Estimate of 2009 H1N1 influenza cases in Shenzhen – the biggest migratory city in China

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SUMMARY

The 2009 novel H1N1 influenza pandemic had a significant impact on Shenzhen's population with 2063 laboratory-confirmed human H1N1 cases and five deaths being reported. We used parameters from two population-based surveys and the Shenzhen Influenza Surveillance System to estimate the total number of H1N1 influenza infections in Shenzhen in the 2009 pandemic. The attack rate of influenza-like illness (ILI) in family households was $11\cdot2\%$ (95% CI 9·4–13·0), with $80\cdot2\%$ (95% CI 77·8–82·5) seeking medical care. The ILI attack rate in workers was $38\cdot1\%$ (95% CI $34\cdot3-41\cdot7$) with $72\cdot5\%$ (95% CI $66\cdot9-78\cdot0$) seeking medical care. The average H1N1 positive rate in individuals reporting ILI and testing by polymerase chain reaction was $22\cdot7\%$. A total of $611\,000-768\,000$ people, or $4\cdot7-5\cdot9\%$ of the Shenzhen population, are estimated to have experienced H1N1 influenza. The estimated total number of cases of H1N1 is likely to be 330 times greater than the number of laboratory-confirmed cases.

Key words: China, H1N1 influenza, pandemic, prevalence, Shenzhen.

INTRODUCTION

Situated adjacent to Hong Kong, Shenzhen is one of the most populous cities in South China. With a large population of migrants, Shenzhen has the highest rate of population mobility in China. Thus, the 2009 H1N1 pandemic had a significant impact on the inhabitants. According to official statistics, in 2008 Shenzhen had 13 million residents of whom

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2.28 million held a Shenzhen 'registered residence' or *hukou*; 6.48 million held temporary residence permits (granted by police to individuals who had resided in Shenzhen for more than 3 months but whose *hukou* were still registered at locations other than Shenzhen); and 4.2 million constituted the 'floating population' [1]. According to the national census data released in 2005, the ratio of family household to non-family household population (i.e. people such as workers, who register their residence at the work-place) was 1.2:1, indicating that there were 7090000 people in family households and 5910000 in non-family households [2]. In 2008, 350000 persons and 120000 vehicles in total passed through the eight

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ports of Shenzhen, accounting for 52% of China's migrants and 72% of its transiting vehicles [3]. The city covers an area of about 1952 km^2 with a population density of 6660 persons/km². The high population density and population mobility favour transmissibility of H1N1 influenza in Shenzhen.

The first case of novel H1N1 influenza in China was an imported case reported on 11 May 2009. The first secondary and community transmission cases were identified on 18 June and 2 July, respectively, following the report of the first imported case in Shenzhen on 28 May. Peaks of pandemic activity appeared in September and November 2009 with an increasing number of outbreaks in schools. Of all the outbreaks reported, 90% occurred among students. Subsequently, a high prevalence of H1N1 persisted despite a mild decrease compared to the peak activity levels. By 31 December 2009, 2063 laboratoryconfirmed cases had been reported to the Shenzhen Centre for Disease Control and Prevention (Shenzhen CDC). As the WHO guidance specified that laboratory confirmation of infection had limited benefit once local cases were prevalent [4], cases were no longer given the polymerase chain reaction (PCR) test after the emergence of the local epidemic. Therefore, it is likely that the number of reported cases underestimated the real situation. In this study, we aimed to estimate the total number of cases based on the Shenzhen Influenza Surveillance System and two population-based surveys of students and workers to provide a more precise estimation of H1N1 prevalence in the Shenzhen population.

METHODS

The total number of H1N1 cases in Shenzhen in 2009 was estimated using a simple multiplier approach and four population indices: the total population, individuals with influenza-like illness (ILI), H1N1 cases, and individuals seeking medication due to H1N1. In this study ILI is defined as symptoms of fever ≥ 38 °C, either cough or sore throat, and no other laboratory-confirmed results [5]. The values for each of these indices were estimated using four parameters based on the conceptual inclusion relationship (Fig. 1). The four parameters were: (A) the ILI attack rate, (B) the average positive rate of H1N1 PCR testing in individuals with ILI, (C) the proportion of individuals with ILI seeking medical care, and (D) the proportion of individuals with ILI among outpatients. Two approaches were used to estimate



Fig. 1. Schematic diagram of inclusion relationship to estimate total cases of pandemic H1N1, 2009. ILI, Influenza-like illness.

the total number of H1N1 cases. The formulae were as follows:

Approach I

- Number of ILI cases in population=total population * A;
- (2) Number of H1N1 cases in population = number of ILI cases * B;
- (3) Number of H1N1 cases seeking medication = number of H1N1 cases * C.

