

## Influenza B Outbreak among Influenza-vaccinated Welfare Home Residents in Singapore

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### Abstract

**Introduction:** Outbreaks of acute respiratory illness occur commonly in long-term care facilities (LTCF), due to the close proximity of residents. Most influenza outbreak reports have been from temperate countries. This study reports an outbreak of influenza B among a highly immunised resident population in a welfare home in tropical Singapore, and discusses vaccine efficacy and the role of acute respiratory illness surveillance for outbreak prevention and control. **Materials and Methods:** During the period from 16 to 21 March 2007, outbreak investigations and active case finding were carried out among residents and nursing staff at the welfare home. Interviews and medical notes review were conducted to obtain epidemiological and clinical data. Hospitalised patients were tested for respiratory pathogens. Further genetic studies were also carried out on positive respiratory samples. **Results:** The overall clinical attack rate was 9.4% (17/180) in residents and 6.7% (2/30) in staff. All infected residents and staff had received influenza immunisation. Fifteen residents were hospitalised, with 2 developing severe complications. Genetic sequencing revealed that the outbreak strain had an 8.2% amino acid difference from B/Malaysia/2506/2004, the 2006 southern hemisphere influenza vaccine strain, which the residents and staff had earlier received. **Conclusions:** A mismatch between the vaccine and circulating influenza virus strains can result in an outbreak in a highly immunised LTCF resident population. Active surveillance for acute respiratory illness in LTCFs could be implemented for rapid detection of antigenic drift. Enhanced infection control and other preventive measures can then be deployed in a timely manner to mitigate the effect of any outbreaks.

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**Key words:** Antigenic drift, Influenza, Long-term care facilities

### Introduction

Influenza has a major impact on the health of residents of long-term residential care facilities (LTCF). Residents of LTCFs are especially vulnerable to influenza infections, due to the closed proximity that they live in. A number of influenza outbreaks involving residents in LTCFs have been reported in the medical literature.<sup>1-13</sup> Influenza A has been implicated in most outbreaks.<sup>3-11</sup> However, influenza B outbreaks have also been reported and can be associated with significant morbidity and mortality.<sup>14,15</sup> Some of these outbreaks have occurred even in highly immunised populations.

Influenza outbreaks in LTCFs are associated with

increased morbidity, hospitalisation and mortality among residents.<sup>16-18</sup> Early recognition of outbreaks is critical for successful outbreak control and the mitigation of its adverse effects.<sup>19</sup> The Ministry of Health has been carrying out virological surveillance of influenza viruses on throat and nasopharyngeal swabs collected by polyclinics, private clinics and hospitals throughout the year.<sup>20</sup> Influenza B accounted for 36.3% of the isolates and it was mainly detected from January through March. The influenza B strains “(B/Ohio/1/05) which made its appearance towards the end of 2005 and had remained active throughout 2006, co-circulated with B/Florida/07/2004-like strains until the later part of the year when the former was not detected. B/

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Shanghai/361/2002-like strains and B/Malaysia/2506/04 strains were occasionally isolated".<sup>20</sup>

Most of the published influenza outbreak reports involving LTCFs have been from temperate countries.<sup>5-10,12-13,21</sup> We report an outbreak of influenza B among a highly-immunised resident population in a LTCF in a tropical city state, Singapore. Furthermore, this report discusses influenza vaccine efficacy and the role of acute respiratory illness surveillance at LTCFs in the rapid detection of antigenic drift and timely institution of outbreak preventive measures.

## Materials and Methods

### Outbreak Setting

On 17 March 2007, a cluster of acute respiratory illness involving 11 residents from a welfare home was admitted to the Communicable Disease Centre (CDC) at Tan Tock Seng Hospital. The 7-storeyed, non-air conditioned welfare home with a bed capacity of 200, provides shelter, care and rehabilitation for male destitute persons with chronic mental illnesses who were employable and able to live independently with minimal supervision. The home provides a supportive environment for the maintenance and promotion of the physical, psychological and social wellbeing of the residents.

The home's resident doctor had reviewed the residents and referred those with acute respiratory illness to CDC for further clinical management.

### Data Collection and Case Definition

On being alerted of the outbreak, the surveillance team at CDC contacted the LTCF's resident doctor and nursing officer to identify further cases, and to collect data on all residents and staff of the home, using the following case definitions:

- (i) Probable case: a resident or staff member who had fever, and either cough or running nose or sore throat, and had contact with a confirmed case during the outbreak period.
- (ii) Confirmed case: a resident or staff member who had fever, and either cough or running nose or sore throat, and a positive PCR test for influenza B, during the outbreak period.

Data collected included age, gender, date of onset of first symptoms, background medical history and influenza vaccination history. In addition, we reviewed the medical notes of each patient admitted to the hospital, to collect data on clinical and radiological findings, the length of hospitalisation, and the outcome of the hospitalisation.

