Epidemiol. Infect. (2012), **140**, 1542–1550. © Cambridge University Press 2011
doi:10.1017/S0950268811002238

Excess mortality associated with the 2009 pandemic of influenza A(H1N1) in Hong Kong

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(*Accepted 12 October 2011; first published online 11 November 2011*)

SUMMARY

Reliable estimates of the burden of 2009 pandemic influenza A(pH1N1) cannot be easily obtained because only a small fraction of infections were confirmed by laboratory tests in a timely manner. In this study we developed a Poisson prediction modelling approach to estimate the excess mortality associated with pH1N1 in 2009 and seasonal influenza in 1998–2008 in the subtropical city Hong Kong. The results suggested that there were 127 all-cause excess deaths associated with pH1N1, including 115 with cardiovascular and respiratory disease, and 22 with pneumonia and influenza. The excess mortality rates associated with pH1N1 were highest in the population aged $\geqslant 65$ years. The mortality burden of influenza during the whole of 2009 was comparable to those in the preceding ten inter-pandemic years. The estimates of excess deaths were more than twofold higher than the reported fatal cases with laboratory-confirmed pH1N1 infection.

Key words: Epidemiology, influenza, statistics.

INTRODUCTION

In 2009 a novel A(H1N1) influenza strain (pH1N1) emerged to cause the worldwide pandemic [1]. In Hong Kong a total of 54 fatal cases with laboratory-confirmed pH1N1 infection were reported by the Centre of Health Protection from 31 December 2009 [2]. However, these numbers probably underestimate the mortality burden associated with pandemic influenza, because the laboratory tests necessary for confirmation of virus infections were often limited by overloaded laboratory capacity during the pandemic and some patients died from secondary bacterial infection or exacerbation of their chronic conditions after clearance of a primary influenza infection [3, 4]. Such case under-ascertainment may be influenced by age, with younger patients being more likely to be investigated and diagnosed. Previous studies have adopted several modelling approaches to estimate the excess mortality, which was defined as the difference in deaths during epidemic periods compared to statistical

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predictions from baseline periods when influenza viruses are not circulating, in order to quantify the disease burden of influenza [5]. For example, the Centers for Disease Control and Prevention in the USA (USCDC) adopted the Serfling method, which fitted a cyclic regression model to the previous 5 years of mortality data during non-epidemic periods and then predicted seasonal baseline mortality for the current year from this cyclic regression model [6]. We, and others, have developed a Poisson regression model to estimate the excess mortality, in which several confounders such as temperature, humidity and seasonality can be simultaneously adjusted for, and the influenza effect is estimated through the coefficient associated with a variable of positive isolation proportions (or numbers) of viruses based on the data from the surveillance network [7–9]. This method has been validated using an empirical dataset of laboratory-confirmed influenza cases [10]. The Poisson model has the advantage that prior determination of an influenza epidemic period is not essential, which makes it particularly suitable for the subtropics and tropics without a clearly defined seasonal pattern for influenza. During a pandemic, however, the proportions or numbers of positive influenza isolates may not be a reliable proxy for virus activity as the health authorities in many countries (including Hong Kong) used extensive laboratory testing in the early phase of the pandemic for containment and later restricted the tests to the high-risk groups because of limited laboratory capacity [11]. To address this problem, we developed a *Poisson prediction* method by modifying our previous Poisson models for disease burden of influenza and demonstrated the application of this method with the examples of the 2009 pandemic as well as seasonal influenza during the period of 1998–2008 in Hong Kong.

METHODS

The known death data coded in the International Classification of Diseases – tenth revision (ICD-10) for the study period of 1998–2009 were obtained from the Census and Statistics Department. There are three categories of underlying causes of deaths we examined in this study: cardiovascular and respiratory (CRD, ICD-10 codes I00–I99, J00–J99), pneumonia and influenza (P&I, ICD-10 codes J10–J18), and all-cause (ICD-10 codes A00–Z99). The virology data were obtained from the microbiology laboratory of Queen Mary Hospital (QMH) which tested all the virus samples collected in Hong Kong Island. The data of weekly proportions of specimens positive for influenza from Hong Kong Island were found to be highly consistent with those from the surveillance network of the Department of Health which covers the entire territory of Hong Kong [12]. Therefore, we used the Hong Kong Island data to represent the virus activity in Hong Kong in our model. The meteorological data were derived from the dataset of Hong Kong Observatory.

