Monitoring respiratory infections amidst COVID-19 epidemic: a complimentary approach to rapidly appraise the effectiveness of general infection control measures

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KEY MESSAGES
- Compartmental modelling studies on COVID-19, although important to inform the epidemic response strategies, have a range of limitations and should not be overly-relied as the only approach in monitoring the pandemic or assessing the effectiveness of infection control measures.   - Simple and rapid assessment of influenza-like illness using widely available surveillance data could be a cost-efficient and complementary approach to compartmental modelling.   - The proposed methods will be particularly useful for resource-deprived countries where testing capacity of COVID-19 and expertise in infectious disease modelling are limited.   - The timely, stringent and community-wide epidemic response action employed in Hong Kong appeared to be effective in controlling local outbreaks of COVID-19 as well as the underlying transmission of influenza and other respiratory infections.

Introduction

The COVID-19 epidemic has grown rapidly from a local outbreak in China to a pandemic with almost 1.3 million confirmed cases and 70,000 deaths worldwide (as of 6 April 2020).[1] Despite the strong connection with mainland China, the number of confirmed COVID-19 cases in Hong Kong Special Administrative Region (HK) has been relatively low (890 as of 6 April),[1] perhaps attributable to its extensive infection control response. However, the relatively small case number and ample uncertainties from under-detection of mild or asymptomatic cases render direct evaluation of the effectiveness of the strategies challenging and inaccurate.[2,3]

Given the limitations of compartmental modelling studies and the severe shortfall of COVID-19 testing capacity worldwide, especially in low- and middle-income countries (LMICs), there is a pressing need of alternative options to appraise the performance of infection control strategies. Since common respiratory infections such as influenza share similar transmission pathways (primarily via droplets and fomites) as COVID-19, [3] most infection control measures should have qualitatively similar effects on these diseases. We hereby propose a simple and rapid approach to indirectly assess the overall effectiveness of a population’s infection control strategies, by examining the more reliable influenza surveillance data (using HK data for in-depth case study), which is more commonly available globally.

Unique challenges to accurate depiction of COVID-19 epidemiology

Compartmental modelling studies have been playing a crucial role in understanding the COVID-19 pandemic. These studies can produce estimates on the current scale (“nowcasting”) of the epidemic and its development over time (“forecasting”), which have been the core foundation of policymakers’ decision on epidemic response worldwide. However, just like any other modelling studies (such as weather forecast), those on infectious disease involve a large number of assumptions (e.g. the contact rate between the infected and susceptible population, probability of transmission per contact), many of which are based on expert opinion because empirical evidence is often not immediately available.[4] A small error in the assumptions can be amplified into a large bias in infectious disease models. For example, the UK government had been heavily criticised for their decision to slaughter 1.2 million livestock based on evidence from modelling studies on the foot and mouth disease epidemic in 2001, which was suggested to have markedly over-estimated the disease impact and under-estimated the effectiveness of conventional public health intervention.[5]

For COVID-19, there have been several unique challenges that make modelling studies particularly difficult. First, there are ample uncertainties about the proportion of undetected, mild or asymptomatic cases, which is suggested to account for the majority of the community transmission.[2] Second, the poor testing capacity and differential testing criteria (e.g. UK currently does not test suspected cases with mild symptoms, whereas HK tests all suspected cases regardless of symptoms) means that the epidemic curves of different populations are not comparable, and they do not necessarily approximate the actual underlying transmission dynamics of COVID-19. Third, the one parameter that is typically more reliable for infectious diseases, case fatality rate, varies dramatically from <1% in some Asian countries to >10% in some European countries.[1] Although adjustment for basic demographic structure can account for some heterogeneity, inference of the actual case number based on fatality rates must be interpreted with great caution.

