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Short Communication

Anti-phase synchronization of influenza A/H1N1 and A/H3N2 in Hong Kong and countries in the North Temperate Zone

Alice P.Y. Chiu[a], Qianying Lin[a], Edwin Yiu Nam Tang[b], Daihai He[a,*]

[a] Department of Applied Mathematics, Hong Kong Polytechnic University, Hong Kong SAR, China
[b] St. Paul's Co-educational College, Hong Kong SAR, China

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ABSTRACT

Objectives: Influenza affects 10% of the global population annually. Hong Kong is a subtropical city close to the North Temperate Zone (NTZ). Influenza-associated mortality rates in Hong Kong were 27.53, 79.55, 36.94, and 48.72 per one million person-years in 2014, 2015, 2016, and January to July 2017, respectively. The aim of this study was to explore the temporal patterns of influenza A subtypes in both Hong Kong and the NTZ.
Methods: Weekly reported cases of influenza A/H1N1 and A/H3N2 from January 2010 to July 2017 were downloaded from the Centre for Health Protection in Hong Kong and FluNet (provided by the World Health Organization). The spatio-temporal patterns of A/H1N1 and A/H3N2 in Hong Kong and the NTZ were explored. Anti-phase synchronization between A/H1N1 and A/H3N2 is indicated by a high for A/H1N1 coinciding with a low for A/H3N2, and vice versa.
Results: Anti-phase synchronization was evident in both Hong Kong and the NTZ. It was found that A/H3N2 clearly dominated in the 2011/2012, 2014/2015, and 2016/2017 influenza seasons.
Conclusions: These results are novel in identifying anti-phase synchronization in influenza A subtypes in Hong Kong and the NTZ. These findings should inform public health preparedness for future epidemics of A/H3N2, which are typically more severe than those of A/H1N1.

Introduction

Influenza affects 10% of the global population annually (Gerdil, 2003). Influenza A/H1N1 and A/H3N2 are two major subtypes of influenza A. A/H3N2 typically has a higher case-fatality ratio among the elderly than A/H1N1, and it has evolved at a higher rate globally (Paules and Subbarao, 2017). In contrast, A/H1N1 strains have been stable since 2009 (Klein et al., 2014) and have shown a large-scale skip-and-resurgence phenomenon (He et al., 2015), i.e., minor or no outbreaks in 2011/2012 and large outbreaks in 2012/2013 in Europe and Asia. In Hong Kong, a sub-tropical city neighbouring Mainland China, the influenza-associated mortality rates were 27.53, 79.55, 36.94, and 48.72 per one million person-years in 2014, 2015, 2016, and January to July 2017, respectively (Centre for Health Protection, 2017). Influenza epidemics in Hong Kong are largely in synchrony with those in Mainland China, as well as those in other countries in the North Temperate Zone (NTZ). The aim of this study was to investigate anti-phase synchronization in Hong Kong and the NTZ, defined as the alternative dominance of A/H1N1 and A/H3N2 (He and Stone, 2003).

Methods

Weekly reported cases of A/H1N1 and A/H3N2 from January 2010 to July 2017 for Hong Kong and the NTZ (the NTZ is defined as those countries that have a latitude between 23.5N and 66.5N) were downloaded from the Centre for Health Protection in Hong Kong and from FluNet, the World Health Organization database for influenza virological surveillance, respectively. The temporal patterns of A/H1N1 and A/H3N2 were explored and compared between Hong Kong and the countries in the NTZ that met the threshold criterion of at least 2000 confirmed cases of each of A/H1N1 and A/H3N2. Wavelet decomposition and reconstruction analyses were performed to explore the temporal trends of anti-phase patterns. WaveletComp and LME4 packages of the statistical software R (version 3.4.1) were used in this study (R Core Team, 2015).

* Corresponding author at: TU804, Yip Kit Chuen Building, Department of Applied Mathematics, Hong Kong Polytechnic University, Hong Kong SAR, China.
E-mail address: daihai.he@polyu.edu.hk (D. He).

