

## Supplementary appendix

### Development of influenza-associated disease burden pyramid in Shanghai, China, 2010–2017: a Bayesian modelling study

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## S1. Negative binomial regression models in a Bayesian framework.

We used negative binomial regression models in a Bayesian framework to estimate the influenza-associated mortality rate, hospitalisation rate, and ILI outpatient visit rate across different age groups and causes of disease from 2010 to 2017 in Shanghai. The basic models were as follow:

$$\left\{ \begin{array}{l} Y_t \sim NB(r, r/(r + \mu_t)) \\ \log(\mu_t) = \beta_0 + \beta_1[A(H1N1)]_{t-i} + \beta_2[A(H3N2)]_{t-i} + \beta_3[B]_{t-i} + ns(t) + ns(AH_t) \end{array} \right.$$

We used the matrix product of a design matrix  $x[, k]$  and a vector of unknown parameters  $b_k$  to describe  $ns(x)$ :

$$\begin{aligned} ns(t) &= \sum_{k=1}^K b_{1k} t[, k] \\ ns(AH_t) &= \sum_{k=1}^4 b_{2k} AH_t[, k] \end{aligned}$$

Where,

- $Y_t$  is the observed number of deaths, hospitalisations, or ILI outpatient visits at week  $t$ . The variable  $Y_t$  is assumed to follow a negative binomial distribution with size parameter  $r$  and probability parameter  $r/(r + \mu_t)$ .
- $A(H1N1)_{t-i}$ ,  $A(H3N2)_{t-i}$  and  $B_{t-i}$  denote the influenza activity proxies (LAB%) for influenza  $A(H1N1)$ ,  $A(H3N2)$  and  $B$  viruses, respectively, at week  $t - i$ ,  $i$  denotes the lag time between influenza infection and health outcome, which varies from 0 to 3 weeks.
- $ns(t)$  and  $ns(AH_t)$  denote the smooth functions of calendar week and absolute humidity respectively.

The priors specified in the Bayesian model were the following:

- $\beta_0 \sim Normal(0, 10^6)$
- $\beta_i \sim Normal(0, 10^6)^+$ ,  $i = 1, 2, 3$ , where  $Normal(0, 10^6)^+$  is the truncated Normal distribution restricted to positive values.

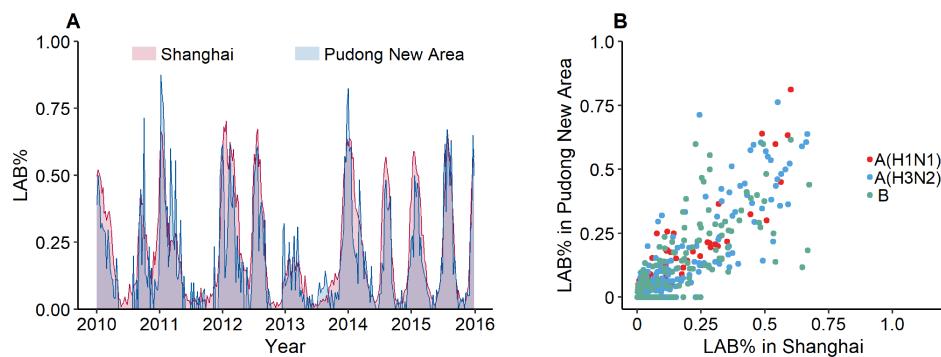
- $b_{1k} \sim Normal(0, 10^6)$
- $b_{2k} \sim Normal(0, 10^6)$
- $r \sim uniform(0, 50)$

**S2. Extrapolation of influenza-associated ILI outpatient visits from surveillance hospitals to general population in Shanghai.**

We assumed that the proportion of ILI outpatient visits among medicine and pediatric outpatient visits in the surveillance hospitals of Pudong New Area is representative of Shanghai. Thus, influenza-associated ILI outpatient visit rates were calculated as the product of the proportion of influenza-associated ILI outpatient visit in surveillance hospitals and the proportion of medicine and pediatric outpatient visits in the population.