## Results

### Influenza B Outbreak

During the outbreak period (16 to 21 March 2007), there

were 180 residents and 30 nursing staff at the LTCF. The outbreak came to the notice of the home's resident doctor on 17 March, when she observed a cluster of 11 residents who were unwell with acute respiratory symptoms. Figure 1 presents the epidemic curve. The outbreak affected a total of 17 residents and 2 nursing staff. The outbreak was over within a week, with no further cases identified after 21 March 2007. Interviews with staff of the home did not identify any earlier cases fulfilling our case definitions for influenza B. All the 17 residents (median age 55 years, range 38 to 75 years) and 2 staff (aged 23 and 25 years) fulfilled our case definitions during the outbreak period. All cases had fever. Dry cough (57.9%) and running nose (47.4%) were the most common respiratory symptoms. Constitutional symptoms were uncommon, with only 1 (5.9%) case presenting with myalgia. One (5.9%) and 6 (35.3%) residents had conjunctivitis and sore throat, respectively.

Table 1 presents a line listing of the 15 residents admitted to CDC during the outbreak period. Their ages ranged from 38 to 70 years (median age 55 years). Most had mild illness and were discharged within a week. However, 2 patients developed serious complications and had prolonged hospitalisation. One patient was hospitalised for 17 days for the management of pneumonia and left lung abscess; another stayed for 16 days, after developing bacteraemia from *Staphylococcus aureus* infection. Neither of them had medical conditions that could have caused them to be immunosuppressed. Interestingly, one resident who was admitted for acute respiratory illness was eventually diagnosed to have acute appendicitis and underwent appendectomy. None of the home's affected nursing staff required hospital admission.

The overall clinical attack rate by the end of the outbreak period was 9.4% in residents and 6.7% in staff (based on individuals who fulfilled our case definitions for probable influenza). A review of the home's vaccination records revealed that 99.5% of their residents and 100% of their staff had been immunised with the trivalent 2006 Southern Hemisphere (SH) influenza vaccine in June 2006. All 17 residents and 2 staff who were infected during the outbreak received the vaccination.

### Microbiological Findings

Seven of the residents were admitted. They were tested for influenza B by an in-house gel-based polymerase chain reaction (PCR) assay for influenza A and B on combined nasal and throat swabs, of which 6 had positive results (Table 1).

Genetic studies performed on all the positive specimens revealed that the influenza B strain that caused the outbreak was closely related to B/Houston/B720/2004. It had an 8.2%

Table 1. Characteristics, Laboratory Results and Discharge Diagnosis of Admitted Patients

No.	Age	Onset date	LOS	CXR	PCR	Discharge diagnosis
1	55	16-Mar-07	4	NAD	Flu B Positive	Upper respiratory tract infection
2	49	16-Mar-07	4	NAD	Flu B Positive	Upper respiratory tract infection
3	54	16-Mar-07	3	NAD	Flu B Positive	Upper respiratory tract infection
4	53	16-Mar-07	6	NAD	Flu B Positive	Upper respiratory tract infection
5	62	16-Mar-07	4	Small nodular opacity in left upper zone	Negative	Tracheobronchitis
6	55	16-Mar-07	17	Left lower zone consolidation	Not tested	Pneumonia with left lung abscess
7	44	17-Mar-07	8	NAD	Flu B Positive	Upper respiratory tract infection
8	43	17-Mar-07	7	NAD	Flu B Positive	Upper respiratory tract infection
9	55	16-Mar-07	4	NAD	Not tested	Viral fever
10	64	16-Mar-07	5	NAD	Not tested	Viral fever
11	46	16-Mar-07	3	NAD	Not tested	Viral fever
12	60	18-Mar-07	10	NAD	Not tested	Appendicitis
13	68	18-Mar-07	16	NAD	Not tested	<i>Staphylococcus aureus</i> infection
14	70	18-Mar-07	3	NAD	Not tested	Viral fever
15	38	20-Mar-07	7	Left middle zone & left lower Zone consolidation	Not tested	Pneumonia

CXR: chest X-ray; LOS: length of stay; NAD: no abnormality detected; PCR: polymerase chain reaction

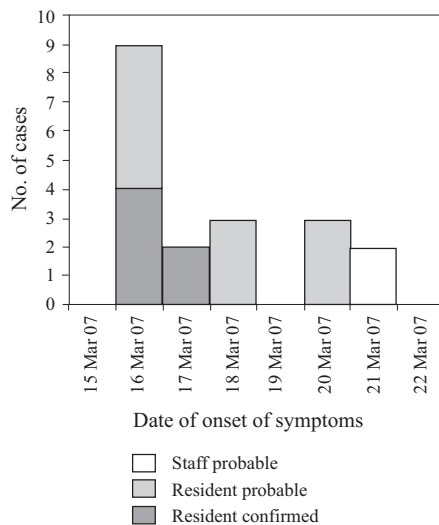


Fig. 1. Epidemic curve of Influenza B outbreak at Welfare home (n = 19).

