***Epidemiology and Infection***

**Real-time estimation of the hospitalization fatality risk of influenza A(H1N1)pdm09 in Hong Kong**

Jessica Y. Wong1, Peng Wu1, Eric H. Y. Lau1, Tim K. Tsang1, Vicky J. Fang1, Lai-Ming Ho1, Benjamin J. Cowling1

**SUPPLEMENTARY MATERIAL**

This supplementary material provides additional information on the data and statistical methods used.

1. E-FLU DATA 2

2. HOSPITALZATION-TO-DEATH INTERVAL 3

3. LIKELIHOOD FUNCTION 5

4. REAL-TIME HFR ESTIMATES 6

# E-FLU DATA

We obtained data on individual patients with laboratory-confirmed H1N1pdm09 infection from the Hong Kong Hospital Authority (the e-flu database) [1, 2]. Summary of the data from 1 May 2009 through 31 December 2009 is shown in Supplementary Figure S1.



Supplementary Figure S1. Hospitalizations, deaths and cases recovered after infection with H1N1pdm09 for all ages in Hong Kong, 2009. (a) Daily number of hospitalizations. (b) Daily number of deaths. (c) Daily number of recoveries.

# HOSPITALZATION-TO-DEATH INTERVAL

We fitted the Weibull distribution to the hospitalization-to-death intervals using all data from 30 June 2009 to 31 December 2009 and stratified by age (Supplementary Figure S2). To examine the effect of the epidemic period, we fitted the distribution using partial data, from 30 June 2009 to 1 September 2009, from 30 June 2009 to 1 October 2009, and from 30 June 2009 to 1 November 2009 (Supplementary Figure S3).



Supplementary Figure S2. Distribution of hospitalization-to-death intervals among patients (a) 20-44y; (b) 45-64y; and (c) ≥65y admitted between 30 June 2009 and 31 December 2009. Dashed lines represent the posterior median and dotted lines show the 95% credible intervals.



Supplementary Figure S3. Distribution of hospitalization-to-death intervals among patients ≥20y admitted (a) between 30 June 2009 and 1 September 2009; (b) between 30 June 2009 and 1 October 2009; (c) between 30 June 2009 and 1 November 2009. Dashed lines represent the posterior median and dotted lines show the 95% credible intervals.

# LIKELIHOOD FUNCTION

We used the method proposed by Garske et al. [3] which is based on the cumulative cases and deaths and a fitted Weibull distribution (“HFR3”) for the hospitalization-to-death distribution. We constructed the likelihood functions for *HFR3(t)* as follow.

Define *Xi(t)* as the indicator of an individual *i* died on or before day *t* with hospitalization on day *ui*.

Then, *Xi(t) ~* Bin*(1, HFR3(t)×F(t-ui))*,where *F(.)* is the Weibull cumulative distribution function of time from hospitalization to death based on data available at time *t*.

We assumed the distribution of the interval from hospital admission to death remained the same over the course of the pandemic. The likelihood for *HFR3(t)* is

****

# REAL-TIME HFR ESTIMATES

We estimated the hospitalization fatality risk of H1N1pdm09 in real-time using three different estimators, starting from August 2009 (Figure 1). Point estimates with 95% credible intervals for the three methods at four different time points are shown in Supplementary Table S1.

Supplementary Table S1. Real-time estimates of the hospitalization fatality risk by 3 methods at 4 different time points.

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **1 Aug** | |  | **1 Sep** | |  | **1 Oct** | |  | **1 Nov** | |
|  | **HFR** | **(95% CI)** |  | **HFR** | **(95% CI)** |  | **HFR** | **(95% CI)** |  | **HFR** | **(95% CI)** |
| **Adults 20-44y** |  |  |  |  |  |  |  |  |  |  |  |
| No. of deaths | 2 |  |  | 4 |  |  | 8 |  |  | 9 |  |
| No. of cases | 105 |  |  | 337 |  |  | 678 |  |  | 846 |  |
| HFR1 | 2.53% | (0.57%, 6.73%) |  | 1.37% | (0.48%, 3.05%) |  | 1.28% | (0.61%, 2.31%) |  | 1.15% | (0.57%, 2.00%) |
| HFR2 | 2.98% | (0.68%, 7.87%) |  | 1.50% | (0.53%, 3.33%) |  | 1.40% | (0.67%, 2.52%) |  | 1.20% | (0.60%, 2.09%) |
| HFR3 | NA |  |  | NA |  |  | 1.54% | (0.72%, 3.03%) |  | 1.25% | (0.63%, 2.28%) |
|  |  |  |  |  |  |  |  |  |  |  |  |
| **Adults 45-64y** |  |  |  |  |  |  |  |  |  |  |  |
| No. of deaths | 1 |  |  | 5 |  |  | 12 |  |  | 19 |  |
| No. of cases | 51 |  |  | 210 |  |  | 419 |  |  | 565 |  |
| HFR1 | 3.26% | (0.50%, 10.34%) |  | 2.68% | (1.03%, 5.39%) |  | 3.01% | (1.64%, 4.93%) |  | 3.47% | (2.17%, 5.23%) |
| HFR2 | 3.93% | (0.60%, 12.35%) |  | 3.17% | (1.23%, 6.40%) |  | 3.35% | (1.83%, 5.45%) |  | 3.71% | (2.32%, 5.58%) |
| HFR3 | NA |  |  | 4.45% | (1.56%, 11.12%) |  | 3.64% | (2.05%, 6.21%) |  | 3.62% | (2.27%, 5.47%) |
|  |  |  |  |  |  |  |  |  |  |  |  |
| **Elderly** ≥**65y** |  |  |  |  |  |  |  |  |  |  |  |
| No. of deaths | 0 |  |  | 1 |  |  | 9 |  |  | 15 |  |
| No. of cases | 22 |  |  | 139 |  |  | 278 |  |  | 359 |  |
| HFR1 | NA |  |  | 1.18% | (0.18%, 4.00%) |  | 3.45% | (1.70%, 6.07%) |  | 4.36% | (2.54%, 6.76%) |
| HFR2 | NA |  |  | 1.51% | (0.23%, 5.00%) |  | 4.09% | (2.03%, 7.17%) |  | 4.63% | (2.70%, 7.16%) |
| HFR3 | NA |  |  | NA |  |  | 4.30% | (2.16%, 7.44%) |  | 4.63% | (2.66%, 7.38%) |

NA=not available due to insufficient number of deaths.

**REFERENCES**

1. Cowling BJ, Lau MS, Ho LM, et al. The effective reproduction number of pandemic influenza: prospective estimation. *Epidemiology* **2010**;21(6):842-6.

2. Wu JT, Ma ES, Lee CK, et al. The infection attack rate and severity of 2009 pandemic H1N1 influenza in Hong Kong. *Clin Infect Dis* **2010**;51(10):1184-91.

3. Garske T, Legrand J, Donnelly CA, et al. Assessing the severity of the novel influenza A/H1N1 pandemic. *BMJ* **2009**;339:b2840.