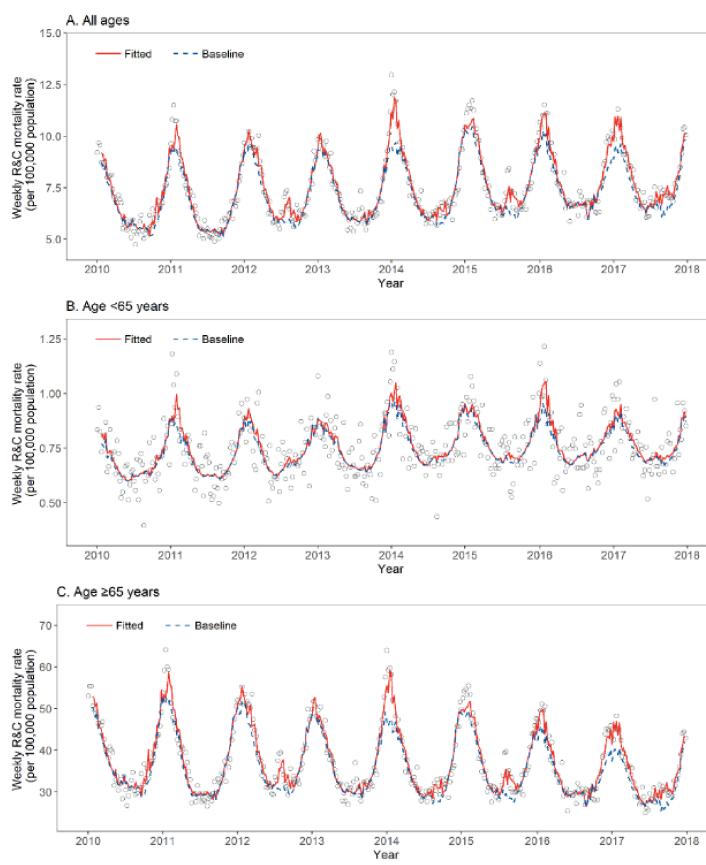
*Influenza – associated ILI outpatient visits in Shanghai*

$$\begin{aligned} & \frac{\text{Total general population in Shanghai}}{\text{Total medicine and pediatric outpatient visits in Shanghai}} \\ = & \frac{\text{Total general population in Shanghai}}{\text{Total influenza – associated ILI outpatient visits in surveillance hospitals}} \\ \times & \frac{\text{Total influenza – associated ILI outpatient visits in surveillance hospitals}}{\text{Total medicine and pediatric outpatient visits in surveillance hospitals}} \end{aligned}$$

