

Estimates of the impact of a future influenza pandemic in China

Hongjie Yu,^{a,1} Luzhao Feng,^{a,1} Zhibin Peng,^a Zijian Feng,^a David K. Shay,^b Weizhong Yang^a

^aOffice for Disease Control and Emergency Response, Chinese Center for Disease Control and Prevention (China CDC), Beijing, People's Republic of China. ^bInfluenza Division, National Center for Immunization and Respiratory Diseases, Coordinating Center for Infectious Diseases, MS A-32, Centers for Disease Control and Prevention, N.E. Atlanta, Georgia

Correspondence: Prof Weizhong Yang, Chinese Center for Disease Control and Prevention, 27# Nanwei Road, Beijing, 100050, China.

E-mail: yangwz@chinacdc.cn

¹These authors contributed equally to this work.

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Background The next influenza pandemic will create a surge in demand for health resources in China, with its current population of >1.3 billion persons and under-developed medical care and public health system. However, few pandemic impact data are available for China.

Objectives We estimated the effects of a future influenza pandemic in China by examining pandemic scenarios of varying severity and described the time distribution of cases during a first wave.

Methods We used a Monte-Carlo simulation model and death rates, hospitalizations and outpatient visits for 1918- and 1968-like pandemic scenarios and data from the literature or experts' opinion to estimate four health outcomes: deaths, hospitalizations, outpatient medical visits and clinical illness for which medical care was not sought. For each of the two scenarios we estimated outcomes by week using a normal distribution.

Results We estimated that a 1968 scenario in China would result in 460 000–700 000 deaths, 1.94–2.27 million hospitalizations, 111–117 million outpatient visits and 192–197 million illnesses for which medical care was not sought. Fifty-two percent of hospitalizations occurred during the two-peak weeks of the first wave. We estimated that patients at high-risk of influenza complications (10–17% of the population) would account for 61–75% of all deaths. For a 1918 scenario, we estimated that 4.95–6.95 million deaths, 20.8–22.7 million hospitalizations and 101–108 million outpatient visits could occur.

Conclusion Even a 1968 pandemic scenario will pose substantial challenges for the medical and public health system in China, and planning to manage these challenges is essential.

Keywords Influenza pandemic, Monte-Carlo method, China, health planning.

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Introduction

The emergence of highly pathogenic avian influenza (HPAI) A (H5N1) viruses, which have caused an unprecedented epizootic and demonstrated an ability to be transmitted directly from birds to humans and cause severe disease with high mortality over the last several years,¹ has increased international planning for a future pandemic. Of the three pandemics that occurred in the 20th century, the 1918 pandemic resulted in especially large tolls in terms of both disease and deaths, and resulted in a catastrophic shock to human health and social economic development.² Limited data on mortality and morbidity are available for China during the early 20th century,³ and assessments of the impact of the 1918 pandemic for the country are limited.

Although another pandemic is likely inevitable, no one can predict when or where the next pandemic will occur.⁴ South-east Asia and southern China are thought to provide an appropriate ecological niche for the emergence of new influenza viruses with pandemic potential.⁵ It is generally accepted the H2N2 pandemic in 1957 and the H3N2 pandemic in 1968 emerged in China, and there is some evidence that H1N1 influenza viruses may have re-emerged in China in 1977.⁶

Even though it is not possible to predict when the next pandemic will occur or how devastating it might be, it will likely cause social disruption because of high rates of illness, sick leave, hospitalization and death. Thus, it is expected that the next pandemic will create a surge in demand for hospital-based services in China, with its current population of more than 1.3 billion persons and

under-developed medical care and public health system. Therefore, pre-pandemic planning is essential to minimize morbidity, mortality and societal disruption by efficiently allocating scarce medical and public health resources and developing ways to decrease the spread of pandemic viruses.^{4,7}

