ORIGINAL ARTICLE

Relationship between population configuration and the spatial pattern of pandemic influenza A (H1N1) 2009 in Hong Kong

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Objective To investigate the association between population structure and the pandemic influenza A (H1N1) 2009 epidemic in a spatial context.

Design A retrospective case-report series study.

Setting Hong Kong.

Patients Laboratory-confirmed cases of human influenza A (H1N1) 2009 reported to the Centre for Health Protection between May and September 2009.

Main outcome measures A geo-referenced database was established comprising age, gender, and residence location of all influenza A (H1N1) 2009 cases reported in the first 5 months of the Kong Kong epidemic's first wave in 2009. They were divided into four age categories: infant, student, adult, and elderly. Correlation coefficients and odds ratios were calculated to explore the association of H1N1 cases with population configurations in 400 District Council Constituency Areas.

Results Of the 24 414 H1N1 cases reported, students accounted for the highest proportion (54.6%), followed by adults (33.4%), infants (11.1%), and the elderly (0.9%). Transmission was initially concentrated in students which then extended to infants and adults. Except for the elderly, the total population size and that of each age category were significantly associated with the H1N1 cases spatially. Mobility indicators as reflected by the number of students studying outside and adults working outside residential District Council Constituency Areas were also positively associated with H1N1 cases.

Conclusions Local population structure and mobility were associated with the spatial distribution of the H1N1 epidemic, despite the small size of the territory of Hong Kong. If an influenza epidemic hits again, an examination of these factors spatially would be useful in supporting the planning of interventions.

New knowledge added by this study

- The incidence of influenza A (H1N1) 2009 was positively associated with population size at sub-district level during the first wave of the epidemic in 2009.
- Mobility of students, followed by that of working adults, was one important determinant of influenza A (H1N1) 2009 transmission in a spatial context within Hong Kong.

Implications for clinical practice or policy

- Delineation of age differentials and population mobility in a spatial context could contribute to a refinement of intervention strategies to control influenza epidemics.
- Regularly collected public health surveillance data coupled with geo-referencing can enhance epidemiological investigations.

Key words
Disease outbreaks; Hong Kong/epidemiology; Influenza A virus, H1N1 subtype; Influenza, human; Population dynamics

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Introduction

When a novel virus is introduced to a human population that has not been previously exposed to that pathogen, potentially an epidemic may occur. Influenza is an example, as shown by its seasonal spread as well as occasional pandemics. Herd immunity aside, the dynamics of influenza transmission can also be shaped by the demographic configuration of the human population. School-age children are usually the main transmitters of human influenza as a result of their high contact intensity with peers.[1,2] When an influenza epidemic occurs, children are often the ones most heavily hit. The proportion of children in a society and their mobility can therefore be important determinants of the epidemic's characteristics. On the other hand, elderly people may have already developed immunity to certain viruses due to previous exposure, while still being more prone to severe disease because of defective immunity and the presence of chronic debilitating illnesses.[3,4] As the demographic composition of the population and their mobility varies from country to country, and also across cities, not surprisingly, the respective epidemic curves may differ considerably in shape, amplitude, and duration. An appreciation of age differentials in influenza cases is naturally an important consideration in the planning of vaccination strategies.

Over the years, the age-related transmission dynamics of influenza have been examined at global and continental levels.[5] However, implications within a country have not been fully investigated, especially in smaller territories that are normally treated as uniform collections of human beings. In Hong Kong, the first case of pandemic influenza A (H1N1) 2009 was reported on 1 May 2009. An earlier study portrayed the spatial heterogeneity of initial diffusion, which was unrelated to population density.[6] The first wave of the pandemic in Hong Kong peaked in September and reached a trough by the end of October 2009.[7] With a population of about 7 million residing over a total area of about 1000 km^2, the clustering of H1N1 cases varied spatially and temporally.[8] From these observations, we hypothesised that the spread of the influenza virus could have been shaped by the local population structure and mobility. An understanding of the space-time distribution of influenza cases and the influence of population structure may have a significant bearing when prioritisation is needed for the introduction of an intervention strategy. Against this background, we set out to explore the relationship of population configuration with the spatial distribution of pandemic influenza A (H1N1) 2009 infection in the territory of Hong Kong.