The details of a Poisson prediction method are described in the Supplementary material (available online). Briefly, the weekly mortality data of 1998–2009 were first detrended by removing the long-term and seasonal trends. Then the detrended dataset of 1998–2008 were fitted by a Poisson regression model with influenza virus variables and covariates of temperature and relative humidity. Temperature and humidity were included as potential confounders because both have been demonstrated to play an important role in influenza virus transmission [13] and have also been linked to mortality by numerous studies (e.g. [14, 15). The baseline mortality for 2009 was predicted from this model by fitting the observed temperature and humidity data in 2009 while setting the influenza variables as zero. A similar modelling process was applied to the inter-pandemic years of 1998–2008 to derive the baseline mortality each year. The excess mortality was defined as the difference between observed mortality and baseline mortality. Since there were few community outbreaks before July 2009 and the first fatal case of pH1N1 in Hong Kong occurred on 16 July 2009, we calculated the excess deaths during the period of 12 July to 26 December 2009 for the pandemic-associated deaths in 2009.

From October 2004 to September 2008, a systematically selected sample of paediatric patients (aged $\leqslant$18 years) who were admitted to two major general public hospitals in Hong Kong Island were all tested for infection of influenza and other respiratory viruses by immunofluorescence tests. We validated the Poisson prediction model by comparing its estimates with this empirical dataset of paediatric hospital admissions with laboratory-confirmed influenza infections, as we previously did for the Poisson regression models [10].

As sensitivity analyses, we tried different combinations of degrees of freedom for natural spline smoothing functions of confounders. In this study the statistical significance was defined as $P<0{\cdot}05$. All the analyses were conducted with R software [16].

https://doi.org/10.1017/S0950268811002238 Published online by Cambridge University Press

Table 1. *Annual rate of all-cause mortality per 100 000 population in Hong Kong*

Year	Age group (years)					All (crude)	All (age-standardized)*
	<20	20–39	40–64	65–84	⩾85		
1998	26·3	54·3	349·3	2829·2	12002·1	494·7	662·4
1999	24·8	51·8	319·2	2812·1	12142·6	494·1	650·1
2000	23·7	48·9	306·2	2763·9	12041·8	496·8	637·0
2001	22·5	52·4	288·0	2628·3	10924·9	487·8	597·9
2002	21·4	52·0	280·3	2607·4	10818·3	498·0	590·7
2003	21·5	55·0	296·3	2768·5	12121·0	551·4	636·4
2004	20·7	49·3	263·6	2576·9	11765·6	528·3	594·9
2005	21·9	46·0	258·7	2680·5	11788·4	551·6	604·2
2006	21·2	42·8	253·2	2486·5	10617·4	527·3	560·7
2007	20·6	41·8	257·4	2532·5	10871·3	549·5	571·1
2008	23·6	41·9	257·5	2525·3	11144·0	562·2	575·2
2009	21·3	41·6	260·9	2507·7	10541·3	564·6	564·5

* The 2009 mid-year population of Hong Kong was adopted as the standard population.

RESULTS

Mortality data

The age-specific mortality rates of 2009 were comparable to those of inter-pandemic years on average, and no remarkable age shift of these rates towards age groups <65 years was observed in 2009 (Table 1, Supplementary Table S1).

