Effect of increased influenza and pneumococcal vaccine coverage on the burden of influenza among elderly people in Hong Kong versus Brisbane: abridged secondary publication

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KEY MESSAGES

1. Influenza and pneumococcal vaccine uptake in older adults of Hong Kong has dramatically increased since the SARS outbreak in 2003. This enables estimation of the effect of increased vaccine coverage by comparing the relative change in influenza disease burden with Brisbane, where vaccine coverage remained stable before and after 2003.
2. Compared with the low vaccination period (pre-SARS), during the first 6 years of high vaccination (post-SARS), influenza-associated excess rates of cardio-respiratory disease, stroke, and ischaemic heart diseases mortality decreased more in Hong Kong than in Brisbane.
3. After the 2009 H1N1 pandemic, excess rates of all-causes mortality increased in Hong Kong but to a lesser extent than in Brisbane.
4. This study provides limited evidence that markedly increased vaccination rates have reduced influenza disease burden in elderly people of Hong Kong.

Hong Kong Med J 2020;26(Suppl 4):S12-6
HMRF project number: 13121282

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Introduction

Influenza is associated with heavy burden of mortality and morbidity globally. Vaccination is an important strategy to reduce disease severity and virus transmission within the community. Few studies have been conducted in high-risk older peoples or those with underlying chronic conditions, although many countries recommend annual influenza vaccination or subsidy programmes to these high-risk groups. An ongoing debate on the true effectiveness of influenza vaccines in the elderly people highlights a need to evaluate the impact of influenza vaccines at the population level.[1]

In Hong Kong, the annual vaccination rate for community-dwelling elders were <3% between 2000 and 2002,[2] but it increased to >50% between 2004 and 2006.[3] In Australia, free influenza vaccine is provided for people aged ≥65 years since 1999, and the coverage rate in older adults was 70% to 80% between 2002 and 2006.[4] Unlike Hong Kong, where the SARS outbreak and new subsidy programme greatly increased the influenza and pneumococcal vaccine coverage in the elders, Brisbane has a fairly stable vaccination rate since 2000.

We compared the long-term trend of influenza burden in those aged ≥65 years in Hong Kong and Brisbane, with the aim to quantify the impact of influenza and pneumococcal vaccine coverage on the reduction of influenza disease burden. Given the similar socioeconomic and climate conditions between the two cities, we hypothesise that the dramatically increased uptake of influenza vaccine among elderly people of Hong Kong since SARS should have reduced mortality and hospitalisation associated with influenza in a larger extent than that in Brisbane where the vaccine uptake remained stable.

Methods

Weekly numbers of specimens tested positive for influenza A and B and weekly total numbers of specimens collected in Hong Kong were obtained from the microbiology laboratory of Queen Mary Hospital. In addition, weekly positive numbers of influenza A and B of Brisbane during 30 April 2001 to 1 January 2010 were obtained from the Queensland Health Australia, but virology data afterwards were not available. Therefore, virology

data of the Queensland state during 2 January 2010 to 16 December 2012 were obtained to approximate the virus activity in Brisbane.

Death registry data were obtained from the Census and Statistics Department of Hong Kong and from Australian Institute of Health and Welfare. Mortality data were aggregated into weekly numbers of deaths with underlying causes of all-causes (ICD10 A00-T99), cardio-respiratory disease (CRD) [ICD10 I00-J99], pneumonia and influenza (P&I) [ICD10 J09-J18], chronic obstructive pulmonary disease (COPD) [ICD10 J40-J47], stroke (ICD9 430-438; ICD10 I60-I69), and ischaemic heart diseases (IHD) [ICD10 I20-I25].

Hospital admission data were obtained from the Hospital Authority of Hong Kong and Queensland Health Australia. Weekly numbers of hospital admissions were aggregated by the discharge diagnosis of CRD (ICD9 390-459), acute respiratory disease (ICD9 460-519), P&I (ICD9 480-487), COPD (ICD9 490-496), stroke (ICD9 001-999), and IHD (ICD9 410-414).

Meteorology data including daily mean of temperature and relative humidity from 2001 to 2013 were obtained from the Hong Kong Observatory and Australian Bureau of Meteorology.

In Hong Kong, seasonal influenza peaks during January to March and June to July, whereas in Australia the influenza peaks during August to October (Fig). Given the difference in seasonal influenza peaks in these two cities, we define the influenza season as January to December in Hong Kong and May to April in Brisbane. The start dates of these seasons are three months after the usual launch dates of the annual seasonal influenza vaccination campaign (March in Brisbane and September in Hong Kong). This should allow valid assessment of the impact of vaccination. The periods defined for influenza associated disease burden estimates in Hong Kong and Brisbane are listed in Table 1.