Methods

In Hong Kong, influenza surveillance forms part of the infectious disease surveillance system managed by the Centre for Health Protection (CHP) of the Department of Health. Beginning 1 May 2009, patients fulfilling both clinical and epidemiological criteria were classified as suspected human swine influenza cases. Taking reference from World Health Organization recommendations and in accordance with the criteria established by the CHP, free testing of specimens from suspected cases submitted by medical practitioners was provided by the Government's Public Health Laboratory. The clinical service was enhanced on 11 June 2009 to include the operation of eight designated flu clinics managed by public hospitals with tests performed by the hospital laboratories.[9] From 27 June 2009 onwards, testing was limited to severe and fatal cases. Throughout the epidemic, polymerase chain reaction was used for the diagnosis of human influenza A (H1N1) infection. We analysed all laboratory-confirmed cases reported to the CHP between May and September 2009 during which period daily reporting of confirmed cases was available, and the testing strategy had not changed. Anonymised data on the reported cases comprising age, gender, and residence location including building level were obtained, following institutional approval from Department of Health, and in accordance with the provision of Privacy Ordinance. For the current study, geocoding was performed to create a geo-referenced dataset.

To explore age-related transmission dynamics of pandemic H1N1, all geo-coded cases were classified into four categories: infants, age 0-4 years; school-age students, age 5-19 years; working adults, age 20-64

香港甲型（H1N1）2009 流感大流行的人口結構和空間分佈的關係

目的 從空間的角度研究甲型（H1N1）2009 流感大流行疫情與人口結構的關係。

設計 案例系列的回顧性分析。

患者 2009年5月至9月期間，香港地區呈報衛生防護中心的感染甲型（H1N1）2009流感病毒實驗室確診病例。

主要結果測量 研究過程成功建立一個地理參考數據庫，包含了在香港2009年第一波疫情首5個月所有H1N1呈報確診病例的年齡、性別和居住地點。他們以四個年齡組別劃分：嬰兒、學生、成年人和長者。我們透過相關係數和勝算比來探討H1N1病例與400區議會選區人口結構的關係。

結果 在24 414 H1N1個案中，學生佔的比例最高（54.6%），其次是成年人（33.4%），嬰兒（11.1%）和長者（0.9%）。疫情初段集中在學生，後來擴散到嬰兒和成年人。除長者外，總人口和各年齡組別人口均與H1N1病例在空間上有顯著關聯。流動性指標如在區外就學的學生數目和成年人在區外上班人數也與H1N1病例數目有正面關聯。

結論 儘管香港相對於全球乃彈丸之地，但是本地人口結構和流動性均與H1N1疫情的空間分佈有關。如果流感疫情再次來臨，這些空間因素的分析將有助規劃干預措施。

years; and elderly, age >64 years. Their time/space distributions were examined and correlated with the local population by district and sub-district, the latter with reference to District Council Constituency Areas (DCCAs), which have been in place as geographic units for electoral purposes. There were a total of 18 administrative districts and 400 DCCAs, each of the latter with a population within a range as determined by the number of elected members for each District Council. Population structural factors under investigation included population size and density in each age category, student mobility, and working adult mobility by DCCA. Population statistics were derived from the 2006 By-census of the Census and Statistics Department, Hong Kong SAR Government. Infrastructural factors potentially affecting population mobility were obtained and calculated in the Geographic Information System (ArcGIS 9.2). Factors evaluated included total length of roads, number of schools, elderly homes and buildings in each DCCA. For the above-mentioned populations, structural and infrastructural factors, including the median of these factors in the 400 DCCAs were used as a threshold for categorisation in subsequent analyses. Pearson's correlation between total number of cases of H1N1 and DCCA population configuration factors was performed using R (http://www.r-project.org/).