Annual excess mortality associated with influenza

The observed weekly mortality data and predicted baseline for all-cause mortality are shown in Figure 1 and the data for CRD and P&I are shown in Supplementary Figure S1. All the estimated annual excess rates of all-cause mortality associated with influenza were significantly higher than zero during the 11 inter-pandemic years (Table 2). The annual estimates ranged from 4·4 to 13·2/100 000 population, with the highest rates found in 2005 and lowest in 1998 (Table 2). The influenza-associated mortality burden of 2009 for all ages was smaller than 2005 and 2007, but higher than the other inter-pandemic years. We estimated that in 2009 there were a total of 641 [95% confidence interval (CI) 364–909] excess all-cause deaths associated with influenza, corresponding to a rate of 9·1/100 000 population (95% CI 5·2–13·0). The estimates for the <20, 20–39 and 40–64 years age groups were not statistically significant ($P>0·05$) in most of the study years. Those aged ⩾85 years were identified as the group with the highest mortality risks associated with influenza in all the study years and more than 90% of deaths were estimated to occur in the 65–84 and ⩾85 years age groups. Similar results were also observed for CRD and P&I mortality (Supplementary Table S2). The age-specific excess rates of all-cause mortality during the pandemic year 2009 were comparable to the average of inter-pandemic years 1998–2008. After standardizing the excess mortality rates by the 2009 mid-year population, the mortality risk of 2009 was similar to that of 2000, but lower than those of 2002, 2005 and 2007, and higher than those in the rest of study period (Table 2).

Pandemic-associated excess deaths

We estimated that there were 127 (95% CI −5 to 256) excess all-cause deaths associated with pH1N1 (Table 3). The excess deaths with underlying cause of CRD and its subcategory P&I were estimated to be 115 (95% CI 29–200) and 22 (95% CI −26 to 68), respectively, corresponding to the excess rates of 1·6 and 0·3/100 000 population. The majority of all-cause, CRD and P&I deaths attributable to the pandemic occurred in the 65–84 and ⩾85 age groups (Table 3). As of 31 December 2009, a total of 54 fatal cases of laboratory-confirmed pandemic influenza were reported via the e-flu database managed by the Hong Kong Hospital Authority and Centre for Health Protection in Hong Kong [11]. Thirty-nine of these cases had any listed diagnosis of CRD while staying in hospital and 28 had P&I. These numbers were larger than our estimates in the younger age groups and markedly smaller in the 65–84 and ⩾85 years age groups, but were almost all within the estimated

https://doi.org/10.1017/S0950268811002238 Published online by Cambridge University Press