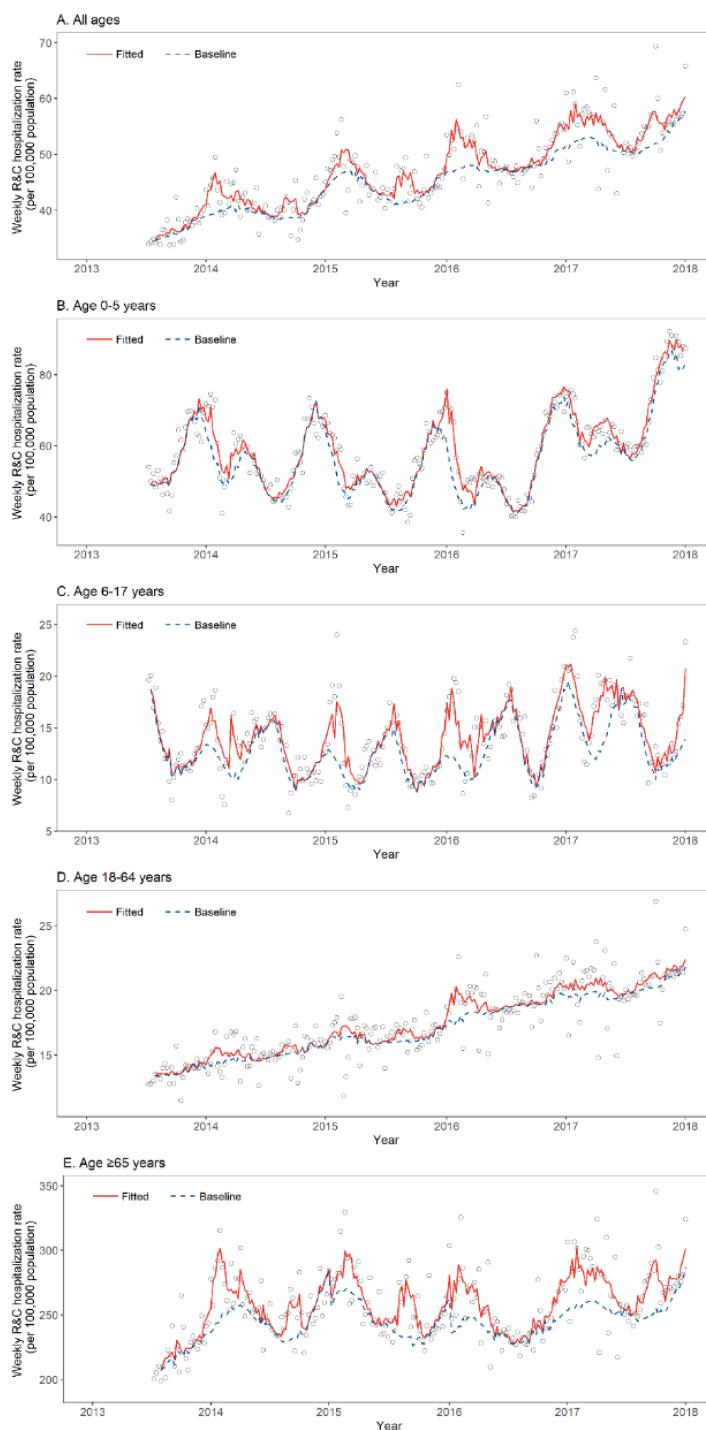


**Figure S1. Weekly LAB% in Shanghai and Pudong New Area, 2010-2015.**

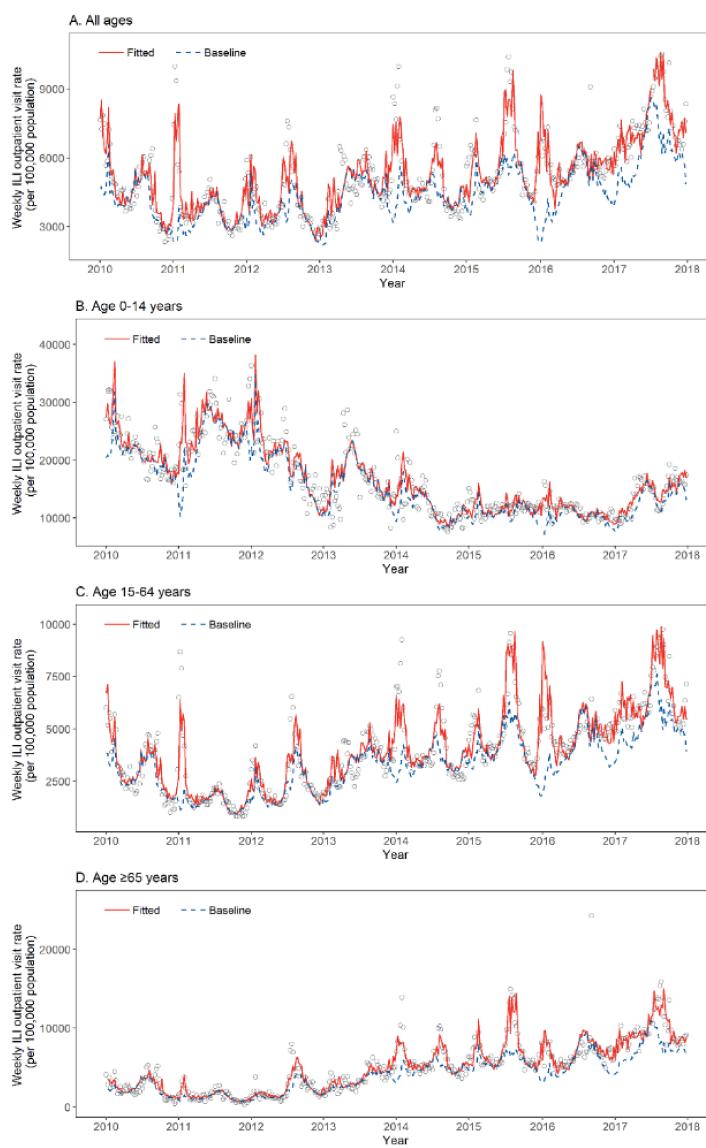
LAB%, weekly positive proportions of laboratory-confirmed influenza. Pearson's correlation coefficients of LAB% between Pudong New Area and Shanghai are 0.93, 0.88 and 0.80 for influenza A(H1N1), A(H3N2), and B, respectively.