Results

Spatiotemporal distribution of pandemic H1N1 cases

Between May and September 2009, a total of 25 473 cases of pandemic H1N1 were reported, of which 24 414 (95.8%) could be successfully geo-coded and evaluated. The monthly reports in the five respective months were: May 19 cases; June 720 cases; July 2721 cases; August 7537 cases; and September 13 417 cases. Except for the first month (May 2009), there was almost an equal proportion of males and females in each month, with a male-to-female ratio of 0.6, 1.1, 1.01, 1.1, and 1.1, respectively. Further analysis of the low male-to-female ratio (0.6:1) in the first month was not possible because of the very small number of cases involved, compared to those in the ensuing months.

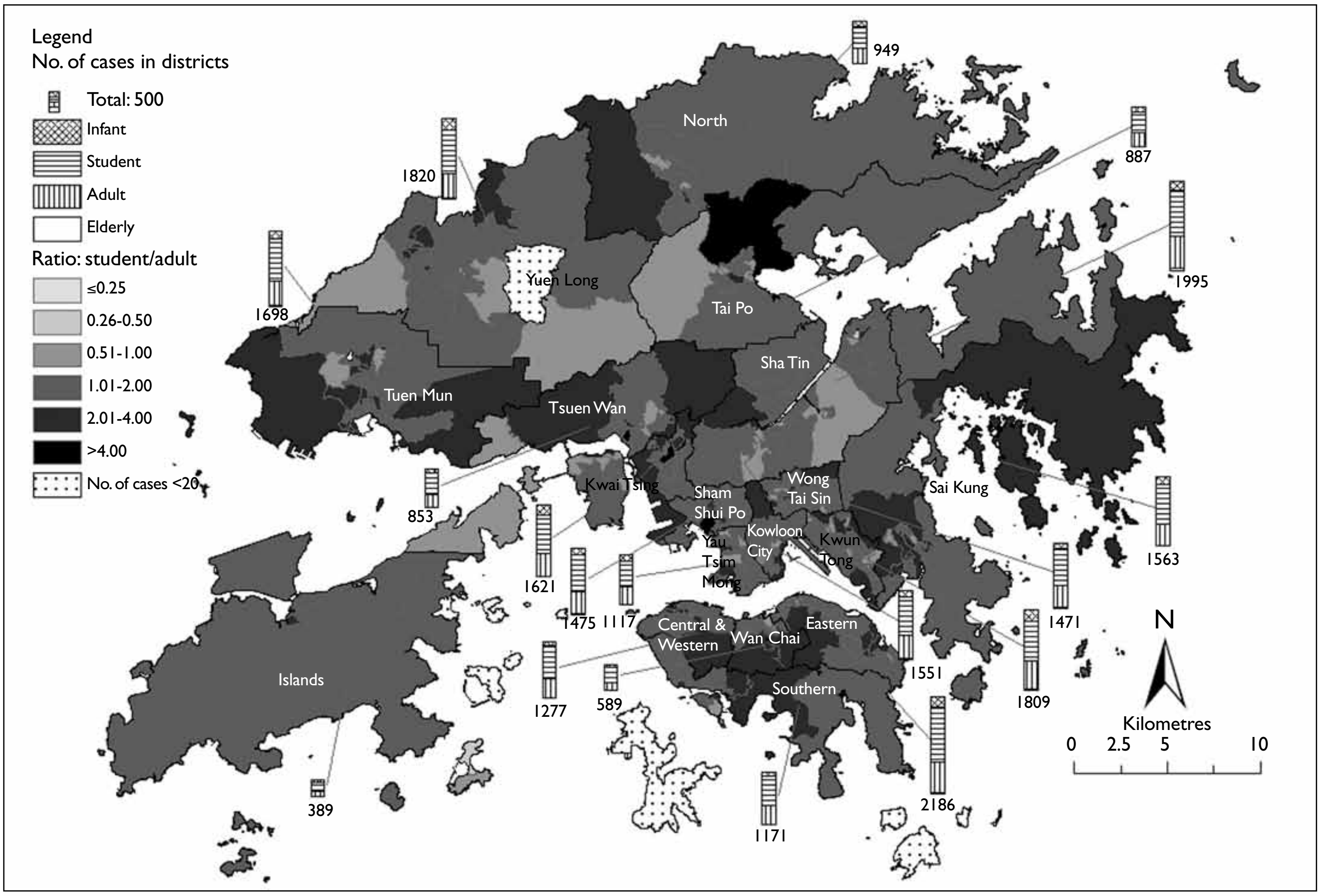

FIG 1. Spatial distribution of pandemic influenza A (H1N1) 2009 cases by age category

Infant (0-4), student (5-19), adult (20-64), elderly (>64) are illustrated by the intensity of greyshade per District Council Constituency Area and the sizes of bars for district

After computing the total cases of H1N1 in the study period, the respective proportions in the four age categories were: infant (11.1%), student (54.6%), adult (33.4%), and elderly (0.9%). Spatially at district level, the proportion of infants, students, adults and elderly in the general population ranged from 2.4-4.2%, 12.0-21.9%, 63.2-70.7%, and 8.3-17.8%, respectively. Without exception, the proportion of adults exceeded that of students in all districts. The distribution of pandemic influenza cases differed for the four age categories, being 7.2-14.9%, 49.9-59.0%, 30.1-36.5%, and 0.5-1.7%, respectively (Fig 1). Elderly people were under-represented in the pandemic H1N1 case counts, as compared to the general population. Breaking down into 400 DCCAs gave a more refined picture of the proportional variations of students and adults. In the general population, the student-to-adult ratio among the 400 DCCAs ranged from 0.1:1 to 0.7:1, whereas for pandemic H1N1 cases it was >0.3:1 (range, 0.3:1 to 8.0:1); 99 (24.8%) of the DCCAs yielded a ratio of >2.0. There was no specific geographic pattern in the distribution of this ratio. Overall, eight DCCAs (scattered in different districts) gave a very high ratio (>4).