A simple, rapid and cost-efficient approach

Common respiratory infection, particularly influenza (or influenza-like illness [ILI]) have long been monitored in the routine disease surveillance systems in many countries, with the Global Influenza Surveillance and Response System (GISRS) established since 1952.[6] Given the common transmission routes between ILI and COVID-19, by monitoring the transmission patterns of ILI, we can approximate the overall performance of a population's general infection control measures, including enhancement of personal and environmental hygiene and social distancing, whereas other measures such as travel restrictions, quarantine and case-isolation targeting specifically on COVID-19 are unlikely to alter local ILI patterns significantly. Unlike COVID-19 which has a long incubation period (up to 16 days),[7] data on ILI (incubation period 1-2 days)[8] are likely to be much more sensitive to the effects of infection control measures, thus allowing a much more timely understanding of the changing transmission intensity of droplet- and fomite-borne disease, including COVID-19. Although changes in health-seeking behaviour and disease surveillance practices are plausible during a pandemic, it is not always the case (see below for the corresponding data from HK) and these can be addressed by examining severe/death cases or institutional outbreaks that are less likely to be confounded.

The case of Hong Kong

We first reviewed the COVID-19 epidemic development in HK and the governmental and community infection control strategies since January 2020. Using published surveillance data,[1] we then compared the length and severity of the 2019/20 winter influenza season in HK with those during 2015-19.[9] We also compared the positive test rates of common respiratory infections in HK before and after 2020 week 5, when most of HK's infection control measures began, and the temporal changes of influenza-like illness (ILI) patterns in selected populations (Southern China [including Hubei, Shanghai, Guangdong and 12 other provinces or municipalities, which recorded 93.1% of all reported COVID-19 cases in China as of 6 April], Singapore, and England).[10-12]

COVID-19 epidemic and infection control measures

There has been two "waves" of COVID-19 local outbreak in HK uptill March 2020, with the first wave occurred during 2020 weeks 6 – 11 (134 cases, 32% imported) and the second wave started since week 11 (688 cases, 61% imported) after a major influx of residents returning from epidemic-struck regions worldwide (**Figure 1a**).

The key infection control strategies undertaken at the community and governmental levels are summarised in **Table 1**. The focus of these are case-identification and isolation, quarantine, social distancing, and mass masking, which serve to reduce the contact rate between the infected and susceptible populations and the probability of transmission per contact. Compared to other populations, the epidemic response in HK is characterised by timeliness and strong civilian commitment. For example, mass masking (75-95% prevalence of frequent mask use in public spaces) was achieved shortly after the first imported cases of COVID-19.[13]

Epidemiology of influenza and other respiratory infections

Compared to the data from 2015-19, the 2020 winter influenza season was 63.2% shorter, the number of institutional (schools or elderly homes) ILI outbreak was 68.4% lower, and the number of deaths from laboratory-confirmed influenza in adults was 62.3% lower (**Table 2**). Notably, although the 2020 season (week 2) began at a similar time as the previous winter influenza (start in week 1-8), there was a sharp decline of laboratory-confirmed influenza cases from >18% in week 3-4 to <1% in week 8, persisting into week 13 (0.1 %), while the total number of respiratory specimens tested remained broadly consistent (~6000/ week) (**Figure 2**). Similar trends have been observed for other respiratory infections during the same period.

Consistently, the outpatient ILI rate in HK started to decrease after the first COVID-19 case in week 4 and the trend continued, with >80% reduction between week 2 and 13 (**Figure 1a**). Similar signs of rapid reduction of ILI transmission have been observed in Singapore (**Figure 1b**; from week 4) and Southern China (**Figure 1c**; from week 5). Interestingly, while the transmission intensity of ILI in Southern China remained low until week 12, that in Singapore started to increase from week 8 to week 11, and dropped again until week 13, which is largely similar to that observed in England during the same period (**Figure 1d**).

