 55% of the total closing measures.

For wave 5, we also evaluated the effectiveness of different types of LPM interventions in controlling H7N9 epidemics in several key sites. Overall, the effectiveness of LPM closure varied with the type of the interventions in these sites during 2016–17. Permanent closure was more effective than long-period closure, short-period closure, and recursive closure. The relatively lower effectiveness of short-period closure was observed in wave 5, but the point estimates of the reduction in daily number of infections inferred from the transmission model were consistent with the effectiveness assessment of a 14-day LPM closure (range 53.0%–89.0%) (*17*). Accompanying the effectiveness assessment of consecutive LPM closure, Yuan et al. (*21*) quantified the effectiveness of periodic LPM closure together with daily cleaning and disinfection (range –47.0% to 34.0%), which was consistent with our minimum point estimates of the effectiveness of recursive closure.

The decline in the number of human infections with H7N9 virus varied among study sites. In addition to being a factor of the type of the intervention, the variations in these declines may have been influenced by the underlying natural transmission dynamics of H7N9. After adjustment for absolute humidity, the most dominant environmental driver for influenza seasonality, the reduction in number of infections did not change significantly in any one of the study sites. Therefore, overall estimates of the effect of LPM closure is unlikely to be confounded by those climatic factors. However, we cannot exclude the possibility that the effectiveness of LPM closure may be delayed because of climatic factors at a specific time, as low temperature and higher humidity always drive the spread of H7N9 virus. In addition, we cannot definitively exclude other unknown seasonal confounders, such as the seasonality of poultry movement. Available evidence supports the seasonal effects of poultry movement on human infection with H5N1 virus around Chinese New Year (*22*). Although we found no quantitative evidence that seasonal variation in poultry trade played a role in human infection with H7N9 virus, the fact that the high-risk season of the H7N9 epidemic was consistent with the peak time of poultry trade around Chinese New Year is notable.

Limited human-to-human transmissibility of H7N9 virus was previously observed during waves 1–4 (*3*). Our low estimates of reproduction number in wave 5 were consistent with previous descriptive analysis of possible clusters of human infection with H7N9 virus (*3*,*23*), confirming that human-to-human transmissibility of H7N9 virus remained unsustainable.

Other factors, such as societal economic costs and residents' behavior toward banning live poultry trade, may affect the effectiveness of LPM closure (*24*) and lead to a displacement effect. LPM closure has threatened the wholesale and retail market chain (*25*); local authorities in epidemic areas even tried to control the spread of H7N9 virus by banning live poultry trade. Consequences of such interventions included loss of consumer confidence, decreases in prices of poultry products, and loss of market shares. In an attempt to reduce adverse effects in economic, less disruptive interventions were introduced, such as rest days, banning live poultry overnight, or periodic cleaning and disinfection (*26*,*27*). These LPM interventions proved to be less effective (*28*).

Besides LPM interventions, several key measures (e.g., culling known infected poultry and direct contacts, vaccinating poultry, or improving biosecurity for poultry-handling practices) have been taken to control zoonotic infection with H7N9 viruses (*29*). These measures are always applied in parallel and have gradually changed human behaviors related to the management, transportation, and trade of poultry. Specifically, traditional poultry handling and trade practices have been replaced by central slaughtering and frozen poultry products in major cities in China, which may have substantially reduced the risk of human exposure to infected poultry. The government of China implanted vaccination of poultry against H7N9 virus to control the 2017–18 epidemic wave after the surge in the reported number of cases in wave 5. The introduction of this H5/H7 bivalent inactivated vaccine substantially reduced the number of cases in the 2017–18 epidemic wave (*30*), although its effectiveness needs to be further assessed quantitatively.

This study has several limitations. First, the timing of the implementation of LPM closures in relation to the progress of the H7N9 epidemic was not considered in the effectiveness assessment of LPM closures, which would lead to an overestimation of the effects of LPM closure if LPM interventions were implemented after the epidemic peak. The incidence reduction might also not be comparable in cities with LPM interventions implemented before reaching the epidemic peak with those implemented near the end of the epidemic. Second, our findings focus only on human cases occurring in urban and semiurban areas in China in wave 5, ignoring H7N9 cases in rural areas, where LPMs are rarely located. More rural cases were reported in wave 5 than in previous epidemic waves, and exposure to poultry in farms and backyards were the main sources of these rural human cases (*9*,*31*). Therefore, LPM closure might be less effective in controlling H7N9 epidemics in these rural areas, and other effective interventions (e.g., vaccination of poultry) need to be further explored. Third, because of the ecologic nature of our study, some anthropogenic factors may have acted as potential confounders that can bias our findings, such as the number of LPM visitors, frequency of LPM visits, improvements in biosecurity for poultry-handling practices, or which live bird species were found in LPMs. These factors and LPM interventions have always existed in parallel, so we cannot rule out the possibility that differences in the reduction in the daily number of infections among different sites may be partially explained by these anthropogenic factors, especially in sites with

Table 3. Estimates of the net effect of LPM closures by comparing the reductions in the number of influenza A(H7N9) infections between study sites with and without closures, adjusting for similar season pattern of absolute humidity, China*

Study sites with LPM interventions	Reference sites without LPM interventions			Reduction in no. infections, % (95% CI)			
	Site no.	Province	Cities	Study sites with LPM interventions, R_1	Reference sites without LPM interventions, R_2	Difference in reduction, $R_1 - R_2$	p value
Site 1	1	Jiangsu	Huaian (Huaian District, Qingpu District), Nantong (Haimen City, Rugao City), Xuzhou (Suining County), Yancheng (Dongtai City), Yangzhou (Hanjiang District)	97.0 (93.0–100.0)	52.0 (12.0–61.0)	45.0 (32.0–88.0)	<0.001
Site 2	1			90.0 (88.0–94.0)	57.0 (16.0–67.0)	33.0 (21.0–78.0)	<0.001
Site 3	1			90.0 (84.0–99.0)	70.0 (42.0–76.0)	20.0 (8.0–57.0)	<0.001
Site 4	1			94.0 (89.0–99.0)	49.0 (10.0–48.0)	44.0 (30.0–89.0)	<0.001
Site 5	1			98.0 (96.0–100.0)	48.0 (20.0–58.0)	51.0 (38.0–80.0)	<0.001
Site 6	1			50.0 (32.0–74.0)	32.0 (21.0–50.0)	18.0 (10.0–23.0)	<0.001
Site 14	1			93.0 (86.0–100.0)	40.0 (27.0–63.0)	52.0 (36.0–59.0)	<0.001
Site 17	1			84.0 (78.0–94.0)	46.0 (39.0–61.0)	38.0 (33.0–39.0)	<0.001
Site 13	2	Hunan	Chenzhou (Beihu District, Yongxing County), Hengyang (Hengdong County, Shigu District, Zhuhui District), Loudi (Shuangfeng District), Shaoyang (Shaodong County, Xinning County, Xinshao County), Zhangjiajie (Yongding District)	86.0 (81.0–87.0)	85.0 (84.0–86.0)	0.5 (–3.0 to 1.0)	0.098

*Similar seasonal patterns of absolute humidity had been observed among study sites with and without closures (e.g., study site 1–6, site 14, site 17, and reference site 1). LPM, live poultry market.

recursive or short-period closures. To more precisely differentiate the effectiveness of each type of LPM interventions, future studies could incorporate additional datasets to try to separate the effects of LPM closure from the natural transmission dynamics of H7N9 virus and other anthropogenic factors. Furthermore, the estimate of the reproduction number in this study relies on the assumption that this parameter is constant among locations. Although the estimate of this parameter did not involve the geographic locations of these cases and the likelihood that these human cases might have been in contact, the estimate was consistent with previous epidemiologic studies (*3*,*23*).