Temporally, the elderly accounted for a small proportion of all cases throughout, and did not exceed 20% in any DCCA at anytime during the 5-month period. There was wider variation for the percentage of infants but the actual number of reported cases was too small for meaningful comparison. The median proportion of student cases was >40% in June, July, August, and September,

TABLE. Influence of population factors on the cumulative number of reported pandemic influenza A (H1N1) 2009 cases*

Population factor >median	% in high cumulative report (>65 cases) DCCA (n=141)	% in low cumulative report (≤65 cases) DCCA (n=259)	OR (95% CI)
All-age population			
Population density >646/ha	42.6	54.1	0.63 (0.42-0.95)
Population size >16 678	78.0	34.7	6.66 (4.15-10.70)
Infant population (0-4 years old)			
Infant population density >16/ha	52.1	47.5	0.83 (0.55-1.25)
Infant population size >450	77.3	34.4	6.51 (4.07-10.41)
Student population (5-19 years old)			
Student population density >98/ha	44.7	52.9	0.72 (0.48-1.09)
Student population size >2577	73.0	37.5	4.53 (2.89-7.09)
Students studying in school >2063	55.3	44.8	1.53 (1.01-2.31)
Students staying in the same DCCA >340	58.2	42.9	1.85 (1.22-2.81)
Students studying outside DCCA >2520	75.2	36.3	5.32 (3.36-8.41)
Total student pool >4668	66.7	40.9	2.89 (1.88-4.43)
No. of schools >6	53.2	37.5	1.90 (1.25-2.88)
Mean distance between schools ≤234 m	42.6	49.8	0.75 (0.49-1.13)
Adult population (20-64 years old)			
Adult population density >440/ha	42.6	54.1	0.63 (0.42-0.95)
Adult population size >11 255	79.4	34.0	7.51 (4.63-12.16)
Adults working outside DCCA >6547	75.2	35.9	5.41 (3.42-8.55)
Adults working outside district >4909	74.5	36.7	5.04 (3.19-7.94)
Elderly population (≥65 years)			
Elderly population density >72/ha	36.9	56.4	0.45 (0.30-0.69)
Elderly population size >1985	46.8	51.4	0.83 (0.55-1.26)
No. of elderly homes >2	27.7	23.9	1.22 (0.76-1.94)
Student-to-adult ratio			
General population >0.23	60.3	51.0	1.46 (0.96-2.21)
Cases >1.65	64.5	42.5	2.47 (1.61-3.77)
Other related factors			
Building density >3 count/ha	38.3	40.5	0.91 (0.60-1.39)
Road density >45 km/km^2	45.4	51.4	0.79 (0.52-1.19)