Interpretation

The markedly shorter and less severe influenza endemic and the rapid decline of incidence of multiple common respiratory infections in HK coincided with its timely, widespread and stringent measures against COVID-19. Although HK is now experiencing a “second wave” of COVID-19 outbreak, this is primarily driven by imported cases from Europe and the US. More importantly, the local transmission in

Hong Kong during the second wave remains limited, with less than 30 daily local cases for more than two weeks. As the number of returning residents start to decline, the rate of expansion of the second wave appears to be levelling off. This is in line with the persistently low ILI transmission intensity, which suggests that the sustained local infection control measures have hampered the chain of local transmissions of respiratory infections in HK.

Beyond HK, Southern China and Singapore have undertaken similarly rapid and stringent epidemic response measures since early-February, and largely consistent signs of declining ILI transmission have been observed during their “first wave” of COVID-19 outbreak. On the other hand, both Singapore and England have experienced a 4-week surge of ILI activities during weeks 8-11, whereas the COVID-19 cases reported in both populations started to increase rapidly from around week 11.

Like HK, Singapore has been experiencing a second wave of COVID-19 driven by imported cases (70% of all cases during 20 March - 2 April).[14] While both HK and Singapore have been relatively successful in capturing and isolating the imported cases, Singapore had less stringent general infection control measures than HK, such as the absence of mass masking and smaller reduction in mobility at public or workplaces (according to Google’s user GPS location data),[15,16] which may explain why Singapore have experienced the resurgence of ILI at the end of the first wave of COVID-19 and a more severe second wave.

The ~3 weeks time gap between the rise of ILI and COVID-19 in Singapore and England appeared to coincide with our understanding that there is a 2-3 weeks time-lag between community transmission and case identification of COVID-19, due to the relatively long incubation period and delays in testing and reporting.[17] Furthermore, the signs of declining ILI activities in Singapore and England during weeks 11-13 are highly consistent with the two populations’ heightened infection control response as their COVID-19 cases rise. In particular, the mobility index in England, which had been stable at normal level during 2020 weeks 1-11, dropped dramatically after the news about the government's “herd immunity” plan (week 11).[15,18] While the latest empirical data on COVID-19 cannot provide reliable information about how effective the response action have been, the changes in ILI transmission seem to offer some promising hints.

Limitations

It is important to note that the ILI data across populations cannot be quantitatively compared due to the substantial heterogeneity in the choice of indicator for ILI activities, the virology of the specific strains, and vaccination efficiency and uptake rate etc. Same is true for COVID-19, given the widely different case-identification systems across populations. The drop of ILI GP consultation rate in England during weeks 2-8 does not seem to coincide with any explicit response action against COVID-19. However, unlike the other populations studied, the influenza season in England started earlier in 2019 week 49, so this may be part of a natural cycle. Overall, the ecological nature of our analysis prevents us from inferring causality or disentangling the independent effect of specific measures, and individual-level analysis is needed for further investigation. Nonetheless, it seems to serve the purpose of simple and rapid assessment of the overall effectiveness of the general infection control measures against primarily droplet-borne infections.

Lesson learned

From the case of HK, we demonstrated the potential value of a simple, cost-efficient approach to analyse well-established surveillance data on influenza and other droplet-borne respiratory infections using existing public health infrastructure. With a relatively manageable COVID-19 epidemic and adequate testing capacity, the epidemic patterns in HK should be relatively well-described compared to other populations such as the UK. Therefore, it is promising that the ILI transmission intensity appeared to be qualitatively consistent with that of COVID-19. The variations in the second wave in HK have been primarily driven by imported cases, which serves as a negative control showing how our analytical approach might tease out the potential effect of general infection control measures. The rapid changes of ILI transmission support our argument that ILI is more sensitive to infection control measures, and analysis of that may enable more rapid appraisal of their impact on the underlying transmission of COVID-19 that cannot be tracked accurately without mass serology testing.