Approach II

- Number of ILI cases in outpatients = number of outpatients * D;
- (2) Number of H1N1 cases seeking medication = number of ILI cases in outpatients * B;
- (3) Number of H1N1 cases in population = number of H1N1 cases seeking medication/C.

Parameters A and C were estimated using two population-based surveys conducted by Shenzhen CDC after identification of the H1N1 pandemic, which started in December 2009. It assumed that student and worker populations represented the two dominant populations of Shenzhen – family household and non-family household populations. The School Outbreak Reporting System was established with the collaboration of all schools and the CDC in Shenzhen. Under the system, the head teacher in a class records all absentees due to sickness and reports to school physicians who verify the clinical diagnosis of each sick child and follow them up. School physicians are also responsible for reporting outbreak events to the district-level CDCs when there are more than five H1N1 cases found in the same class within a week. Until the end of November, more than 50% (290/514) of schools in Shenzhen had reported H1N1 influenza outbreak events to the CDC. In order to estimate the overall ILI rates for students in the whole city, both infected schools (those that had reported outbreaks) and non-infected schools (those that had not reported any outbreaks) were recruited in our sample pool in equal proportions in order to represent both the high- and low-risk student population. We randomly selected four districts for the infected school sampling and another four for the noninfected school sampling and all infected or noninfected schools, as appropriate, in each district constituted the sampling pool of that district. One school was then randomly selected from each district. The resulting four infected schools and non-infected schools from eight districts included two primary schools, three junior high schools and three senior high schools. One class was then randomly sampled from each grade in each target school and all students in the target classes were recruited. The survey included questions on personal details, ILI symptoms and medical consultations for both students and their families between June 2009 and the time of the survey. Surveys were completed by students' parents or guardians. The overall ILI attack rates of students and family households (the percentage of households which contained a child who experienced ILI) were weighted by the proportion of schools in a district and size of the student population. Parameter A used the question: How many people including you and any of your family members have ever experienced fever \geq 38 °C, and either cough or sore throat in the past six months? Parameter C used the question: How many people including you and your families have ever visited a doctor when you (your family members) experienced ILI symptoms? The second questionnaire was targeted at workers as the non-family household population defined by the 2009 statistical report of the Shenzhen government. This report showed that more than 80% of migrant workers were employed in the manufacturing industry [6]. The factory workers were asked to complete a self-administered questionnaire similar to the one used in the student survey. One small factory (<800 workers) and one large factory (≥800 workers) were randomly selected from each of the three industrial districts in Shenzhen. All workers in the target factories were recruited as subjects. Workers' children were sampled independently in the student-based survey. Two surveys were completed at the end of the second week of December (week 50 in 2009).

Parameter B was estimated using data from the Shenzhen Influenza Surveillance System, which was established in the late 1980s alongside the development of two national sentinel hospitals, one city-level general hospital with the highest number of outpatient visits in Shenzhen and one city-level maternal and children's hospital. The 100 public hospitals in Shenzhen are the main healthcare provider with outpatient visits to these hospitals comprising more than 80% of the visits to all healthcare facilities [3]. Within these two sentinel hospitals ILI surveillance was conducted among the outpatients of the departments of internal and paediatric medicine on a weekly basis. The weekly number of outpatients, the number of ILI cases, the number of samples collected and the number of H1N1-positive samples were obtained from the system. The average H1N1 PCR-positive rate in individuals with ILI (B) was calculated using the weekly positive rate from June to week 2 of December weighted by the weekly number of ILI cases. The adjusted H1N1 PCR-positive rate in outpatients with ILI was assumed to be the average rate in the general population with ILI in our models. The number of ILI cases divided by the number of outpatients was used as parameter D (the proportion of ILI in outpatients).

Epidata 3.0 (Denmark) and SPSS v. 15.0 (SPSS Inc., USA) were used for data entry and analysis, respectively. Proportions and 95% confidence intervals (CI) were calculated to describe the variance of parameters. The differences and trends in ILI attack rates and doctor consultation rates across different types of school were tested using χ^2 tests.