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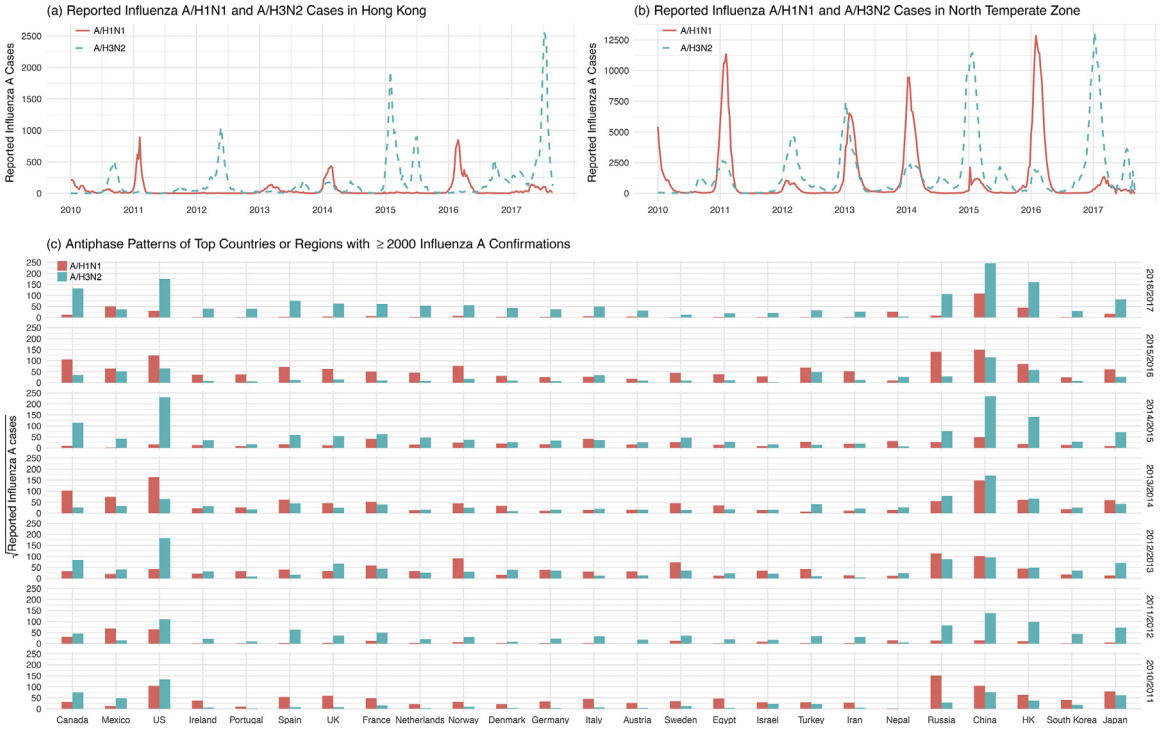

Figure 1. Temporal patterns of A/H1N1 and A/H3N2 in (a) Hong Kong, and (b) the North Temperate Zone. (c) Spatial patterns of the annual totals of A/H1N1 and A/H3N2 in Hong Kong and 24 countries and regions in the North Temperate Zone, which are ranked according to their longitudes. It is evident that A/H1N1 and A/H3N2 alternately dominated in the recent 4 years. A/H1N1 skipped (i.e., very low numbers of cases) in most countries or regions in 2011/2012 and 2016/2017. Since A/H1N1 resurged in 2012/2013, a resurgence could happen in 2017/2018.

Results

The temporal patterns of the weekly reported cases of A/H1N1 and A/H3N2 from Hong Kong and 71 of 150 countries in the North Temperate Zone are presented in Figure 1a and b. It can be seen that anti-phase patterns formed between A/H1N1 and A/H3N2 after a transient period of several years. Figure 1c shows the spatio-temporal patterns of the square roots of the annual totals of