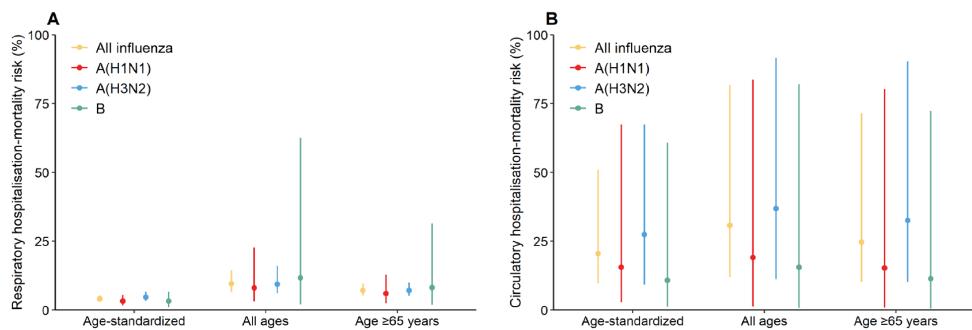
**Figure S2. Weekly observed, fitted, and baseline respiratory and circulatory mortality rates by negative binomial regression model in Shanghai, 2010-2017.** R&C, respiratory and circulatory disease.



**Figure S3. Weekly observed, fitted, and baseline respiratory and circulatory hospitalisation rates by negative binomial regression model in Shanghai, 2013-2017.** R&C, respiratory and circulatory disease.



**Figure S4. Weekly observed, fitted, and baseline influenza-like illness outpatient visit rates by negative binomial regression model in Shanghai, 2010-2017.** ILI, influenza-like illness.



**Figure S5. Clinical severity of influenza with different influenza virus types/subtypes and age groups.** (A) Respiratory hospitalisation-mortality risk; (B) Circulatory hospitalisation-mortality risk.

**Table S1. Posterior parametric coefficients of the influenza activity proxy.**

	R&C mortality			R&C hospitalisation				ILI outpatient visit				
	All ages	<65 y	≥65 y	All ages	0-5 y	6-17 y	18-64 y	≥65 y	All ages	0-14 y	15-64 y	≥65 y
Lag0												
$\beta_1$	0.314	0.354	0.313	0.168	0.389	0.563	0.121	0.142	1.750	0.970	2.071	1.431
$\beta_2$	0.250	0.094	0.270	0.158	0.074	0.231	0.090	0.195	0.733	0.270	0.814	0.921
$\beta_3$	0.148	0.075	0.165	0.162	0.287	1.061	0.158	0.160	0.724	0.512	0.601	0.668
DIC	5104.645	3291.688	5044.033	3986.287	2653.707	2381.019	3412.148	3784.309	5239.731	4261.237	4979.646	3558.903
Lag1												
$\beta_1$	0.247	0.265	0.246	0.236	0.376	0.565	0.168	0.220	1.193	0.381	1.526	1.385
$\beta_2$	0.327	0.152	0.345	0.181	0.107	0.212	0.094	0.225	0.794	0.275	0.891	1.089
$\beta_3$	0.122	0.048	0.137	0.216	0.285	0.986	0.161	0.227	0.512	0.247	0.566	0.644
DIC	5086.597	3288.968	5019.691	3967.744	2639.012	2370.057	3395.326	3766.228	5332.93	4298.581	5054.482	3529.121
Lag2												
$\beta_1$	0.214	0.249	0.208	0.209	0.261	0.395	0.163	0.197	0.349	0.042	0.703	0.945
$\beta_2$	0.333	0.131	0.351	0.172	0.115	0.167	0.075	0.239	0.775	0.214	0.834	1.067
$\beta_3$	0.120	0.066	0.128	0.160	0.276	0.616	0.110	0.174	0.203	0.075	0.307	0.395
DIC	5070.362	3276.906	5008.069	3952.272	2633.324	2380.595	3385.27	3747.855	5403.211	4302.206	5127.471	3571.984
Lag3												
$\beta_1$	0.139	0.179	0.133	0.228	0.147	0.164	0.195	0.237	0.066	0.028	0.161	0.440
$\beta_2$	0.273	0.070	0.297	0.193	0.138	0.133	0.092	0.258	0.519	0.121	0.530	0.529
$\beta_3$	0.112	0.081	0.117	0.175	0.189	0.352	0.104	0.210	0.183	0.048	0.346	0.571
DIC	5069.297	3276.217	5002.212	3931.903	2626.978	2387.809	3370.539	3726.269	5435.554	4294.45	5161.446	3638.945