A number of research questions need to be further clarified in future studies. The optimal time and duration to implement LPM closure to balance the economic loss and transmission risk reduction needs further investigation, combined with a time-varying force of infection. Moreover, it could be possible to estimate key epidemiologic parameters (e.g., animal-to-human transmissibility and reproduction number) by considering the spatial–temporal dynamics of H7N9 epidemics in poultry and related environments, potential market functioning effects, and the frequency of human exposure to H7N9 virus to explain the differences in effectiveness.

In conclusion, the characteristics of LPM interventions can potentially affect their effectiveness. Although possibly more challenging from an operational point of view, permanent and long-period closures were found to be more effective in reducing human H7N9 cases during waves 1–5. In the long term, structural changes in the poultry value chain linked to permanent LPM closure may be required to maintain sufficient effectiveness of interventions and prevent the occurrence of H7N9 epidemics.

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Effectiveness of Live Poultry Market Interventions on Human Infection with Avian Influenza A(H7N9) Virus, China

Appendix

Live Poultry Market Closure Database

We obtained a database of live poultry market (LPM) closures at district or county levels through the official website of the Agricultural Bureaus and the Animal Husbandry and Veterinary Bureau at province and county levels; the municipal social media; and internet searches through the Baidu, Sougou, and Bing search engines by using the search terms “live poultry market closure,” “live poultry market,” “live poultry trade,” and “H7N9-positive,” with predefined locations corresponding to the prefectures with $\geq$1 H7N9 case over the 5 epidemics (Appendix Figure 1). Two independent investigators applied the same search procedure for cross-checking and comprehensiveness.

Assessment of Type of LPM Closure on H7N9 Daily Incidence Rate

We defined the H7N9 daily incidence rate (DIR) as the number of new cases during the timespan / (population × total number of days during the timespan). We defined the timespan differently according to the dates of the first LPM closure. In counties without LPM closure, the timespan was the duration of the epidemic wave (i.e., the 5th to the 95th percentiles of the days of onset of illness in each wave). In counties with LPM closure, we considered 2 timespans: the first was the period preceding the implementation of the first LPM closure and the second was the period after the implementation of the first measure until the 95th percentiles of the days of onset of illness. We used the proportion of closing days after the first LPM closure to contrast different levels of closures in that period: low (<25% of closing days), intermediate (25–75% of closing days), and high (>75% of closing days).

The generalized linear mixed effect models (GLMMs) were formulated with a Poisson distribution taking the county level as random effects (2 observations of the same county, before and after the closure, may be considered separately in the models and represent a bias to the assumption of independence of observations). In addition, DIRs estimated from very short periods of time may have extreme variation because of the stochasticity of case reports. Therefore, the GLMM included DIR estimates only for durations >20% of the full epidemic wave duration. We excluded groups with <20 LPM closures from multiple comparison procedures considering GLMM convergence. We compared the performances of GLMMs with various types and closing levels using the Akaike information criterion.

Assessment of LPM Interventions on Risk of Animal-to-Human and Human-to-Human Transmission in 2016–2017 Epidemic

Study Site Selection

We initially included 271 districts/counties in 26 cities with ≥5 urban and semiurban human H7N9 cases in the 2016–2017 epidemic. Of these, we excluded 211 districts/counties for 1 of 3 reasons: permanent closure before the fifth wave, without H7N9 cases, or without LPMs closure (Appendix Figure 3). We aggregated the onset data in the remaining 60 districts/counties based on the same LPM closure measure within the same cities.

Transmission Model

In the transmission model, we assumed human cases to be generated by two processes: index cases infected from animal exposure and secondary cases generated by previous infections. Therefore, the expected number of human cases with onset of day *t* depends on the animal-to-human transmission function $h_{A,i}(t)$ and 2 human-to-human transmission parameters: mean serial interval (the time between successive cases in a chain of transmission, S_p) and the effective reproduction number (R_e). A similar approach has been applied and validated in other modeling studies (*1*,*2*).

Animal-to-Human Transmission Model

In study sites, the mean incubation period of H7N9 infection was assumed to be 3.3 days and followed the same probability Weibull distribution F with scale μ and shape σ for all study sites (*3*).

For study sites with 1 LPM closure measure, the new animal-to-human infections in study site *i* followed a Poisson distribution with mean $\lambda_{pre,i} = p_i \cdot \pi_{pre,i}$ for $\mathrm{t} \in [\mathrm{t_a}, \mathrm{t_b})$, and $\lambda_{post,i} = p_i \cdot \pi_{post,i}$ for $\mathrm{t} \in [\mathrm{t_b}, \mathrm{t_c})$ where p_i was the ascertainment proportion associated with the confirmed cases. We thus defined the transmission function $h_{A,i}(t)$ to be the number of cases due to exposure to animals in study site *i*:

$$h_{A,i}(t) = \begin{cases} F(t) \cdot \lambda_{pre,i} & t \in [t_\mathrm{a}, t_\mathrm{b}) \\ F(t-t_b) \cdot \lambda_{post,i} + [1 - F(t-t_b)] \cdot \lambda_{pre,i} & t \in [t_b, t_c) \end{cases}$$

where $\lambda_{pre,i}$ and $\lambda_{post,i}$ were the number of new animal-to-human infections in study site *i* before and after LPM closure, t_b was the start date of LPM closure, and t_a and t_c were the start and end times of the time horizon for study site *i* in our analysis. We also assumed that the population in site *i* was subject to the a daily per capita force of infection, $\pi_{pre,i}/N_i$ and $\pi_{post,i}/N_i$, where N_i is the population in site *i*. We assessed the effect of LPM closure by the form $(1–\lambda_{post,i}/\lambda_{pre,i}) \times 100\%$, which indicated the proportionate reduction in the number of infections after LPM closure.