Meltzer *et al.* used Monte-Carlo methods to estimate the possible effects of the next influenza pandemic in the United States and analysed the economic impact of vaccine-based interventions.⁸ Subsequently, many studies have been conducted to simulate or predict the impact and health utilization of a future pandemic in other countries, including the use of a Monte-Carlo model in France,⁹ use of FluAid and FluSurge software¹⁰ in Canada, England, New Zealand, Australia and Pacific Islands,^{11–16} and use of a static model in Netherlands.^{17,18} However, few pandemic impact data are available in China, except for a regression modelling study that included China in making worldwide estimates of mortality in 2004.¹⁹ Here we used a Monte-Carlo simulation model to estimate the overall health burden posed by a relatively mild and a severe future pandemic in China.

Methods

The model

Because of the difficulties in calculating realistic estimates of the numbers of cases in the next influenza pandemic, we used a previously described Monte-Carlo mathematical simulation model to examine the potential impact of the next pandemic in China.^{8,20} This model used predefined probability distributions of key input variables to estimate the numbers of illnesses and deaths that could result from an influenza pandemic in China, and produced a range of estimated effects, rather than a single point estimate.

Input variables

Gross attack rates were examined at pre-determined intervals and values for other important input variables, including age distribution of patients, percentages of persons at high risk for severe complications of influenza infections, and population-based rates of illness and death, were chosen from pre-determined probability distributions available from earlier influenza pandemics and epidemics.^{21–24} If specific data were not available in published reports for some variables, we used recommendations from an invited group of Chinese experts.

We used gross attack rates (the percentage of clinical influenza illness cases per population) of 15–35%, in steps of 5%, in our models. Infected individuals who continued to work were not considered to have a clinical illness of influenza and were not included in estimates of health outcomes. The number of cases generated by a given attack

rate was distributed among China population for 2000 census²⁵ first by age and then by high-risk status.

The Chinese population was categorized into three age groups: 0–19 years, 20–59 years and ≥60 years. Since the age distribution of patients in the next pandemic cannot be predicted, we calculated two age-related distribution of cases, reflecting either a 1968-type or a 1918-type pandemic scenario (Table 1), and based on lower and upper estimates of age-specific attack rates from 1918, 1957 and 1968 pandemics.^{21–24}

The number of cases in each age group was further divided into those at high risk for influenza complications and those not at high risk by using the lower and upper estimates of age-defined percentages of high-risk persons in each age group (Table 1). Populations at high risk were defined as persons with a pre-existing medical condition making them more susceptible to complications from influenza, based on the medical conditions used by the US Advisory Committee on Immunization Practices (ACIP)²⁶ to recommend annual vaccination for certain groups. Persons 60 years and older were assumed to have higher rates of severe illnesses and death than younger persons (Table 2).

Table 1. Estimates of age distribution of cases and percentages of population at high risk used to examine the impact of influenza pandemic in China*

	1918-type		1968-type	
	Lower estimate	Upper estimate	Lower estimate	Upper estimate
Percentage of all cases**				
0–19 years old	39.0	35.4	46.6	36.7
20–59 years old	56.7	59.6	48.8	58.1
≥60 years old	4.4	5.0	4.6	5.2
Total***	100	100	100	100
Percentage at high risk†				
0–19 years old	7.5	12.4	7.5	12.4
20–59 years old	5.6	13.5	5.6	13.5
≥60 years old	40.0	50.0	40.0	50.0
Average††	10.0	17.0	10.0	17.0

*Chinese Population was obtained from the latest population census data in 2000.²⁵

**The actual number of cases will depend upon the assumed gross attack rate. The distribution of cases was based on lower and upper estimates of age-specific attack rates from 1918, 1957 and 1968 pandemics in different countries.^{21–24}

***Totals may not exactly add to 100 percent due to rounding up.

†The percentage of person in each age group that were at high risk were obtained from literature (Appendix S1) or experts' opinion.

††Average by age-weighted, using each age group's proportion of the total Chinese population.