$\beta_1$ ,  $\beta_2$ ,  $\beta_3$  are the coefficients of influenza A(H1N1), A(H3N2) and B viruses, respectively.

**Table S2. Ratios of influenza-associated excess mortality rates to ILI outpatient visit rates, excess hospitalisation rates to ILI outpatient visit rates, and excess mortality rates to hospitalisation rates by influenza virus types/subtypes and age groups.**

	All influenza	A(H1N1)	A(H3N2)	B
<b>Outpatient-mortality risk (%)</b>				
Age-standardised	0.76 (0.48, 1.09)	0.32 (0.08, 0.68)	1.20 (0.69, 1.83)	0.51 (0.08, 1.28)
All ages	1.69 (0.97, 2.48)	0.71 (0.06, 1.63)	2.51 (1.23, 3.99)	1.16 (0.06, 3.26)
≥65 years	7.45 (4.53, 11.18)	4.27 (0.36, 11.14)	7.98 (4.34, 12.28)	7.82 (0.51, 24.61)
<b>Outpatient-hospitalisation risk (%)</b>				
Age-standardised	10.01 (7.04, 13.46)	6.03 (2.94, 9.60)	12.32 (7.03, 19.16)	10.41 (5.33, 18.66)
All ages	11.09 (5.23, 17.39)	6.56 (0.78, 13.40)	14.22 (4.63, 25.20)	9.21 (0.68, 25.49)
≥65 years	63.12 (34.84, 92.66)	47.24 (6.03, 93.48)	60.36 (26.97, 93.64)	54.42 (5.21, 97.30)
<b>Hospitalisation-mortality risk (%)</b>				
R&C				
Age-standardised	7.53 (4.59, 12.31)	5.28 (1.25, 14.64)	9.66 (5.11, 18.27)	4.84 (0.74, 14.46)
All ages	15.29 (7.68, 34.85)	10.61 (0.89, 60.86)	17.55 (7.50, 51.15)	11.93 (0.64, 74.56)
≥65 years	11.79 (6.37, 23.08)	8.76 (0.69, 52.20)	13.04 (6.40, 30.63)	9.56 (0.58, 60.09)
Respiratory disease				
Age-standardised	4.03 (3.06, 5.26)	3.26 (1.74, 5.45)	4.72 (3.35, 6.60)	3.23 (1.01, 6.67)
All ages	9.55 (6.54, 14.36)	8.09 (3.12, 22.68)	9.40 (6.08, 16.06)	11.70 (2.00, 62.60)
≥65 years	7.11 (5.21, 9.58)	6.02 (2.45, 12.77)	7.12 (5.10, 10.05)	8.19 (1.88, 31.38)
Circulatory disease				
Age-standardised	20.49 (9.71, 50.86)	15.65 (2.82, 69.43)	27.51 (9.17, 81.93)	10.78 (1.25, 60.79)
All ages	30.75 (11.97, 81.79)	19.14 (1.27, 83.69)	36.89 (11.21, 91.73)	15.59 (0.67, 82.09)
≥65 years	24.70 (10.17, 71.43)	15.35 (0.78, 80.25)	32.62 (10.17, 90.30)	11.48 (0.49, 72.26)

We assumed that the excess R&C deaths or hospitalisations approximate the totality of the influenza-associated deaths or hospitalisations. R&C, respiratory and circulatory disease.