For study sites with 2 LPM closure measures, we assumed that the new animal-to-human infections in these study sites followed a Poisson distribution with mean $\lambda_{1st,i} = p_i \cdot \pi_{1st,i}$ for the period before the first LPM closure, $\lambda_{2nd,i} = p_i \cdot \pi_{2nd,i}$ for the period during the first LPM closure, and $\lambda_{3rd,i} = p_i \cdot \pi_{3rd,i}$ for the period after the first LPM closure (or during the second LPM closure). The transmission function was given by:

$$h_{A,i}(t)=\begin{cases}F(t)\cdot\lambda_{1\mathrm{st},i} & t\in[t_0,t_1)\\ F(t-t_1)\cdot\lambda_{2nd,i}+[1-F(t-t_1)]\cdot\lambda_{1st,i} & t\in[t_1,t_2)\\ F(t-t_2)\cdot\lambda_{3rd,i}+[1-F(t-t_2)]\cdot\left(\lambda_{1st,i}+\lambda_{2nd,i}\right) & t\in[t_2,t_3)\end{cases}$$

where $\lambda_{1st,i}$, $\lambda_{2nd,i}$, and $\lambda_{3rd,i}$ were the number of new animal-to-human infections in study site i; t_1 and t_2 were the start dates of the first and second LPM closure; and t_0 and t_3 were the start and end times for study site *i* in the analysis. The population in site *i* was assumed to be subject to a daily per capita force of infection $\pi_{1st,i}/N_i$, $\pi_{2nd,i}/N_i$ and $\pi_{3rd,i}/N_i$. (1–$\lambda_{2nd,i}/\lambda_{1st,i}$) $\times 100\%$ and (1–$\lambda_{3rd,i}/\lambda_{2nd,i}$) $\times 100\%$ were used to evaluate the effect of different period of LPMs closure.

Human-to-Human Transmission Model

In the human-to-human transmission model, we assumed that human infections had an infectiousness profile following a Poisson distribution with mean serial interval (S_p) of H7N9 infection. The human-to-human transmission model was defined as follows:

$$h_{H,i}(t)=\sum_{j=1}^{\min(k.t)} R_e N(t-j-1)\frac{S_p^{\,j}e^{-S_p}}{j!} \qquad t\in(0,t_n)$$

where *N(t)* was the number of new human infections each day chosen from a Poisson distribution with mean $h_{A,i}(t)$+$h_{H,i}(t)$. The expected number of cases on day *t* was given by:

$$h_i(t)=\begin{cases}h_{A,i}(t) & t=0\\ \displaystyle\sum_{j=1}^{\min(k.t)} R_e N(t-j-1)\frac{S_p^{\,j}e^{-S_p}}{j!}+h_{A,i}(t) & t\in(0,t_n)\end{cases}$$

where *k* is the maximum value the serial interval distribution can take; we fixed *k* = 14 days in main analyses.

We used a Markov chain Monte Carlo (MCMC) method to jointly estimate the expected number of new animal-to-human infections during each period and the effective reproduction number, on the basis of illness onset data. Each parameter was assumed to be positive and with noninformative uniform priors. We used a likelihood-based method to estimate epidemiologic parameters. The likelihood of a time series of observed human cases was:

$$L(\lambda_{pre,i},\lambda_{post,i},\mu,\sigma,R_e) = \prod_{t=0}^{t_n\text{-}1} \frac{h_i(t)^{N(t+1)} e^{-h_i(t)}}{N(t+1)!}$$

Sensitivity Analysis

Analysis of Influence of Proportion of Unreported Cases and Mean Serial Interval on the Effective Reproduction Number

We incorporated the proportion of unreported cases ($1-p_i$) and mean serial interval into the model in a sensitivity analysis. For patients with known exposure, an estimate of the serial interval is 7.5 days (95% CI 4.9–9.0) (*4*). We therefore assumed a serial interval of 7.5 days for our main analysis and tested a range of 5.5–9.5 days (*4*) during the sensitivity analysis; we adjusted for 4 days (*5*) for any potential delays such as symptom onset and case reports. Many unreported mild or asymptomatic H7N9 cases may have occurred (*6*), and this may potentially affect the pool of susceptible humans. Thus, the proportion of unreported cases was assumed to be 0.0, 0.2, 0.4, or 0.6, based on previous studies (*6*,*7*).

Analysis of Potential Effect of Absolute Humidity

The number of new animal-to-human infections and effective reproduction number on day *t* was extended to analyze how absolute humidity modulates the onset of H7N9 infection (*3*,*7*). Incorporating the potential effect of the seasonality of H7N9 epidemic into animal-to-human and human-to human transmission model, the extended models were

$$h_{\mathrm{A},i}(t)=\begin{cases}F(t)\cdot\alpha_{pre,i}\cdot Q(H_{t,i}) & \mathrm{t}\in[t_a,t_b)\\ F(t)\cdot\alpha_{\mathrm{post},i}\cdot Q(H_{t,i})+(1-F(t))\cdot\alpha_{pre,i}\cdot Q(H_{t,i}) & \mathrm{t}\in[t_b,t_c)\end{cases}$$

$$h_{H,i}(t)=\sum_{j=1}^{\min(k,t)}k\cdot(R_{0\min}+\exp(b+a\cdot H_{t,i}))\cdot\mathrm{N(t - j+1)}\cdot\frac{S_p^{j}e^{-S_p}}{j!}\qquad t\in(0,t_c)$$

where $H_{t,i}$ was the daily average absolute humidity on day *t* in study site i; $Q\left(H_{t,i}\right)=1+exp\left(b+a\cdot H_{t,i}\right)$ $(a>0)$ represented how absolute humidity modulated the force of infection (*8*,*9*); $\alpha_{pre,i}\cdot Q(H_{t,i})$ and $\alpha_{post,i}\cdot Q(H_{t,i})$ were the number of new animal-to-human infections on day *t* before and after LPM closure and followed a Poisson distribution; the ratio $1-\frac{\alpha_{pre,i}}{\alpha_{post,i}}$ (i.e., equivalent to $1-\lambda_{post,i}/\lambda_{pre,i}$ in the base model) represented the reduction in force of infection as a result of LPM closure; *k* was the susceptibility of population and was assumed to be approximately 100.0%; R_{0min} was the minimum basic reproduction number. For study sites with 2 LPM closure measures, the number of new animal-to-human infections on day *t* followed a Poisson distribution with mean $\alpha_{1st,i}\cdot Q(H_{t,i})$ for $\mathrm{t}\in[t_0,t_1)$, $\alpha_{2nd,i}\cdot Q(H_{t,i})$ for $\mathrm{t}\in[t_1,t_2)$, and $\alpha_{3rd,i}\cdot Q(H_{t,i})$ for $\mathrm{t}\in[t_2,t_3)$, where the ratio $1-\alpha_{2nd,i}/\alpha_{1st,i}$, and $1-\alpha_{3rd,i}/\alpha_{2nd,i}$ represented the reduction in force of infection resulting from LPM closure. Parameter *a* and *b* were assumed to be followed a semi-informative distribution (normal distribution with mean 0 and deviation 5).