Given the limited testing capacity of COVID-19 worldwide, our indirect evaluation method capitalising the more widely available and reliable influenza surveillance data could be a complimentary and cost-efficient alternative to understand different countries' performance in controlling COVID-19, especially for LMICs with limited resources in tracking COVID-19. For countries where no influenza surveillance system is in place (mostly due to resource limitations), an alternative approach is to rapidly establish a symptom-based surveillance system reporting ILI and suspected COVID-19 cases based on known symptoms, while waiting for COVID-19 testing capacity to build up gradually. The present article serves to demonstrate a simple analytical framework with minimal demand on statistical expertise, which may not be always available in populations with little testing capacity for COVID-19, but more sophisticated nowcasting and time-series analysis can be employed to further enhance the value of monitoring influenza and other respiratory infection during this pandemic.

Contributors and sources:

All authors conceived the study together; PL and CYC collated and analysed the data; PL and KHC prepared the first draft of the report; all authors contributed to the subsequent revision and final approval of the present manuscript. KHC is the guarantor of the paper.

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Conflict of interest

No conflict of interest is declared.

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Table 1. Key epidemic response against COVID-19 as of 18 March 2020 in Hong Kong

Community level*

- Enhanced personal hygiene, especially on hand hygiene and cough etiquette
- Regular environmental disinfection
- Social distancing
- Widespread symptoms screening (primarily body temperature)
- Widespread medical facemask usage (since 25 Jan) [13]

Governmental level [20]

- **Since 23 Jan:** Contact tracing and isolation for all confirmed cases
- **Since 25 Jan:**
    - Activation of the "Emergency Response Level" of the Preparedness and Response Plan against infectious disease outbreak
    - Closure of all schools
    - Postponement and cancellation of major social and sporting events
    - Mandatory quarantine in quarantine centre for 14 days for all close contacts of confirmed cases
- **Since 27 Jan:** Entrance restriction of non-Hong Kong residents who have visited the Hubei Province
- **Since 29 Jan:** Work from home policy for most government employees (stopped on 2 March)
- **Since 8 Feb:** Mandatory home quarantine for 14 days for all travellers from Mainland China
- **Since 13 Mar:** Mandatory quarantine in quarantine centre for 14 days for people arriving from Daegu and Gyeongsangbuk-do in Korea, Iran, and Emilia-Romagna, Lombardy and Veneto regions in Italy.
- **Since 25 Mar**: Mandatory home quarantine for 14 days for all travellers from worldwide. Free testing service for asymptomatic travellers arriving from the United Kingdom, Europe and the United States.
- **Since 28 Mar:** Closure of recreational businesses by types of industry when a cluster of cases occurs.
- **Since 29 Mar:** Ban on gatherings of more than four people in public places.

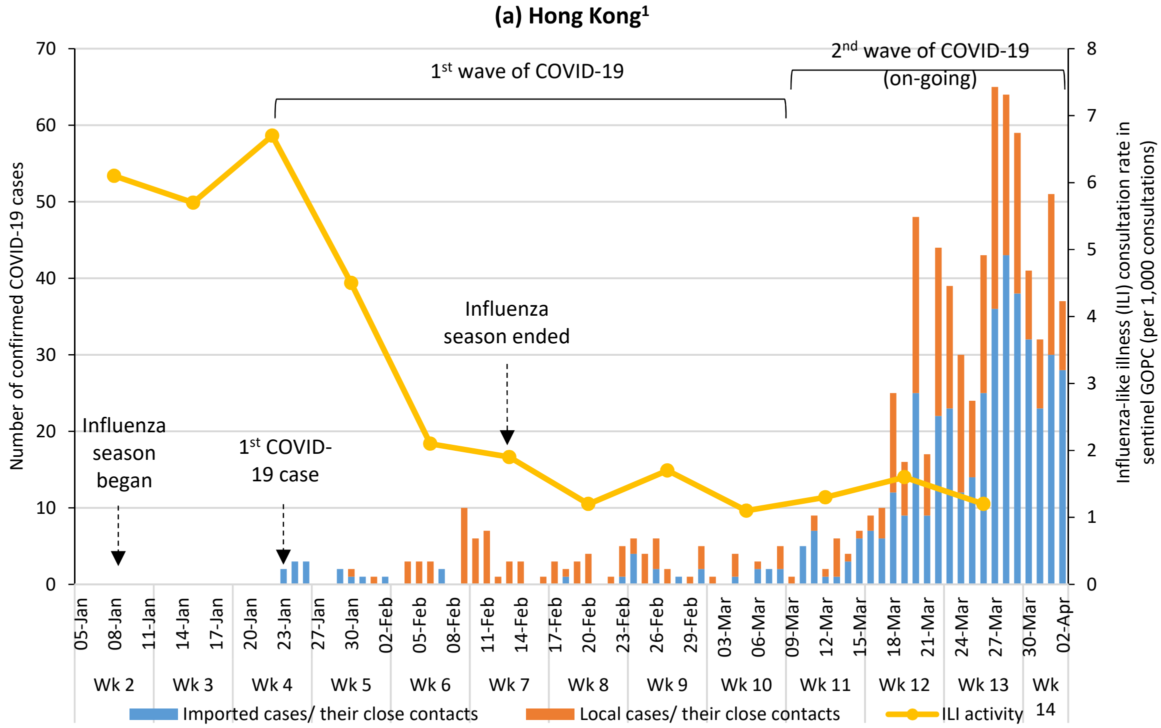
*Based on extensive media report and observations in community and healthcare settings.