We constructed time series segmented regression models to estimate mortality or hospitalisation risks associated with influenza in elderly people during the pre-SARS, post-SARS, and post-pandemic period for Hong Kong and Brisbane. The proxy variable of influenza in the model is the percentage of specimens positive for influenza each week among the annual total number of positive specimens in each city. The confounders of seasonal trend, temperature, humidity, and other respiratory

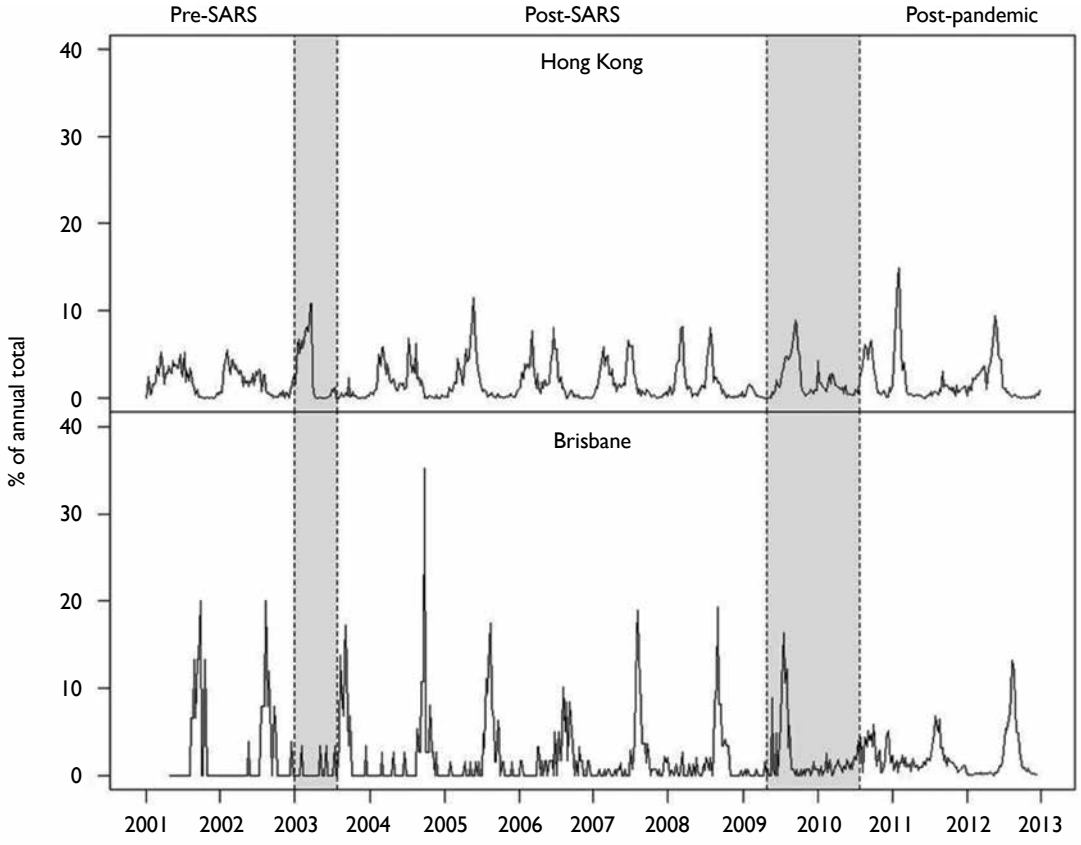

FIG. Time series plots of laboratory confirmed influenza in Hong Kong and Brisbane, 2001-2012. The gray bands highlight the SARS period and the 2009 H1N1 pandemic.