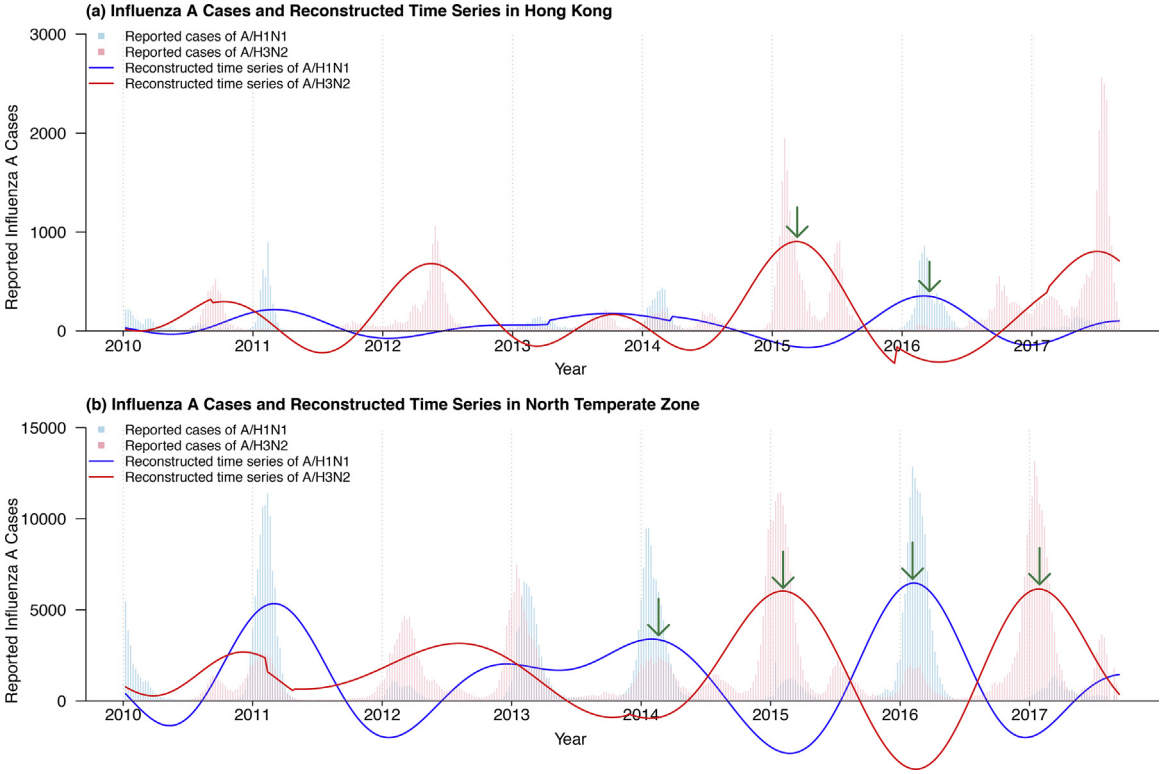

Figure 2. Temporal patterns of reported influenza A/H1N1 and A/H3N2 cases and their reconstructed time-series in (a) Hong Kong, and (b) the North Temperate Zone. Arrows indicate the remarkable anti-phase patterns from 2015 to 2017 in Hong Kong, and from 2014 to 2017 in the North Temperate Zone.

A/H1N1 and A/H3N2 for Hong Kong and 24 NTZ countries ordered according to their longitude. The square root transformation was used to make the small-scale epidemic more visible graphically. It can be seen that individual countries/regions exhibited the same anti-phase patterns.

Time-series decomposition analyses and wavelet analyses were performed on the reported cases of A/H1N1 and A/H3N2 from January 2010 to July 2017 for both Hong Kong and the NTZ (see **Supplementary Material**). Figure 2a and b shows the reconstructed time series of A/H1N1 and A/H3N2 for both Hong Kong and the NTZ. Again, anti-phase synchronization is observed in these time series.

Discussion

The results of the present study appear to be novel in identifying anti-phase synchronization patterns between influenza A/H1N1 and A/H3N2 in Hong Kong and the NTZ for the years 2014 to 2017. Influenza epidemics in Hong Kong are largely in synchrony with those in the NTZ. The study results are in line with those of a previous study by Finkelman et al., who identified interhemispheric synchrony for A/H3N2 (Finkelman et al., 2007). The present exploratory analyses suggest that these patterns could be due to the following factors: (1) the two subtypes competing on susceptibles; (2) partial cross-immunity between the two subtypes; (3) viral evolution; and (4) herd immunity and waning of immunity. The finding that many countries displayed similar patterns across multiple years suggests that the anti-phase pattern is unlikely to be a stochastic event.

This study is strengthened by the use of data from FluNet, a global tool for influenza surveillance that has recorded influenza data from more than 100 countries over an extended period of time. However, the study has some limitations. FluNet data, while comprehensive, may be subject to some biases, due to country variations in testing policies, or surveillance data coming from hospitals rather than being representative of the general population (He et al., 2015).

In this study, the temporal patterns of influenza A/H1N1 and A/H3N2 in Hong Kong and the NTZ were examined. An anti-phase synchronization pattern between A/H1N1 and A/H3N2 was found. If this pattern persists in the next few years in Hong Kong, A/H3N2 will likely dominate in 2018/2019 and 2020/2021. It is therefore recommended that the Hong Kong government initiates public health preparedness against this potential future influenza epidemic. Furthermore, hospitals should make plans to prepare for larger numbers of patients requiring hospitalization than expected for an A/H1N1 epidemic. This anti-phase synchronization also implies that the patterns of A/H1N1 and A/H3N2 epidemics will repeat biennially. Namely, the epidemic in 2018 could be a repeat of that in 2016 (i.e., 2 years ago), or a simple averaging of the epidemics in 2014 and 2016. A simple prediction formula is provided in the **Supplementary Material**. More rigorous statistical model fitting can be done in the future. In summary, an anti-phase synchronization pattern between A/H1N1 and A/H3N2 was found for both Hong Kong and the NTZ in recent years.

Conflict of interest

No conflict of interest to declare.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.ijid.2017.11.006.

References

Centre for Health Protection. Local situation of influenza activity. Flu Express 2017;14(38):1–5.
Finkelman BS, et al. Global patterns in seasonal activity of influenza A/H3N2, A/H1N1, and B from 1997 to 2005: viral coexistence and latitudinal gradients. PLoS One 2007;2:e1296.
Gerdil C. The annual production cycle for influenza vaccine. Vaccine 2003;21:1776–9.
He D, Stone L. Spatio-temporal synchronization of recurrent epidemics. Proc Biol Sci 2003;270:1519–26.
He D, et al. Global spatio-temporal patterns of influenza in the post-pandemic era. Sci Rep 2015;5:11013.
Klein EY, et al. Influenza A H1N1 pandemic strain evolution–divergence and the potential for antigenic drift variants. PLoS One 2014;9:e93632.
Paules C, Subbarao K. Influenza. Lancet 2017;390:697–708.
R Core Team. R: a language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2015 Available from: https://www.R-project.org/.