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Appendix Table 1. Action lists for live poultry market closures in China, 2013–2017

Action Code	Action	Frequency of LPM
1	Close 1 d per month	Recursive
2	Close 1 d per month, disinfection on close day	Recursive
3	Close 1 d per month, clean 1 d per week	Recursive
4	Close 1 d per month, disinfection per week	Recursive
5	Close 1 d per month, clean per day, disinfection per week	Recursive
6	Close 1 d per month, clean 1 d per week, No stay overnight	Recursive
7	Close 2 d per month	Recursive
8	Close 2 d per month, clean 1 d per week	Recursive
9	Close 1 d per 2 weeks, disinfection on the close day	Recursive
10	Close in 3 fixed time	Recursive
11	Close 3 d per month	Recursive
12	Close 3 d per month, clean 1 d per week	Recursive
13	Close 1 d per week	Recursive
14	Close 1 d per week in wholesale market, close 1 d per 2 weeks in retail level	Recursive
15	Close 1 d per week, disinfection on close day	Recursive
16	Close 2 d per week	Recursive
17	Close 3 d per month, disinfection per day	Recursive
18	Disinfection per 2 weeks	Recursive
19	Disinfection per week	Recursive
20	Disinfection per week, clean per day	Recursive
21	Disinfection per day	Recursive
22	Disinfection and clean per day	Recursive
23	Disinfection twice per day	Recursive
24	Close 1 d to clean and disinfect	Short
25	Close 3 d	Short
26	Close 5 d	Short
27	Close 1 week	Short
28	Close 2 weeks	Short
29	Temporarily close in >1 markets	Long
30	Temporarily close	Long
31	Gradually cancel live poultry trading	Long
32	Permanent close	Permanent

Appendix Table 2. Regression coefficients of fixed effect of various types and closing levels of live poultry market closure on daily incidence rate using general linear mixed model across waves, China

Types and closing levels of	Wave	Category	β_i	Standard error	Z value	p value
Proportion of closing days	1	No closure	1.376	0.362	3.797	<0.001
		<25% closing days	–1.653	0.722	–2.287	0.022
	2	No closure	0.244	0.251	0.973	0.331
		25%–75% closing days	–4.479	1.010	–4.434	<0.001
		>75% closing days	–1.350	0.248	–5.446	<0.001
	3	No closure	0.698	0.226	3.094	0.002
		<25% closing days	–3.043	0.717	–4.244	<0.001
		25%–75% closing days	–3.204	1.022	–3.135	0.002
		>75% closing days	–1.972	0.380	–5.183	<0.001
	4	No closure	1.489	0.368	4.049	0.175
		>75% closing days	–0.613	0.452	–1.355	<0.001
	5	No closure	0.526	0.131	4.006	<0.001
		<25% closing days	–1.652	0.240	–4.676	<0.001
		25%–75% closing days	–1.361	0.209	–6.514	<0.001
		>75% closing days	–1.131	0.182	–6.232	<0.001
Type of closure	1	No closure	4.499	0.727	6.191	<0.001
		Before closure	1.610	0.784	2.052	0.040
		Permanent closure	0.847	0.784	1.081	0.280
	2	No closure	1.904	0.376	5.059	<0.001
		Before closure	0.955	0.369	2.585	0.010
		Long-period closure	–0.876	0.371	–2.361	0.018
		Permanent closure	–2.292	0.703	–3.259	0.001
	3	No closure	3.121	0.395	7.911	<0.001
		Before closure	1.149	0.364	3.158	0.002
		Long-period closure	–3.019	1.062	–2.842	0.005
		Permanent closure	–0.859	1.495	–1.735	0.083
	4	No closure	4.499	0.727	6.191	<0.001
		Before closure	1.610	0.784	2.052	0.040
		Permanent closure	0.847	0.784	1.081	0.280
	5	No closure	2.064	0.201	10.289	<0.001
		Before closure	0.491	0.177	2.777	0.006
		Short-period closure	–0.829	0.321	–2.586	0.010
		Long-period closure	–0.744	0.226	–3.289	0.001
		Permanent closure	–0.729	0.266	–2.737	0.006

Appendix Table 3. Multiple comparisons of the reduction in number of infections before and after live poultry market closure among study sites with different types of live poultry market closure in the 2016–17 H7N9 epidemic wave, China.

Type of live poultry market closure		Mean difference of the reduction in number of	p value
Permanent closure	Long-period closure	45.0 (40.3–49.7)	<0.001
	Short-period closure	28.2 (23.8–32.7)	<0.001
	Recursive closure	15.3 (11.3–19.3)	<0.001
Long-period closure	Short-period closure	12.9 (10.4–15.4)	<0.001
	Recursive closure	29.7 (26.8–32.7)	<0.001
Short-period closure	Recursive closure	16.8 (13.3–20.3)	<0.001

*Difference in the effectiveness of the 2 LPM interventions presented in the first and second columns.

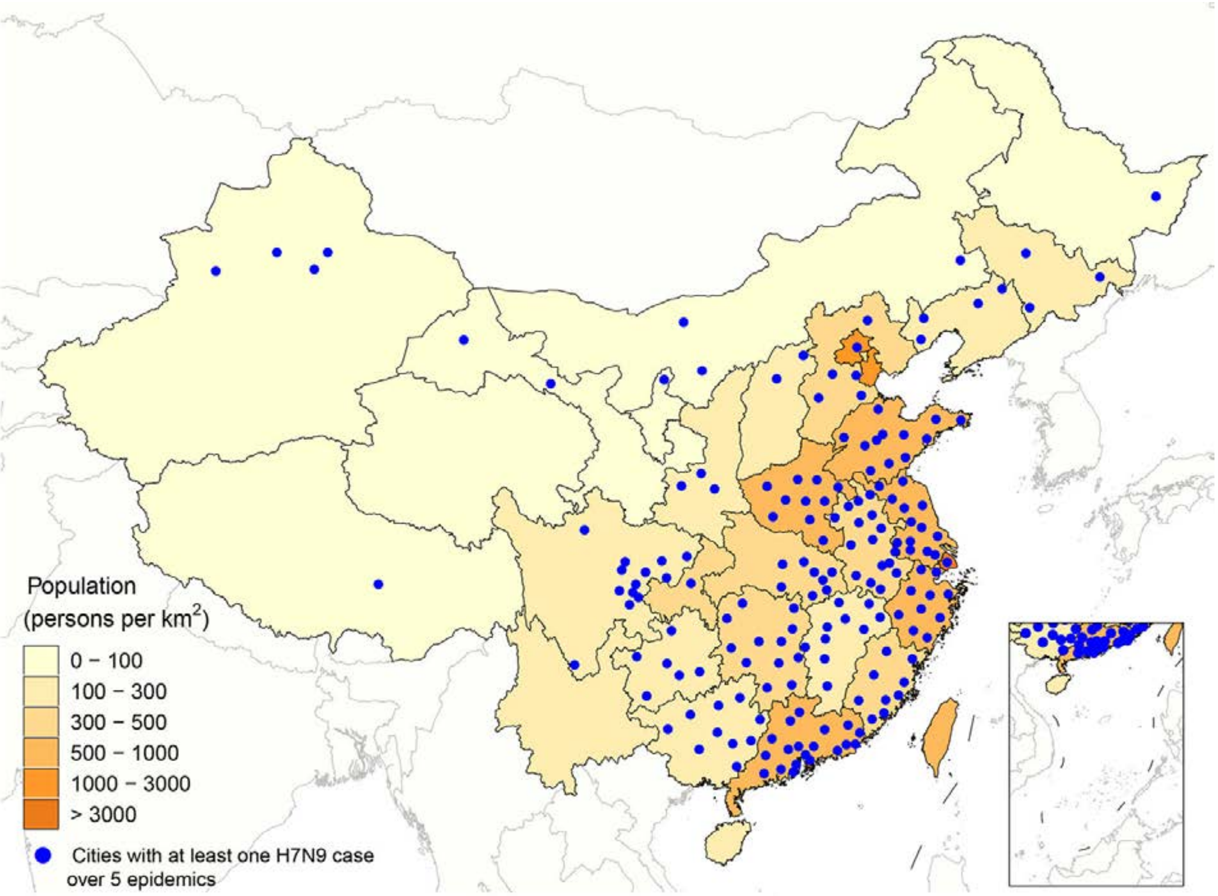
Appendix Table 4. Estimates of the effective reproduction number in the 2016–17 epidemic wave of H7N9, China, considering the impact of the proportion of unreported cases and the mean serial interval on the effective reproduction number.