* DCCA denotes District Council Constituency Area, OR odds ratio, CI confidence interval, and ha hectare

during which period the testing strategy of the hospital laboratories and Public Health Laboratory had remained unchanged, whereas it was >40% for adult cases in July and August only.

Associations of H1N1 cases with population configurations

Cumulatively over the 5-month study period, the mean number of H1N1 cases in the 400 DCCAs was 61 (standard deviation, 28). Using the cumulative total of 65 (the nearest round-up figure for the mean number of reported H1N1 cases) as the cut-off, all DCCAs were divided into two categories—high- and low-caseload DCCAs. The population structures of the two categories were then compared, using population data from the 2006 By-census. The results are shown in the Table. A higher population density, either for all ages or in any of the four age categories, was not associated with a high H1N1 caseload in the respective DCCA. There was positive correlation between the case number and the population size (results not shown). The correlation coefficient between cumulative case counts and population density was, however, negative (-0.08; P>0.05) [Fig 2a]. In these comparisons, population density was calculated after exclusion of uninhabitable areas, defined as an altitude of >200 m and bodies of water. The population sizes in numbers were better predictors of a high caseload. This applied to all ages (odds ratio [OR]=6.66), infants (OR=6.51), students (OR=4.53), and adults (OR=7.51), but not to the elderly (OR=0.83). For students, the OR was higher for those in the resident population (OR=4.53) than in schools (OR=1.53), the latter being derived from a summation of all students in schools in each DCCA. There was, however, a higher OR for DCCAs with more schools (OR=1.90). The mean distance among schools (OR=0.75) did not differ between high and low H1N1 caseload DCCAs.