Table 2. Variables used to define distribution* of health outcomes of those with clinical cases of influenza for 1968-type and 1918-type pandemic scenario

	Rates per 1000 persons					
	1968-type			1918-type**		
	Lower	Most likely	Upper	Lower	Most likely	Upper
Outpatient visits ^{8,21,27}						
Not at high risk						
0–19 years old	165	–	230	–	–	–
20–59 years old	40	–	85	–	–	–
≥60 years old	45	–	74	–	–	–
High risk						
0–19 years old	223	–	311	–	–	–
20–59 years old	54	–	115	–	–	–
≥60 years old	61	–	100	–	–	–
Hospitalizations ^{8,24,27,28}						
Not at high risk						
0–19 years old	0.2	0.5	2.9	–	–	–
20–59 years old	0.18	–	2.75	–	–	–
≥60 years old	1.5	–	3.0	–	–	–
High risk						
0–19 years old	2.1	2.9	9.0	–	–	–
20–59 years old	0.8	–	5.1	–	–	–
≥60 years old	4.0	–	13.0	–	–	–
Deaths ^{8,29–32}						
Not at high risk			Deaths ^{19,30,33,34}			
0–19 years old	0.044	0.091	0.149	2.68	2.85	3.17
20–59 years old	0.041	0.085	0.126	3.18	4.67	6.19
≥60 years old	0.46	1.51	3.02	0.90	3.68	6.78
High risk						
0–19 years old	0.40	0.83	1.36	24.4	26.0	28.8
20–59 years old	0.10	–	5.72	26.1	38.3	50.8
≥60 years old	2.76	–	5.63	2.8	11.4	21.0

*For Monte-Carlo simulations, rates were presented as lower and upper for uniform distributions and lower, most likely, and upper for triangular distributions.

**Rates of hospitalizations and outpatient visits for the 1918 pandemic were not available from literatures.

We used data published in the Chinese literature (Appendix S1) on the percentages of individuals in the 0–19 and 20–59 age groups with any of the ACIP conditions to define the medical high-risk group. For ≥60 age group, we used experts' opinion to estimate the percentage with any ACIP condition due to the lack of published data from China (Table 1).

The health outcomes we studied include deaths, hospitalizations, outpatient medical visits and clinical illness for which medical care was not sought. The rates of death, hospitalization and outpatient medical visits, by age and risk group, were obtained from the literature or from experts' opinion (Table 2). These rates were used to determine the numbers of persons in each category.

Estimating health outcomes

The potential health outcomes of a 1968-type and a 1918-type scenario were estimated separately, when the

variables described above were used in the Monte-Carlo model. Every scenario was divided into lower and upper estimate for attack rates. For each series of estimations, the model was run for 1000 iterations using @RISK software (Version 4.5. Palisade Corporation, NY, USA, June, 2005), and the descriptive statistics (mean, minimum and maximum) of four health outcomes described above were calculated.

Based on the epidemic curves of the first waves of past pandemics and hypotheses from previous studies,^{29,35,36} we assumed that the first wave of next pandemic might last for 6, 8 or 12 weeks and that cases would follow an approximate normal distribution. We did not model subsequent pandemic waves, as it was assumed that the first wave would place the greatest strains on the medical and public health system. We distributed deaths, hospitalizations and outpatient visits for each of the two scenarios

into each week and each day by using a normal distribution curve and function.

Results

Impact of a 1968-type pandemic in China

If the next influenza pandemic resembled a 1968-type pandemic with an attack rate of 25%, we estimated that 460 000 to 700 000 deaths, 1.94–2.27 million hospitalizations, 111–117 million outpatient visits and 192–197 million illnesses for which medical care was not sought would occur (Table 3). Those aged 60 years and older accounted for a highest percentage of all deaths (a mean of 51–60%), while the 20–59 age group accounted for the highest percentage of all hospitalizations (a mean of 42–46%) and the 0–19 age group accounted for the highest percentage of all outpatient visits (a mean of 54–64%). Approximately 61–75% of deaths, 34–46% of hospitalizations and 11–20% of outpatient visits occurred in the high-risk groups, although these groups represented only for 10–17% of total population in each age group.