Parameters		Reproduction number (95% CI)
Proportion of unreported cases	0.0	0.147 (0.034–0.285)
	0.2	0.151 (0.042–0.283)
	0.4	0.125 (0.033–0.232)
	0.6	0.162 (0.063–0.265)
Mean serial interval (S_p)	5.5 d	0.156 (0.043–0.298)
	6.5 d	0.150 (0.037–0.292)
	7.5 d	0.147 (0.034–0.285)
	8.5 d	0.138 (0.029–0.273)
	9.5 d	0.131 (0.021–0.274)

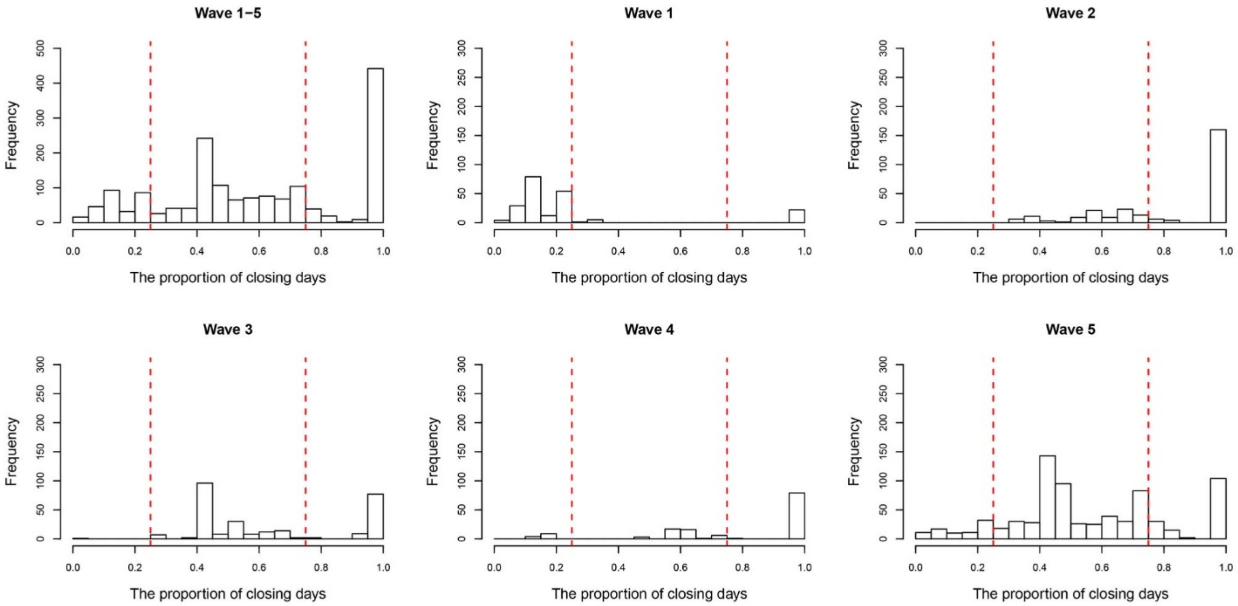
Appendix Table 5. Comparison of parameter estimates from models with and without an effect of absolute humidity in the 2016–17 H7N9 epidemic wave, China.

Site	Type of closures	Reduction in force of infection due to live poultry market closure			
		Model without an effect of absolute		Model with an effect of	
Site 1	Permanent	97.0 (94.0–100.0)		97.0 (93.0–100.0)	
	Site 2	Long	90.0 (87.0–95.0)		90.0
	Site 3	Long	92.0 (87.0–100.0)		90.0
	Site 4	Long	95.0 (90.0–100.0)		94.0
	Site 5	Long	98.0 (96.0–100.0)		98.0
	Site 6	Long	48.0 (35.0–81.0)		50.0
	Site 7	Recursive	34.0 (15.0–70.0)		36.0
		Short	73.0 (53.0–77.0)		70.0
	Site 8	Short	96.0 (93.0–99.0)		96.0
	Site 9	Long	84.0 (75.0–96.0)		84.0
	Site 10	Long	89.0 (80.0–99.0)		90.0
	Site 11	Long	92.0 (84.0–99.0)		92.0
	Site 12	Long	78.0 (72.0–92.0)		78.0
	Site 13	Long	86.0 (83.0–87.0)		86.0
	Site 14	Long	92.0 (86.0–100.0)		93.0
	Site 15	Short	95.0 (92.0–98.0)		95.0
	Site 16	Recursive	71.0 (47.0–97.0)		73.0
Site 17	Long	84.0 (79.0–94.0)		84.0 (78.0–94.0)	
Minimal basic reproduction number (95% CrI)					
Parameter*				0.061 (0.004–0.147)	
	a			0	2.89
b		∞		–0.85 (–6.52–+4.76)	