Table 2. Comparison of the winter influenza season in 2020 with those in 2015-2019 [9]

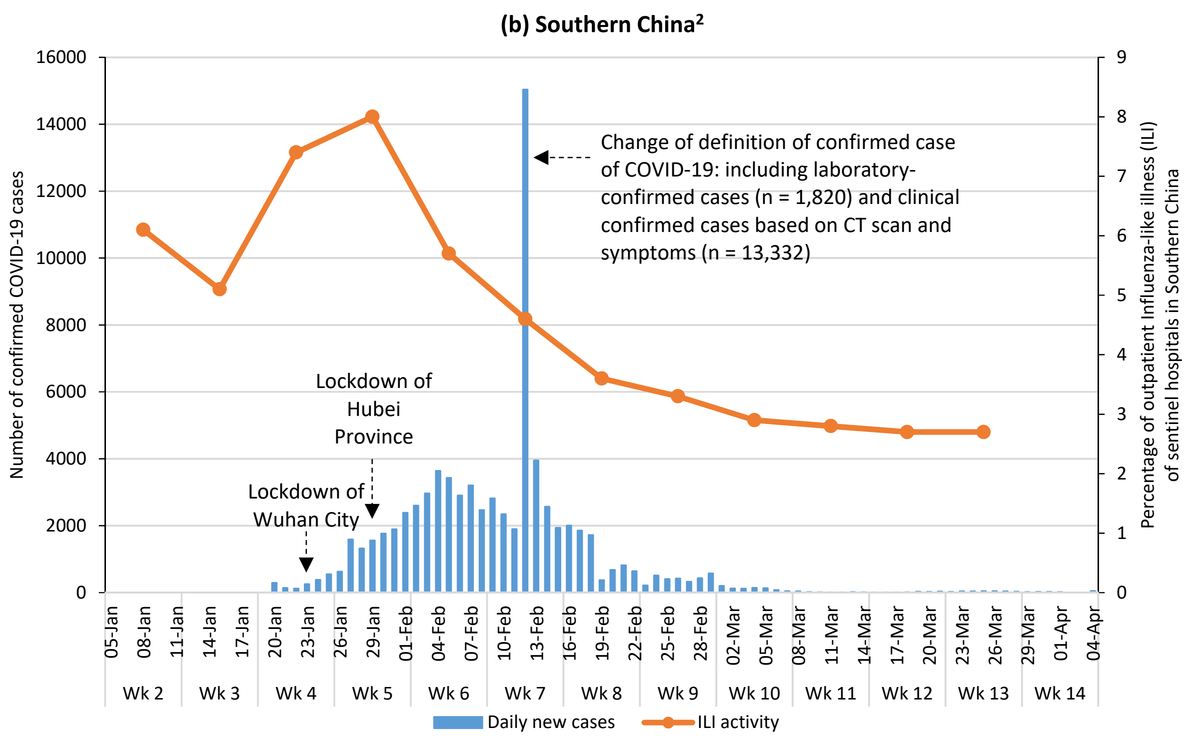
Winter influenza season	Week of the year	Length (weeks)	Number of institutional outbreaks*	Number of deaths
2015	1 to 17	17	433	502
2016	5 to 21	17	435	214
2017	8 to 15	8	87	42
2018	2 to 13	12	600	384
2019	1 to 14	14	863	357
2015-2019, mean (SD)	NA	13.6 (2.5)	483.6 (191.7)	299.8 (107.0)
2020	2 to 7	5	153	113