Time distribution of cases in a 1968-type pandemic

If a first pandemic wave lasted for 8 weeks, there were an estimated 120 000 to 180 000 deaths, 500 000 to 590 000 hospitalizations and 28.7–30.2 million outpatient visits in the fourth or the fifth weeks of the wave. During the 2 days when the pandemic wave peaked (the 28th and 29th days after the first cases) there were an estimated 19 000 to 28 000 deaths, 79 000 to 92 000 hospitalizations and 4.49–4.72 million outpatient visits (Figure 1).

If a first pandemic wave lasted for 6 weeks, there were an estimated 120 000 to 180 000 deaths, 520 000 to 600 000 hospitalizations and 29.4–30.9 million outpatient visits in the third or the fourth weeks of the wave. During the 2 days when the pandemic wave peaked (the 21st and 22nd days after the first cases) there were an estimated 19 000 to 29 000 deaths, 80 000 to 94 000 hospitalizations and 4.59–4.83 million outpatient visits (Appendix S2). If a first pandemic wave lasted for 12 weeks, there were an estimated 80 000 to 130 000 deaths, 350 000 to 410 000 hospitalizations and 20.0–21.1 million outpatient visits in the sixth or the seventh weeks of the wave. During the 2 days when the pandemic wave peaked (the 42nd and 43rd days after the first cases) there were an estimated 12 000 to 19 000 deaths, 52 000 to 61 000 hospitalizations and 2.98–3.14 million outpatient visits (Appendix S2).

Impact of 1918-type pandemic in China

If the next influenza pandemic resembled a 1918-type pandemic with an attack rate of 25%, we estimated 4.95–6.95 million deaths, 20.8–22.7 million hospitalizations, 101–108

million outpatient visits and 177–180 million illnesses for which medical care was not sought would occur (Table 3). Those aged 20–59 years accounted for the highest percentage of all deaths (56–66%). The 0–19 age group accounted for 23–32% of all deaths, while those aged 60 years and older accounted for the lowest percentage of all deaths (11–12%). Approximately 40–58% of all deaths occurred among those in a group at high risk for influenza-associated complications.

Time distribution of cases in a 1918-type pandemic

If the pandemic wave lasted for 8 weeks, there were an estimated 1.28–1.80 million deaths, 5.38–5.88 million hospitalizations and 26.24–27.91 million outpatient visits during the fourth or the fifth week of the wave. Again, if the pandemic wave peaked on the 28th and the 29th days after beginning, there were an estimated 200 000 to 280 000 deaths, 840 000 to 920 000 hospitalizations and 4.10–4.36 million outpatient visits (Figure 2).

If the pandemic wave lasted for 6 weeks, there were an estimated 1.32–1.84 million deaths, 5.51–6.02 million hospitalizations and 26.88–28.60 million outpatient visits during the third or the fourth week of the wave. If the pandemic wave peaked on the 21st and the 22nd days after beginning, there were an estimated 210 000 to 290 000 deaths, 860 000 to 940 000 hospitalizations and 4.19–4.46 million outpatient visits (Appendix S2). If a first pandemic wave lasted for 12 weeks, there were an estimated 0.90–1.26 million deaths, 3.75–4.10 million hospitalizations and 18.31–19.48 million outpatient visits during the sixth or the seventh weeks of the wave. Again, if the pandemic wave peaked on the 42nd and 43rd days after beginning, there were an estimated 130 000 to 190 000 deaths, 560 000 to 610 000 hospitalizations and 2.73–2.90 million outpatient visits (Appendix S2).