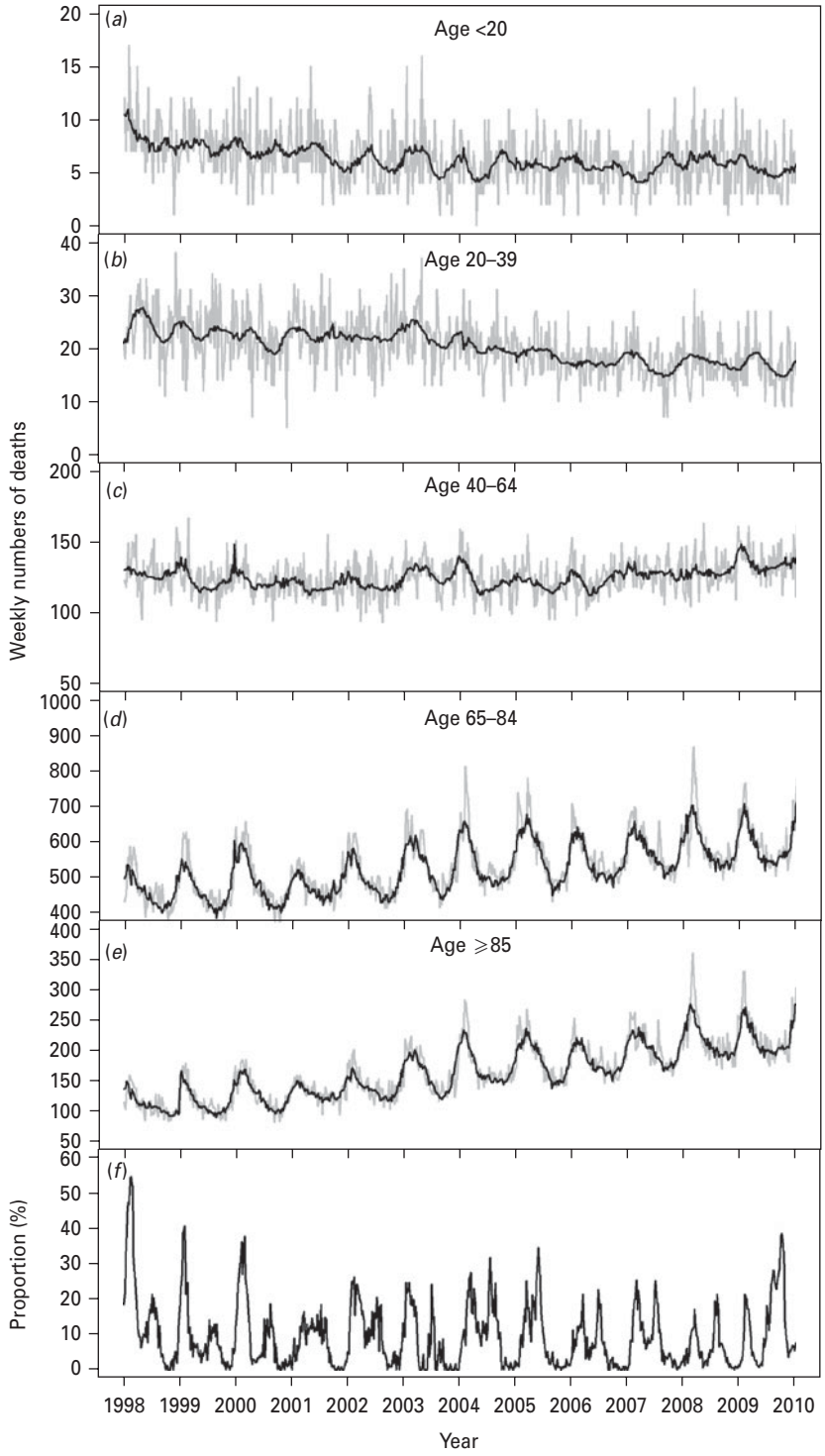

Fig. 1. Time-series plots of data. (*a–e*) Observed weekly all-cause mortality (grey line) and predicted baseline mortality from Poisson models (black line), for the <20, 20–39, 40–64, 65–84 and ⩾85 years age groups. (*f*) Weekly proportion of specimens positive for influenza A or B.

95% CI, with the exception of all-cause deaths in the 20–39 years age group, P&I in the 40–64 years group (slightly larger than upper bound) and CRD in the 65–84 years agegroup (below lower bound).

Sensitivity analysis and validation of model

The sensitivity analysis showed that changing the degrees of freedom for smoothing functions of

https://doi.org/10.1017/S0950268811002238 Published online by Cambridge University Press

Table 2. *Annual excess rate of all-cause mortality (ER) per 100 000 population associated with influenza for different age groups*