*Refers to outbreaks at schools or elderly homes.

Figure 1. Incidence of COVID-19 and indicators of transmission intensity of influenza-like illness from 2020 week 2 to 14 in (a) Hong Kong (b) Southern China (c) Singapore and (d) England

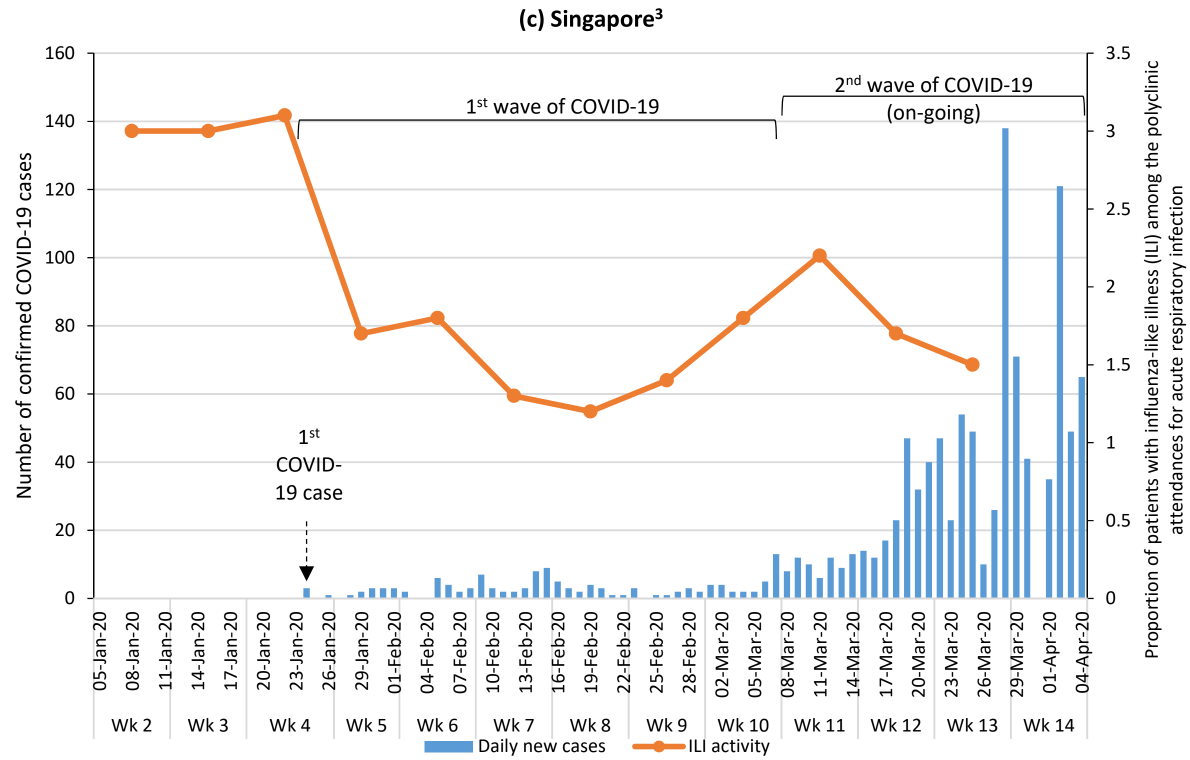


[1]Influenza season is defined as the period during which the positive rate of influenza cases in the respiratory tract specimens tested in the public health laboratory and hospital admission rate for influenza is above the usual baseline level. GOPC: public general outpatient clinics. Data source: Centre for Health Protection. [9]