Discussion

We found that the next influenza pandemic in China, whether mild and resembling a 1968-type pandemic or severe and resembling a 1918-type pandemic, will likely cause considerable social disruption. Although the Chinese population at high risk for influenza-related complications accounts for only 10–17% of the total population, this group could bear a heavy burden of deaths and hospitalizations. If the next pandemic resembled a 1918 pandemic, the number of estimated deaths and hospitalizations was approximately 10 times greater than that estimated for a 1968-type scenario. Such a severe pandemic would place a considerable stress on the medical and public health sectors of China. However, there is a great deal of uncertainty associated with any estimate of the potential impact of a

Table 3. Estimated impact of pandemic influenza for 1968-type and 1918-type scenario

	Mean (min; max) of outcomes (10 000)				
	15%	20%	25%	30%	35%
1968-type scenario					
Lower estimate for AR					
Deaths	28 (15; 44)	37 (20; 59)	46 (25; 73)	56 (30; 88)	65 (35; 103)
Hospitalizations	116 (50; 210)	155 (67; 280)	194 (84; 350)	233 (100; 420)	272 (117; 490)
Outpatients visits	6994 (5242; 9507)	9325 (6990; 12 676)	11 657 (8737; 15 845)	13 988 (10 484; 19 014)	16 319 (12 232; 22 182)
Illnesses not seeking medical care	11 501 (8962; 13 201)	15 335 (11 949; 17 601)	19 168 (14 936; 22 002)	23 002 (17 924; 26 402)	26 836 (20 911; 30 802)
Upper estimate for AR					
Deaths	42 (19; 70)	56 (26; 93)	70 (32; 117)	83 (38; 140)	97 (45; 163)
Hospitalizations	136 (62; 236)	182 (83; 314)	227 (104; 393)	272 (124; 472)	318 (145; 550)
Outpatients visits	6654 (4901; 9192)	8872 (6535; 12 256)	11 090 (8169; 15 320)	13 308 (9802; 18 384)	15 525 (11 436; 21 448)
Illnesses not seeking medical care	11 807 (9235; 13 600)	15 743 (12 313; 18 133)	19 679 (15 391; 22 666)	23 615 (18 469; 27 199)	27 551 (21 548; 31 733)
1918-type scenario					
Lower estimate for AR					
Deaths	297 (232; 377)	396 (309; 502)	495 (386; 628)	595 (463; 753)	694 (540; 879)
Hospitalizations*	1246 (537; 2248)	1661 (716; 2997)	2076 (895; 3746)	2491 (1074; 4495)	2907 (1253; 5245)
Outpatients visits**	6465 (6056; 6758)	8620 (8075; 9011)	10 775 (10 094; 11 263)	12 930 (12 112; 13 516)	15 085 (14 131; 15 769)
Illnesses not seeking medical care**	10 631 (9959; 11 113)	14 175 (13 278; 14 817)	17 719 (16 598; 18 521)	21 262 (19 917; 22 226)	24 806 (23 237; 25 930)
Upper estimate for AR					
Deaths	417 (304; 561)	556 (405; 748)	695 (507; 935)	834 (608; 1122)	973 (709; 1309)
Hospitalizations*	1361 (621; 2356)	1815 (828; 3141)	2269 (1036; 3926)	2722 (1243; 4711)	3176 (1450; 5496)
Outpatients visits**	6077 (5667; 6384)	8103 (7556; 8513)	10 128 (9444; 10 641)	12 154 (11 333; 12 769)	14 180 (13 222; 14 897)
Illnesses not seeking medical care**	10 784 (10 056; 11 329)	14 379 (13 408; 15 106)	17 973 (16 760; 18 882)	21 568 (20 112; 22 659)	25 163 (23 463; 26 435)

*Hospitalizations for a 1918-type scenario were estimated by following steps: (i) To calculate the ratio of hospitalizations and deaths for the 1968-type scenario; (ii) Hospitalizations for a 1918-type scenario was produced by using the above ratio multiply the deaths for the 1918-type scenario.