Year	Dominant subtypes*	<20 yr		20–39 yr		40–64 yr		65–84 yr		⩾85 yr		All ages (crude)		All ages (standardized)†	
		ER	(95% CI)	ER	(95% CI)	ER	(95% CI)	ER	(95% CI)	ER	(95% CI)	ER	(95% CI)	ER	(95% CI)
1998	H3N2	0·3	(−1·1 to 1·6)	0·1	(−1·4 to 1·8)	3·6	(−0·8 to 7·7)	29·4	(2·8 to 55·2)	175·2	(12·0 to 327·7)	4·4	(0·5 to 7·9)	7·6	(−0·4 to 15·1)
1999	H3N2	0·7	(−0·4 to 1·8)	−0·8	(−2·2 to 0·6)	−0·7	(−4·2 to 2·9)	45·0	(21·1 to 68·3)	142·1	(−10·9 to 284·1)	7·6	(4·2 to 11·0)	6·9	(−0·2 to 13·8)
2000	H1N1/B	0·6	(−0·5 to 1·8)	−0·5	(−2·0 to 1·0)	1·6	(−2·4 to 5·2)	51·4	(24·3 to 76·3)	159·0	(−7·2 to 315·5)	7·6	(3·6 to 11·2)	8·9	(1·0 to 16·2)
2001	H1N1/B	0·1	(−1·1 to 1·3)	0·3	(−1·3 to 1·8)	1·4	(−2·2 to 4·8)	29·4	(5·3 to 52·6)	75·4	(−63·4 to 202·1)	5·0	(1·1 to 8·7)	5·1	(−1·9 to 11·7)
2002	H3N2	1·0	(0·1 to 2·1)	0·1	(−1·5 to 1·6)	3·3	(0·1 to 6·4)	44·6	(20·9 to 66·0)	204·5	(68·2 to 327·8)	8·8	(4·8 to 12·2)	9·7	(3·0 to 15·9)
2003	H3N2	−0·6	(−1·7 to 0·5)	0·0	(−1·7 to 1·6)	1·5	(−2·2 to 4·9)	51·2	(26·9 to 76·1)	130·9	(−33·9 to 276·4)	7·6	(3·4 to 11·5)	8·2	(0·8 to 15·3)
2004	H3N2	0·7	(−0·3 to 1·6)	0·7	(−0·7 to 2·0)	−0·4	(−3·4 to 2·5)	31·4	(9·3 to 54·1)	191·8	(47·1 to 334·1)	6·3	(2·5 to 10·1)	6·7	(0·2 to 13·2)
2005	H3N2	0·4	(−0·7 to 1·6)	−0·3	(−1·9 to 1·2)	5·3	(2·2 to 8·7)	69·4	(44·5 to 94·1)	258·2	(90·8 to 429·1)	13·2	(8·5 to 17·3)	13·9	(6·6 to 21·3)
2006	H1N1/B	0·4	(−0·8 to 1·5)	−0·2	(−1·6 to 1·2)	0·6	(−2·6 to 3·6)	28·3	(6·5 to 52·2)	183·7	(35·0 to 336·6)	6·4	(2·2 to 10·4)	6·3	(−0·4 to 13·2)
2007	H3N2	0·4	(−0·6 to 1·3)	0·8	(−0·5 to 1·9)	0·9	(−2·0 to 3·9)	55·5	(34·9 to 76·2)	196·8	(62·0 to 332·7)	10·0	(6·2 to 13·6)	10·0	(3·8 to 16·1)
2008	H1N1/B	−0·2	(−1·5 to 1·0)	−0·9	(−2·3 to 0·4)	1·0	(−2·3 to 4·0)	29·5	(7·8 to 51·0)	298·7	(142·6 to 455·8)	8·1	(3·8 to 11·9)	8·1	(1·3 to 14·8)
2009	pH1N1	0·4	(−0·6 to 1·3)	0·0	(−1·2 to 1·1)	1·3	(−1·6 to 4·3)	34·1	(13·0 to 55·7)	276·2	(157·1 to 396·4)	9·1	(5·2 to 13·0)	8·8	(2·9 to 14·8)

* Dominant subtypes were defined as more than 50% of virus isolates belonging to those subtypes that year. Information was obtained from the Centre for Health Protection website (www.chp.gov.hk).

† The 2009 mid-year population of Hong Kong was adopted as the standard population.

meteorological variables did not substantially alter the estimates. We did not observe any decreasing or increasing trend in estimates that was associated with changing model parameters (Supplementary Table S3). Validation using paediatric hospitalization data showed that the Poisson prediction method performed equally well as did the Poisson regression models, in terms of providing estimates reasonably close to the directly observed hospitalization rates of laboratory-confirmed influenza cases. However, both methods tended to overestimate the true morbidity burden when compared to laboratory-confirmed pandemic hospitalizations (Supplementary Table S4).