RESULTS

Student-based survey

Of the 1333 student questionnaires distributed, 1165 were completed by a total of 4863 students and family members, a response rate of 87.4%. Of the 1165 students, 59.9% were male, 38.2% were in primary school, 28.1% were in junior secondary school, and 33.7% were in senior secondary school (Table 1). Almost half of students (49.5%, 95% CI 46.6-52.4),

	Students $(n = 1293)$		Workers $(n=692)$		Total (<i>n</i> = 1985)	
	No.	%	No.	%	No.	%
Sex						
Male	698	59.9	303	46.6	1001	55.2
Female	467	40.1	347	53.4	814	44.8
Age (mean)			24			
Classification of schools*						
Primary school	445	38.2				
Lower secondary school	327	28.1				
Upper secondary school	393	33.7				
Family population, <i>n</i> *	4863					
Hukou, n (%)						
Local	629	54.0	33	5.1	662	36.5
Non-local	536	46.0	617	94.9	1153	63.5
Parents' age (mean)*	40					
Parent/worker education level						
Primary school or lower	59	5.1	0	0		
Lower secondary	378	32.4	119	18.3		
Upper secondary	427	36.7	422	64.9		
College	138	11.8	70	10.8		
University	163	14.0	39	6.0		
Parents' occupation, n (%)*						
Worker	156	13.4				
Administrative	198	17.0				
Private proprietor	408	35.0				
Housewife	127	10.9				
Others	276	23.7				
Worker's position						
General worker			455	70.0		
Civilian staff			70	10.8		
Administrative			69	10.6		
Support staff			27	4.2		
Others			29	4.5		

Table 1. Demographic characteristic of subjects in two population influenza-like illness surveys

* Items were not suitable to worker subjects.

reported experiencing symptoms of ILI between June 2009 and the time of the survey (Table 2). Of those who had experienced ILI during this time, 74.5% reported having symptoms on one occasion, 19.4% reported two separate occasions of ILI, and 6.1% reported more than two occasions of ILI. The proportion of students with ILI who sought medical care was 84.6% (95% CI 81.9-87.4) and this decreased significantly with advancing grade ($\chi^2 = 7.936$, P < 0.01). Of the students, 67.7 % (95 % CI 64.1–71.3) reported that, in the week preceding the onset of ILI, their classmates had experienced fever and cough or sore throat; 14.6% (95% CI 11.9-17.3) of students reported that, in the week preceding onset of ILI symptoms, family members had experienced symptoms of fever with cough or sore throat.

Of 4863 students and family members, $11\cdot 2\%$ (95% CI 9·4–13·0) reported having ever experienced symptoms of ILI between June and the time of the survey, 2009. Of these, $80\cdot 2\%$ (95% CI 77·8–82·5) had sought medical care (Table 2). These two outcomes were used as parameter A (ILI attack rate) and parameter C (proportion of individuals with ILI seeking medical care), respectively, in the family household model (Table 4).

Factory worker-based survey

Of the 750 worker-based questionnaires distributed, 650 were completed representing a response rate of 86.7%. Of the respondents, 46.6% were male, the

	No.	No. of ILI cases	ILI attack rate (%)	No. seeking medical care	Proportion of ILI cases seeking medical care (%)
Student					
Primary school	445	260	58.4	230	88.5
Junior middle school	327	188	57.5	161	85.6
Senior middle school	393	203	51.7	160	78.8
Total	1165	651	49.5*	551	84·6†
Family					
Primary school	1827	442	24.2	362	81.9
Junior middle school	1330	298	22.4	244	81.9
Senior middle school	1706	355	20.8	272	76.6
Total	4863	1095	11.2‡	878	80.2

 Table 2. Attack rate of influenza-like illness (ILI) and health-seeking behaviour of students and their families

* χ^2 test for difference between groups: $\chi^2 = 4.363$, P = 0.113; the overall ILI attack rate of students was weighted by the proportion of schools and the student population size.

† χ^2 test for difference between groups: $\chi^2 = 8.357$, P = 0.015; χ^2 test for trend across groups: $\chi^2 = 7.936$, P < 0.01.