**Outpatient visits and illnesses for which medical care was not sought for a 1918-type scenario were estimated by following steps: (i) To calculate the total number of clinical cases by age group, using the population multiply gross attack rate and percentage of all cases in different age groups separately; (ii) To calculate the residual total number of outpatient visits plus illness for which medical care was not sought for a 1918-type scenario, by subtracting deaths and hospitalizations from total clinical cases; (iii) To distribute the total residual patients into outpatient visits and illness for which medical care was not sought using the proportions from the 1968-type scenario.

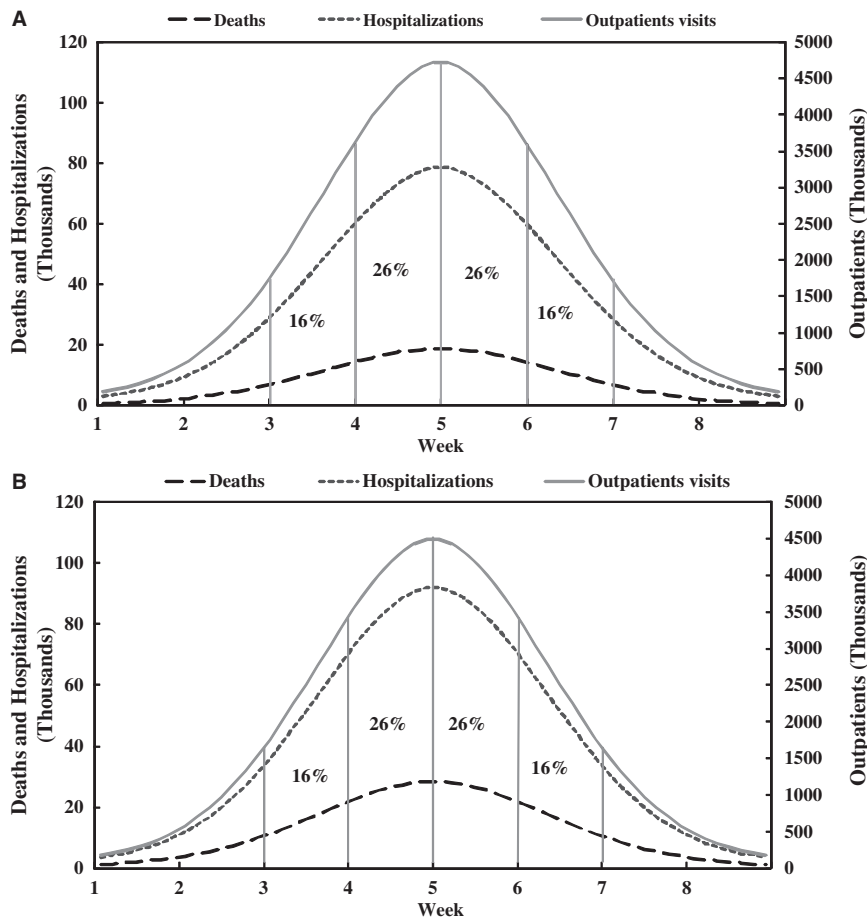


Figure 1. Time distribution of cases during 8 weeks in a 1968-type pandemic in China. Panel A: lower estimate for AR; panel B: upper estimate for AR.

future influenza pandemic. These uncertainties suggest that the most prudent course for public health authorities is to prepare for a relatively severe pandemic.