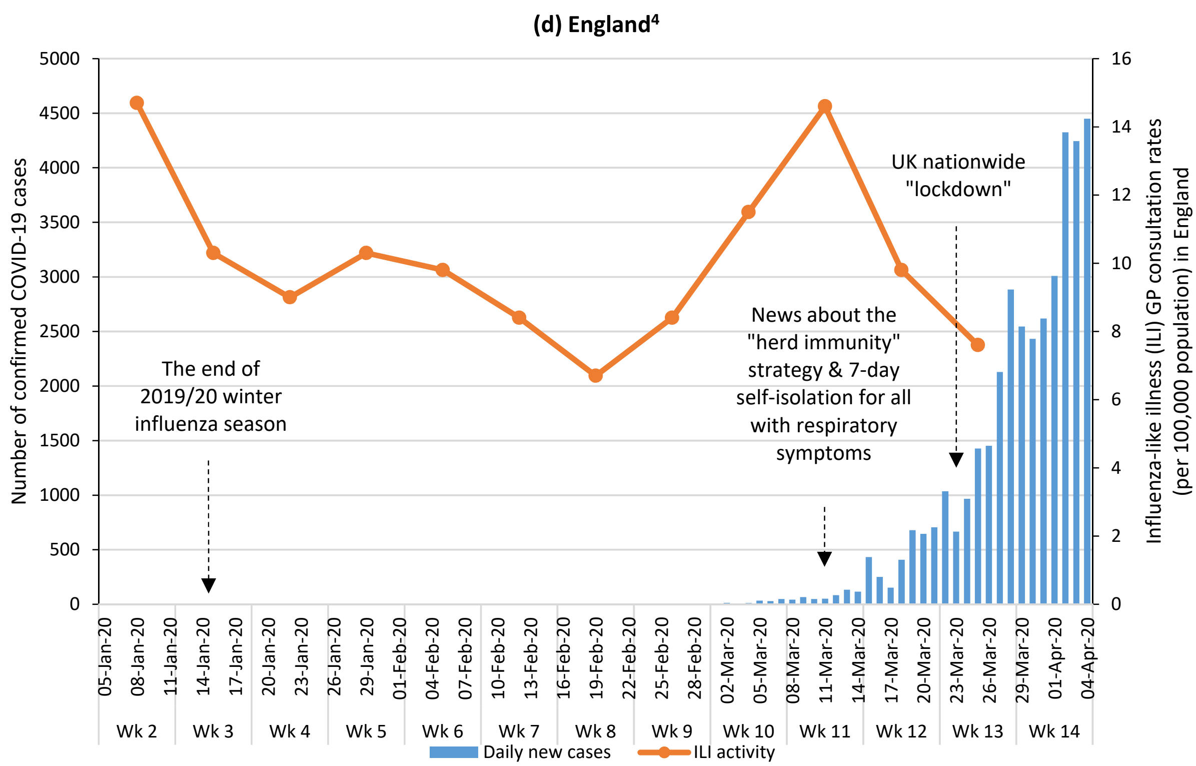


[2]Southern China: Hubei, Shanghai, Guangdong, Jiangsu, Zhejiang, Anhui, Fujian, Jiangxi, Hunan, Guangxi, Hainan, Chongqing, Sichuan, Guizhou, Yunnan. Lockdown of Wuhan City and Hubei Province involved shutting down all

transportations in and out of the region and local transportation, restricted local travel/ banning all travel. Data source: Chinese National Influenza Centre. [10]