‡ The overall ILI attack rate of students' families was weighted by the proportion of schools and the student population size.

average age was 24 years, 94.9% were migrant workers, 64.9% reported an educational level of senior high school, and 50.8% lived in factory dormitories (Table 1). The proportion who reported ever having symptoms of ILI between June and the time of survey (parameter A) was 38.1% (95% CI 34.3–41.7) (Table 4). Of those reporting ILI, 62.8% reported a single episode of ILI, 21.9% reported two episodes, and 15.3% reported more than two episodes. Of these, 72.5% (95% CI 66.9-78.0) had sought medical care (parameter C) (Table 4); 45.7% (95%) CI 39.4-51.9) of workers reported that, in the week preceding onset of ILI, their departmental colleagues had experienced fever with cough or sore throat while 26.5% (95% CI 20.8-32.2) reported that members of their families or room-mates had symptoms of fever with cough or sore throat in that week.

Influenza surveillance system

According to the influenza surveillance system, the weekly positive rate of influenza A/H1N1 in ILI samples sent for testing ranged from 0% to 77.3%. The average positive rate of influenza A/H1N1 from June to week 2 of December was 22.7% weighted by the weekly number of ILI cases (Table 3).

Estimates of influenza A/H1N1 cases

As mentioned above, the Shenzhen population is generally classified into two groups - family household population and non-family household population. The two surveys in this study were used to estimate the number of cases of influenza A/H1N1 in the two populations. Estimates were based on the calculations of Approach I and Approach mentioned above by applying four parameters (Table 4). Using Approach I, we estimated that 611000-768000 citizens in Shenzhen experienced influenza A/H1N1 with symptoms, of whom 454000-573000 sought medical care (Table 5). We estimated the age-specific number of cases and rates of influenza A/H1N1 using the age distribution of laboratory-confirmed cases in Shenzhen from June to December 2009. The incidence was highest in the 0-4 years age group compared to other age groups (Table 6).

Statistical data from the Shenzhen Health Bureau showed that the number of outpatients in Shenzhen was 34.7 million. According to the average proportion of ILI cases in outpatients (8.5%) and the average positive rate of influenza A/H1N1 (22.7%), we estimated, using Approach II that between June and December 2009 there were 670 000 cases of influenza A/H1N1 in Shenzhen that sought medical care. As the

Month	Week	Outpatient	ILI	Samples for testing	Positive rate of H1N1 in samples for testing (%)	Adjusted positive sample of H1N1
6	23	13 598	1177	25	0	0
•	24	15 782	1362	19	0	0
	25	16 646	1515	52	0	0
	26	18862	2005	45	0	0
7	27	19 706	2321	41	0	0
	28	21 374	1990	44	0	0
	29	18 766	1776	47	2.1	38
	30	17870	1444	43	2.3	34
	31	15633	1276	37	0	0
8	32	15106	1122	38	2.6	30
	33	15603	1324	42	7.1	95
	34	16207	1525	42	4.8	73
	35	15 690	1368	41	4.9	67
9	36	16219	1481	43	18.6	276
	37	15927	1610	45	42.2	680
	38	16 683	1690	46	32.6	551
	39	12965	1269	47	70.2	891
10	40	13 649	1028	34	23.5	242
	41	14 361	1064	37	32.4	345
	42	15 446	1148	46	21.7	250
	43	16639	1283	42	40.5	519
	44	17 577	1309	40	50.0	655
11	45	17908	1357	46	43.5	590
	46	17 565	1296	42	50.0	648
	47	21 513	1783	44	77.3	1378
	48	17964	1510	44	54.5	824
12	49	15155	1162	44	43.2	502
	50	12919	842	39	46.2	389
	51	13 560	846	39	48.7	412
	52	12609	674	45	22.2	150
Total		489 502	41 557			9639

 Table 3. Influenza surveillance system (June–December 2009)

ILI, Influenza-like illness.

Table 4. Parameters and sources of data included in the model

Parameter		Source	Value (95% CI)
A	ILI attack rate	Student-based survey	11.2% (9.4–13.0)
		Factory worker-based survey	38.1% (34.3-41.7)
В	Average H1N1 positive rate in ILIs	Influenza surveillance system	22.7%
С	Proportion of individuals with ILI seeking medical care	Student-based survey	80·2 % (77·8–82·5) 72·5 % (66·9–78·0)
D	Proportion of ILI in outpatients	Influenza surveillance system	8·5 %

CI, Confidence interval; ILI, Influenza-like illness.

proportion of people with ILI seeking medical care was 72.5-80.2%, this represents a total of $835\,000-$ 924000 cases of influenza A/H1N1 in Shenzhen between June and December 2009.