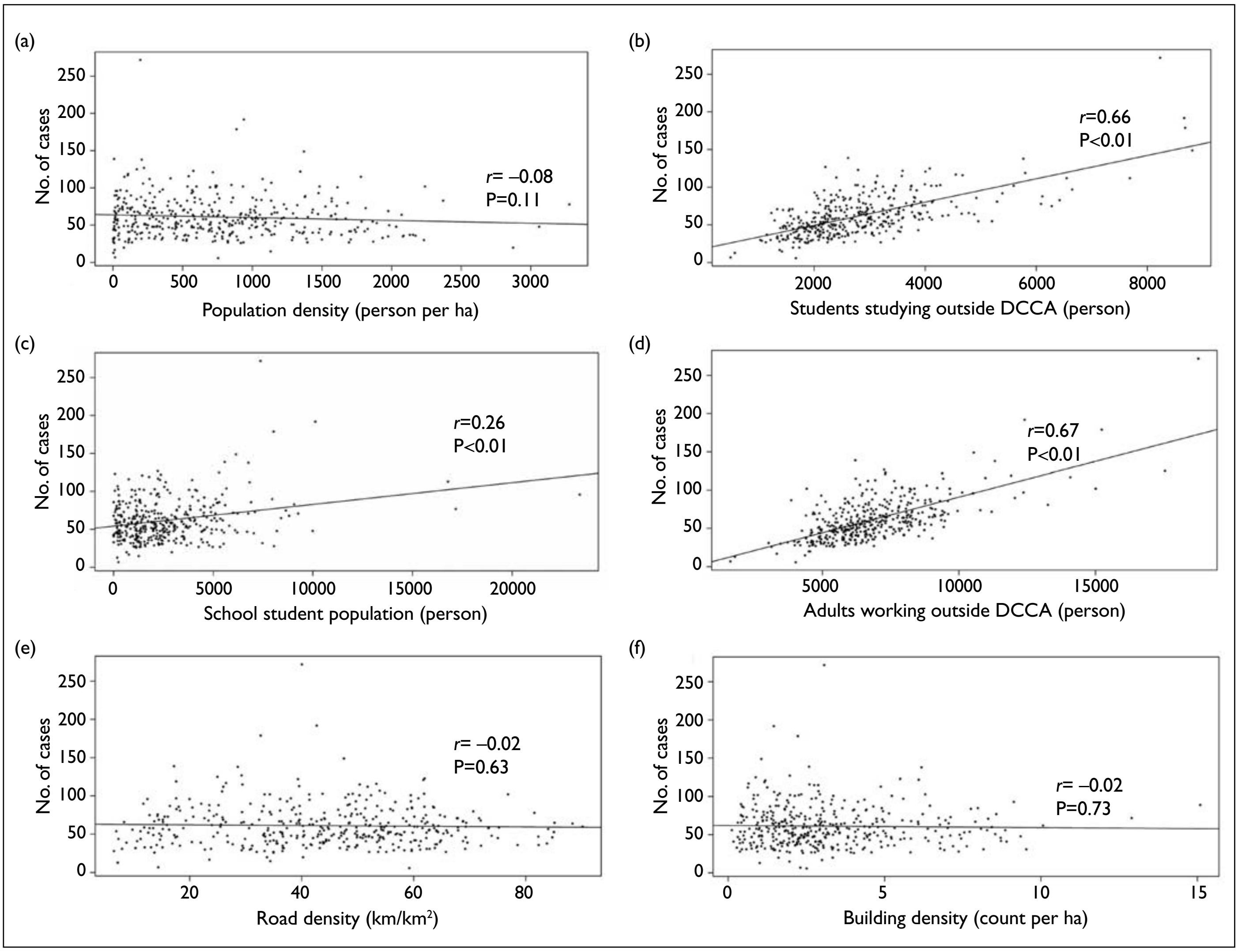

FIG 2. Correlation between reported pandemic influenza A (H1N1) and (a) population density, after exclusion of uninhabitable areas, (b) number of students studying outside District Council Constituency Area (DCCA); (c) school student population by DCCA; (d) adults working outside DCCA; (e) road density; and (f) building density

The influence of student mobility was assessed using two indices: number of students studying outside the DCCA of their residence, and the number of students studying in a school within a DCCA. The first index showed a higher degree of correlation (*r*=0.66; P<0.01) [Fig 2b] with H1N1 cases than the second (*r*=0.26; P<0.01) [Fig 2c]. Likewise, there was positive association between caseload with the number of adults working outside the DCCA of their residence (*r*=0.67; P<0.01) [Fig 2d] or district (*r*=0.62; P<0.01), which was another surrogate marker of population mobility. Road density (Fig 2e) and building density (Fig 2f) did not yield any association with high caseloads. The correlation coefficient between caseload and building density was -0.02, and -0.02 for road density, both being statistically insignificant.

Discussion

We describe here, for the first time, the association between the incidence of pandemic influenza (H1N1) 2009 cases at the community level with population structure and mobility, from a spatial perspective applied to Hong Kong. This has been made possible through the availability of case-based surveillance data collected by the Hong Kong CHP over an extended period (reporting of the first case up to shortly after the peak was reached).[10] The results have allowed us to examine the epidemiology of the infection from two angles—age-related susceptibility of the population, and the driving force of the epidemic.