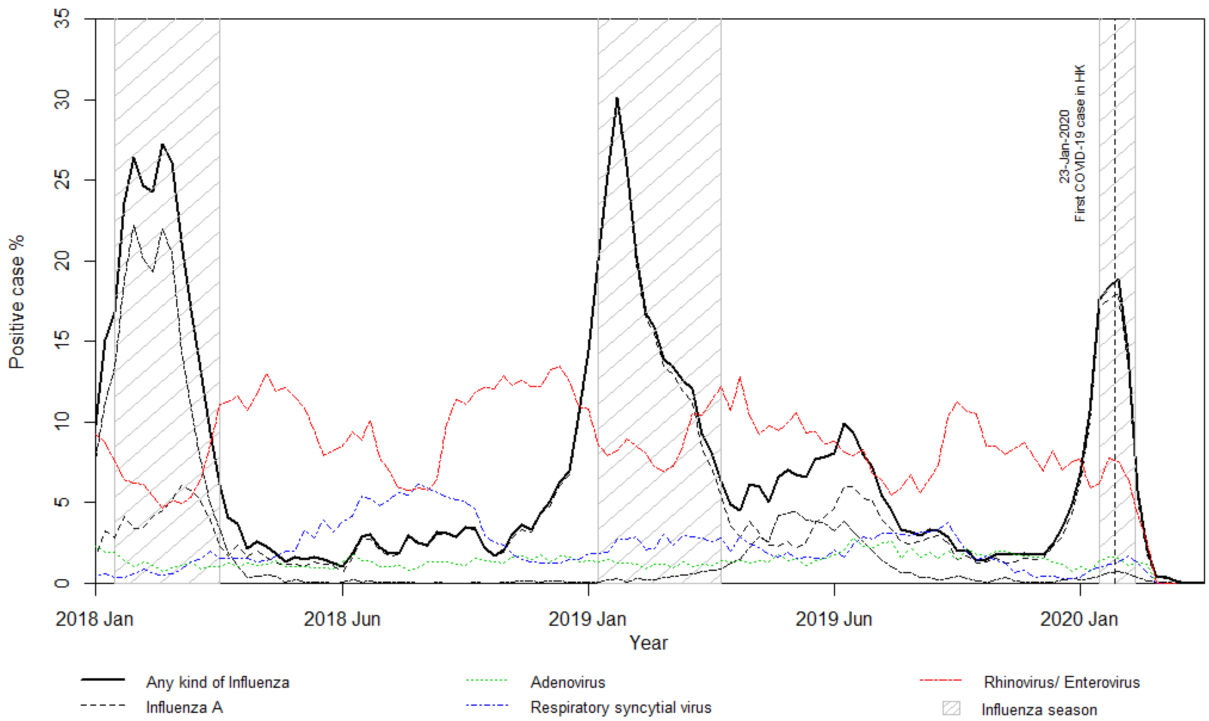
[3]Data source: Singapore Ministry of Health. [11]



[4]The 2019/20 winter influenza season started in 2019 week 49 and ended in 2020 week 3. UK nationwide lockdown involved shutting all non-essential shops (except supermarkets, pharmacies, newsagents, vets, petrol stations, hardware, banks, laundrettes and undertakers), banning of gatherings of >2 people except for households,

mandating all residents to stay at home unless for essential travel (shopping for food or medicine, one type of exercise a day, medical appointments/ as a carer visiting a vulnerable person, for essential work). Data source: Public Health England. [12]

Figure 2. Time series of positive percentages of different pathogens in all respiratory specimens analysed during 2018-2020 in Hong Kong[1]



[1]Influenza season is defined as the period during which the positive rate of influenza cases in the respiratory tract specimens tested in the public health laboratory and hospital admission rate for influenza is above the usual baseline level. [9]