The burden of any future pandemic will depend on relative attack and complication rates for various population groups. For example, in a 1968-type scenario, those aged 60 years and older in China would account for the greatest proportion of pandemic-associated deaths. Such a pattern is in accordance with the 'U' or 'J' shaped mortality curves seen in America and Britain during the 1968–1969 pandemic,^{21,37} and in the Netherlands.^{17,18} However, these findings differ from those from other modelling studies conducted in the United States⁸ and in France.⁹ In these studies, a greater percentage of the US than the Chinese adult population was estimated to be at high-risk of influenza complications,⁸ and the criteria used to estimate death and hospitalization rates were different in the French study.⁹ In a 1918-type pandemic scenario, we estimated that the 20–59 age group would bear the heaviest mortality burden, reflected in a characteristic 'W' shaped excess mortality curve similar to that seen during the 1918 pandemic.^{21,37} Our results contrast with those from other studies estimating the pandemic disease burden in China.

For example, in a 1918-type scenario, our maximum number of deaths (13 090 000) was 8.1% lower than the deaths found for a severe scenario (14 240 000) in a study by McKibbin *et al.* using an APG-Cubed model.³⁸ Our death estimate was 26.7% lower than the 90th percentile for deaths (17 860 000) in the Murray *et al.* study, which used an ordinary least squares regression model.¹⁹ Our lower estimates in this case may be due to the use of different mathematical models, and the use of Chinese census data for the year 2000 in our study, while sampled Chinese population data for the years 2004³⁸ and 2006¹⁹ were used in the other two studies.

It is clear that the demands of a severe influenza pandemic would overwhelm the Chinese hospital system. The number of hospitalizations we estimated during the peak weeks of a pandemic could approach 590 000 for a 1968 scenario and 5.88 million for a 1918 scenario. In 2005, China had a total number of 3 135 000 hospital beds available to care for inpatients with all diagnoses.³⁹ Even if plans to mitigate the health effects of the next pandemic are effective, it will be necessary to develop alternative methods to provide care to large numbers of patients with illnesses that at present would result in hospital admission.

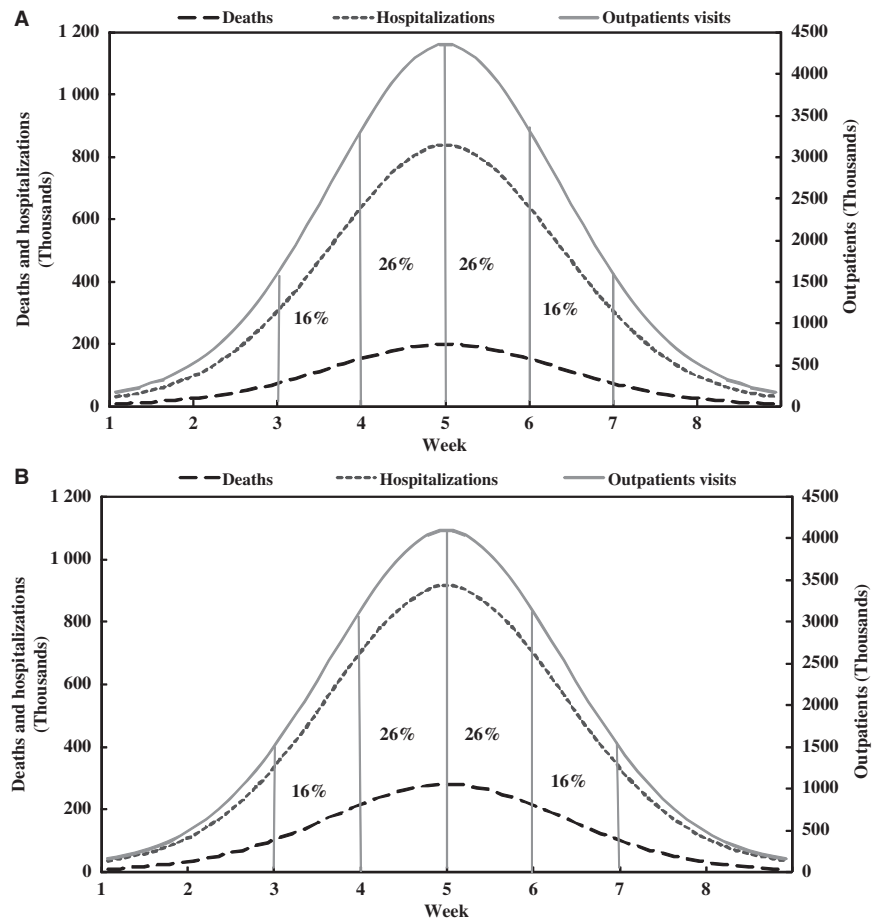


Figure 2. Time distribution of cases during 8 weeks in a 1918-type pandemic in China. Panel A: lower estimate for AR; panel B: upper estimate for AR.