From the outset it was clear that transmission of the H1N1 virus was neither a random nor a homogeneous process. Certain segments of the population appeared to have been preferentially affected. Division of the population into four age-specific categories—infants, school-age children, adults, and elderly—has been used in other studies to describe the changing demographic landscape of influenza.[11] Using a similar framework, we endeavoured to assess the proportional distribution of reported infections, against the population structure in the city. The most heavily affected were students, followed by working adults. Infants accounted for a small proportion, while elderly people were minimally affected. The predominance of the H1N1 (2009) in school-age children has also been reported elsewhere.[2,12,13] In our study, there was clearly a spatial and temporal variation of the proportional distribution of different age categories. In some DCCAs, adults were as severely affected as students in terms of numbers, while the proportion of elderly was universally small. Over time, students were predominantly affected in the first 2 months and also during the last month of data collection. During the third and fourth month (summer months of July and August), the contribution of student and adult cases were similar (Fig 3). The low attack rate in elderly was probably related to their partial immunity to the virus, as has already been demonstrated in some studies.[14] While the age of 65 years was used as a cut-off for facilitating correlation with population characteristics, the number of reported cases was in fact very low above the age of 60 years. Unlike elderly people, the variability of caseload in the younger population was more a reflection of exposure risk than the level of immunity. There was a higher median ratio of adult-to-student in the population

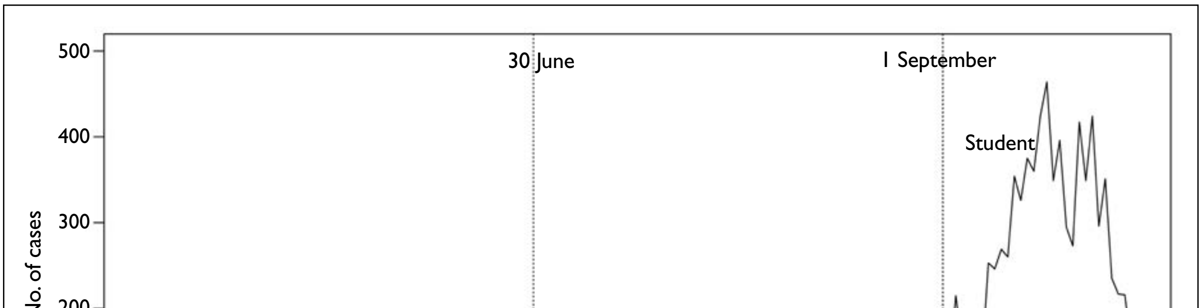

FIG 3. Temporal distribution of pandemic influenza A (H1N1) 2009 cases by age category
Infant (0-4 years old), student (5-19 years old), adult (20-64 years old), and elderly (>64 years old)

(4.3:1) than that in the reported cases (0.6:1). Conversely, the cumulative caseload of the infection was much higher in students than adults. It has been shown that prolonged close contacts was the main predisposing factor for H1N1 transmission.[15] Schools were obviously an ideal setting for population mixing of students, which provided an opportunity for the epidemic to grow except during the long summer vacation.[16] Very young infants were presumably home-bound, thus limiting their exposure to students and adults in the family.