DISCUSSION

This study reports the excess deaths with underlying causes of CRD and P&I as well as all-cause mortality associated with 2009 pH1N1. We estimated that influenza was associated with a total of 127 excess deaths from all causes, 115 for CRD and 22 for P&I during the pandemic period of July–December 2009. These numbers were equivalent to the rates of 1·8, 1·6 and 0·34/100 000 population. A recent Australian study has reported that their pandemic estimates for all-cause mortality based on Serfling regression methods were significantly lower than their baseline levels, which was probably due to low death rates observed in the older population during the pandemic [17]. The USCDC adopted a probability model that utilized data from some health-seeking behaviour surveys, and estimated that pH1N1-related deaths ranged from 2500 to 6000 (2·9–6·0 deaths/100 000 population) between April and October, 2009 [18, 19]. Our estimates are lower than the USCDC estimates, and also substantially lower than the preliminary estimates by Viboud *et al.*, who projected 7500 excess deaths for P&I (2·5/100 000 population) and 44 100 excess deaths for all-cause (14·7/100 000 population) attributable to influenza based on the provisional mortality surveillance data of the 122 cities in the USA [20]. A study in Navarre, Spain calculated the excess mortality of the pandemic as the difference between the observed mortality in 2009 and the annual average rate of 2006–2008 during the same period of the year (weeks 24–52) [21]. This study estimated an excess rate of 102/100 000 population for persons aged ⩾65 years, which is also much higher than our estimate. This could potentially be explained by regional heterogeneity in disease severity, population susceptibility and also control measures adopted by

https://doi.org/10.1017/S0950268811002238 Published online by Cambridge University Press

Table 3. *Excess deaths associated with the pH1N1 during July–December 2009*

Disease	Age (years)	Excess number (95% CI)		Excess rate (95% CI)*		Confirmed number†	Confirmed rate (95% CI)	
All-cause	<20	1	(−5 to 6)	0·1	(−0·4 to 0·5)	2	0·2	(−0·1 to 0·4)
	20–39	−6	(−17 to 5)	−0·3	(−0·8 to 0·2)	10	0·5	(0·2 to 0·8)
	40–64	16	(−22 to 54)	0·6	(−0·8 to 2·0)	25	0·9	(0·6 to 1·3)
	65–84	73	(−10 to 153)	9·3	(−1·3 to 19·5)	13	1·7	(0·8 to 2·6)
	⩾85	49	(−16 to 114)	44·3	(−14·5 to 102·7)	4	3·6	(0·1 to 7·1)
	All ages	127	(−5 to 256)	1·8	(−0·1 to 3·7)	54	0·8	(0·6 to 1·0)
CRD	40–64	18	(−2 to 37)	0·7	(−0·1 to 1·4)	18	0·7	(0·4 to 1·0)
	65–84	72	(21 to 124)	9·2	(2·7 to 15·9)	6	0·8	(0·2 to 1·4)
	⩾85	26	(−27 to 74)	23·4	(−23·9 to 66·3)	3	2·7	(−0·4 to 5·7)
	All ages	115	(29 to 200)	1·6	(0·4 to 2·9)	39	0·6	(0·4 to 0·7)
P&I	40–64	0	(−9 to 9)	0·0	(−0·3 to 0·3)	11	0·4	(0·2 to 0·7)
	65–84	15	(−11 to 40)	1·9	(−1·4 to 5·2)	3	0·4	(−0·1 to 0·8)
	⩾85	8	(−22 to 37)	7·3	(−19·4 to 33·1)	3	2·7	(−0·4 to 5·7)
	All ages	22	(−26 to 68)	0·3	(−0·4 to 1·0)	28	0·4	(0·3 to 0·5)

CRD, Cardiovascular and respiratory diseases; P&I, pneumonia and influenza.

* Rates were calculated as deaths per 100 000 population.