DISCUSSION

Similar to other countries, laboratory-confirmed cases of H1N1 form the main source of statistics on the

Category	Population	ILI	H1N1	H1N1 cases seeking medical care
Family household	709·1	66·7–92·2	15·1–20·9	12·1–16·8
Non-family household	590·9	202·7–246·4	45·9–55·9	33·3–40·5
Sum	1300	269·3–338·6	61·1–76·8	45·4–57·3

Table 5. Estimates of influenza A/H1N1 cases (per 10000 people)

ILI, Influenza-like illness.

Table 6. Estimates of H1N1 cases and rates of illness by age group

Age group (yr)	Proportion of notifiable cases*	Estimated no. cases	Estimated rate (%)	
0–4	0.118	71 969-90 462	16.8-21.1	
5-24	0.725	442775-556549	8.2-10.3	
25-49	0.143	87 370-109 821	1.4-1.8	
50-64	0.013	7997-10051	1.5–1.9	
≥65	0.002	889–1117	0.42-0.53	

* The age-specific number of cases and rates of influenza A/H1N1 were estimated by the age distribution of laboratory-confirmed cases from June to December 2009 in terms of statistics from Shenzhen CDC.

number of infections in China as well as in Shenzhen. It has been suggested that these statistics significantly underestimate actual cases of illness [4]. One study suggested that only 10% of H1N1 cases in developed countries were identified by laboratory assays in the early stages of the pandemic [7]. This might affect policy makers' judgements on the impact and the severity of the pandemic. In addition, the perception of severity and risk among the public was also influenced by the health authorities' data, which in turn affected compliance with official control measures such as the vaccination strategy [8]. Not all H1N1 influenza cases were reported by the sentinel points in Shenzhen for several reasons. First, mild cases were more likely to self-medicate rather than seek medical care. Hospital and laboratory surveillance systems therefore represented primarily the more severe cases. Second, negative laboratory results may be associated with the quality or timing of the sample collection. Furthermore, the capacity of the surveillance system may have changed as the pandemic developed [9]. Initially, monitoring was enhanced in response to political demand. When new cases exceeded the capacity of the surveillance system and as the costs of serological testing increased, the surveillance system could have missed greater numbers of mild cases. Thus, we estimated the actual impact of the H1N1 pandemic in 2009 in Shenzhen using two population-based surveys and the surveillance system.

Some studies have already evaluated the extent of actual illness in the early stages of the 2009 pandemic. Reed et al. [10] applied a probabilistic multiplier model to the number of reported cases and estimated that there were between 1.8 and 5.7 million symptomatic cases of H1N1 in the USA between April and July 2009 - a figure 140 times greater than the number of laboratory-confirmed cases. Another study modeLled the size of the epidemic in Mexico during its early stage using Global Epidemic and Mobility (GLEaM), and estimated the total infections to be between 121000 and 1394000, 36-416 times greater than the number of notified cases [9]. Barker et al. suggest that 7.5% of the population of New Zealand was infected with symptoms based on ILI surveillance [11]. In China, estimation of actual prevalence of H1N1 in the first wave of the H1N1 pandemic has seldom been done. We estimated that 611000 to 768 000 people, or 4.7-5.9% of the population in Shenzhen, experienced H1N1 influenza in 2009, which was about 330 times higher than the number of reported laboratory-confirmed cases (2063). In contrast with the distribution of seasonal influenza, the frequency of H1N1 was higher in younger age groups

than in older age groups. Similar age shifts have been highlighted in other studies [10-12]. The findings of highest prevalence within the 0-4 years age group in our study was consistent with findings in the New Zealand population [11], but differed from the US study [10] in which the highest prevalence was seen in the 5-24 years age group. Because the estimated cases by age group were weighted by the distribution of age groups in laboratory-confirmed cases, the high proportion of H1N1 cases in the 0-4 years age group was related to the high estimated prevalence. High hospitalization rates and a high prevalence of severe cases or death in this age group contributed to the high ascertainment of H1N1 cases. In addition, the high prevalence of estimated cases in this age group might have resulted from the age distribution in Shenzhen.