TABLE 1. Study periods defined for Hong Kong and Brisbane

Period	Hong Kong			Brisbane		
	Start date	End date	No of weeks	Start date	End date	No of weeks
Pre-SARS	31/12/2000	29/12/2002	104	30/04/2001	29/12/2002	87
SARS	30/12/2002	02/08/2003	31	30/12/2002	03/08/2003	31
Post-SARS	03/08/2003	25/04/2009	299	04/08/2003	26/04/2009	299
Pandemic	26/04/2009	31/07/2010	66	27/04/2009	01/08/2010	66
Post-pandemic	01/08/2010	29/12/2012	126	02/08/2010	16/12/2012	124

viruses were added into the model to assess influenza-associated excess risk. Dummy variables for the pre-SARS, post-SARS, and post-pandemic periods, together with the interaction terms between these period dummies and virus activity variables, were also added to test the statistical difference in the risk estimates between the different periods within each city. Baseline rates of cause-specific mortality and hospitalisation associated with influenza were calculated for different periods by setting the virus proxy to zero and the corresponding period dummy to one (other dummies set to zero simultaneously). Excess numbers were derived by subtracting baseline rates from observed data, and excess rates were further calculated by dividing age-specific population size. The 95% confidence interval of the excess rate was calculated by bootstrapping for 1000 times. Due to the different length of periods, we calculated annual rates of excess mortality (or hospitalisation) to facilitate the comparison between different periods.

The pre-SARS period was the reference period. For each disease category, the rate ratio (RR) of post-SARS (or post-pandemic) versus pre-SARS was derived by dividing the annual excess rates during the post-SARS (or post-pandemic) period to those in the pre-SARS period: RR = annual excess rate (post-SARS) / annual excess rate (pre-SARS). The ratio of RR (RRR) was calculated by dividing RR of Hong Kong with RR of Brisbane. We used the ratio of RR as measurement of relative change in influenza disease burden, because the ratio of RR is less likely to be affected by the regional heterogeneity of these factors between Hong Kong and Brisbane, compared to the commonly adopted excess mortality/hospitalisation. The 95% confidence interval and P value of RR and RRR were derived from normal approximation of their logarithm transformations. All analyses were conducted in R software version 2.5.1. Significance level was set to 0.05.

Results

Compared with the pre-SARS period, the post-SARS period had increased influenza-associated mortality rates in terms of all-causes (RR=1.22) and COPD (RR=1.04). In Brisbane, all-causes mortality reduced (RR=0.87) and COPD mortality increased but to a slightly less extent than in Hong Kong (RR=1.03, RRR=1.01, P=0.98) [Table 2]. Decreased excess rates of mortality in Hong Kong were observed for CRD (RR=0.90), stroke (RR=0.74), and IHD (RR=0.45) mortality; the corresponding RRs in Brisbane were 0.79, 0.33, and 1.09, respectively. Only IHD mortality shows a significantly greater reduction in Hong Kong than in Brisbane (RRR=0.41, P=0.005).

Compared with the pre-SARS period, in the post-SARS period, excess rates of CRD hospitalisation decreased in Hong Kong but markedly increased in Brisbane (RR=0.86 vs RR=26.82, RRR=0.03, P<0.001). Influenza-associated hospitalisation of P&I and COPD increased more in Brisbane (RR=3.49 and RR=1.33, respectively) than in Hong Kong (RR=2.79 and RR=1.04, respectively), but the differences were not significant (RRR=0.80 and RRR=0.79, respectively). However, the extremely large point estimate for the RR of CRD hospitalisation in Brisbane is due to the very small point estimate of excess CRD hospitalisation rate for the pre-SARS period, which requires a cautious interpretation.

Compared with the pre-SARS period, in the post-SARS period, the excess mortality rates increased in Hong Kong for all the disease categories except IHD, but only all-causes and COPD mortality also increased in Brisbane. The differences between Hong Kong and Brisbane were significant for all-causes and stroke mortality. Annual excess rates of all-causes mortality increased in Hong Kong to a lesser extent than in Brisbane (RR=1.41 vs RR=2.39, RRR=0.59, P<0.001), whereas an opposite changing trend was observed for stroke mortality (RR=1.26 vs RR=0.29, RRR=4.37, P=0.003).

Due to the negative estimates in annual excess rates of mortality, the post-SARS RR could not be estimated for IHD hospitalisation of Hong Kong, P&I mortality, stroke and IHD hospitalisation of Brisbane. Similarly, the post-pandemic RR could not be estimated for P&I and IHD of Hong Kong, and stroke and COPD of Brisbane.