† The numbers of laboratory-confirmed pandemic fatal cases were obtained from the e-flu database managed by the Hong Kong Hospital Authority and Centre for Health Protection. The disease-specific deaths were calculated as the fatal cases with any listed diagnosis of CRD or P&I.

governments. According to our estimates, the majority of pH1N1-associated excess deaths had CRD as the underlying cause of death. This finding is consistent with laboratory-confirmed data, of which 72% had CRD as any listed diagnosis. The USCDC also reported 78% of pandemic deaths in the USA had pre-existing medical conditions [22]. Taken together, people with chronic conditions were still the primary victims of pH1N1, as we observed for seasonal influenza.

Our previous Poisson models with pH1N1 proportions as a proxy variable returned a markedly large estimate of 247 (95% CI −335 to 835) for pH1N1-associated deaths, compared to the estimates of 127 (95% CI −5 to 256) from the present Poisson prediction method. The estimates for inter-pandemic years were simultaneously inflated, probably due to the offseason spike of virus proportions during the pandemic (Supplementary Table S3). In this study we revised the previous Poisson modelling approach to develop a Poisson prediction method, in which the Poisson models with influenza virus variables from relatively stable surveillance of 11 consecutive years preceding 2009 were used to predict the baseline mortality in the absence of influenza in 2009. In this way, we expected to minimize the potential bias introduced by sudden changes in surveillance practice and also the influence of offseason peaks caused by the pH1N1 pandemic. The estimates for inter-pandemic years produced by this method were lower than the mortality burden estimates for 1998–2007 by a US study and also lower than our previous estimates for 1996–1999, both of which were from Poisson regression models [23]. Although it is almost impossible to validate this model by a dataset of laboratory-confirmed influenza deaths, we chose an alternative empirical dataset of paediatric hospital admissions with laboratory-confirmed influenza [24]. The performance of this new method was comparable to the previous Poisson regression model when compared to a 'gold-standard' of virologically confirmed hospital admissions in children during the inter-pandemic period. Furthermore, given the relatively intensive survey during the pandemic and great attention paid to children and young adults, the laboratory-confirmed pandemic deaths were a reliable indicator of mortality burden in children and young adults. Further comparison with these data, as shown in Table 3, suggested that our estimates were quite close to the reported fatalities in children and young adults. The only exception is the negative estimate in the 20–39 years age group. This could be due to the relatively small number of deaths in this group, which makes it difficult to obtain a good estimate for this age group during the short pandemic period. Nevertheless, overall our model is good and valid in providing

https://doi.org/10.1017/S0950268811002238 Published online by Cambridge University Press

estimates for excess mortality associated with the pandemic. The Poisson prediction method can be recommended for estimation of excess mortality or hospitalization associated with pandemic influenza, when influenza virology data are unlikely to be a reliable proxy for influenza virus activity due to interrupted or changed surveillance practices or other reasons.

Case-fatality rate (CFR) is one of the key severity measures for the pH1N1 pandemic. However, it is difficult to obtain reliable estimates for both denominator (infection or symptomatic cases) and numerator (death from pH1N1) [25]. The denominator of infection cases could be derived from two serological studies conducted in Hong Kong. One study estimated the cumulative incidence of infection was 10·7% of persons aged 5–59 years between June and November 2009 [26]. Another study analysed 770 paired sera that were obtained from 469 households during July 2009 and February 2010, and estimated that the attack rates by pH1N1 up to the end of January 2010 were 39%, 8·9%, 5·3%, and 0·77% for the 3–19, 20–39, 40–59, and $\geqslant$60 years age groups, respectively, and 16% for the whole Hong Kong population [27]. These data imply denominators of 1 098 296 infection cases and 6567 for the all-age and older age groups, respectively. With our mortality estimates as numerators, the CFR per *infection* case was 0·01% and 1·8% for these two age groups. Presanis and colleagues estimated that the CFR per *symptomatic* case was 0·048% (95% CI 0·026–0·096), based on data from health-seeking behaviour surveys in two cities of the USA [28]. Given the presence of asymptomatic cases, the CFR per *symptomatic* case in Hong Kong could be even higher than the CFR per *infection* case, and closer to the range of the US estimates. Previous studies have reported that the CFR of the 1918 'Spanish flu' pandemic was 2%, and the 1957 'Asian flu' pandemic was 0·1% [29, 30]. Although it is difficult to directly compare our estimates with these because of different denominators, the 2009 pH1N1 pandemic appears to have had a substantially lower mortality burden than previous pandemics.