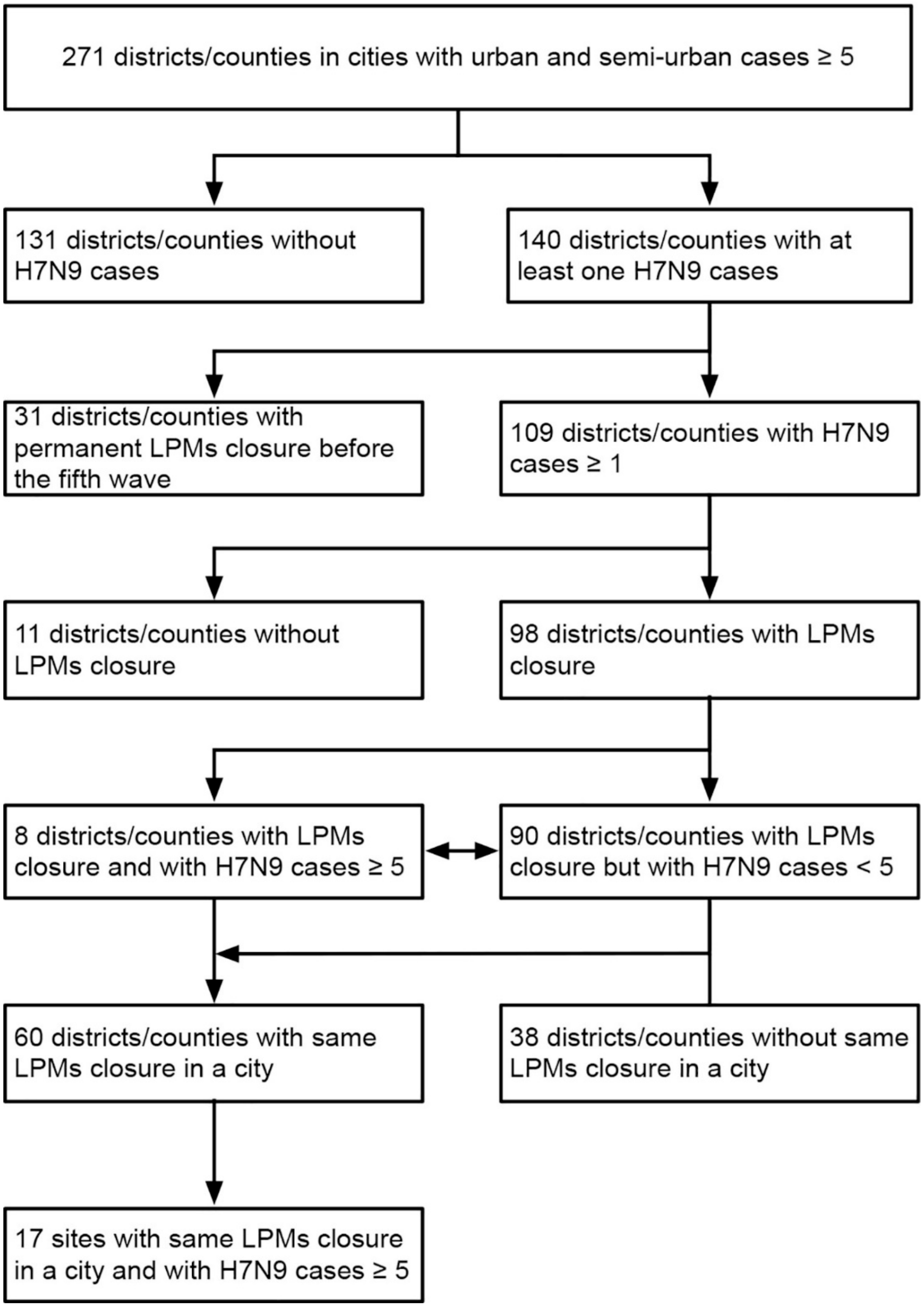
*a and b are key parameters used to modulate the impact of absolute humidity on the force of infection.



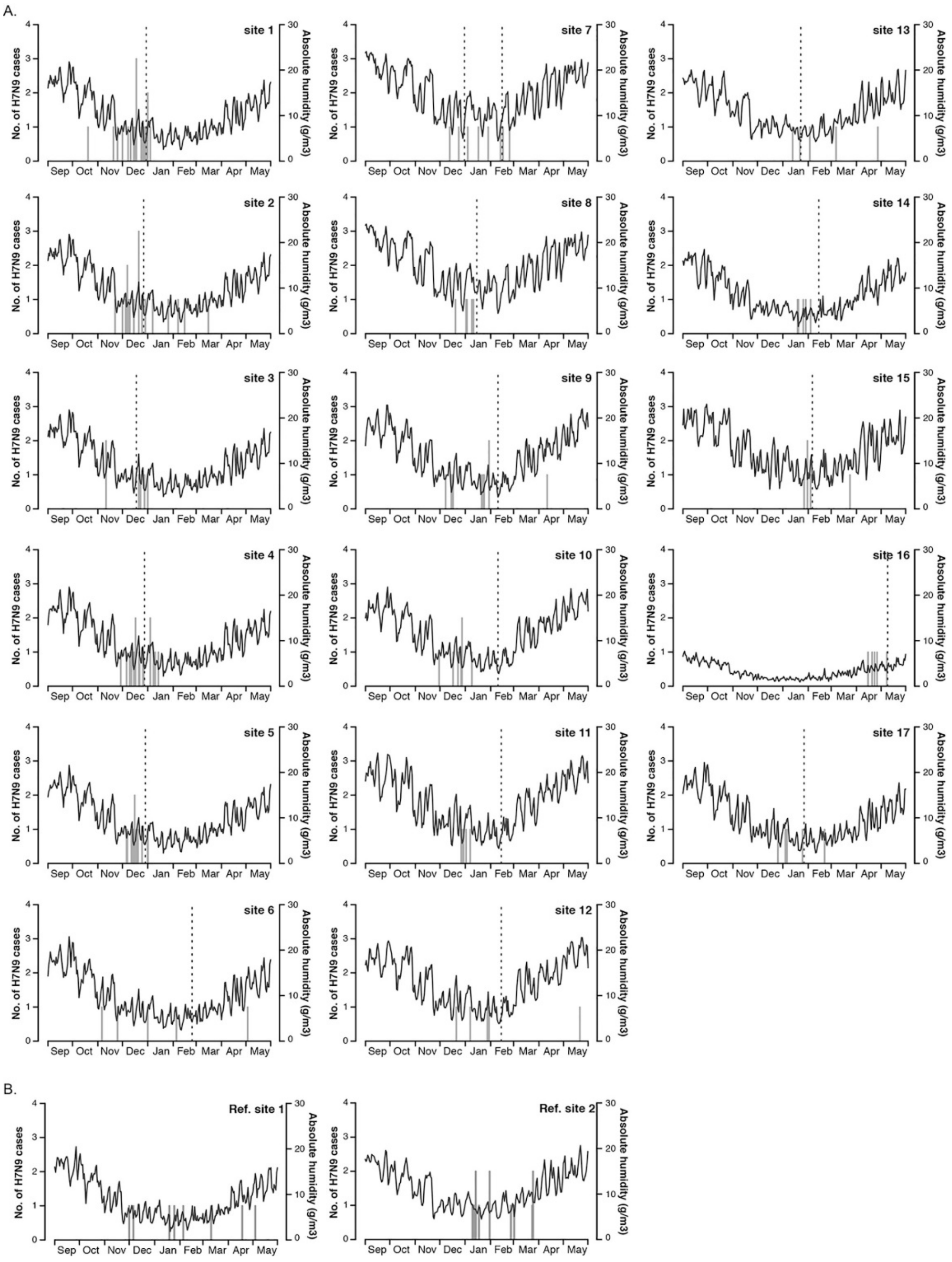
Appendix Figure 1. Geographical distribution of predefined locations when using search engines to update the live poultry market closure measures, China. The blue dots refer to the cities with $\geq$1 H7N9 case over 5 epidemic waves.