Our study has several limitations. Our estimates of the outcomes of pandemic impact in China depend on historical rates of death, hospitalizations and outpatient visits; however, most of these rates were derived from other countries, and they may not reflect the situation in China during past pandemics. It was not possible to determine the proportion of older persons in China with chronic medical conditions, and thus we had to depend on the expert opinions of Chinese authorities. The Monte-Carlo model is a deterministic model and can only provide an estimate of the overall impact of a future pandemic, but not describe or predict the spread of the disease through a population. In addition, although a pandemic may cause two or three waves of disease, we only simulated a first pandemic wave in this study. We did not consider the effects of interventions designed to mitigate a pandemic, such as vaccination programmes or the implementation of non-pharmaceutical interventions. However, the major goals of our study were to estimate the health impact of unmitigated pandemics – from mild to severe – to inform medical and public health pandemic planning in China.

We may have substantially underestimated the impact of the next influenza pandemic in China. The percentage of

persons at high risk for serious complications of influenza infections might be larger than the estimates used in this study, as the proportion of individuals characterized as high-risk persons was based on limited data. Furthermore, given the speed and volume of international air travel today, a pandemic virus will spread rapidly, possibly reaching all continents in less than 3 months. China's huge population and high population density may result in more rapid transmission and this could result in more morbidity and mortality than other in less densely populated countries.

Conversely, we may overestimate of the impact of next pandemic influenza, particularly for a severe 1918-type pandemic. The First World War may have increased the 1918 pandemic's effects, because of crowding of soldiers and the difficulty in providing appropriate care. Improvements since 1918 in prevention, control and treatment measures could result in lower hospitalizations and mortality rates for a future severe pandemic, although there are few data to directly support this contention. We did not attempt to assess the effects of influenza vaccines and antiviral drugs, which are the two most important medical interventions for reducing illness and deaths during a pandemic.⁷

Non-pharmaceutical interventions such as isolation, quarantine, social distancing and travel restrictions may decrease transmission and slow the progression of a pandemic, thus providing additional time for the production of vaccines and decreasing the overall health burden.^{40,41}

Our estimates of deaths, hospitalizations and outpatient visits caused by a future pandemic and the associated time distribution of cases provide important data for updating China's national pandemic preparedness plan, and may influence decisions regarding the stockpiling of health resources, pre-pandemic vaccines, antiviral drugs and the use of intervention measures. Non-pharmaceutical interventions may be particularly important for China in the early stages of the next pandemic, given the current low production capacity for influenza vaccines and antivirals. In contrast to some European countries which locally manufacture enough seasonal influenza vaccine to vaccinate for their entire populations, China's estimated maximum production capacity of seasonal influenza vaccine is only about 83 million doses (CDC, China; unpublished data).

Our initial estimates of the health effects of mild and severe pandemics for China represent only a first step in pandemic planning. The next steps in research might include studies evaluating the effects of different intervention measures, including quarantine, social distancing, vaccination and use of antiviral drugs for treatment and prophylaxis. These studies can help health authorities in China better understand the dynamics of transmission of pandemics and suggest strategies to decrease the health impact of the next pandemic.

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Conflict of interest

No authors have any conflicts of interest.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. References only available in Chinese.

Appendix S2. Figure Legends for Time distribution of cases during 6 and 12 weeks in a 1968-type and 1918-type pandemic.

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