School-age children did not just constitute the main patient load but were the driving force of the epidemic, an observation that has also been reported elsewhere.[17] In our study, infections were first reported predominantly in the student population, irrespective of locations and time (result not shown). In the summer months of July and August, transmission among students continued to occur, while adults gradually assumed a more prominent role in contributing to the continued growth in each DCCA. In 55 (14%) of the DCCAs, the adult-to-student ratio for pandemic H1N1 cases was ≥1, suggesting that adults could be the driving force of the epidemic in a small number of places. There was obviously some degree of spill-over from students or adults to the elderly. The overall number of elderly H1N1 cases remained small, as reported in other populations, though such patients were more prone to complications.[12,18] Of the population factors assessed, population density did not appear to be important in shaping the epidemic. Population density refers to the number of residents per unit area (hectare), which is an averaged figure that cannot effectively reflect the heterogeneity of distribution. It is probably a less sensitive index of the non-random population compared to population size and mobility. Higher population size, particularly that of sub-populations (students, adults, or infants), suggests a higher degree of connectivity and was associated with a higher cumulative caseload by DCCA. We have used two sets of indices to assess the possible impact of population mobility. For students, the first index, that of the number studying in another DCCA reflected the potential risk of virus transmission through commuting. The second index, that of the number of students in schools, inferred the potential risk associated with virus transmission within school settings in the same geographic location. Both indices were higher in DCCAs with high cumulative case counts. The same correlation was also evident for adults working outside their resident DCCAs/districts, suggesting that commuting to work and study have probably contributed to the growth of the epidemic. In our study, road and building density were unimportant determinants, possibly because of the almost universal pattern of urbanisation that has taken place in the whole territory.

What are the implications of our results? If an influenza epidemic hits again, an examination of age differentials and respective mobilities could be useful in the planning of interventions, for example by resorting to social distancing or vaccination. The simple classification of the susceptible population by age categories allows us to characterise major transmitters as well as to rank population categories by their level of vulnerability. For an influenza outbreak with characteristics similar to H1N1, our study implies that students play an important role in driving the epidemic. Social distancing by closure of schools has been introduced as a strategy in responding to an emerging influenza pandemic.[16,19] However, this would only be effective in slowing the course of the epidemic, as evidenced by the reduction in the proportion of students in cases reported during summer holidays. Simulation studies suggested that school closures only delay the epidemic peak.[20] In view of the spatial heterogeneity of the spread of H1N1, localised forms of school closure, for example, at district or even sub-district level (as supported by analysis from geo-referenced surveillance data), may theoretically be a more practical approach to slow transmission. However, the effectiveness of such measures remains to be confirmed.[21] Transmission through working adults would invariably continue, though at a slower pace, because of varied networking patterns, which are less concentrated than those for students. Social distancing of the adult population is also more difficult to enact as a strategy, because of the age heterogeneity of the population and the diverse networking patterns implicated. Rolling out of social distancing can however be considered, depending on the specific time-point on an epidemic curve and its location. Vaccination, on the other hand, would be hard to prioritise for two reasons. First, it takes a long time for the appropriate vaccine to become available, and second, division of the population by age category is too arbitrary for achieving an effective outcome. By the time a relevant vaccine is available, a significant proportion of the at-risk population would have become immune through exposure to the circulating virus.[22]

The fact that we relied exclusively on the use of surveillance data for conducting this assessment is an important limitation. Despite the aggressiveness of the Department of Health in attempting to control the epidemic through case-based surveillance, biases due to self-selection, delayed reporting, and missed diagnoses were inevitable. The mild nature of the infection also means that infected persons were less likely to present for treatment as the epidemic matured. On the other hand, the laboratory testing strategy and criteria of sampling changed in the middle of the study period, making temporal assessment relatively ineffective. Furthermore, there might be ecological fallacies, as data for analysis were aggregated according to DCCAs. Possible immeasurable confounding factors, such as social networking patterns and population immunity, were not included in the analysis. However, the dataset was robust for spatial assessment, especially during July, August, and September 2009 (when the reporting strategy remained consistent). The dataset used in this study was also relatively large, with the geo-coded cases accounting for 67% (24 414/36 546) of all cases reported over a 1-year period between May 2009 and May 2010.[11] Despite the high number of cases for evaluation, this may reflect only the tip of the iceberg. Interpretation of the resultant analysis therefore requires caution. In practice, the use of reporting data also carries the advantage that it supports the development of a consistent surveillance system, the results of which can contribute to the planning of intervention strategies, rather than depending on the development of real-time responses.

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