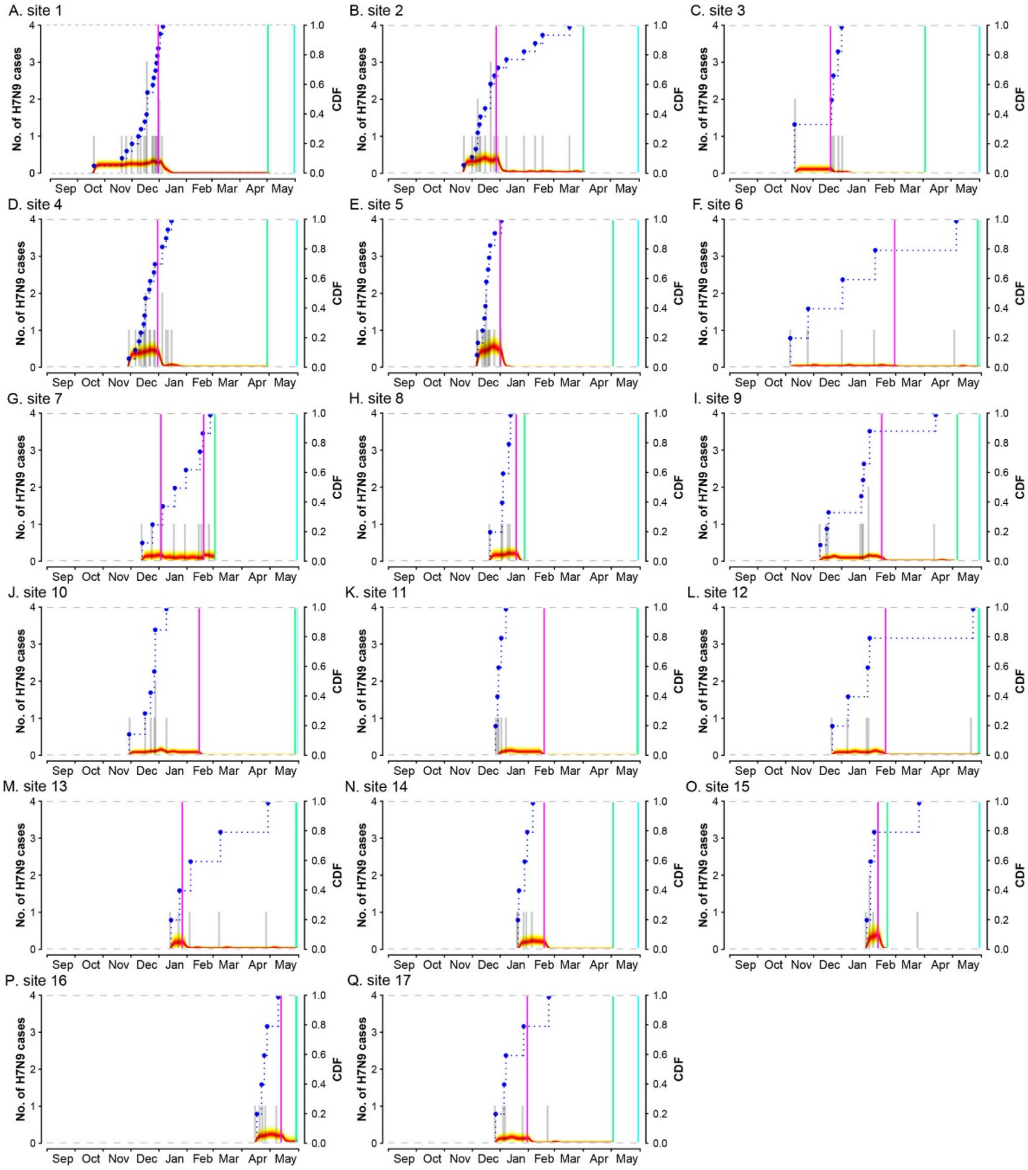
Appendix Figure 2. Distribution of the proportion of days of closing out of the total epidemic wave duration in 2013–2017. The red vertical lines refer to 25% and 75% of the total epidemic wave duration.



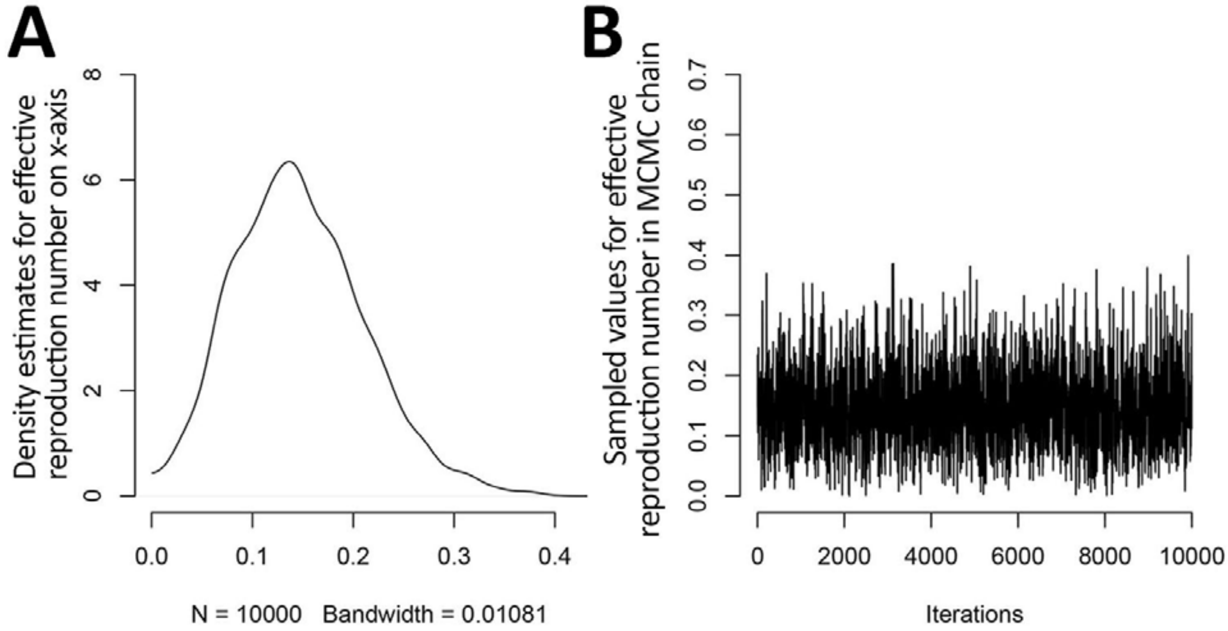
Appendix Figure 3. Flowchart of the selection of sites in quantitative evaluation of live poultry markets closure in the 2016–17 H7N9 epidemic wave, China.