TABLE 2. Rate ratio (RR) for excess mortality or hospitalisation associated with influenza between the post-SARS and pre-SARS (reference) periods and the ratio of RR (RRR) in Hong Kong and Brisbane

	Hong Kong	Brisbane	Hong Kong vs Brisbane	
	RR (95% confidence interval)	RR (95% confidence interval)	RRR (95% confidence interval)	P value (z-test)
Mortality of post-SARS vs pre-SARS				
All-causes	1.22 (1.10-1.35)	0.87 (0.62-1.21)	1.40 (0.99-1.98)	0.058
Cardio-respiratory disease	0.90 (0.80-1.01)	0.79 (0.54-1.15)	1.14 (0.77-1.69)	0.516
Pneumonia and influenza	2.50 (2.00-3.13)	NE	NE	-
Chronic obstructive pulmonary disease	1.04 (0.78-1.38)	1.03 (0.44-2.39)	1.01 (0.41-2.47)	0.980
Stroke	0.74 (0.50-1.09)	0.33 (0.13-0.80)	2.27 (0.85-6.05)	0.102
Ischaemic heart diseases	0.45 (0.34-0.58)	1.09 (0.62-1.90)	0.41 (0.22-0.76)	0.005
Hospitalisation of post-SARS vs pre-SARS				
Cardio-respiratory disease	0.86 (0.82-0.91)	26.82 (9.56-75.24)	0.03 (0.01-0.09)	<0.001
Pneumonia and influenza	2.79 (2.57-3.03)	3.49 (1.96-6.21)	0.80 (0.45-1.43)	0.451
Chronic obstructive pulmonary disease	1.04 (0.96-1.14)	1.33 (0.91-1.93)	0.79 (0.54-1.15)	0.217
Stroke	0.15 (0.12-0.19)	NE	NE	-
Ischaemic heart diseases	NE	NE	NE	-
Mortality of post-pandemic vs pre-SARS				
All-causes	1.41 (1.28-1.56)	2.39 (1.83-3.12)	0.59 (0.44-0.79)	<0.001
Cardio-respiratory disease	1.16 (1.04-1.29)	0.98 (0.69-1.38)	1.19 (0.83-1.71)	0.352
Pneumonia and influenza	2.44 (1.95-3.05)	NE	NE	-
Chronic obstructive pulmonary disease	1.07 (0.81-1.41)	1.75 (0.83-3.67)	0.61 (0.28-1.35)	0.225
Stroke	1.26 (0.90-1.77)	0.29 (0.12-0.72)	4.37 (1.66-11.48)	0.003
Ischaemic heart diseases	0.74 (0.59-0.92)	NE	NE	-

Abbreviation: NE denotes not estimated owing to negative estimates in annual excess rates

Discussion

We estimated the excess rates of mortality or hospitalisation attributable to influenza in pre-SARS, post-SARS, and post-pandemic periods for Hong Kong and Brisbane. We hypothesised that influenza disease burden decreased more or increased less in Hong Kong than in Brisbane since 2003, because the uptake rate of influenza and pneumococcal vaccines was more markedly increased in Hong Kong than in Brisbane at the same time. In a study comparing the relative change in disease burden in Ontario (after a universal influenza vaccination programme was launched) and other Canadian provinces without such a policy.[5] Influenza-associated mortality reduced in both Ontario and other provinces, but the former had a larger reduction (RRR=0.61).[5] In the current study, compared with the pre-SARS period, during the post-SARS period, annual excess rates of IHD mortality decreased more in Hong Kong than in Brisbane, but for all the other mortality outcomes, excess rates increased more in Hong Kong (although the differences were not significant). For hospitalisation in the post-SARS period, significantly reduced excess rates were only found for CRD in Hong Kong. P&I and COPD hospitalisation rates increased in both cities, and the ratio of RRs of Hong Kong versus Brisbane was <1, although none of these estimates were significant.

Conclusion

Our findings provided limited evidence on the effective reduction of influenza-associated disease burden in older adults after the markedly increase of influenza vaccination coverage.

Acknowledgement

We thank the Census and Statistics Department, Hospital Authority of Hong Kong, Hong Kong Observatory, Australian Bureau of Meteorology, Australian Institute of Health and Welfare, Department of Health of the Australian Government, and Queensland Health Australia for providing the datasets.

Funding

This study was supported by the Health and Medical Research Fund, Food and Health Bureau, Hong Kong SAR Government (#13121282). The full report is available from the Health and Medical Research Fund website (https://rfs1.fhb.gov.hk/index.html).

Disclosure

Results from this study have been previously published in:
(1) Wang XL, Wong CM, Yang L, et al. Developing an epidemic forecasting model for influenza A in Brisbane, Australia based on climate and Hong Kong influenza A surveillance data. Clin Infect Dis 2014:59:1508-9.
(2) Yang L, Chan KP, Wong CM, et al. Comparison of influenza disease burden in older populations of Hong Kong and Brisbane: the impact of influenza and pneumococcal vaccination. BMC Infect Dis 2019;19:162.

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