Unlike in the previous pandemics [31, 32], evidence was limited to support an age shift of mortality towards younger people in the 2009 pH1N1 pandemic. We found the all-cause mortality risks attributable to the 2009 pandemic were still higher in the elderly, which is consistent with the findings of many observational studies [33–35], but contradictory to the findings of a US study that 87% of excess deaths of pH1N1 occurred in the population aged $<$65 years [36]. However, the US study adopted a different method which assumed the numbers of deaths proportional to hospitalizations; therefore their estimates reflect the higher proportion of pH1N1 hospital admissions in the younger ages. The gap between the numbers of reported fatal cases and our estimates in the older population probably reflects a major under-ascertainment of influenza-related illness in this age group. This may be due to the fact that many influenza-initiated fatalities are attributed to secondary bacterial complications and to exacerbation of underlying diseases such as chronic obstructive airways disease or ischaemic heart disease. Although many older persons were protected from the 2009 pH1N1 virus by pre-existing immunity [37], those who were susceptible and had acquired infection appear to have been more likely to get serious complications. Enhancing community-based laboratory surveillance could help capture these influenza cases in older adults. Laboratory-confirmed cases for young age groups were all close to the upper bound of our estimates, suggesting that the true mortality burden of influenza could be obtained by intensive virological surveillance in hospitals for these age groups.

There are several limitations in our study. First, there were still some seasonal influenza viruses isolated during the 2009 pandemic, so our estimates probably also included the excess deaths attributable to seasonal influenza. According to the QMH data, around 20% of laboratory-confirmed influenza cases had seasonal influenza infections during July–December 2009. The Poisson prediction method did not differentiate the excess deaths attributed to seasonal or pandemic influenza. In an attempt to adjust for seasonal influenza, we calculated the weekly numbers of excess mortality specifically attributable to pH1N1 according to the weekly proportions of specimens positive for pH1N1 among all the specimens positive for influenza. The estimates of excess deaths specifically allocated to pH1N1 were similar to those without adjustment (data not shown). However, such allocation is rather crude because it is difficult to know whether seasonal influenza posed a similar mortality risk as pH1N1 did in the pandemic period and whether the two viruses had a comparable impact across different age groups. Second, our models could not simultaneously estimate the effects of co-circulating respiratory viruses. Third, the Poisson prediction method requires several years of virology

data with the surveillance networks following consistent surveillance criteria, which may not be available in some countries. The Poisson prediction method can be combined with the widely used Poisson models to provide the full-range estimates. The latter can be used for estimation of disease burden when the sample collection procedure does not change, but the former method should be considered when the virus surveillance practices are markedly changed in the short term, thus leading to short-term distortions of the trend of true virus activity.

In this study we demonstrated that pH1N1 posed a disease burden comparable to that of inter-pandemic seasonal influenza. The mortality rates associated with pandemic influenza were found highest in the elderly. The difference between estimated excess deaths and reported laboratory-confirmed deaths was greatest in the elderly, which highlights the need to enhance influenza surveillance in both private and public clinic sectors as well as in the community.

NOTE

Supplementary material accompanies this paper on the Journal's website (http://journals.cambridge.org/hyg).

ACKNOWLEDGEMENTS

We thank Dr E. H. Y. Lau and Dr L. M. Ho for their assistance in data collection. This work was supported by the Research Fund for the Control of Infectious Diseases (11100582) and the Area of Excellence Scheme of the University Grants Committee (AoE/M-12/06) of the Hong Kong Special Administrative Region Government.

DECLARATION OF INTEREST

None.

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