Our subjects from the two surveys had relatively good representativeness of the family household and non-family household populations, the predominant population groups in Shenzhen. As we randomly sampled schools stratified by outbreak records, students with lower risk of H1N1 infection were also included in the survey. In addition, about 70% of parents had reached secondary education level in our survey, which was similar to that of the general household population (74%) [2]. In the worker-based survey, factories were stratified by size of the worker population, a variable that might be critical to H1N1 transmission. The proportion of female workers (53%) in our survey was higher than that of males (47%), which is close to government statistics for migrant workers (female 52%, male 48%) [6] but different to the ratio of the registered resident population (male:female ratio 1.03:1) [2]. These demographic characteristics justify the representativeness of both our survey samples.

The student-based survey indicated a high ILI attack rate (49.5%) in students which was consistent with the high proportion of H1N1 outbreaks (90%) occurring in school settings. There was an insignificant downward trend in the ILI attack rate, but the proportion of symptomatic cases seeking medical care also decreased significantly with increasing student grade. Furthermore, classmates of respondents had higher ILI attack rates (67.7%) than their parents (14.6%), according to students' reports. Workers who responded also reported higher attack rates among their colleagues (45.7%) than their room-mates (26.5%). These findings could result from high population density and close contact in school and at work, which was likely to increase students' and workers' risks of acquiring H1N1 infection. The population-based surveys were developed to complement ILI surveillance and to include those who did not seek medical care [13]. Furthermore, workers had higher ILI attack rates ($38\cdot1\%$) than students' families ($11\cdot2\%$), indicating that the non-family household population might be more likely to be affected by H1N1 than the family household population because of the high mobility of migrant workers.

National sentinel sites have been in place to monitor ILI in outpatients for 20 years. The surveillance of H1N1 influenza was added to seasonal flu surveillance from June 2009. As the trend in detection of H1N1 cases through the Shenzhen Influenza Surveillance System was in accordance with the epidemic in the whole city, the average H1N1 PCR-positive rate in consistent samples used in our estimation has good representativeness, and we suggest that it be used to estimate the overall burden of the pandemic [13]. The system indicated the average value of parameter D before June in 2009 was similar to the average level in 2008 (5.92%), while the ILI rate in outpatients reached 8.5% after June in 2009 accord with the H1N1 influenza pandemic. Moreover, the high frequency of H1N1 samples with positive results improved the accuracy of detection even with small numbers of ILI case samples. When we used two approaches to calculate the total number of cases, the numbers estimated from Approach (611000-768000) and Approach II (835000-924000) were close.

We noticed that there were some potential confounders in our survey due to the sampling methods but the incidence of H1N1 in schools was the key factor we accounted for in the students' sampling frame. Because the ILI rate in outpatients in 2009 did not vary significantly in districts (3-9%) according to the Shenzhen Influenza Surveillance System, we assumed there was no difference in endemicity of H1N1 in districts in Shenzhen when sampling schools in each district. Eight target schools might be a small proportion of the total schools in Shenzhen but we were able to collect the ILI attack rate in family households in a short time period. In addition, there was no significant age difference between students in the infected and uninfected groups. We also weighted the student and family ILI attack rates by the proportion of schools and the student population size. Another limitation was that the average A/H1N1-positive rate in outpatients with ILI in the two sentinel hospitals was assumed to match the general population rate in Approach I and the general outpatient rate in Approach II. The higher probability of more severe cases seeking medical care in the two national sentinel hospitals s compared to milder cases may have overestimated the H1N1 PCR-positive rate in the general community or in general outpatients with ILI. However, as residents normally seek medical care in public hospitals [3] the two sentinel hospitals should be the most reliable places to monitor ILI. The relatively small number of ILI samples for testing might lead to a high variance in the estimate of positive results even with random sampling. However, the highest H1N1 PCR-positive rates were found in September (week 39, 70.2%) and November (week 47, 77.3%), matching the two peaks of the pandemic in the Shenzhen CDC data of notifiable H1N1 influenza cases. Furthermore, our study has a limitation in demonstrating the discrepancy between symptomatic and asymptomatic H1N1 infections, which could be identified by serological research. Other limitations arise from the survey methods. Respondents from the worker survey may have exaggerated their medication-seeking behaviour when they completed the questionnaires. A representative study concerning migrant workers found that over 50% of research subjects did not have medical insurance, and over 60% of workers did not seek medical care when they became ill [1]. Those who reported seeking medical care for ILI may have purchased medicines from pharmacies without prescriptions, or visited private, unlicensed clinics that accept cash payments or were physically more convenient. Those who were unable to access the formal and better quality hospitals would not be sampled to test for H1N1, leading to an underestimation of the actual burden of the disease. The two population-based surveys did not cover all population groups. For instance, households without children and households with pre-schoolchildren were missed out in these surveys. The surveys were carried out throughout the pandemic period, which should have minimized subjects' recall bias for ILI symptoms and their behaviours in seeking medical care, similar to one random telephone interview in Sweden in 2005 which estimated the attack rate of influenza during epidemic seasons [14]. Finally, subjects not only had to respond on their ILI events but also their detailed symptoms and approaches to seeking medical care which should have made them less likely to overestimate the number of attacks, even if they perceived themselves at high risk.