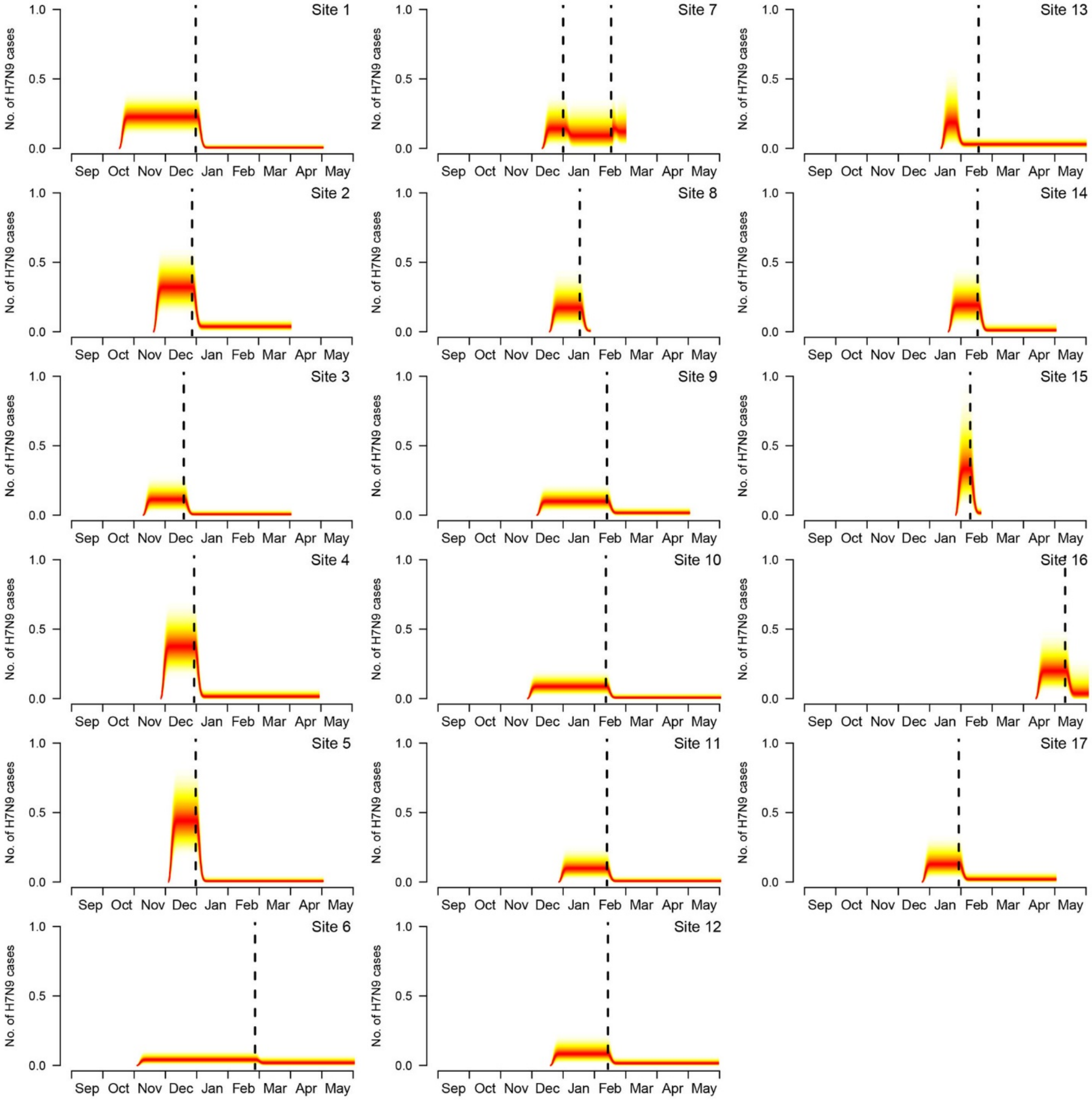
Appendix Figure 4. Time series of absolute humidity and illness onset of human H7N9 cases in sites with and without live poultry market closures, China. The gray bars indicate the number of cases with onsets on that day. Red vertical lines indicate the start date of live poultry market closures in each study site. The blue curves refer to the daily average absolute humidity in each site. A) Absolute humidity and illness onset of human cases in 17 study sites with closures and B) in 2 reference sites without closures.



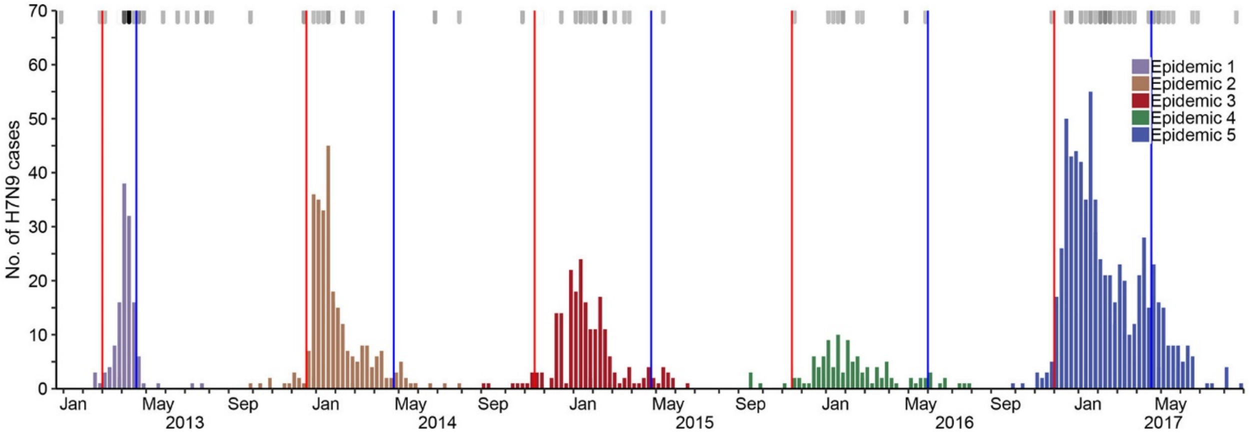
Appendix Figure 5. Dates of H7N9 cases and posterior estimates of the expected daily number of illness onsets of cases in 17 sites in the 2016–17 H7N9 epidemic wave. The gray bars indicate the number of cases with onsets on that day. The magenta vertical lines refer to the start date of live poultry market closures, the green vertical lines indicate the end date of live poultry market closures, and the cyan vertical lines indicate the last date used in analyses. The blue points and dashed lines represent the cumulative distribution function (CDF) of H7N9 epidemics in humans. The red and yellow colors in each panel refer to whether the value of posterior estimates is included within the 95th prediction intervals on a given day.



Appendix Figure 6. The posterior distribution and Markov chain Monte Carlo (MCMC) sampling process of effective reproduction number. A) The posterior distribution for effective reproduction number. B) The MCMC sampling process of effective reproduction number.



Appendix Figure 7. Posterior estimates of the expected daily number of illness onsets of H7N9 cases resulting from animal-to-human transmission in 17 sites in the 2016-17 epidemic wave, China. The red and yellow colors in each panel refer to whether the value of these estimates is included within the 95th prediction intervals on a given day. Black vertical lines indicate the start date of live poultry market closures in each study site.



Appendix Figure 8. Temporal pattern of laboratory-confirmed H7N9 cases and the implementation of live poultry market interventions in mainland China across epidemic waves. The small and partially transparent lines represent the implementation of live poultry market measures; darker colors indicate higher frequency of the implementation of live poultry market interventions. Red vertical lines and blue vertical lines refer to the 5th and 95th percentiles of the days of onset of illness in each epidemic wave. The epidemic peak of H7N9 in each wave appeared to coincide with the period in which the closure measures were implemented.