Although the estimation method in this study was simple compared with other dynamic or probabilistic models, the parameters were based on original local data and surveys rather than literature review and so were more appropriate to estimate the extent of the pandemic in Shenzhen. Based on the estimates in this study, dynamic models are being considered for simulating the transmission of the H1N1 influenza during the pandemic in Shenzhen in future work. Serological investigations are expected to be used to estimate the overall infected population both with and without symptoms during the pandemic. In general, the estimates of actual H1N1 influenza cases are crucial for the development of mitigation and control measures for any novel H1N1 pandemic, particularly in Shenzhen, with high population mobility and density.

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DECLARATION OF INTEREST

None.

REFERENCES

- 1. Mou J, et al. Health care utilisation amongst Shenzhen migrant workers: does being insured make a difference? BMC Health Services Research 2009; 9: 214.
- Shenzhen Statistics Bureau. 2005 Shenzhen report of the national 1% population sampling survey. Shenzhen, Guangdong, China, 2005 (http://www.sztj.com/main/ xxgk/tjsj/tjgb/pcgb/200605181682.shtml). Accessed 13 December 2009.
- Shenzhen Government. Shenzhen Yearbook 2008. Shenzhen, Guangdong, China, 2008. (http://www.sztj. com/main/xxgk/tjsj/tjgb/gmjjhshfzgb/200903243520. shtml). Accessed 13 December 2009.
- 4. World Health Organization. Human infection with (pandemic) H1N1 2009: updated interim WHO guidance on global surveillance 2009. (http://www.who.int/ csr/resources/publications/swineflu/interim_guidance/ en/index.html). Accessed 23 March 2010.

- World Health Organization. A practical guide for designing and conducting influenza disease burden studies, 2008 November (http://www.wpro.who.int/ internet/resources.ashx/CSR/Publications/Guidefor DesigningandConductingInfluenzaStudies.pdf). Accessed 10 November 2009.
- Shenzhen Government. Shenzhen Migrant workers: safeguard and employment. Shenzhen, Guangdong, China, 2009 (http://www.szhrss.gov.cn/tjsj/zxtjxx/200910/ t20091023_1214416_7374.htm). Accessed 25 June 2010.
- 7. Wilson N, Baker MG. The emerging influenza pandemic: estimating the case fatality ratio. *Euro-surveillance* 2009; 14.
- Bootsma MC, Ferguson NM. The effect of public health measures on the 1918 influenza pandemic in U.S. cities. *Proceedings of the National Academy of Sciences USA* 2007; 104: 7588–7593.
- 9. Colizza V, *et al.* Estimate of Novel Influenza A/H1N1 cases in Mexico at the early stage of the pandemic with

a spatially structured epidemic model. *PLoS Currents: Influenza* 2009; RRN1129.

- Reed C, et al. Estimates of the prevalence of pandemic (H1N1) 2009, United States, April–July 2009. Emerging Infectious Diseases 2009; 15: 2004–2007.
- 11. **Baker MG**, *et al.* Pandemic influenza A(H1N1)v in New Zealand: the experience from April to August 2009. *Eurosurveillance* 2009; **14**.
- 12. **Tuite AR**, *et al.* Estimated epidemiologic parameters and morbidity associated with pandemic H1N1 influenza. *Canadian Medical Association Journal* 2010; **182**: 117.
- Lipsitch M, et al. How to maintain surveillance for novel influenza A H1N1 when there are too many cases to count. Lancet 2009; 374: 1209–1211.
- 14. **Payne L, et al.** 'Did you have flu last week?' A telephone survey to estimate a point prevalence of influenza in the Swedish population. *Eurosurveillance* 2005; **10**: 241–244.