amino acid difference from B/Malaysia/2506/2004; the strain contained in the 2006 SH influenza vaccine, which the residents and staff had earlier received. The vaccine strain of B/Malaysia/2506/2004 used in 2006 to 2007 belonged to the Victoria lineage. Our clinical isolates clustered with isolates from the Yamagata linkage, such as B/Florida/4/2006, B/Florida/7/2004 and B/Jiangsu/10/2003. We used the haemagglutinin gene for building the phylogenetic tree, all the sequences were downloaded from The National Center for Biotechnology Information (NCBI). The coding

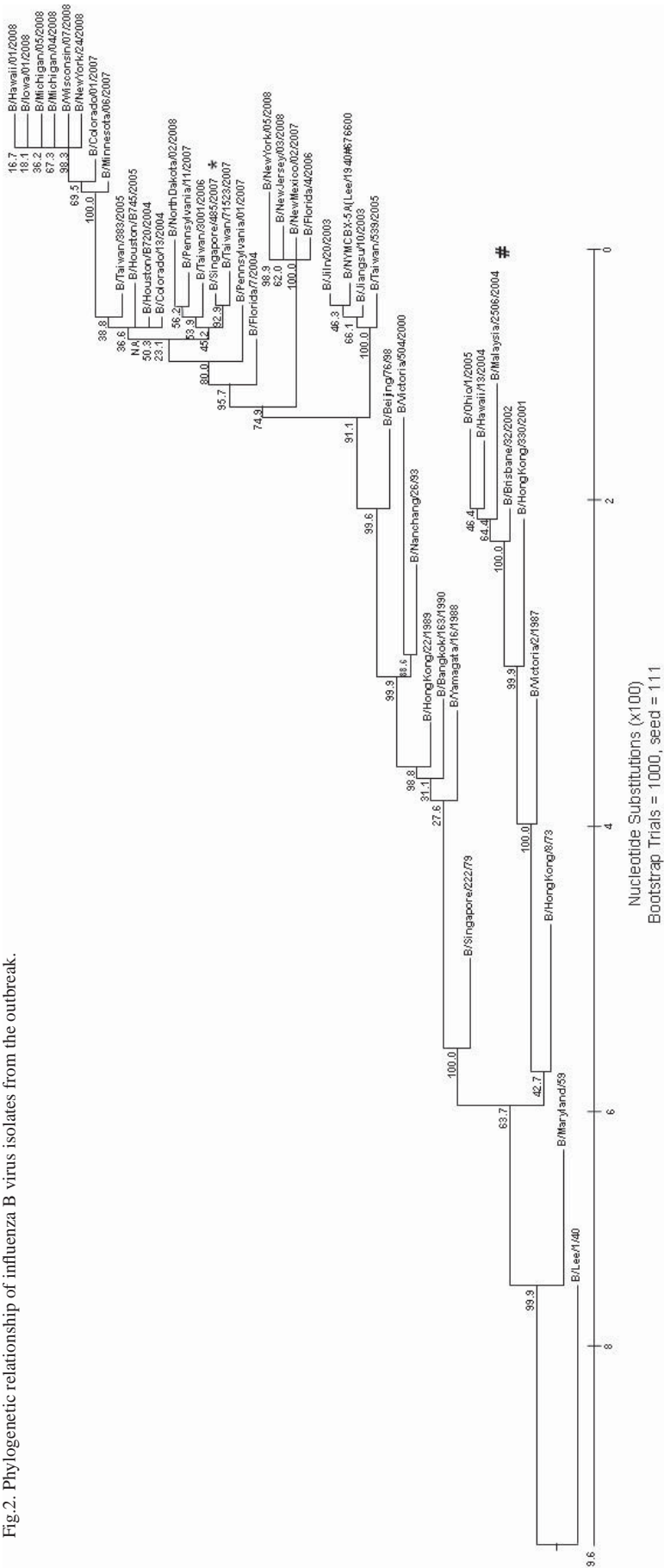
sequence without the signal sequence was aligned and the phylogenetic tree was built using MegAlign (DNASTAR, Inc. WI, USA). The strain from our clinical isolates and the vaccine strain are highlighted with '\*' and '#', respectively, in Figure 2.

## Discussion

Although there have been many reports of outbreaks of influenza in institutionalised populations,<sup>5-10,12,13,20</sup> very few of these reports have been from the tropics. In this paper, we describe an outbreak of influenza B in a highly vaccinated institutionalised population in a tropical country. Many reports on outbreaks of institutionalised elderly populations have reported a low vaccine efficacy.<sup>4,13</sup> The most common explanation for the lack of vaccine efficacy is a mismatch between the vaccine strain and the circulating viral strain,<sup>22</sup> as was the case in this outbreak. However, there have also been reports of influenza B outbreaks in highly immunised nursing home populations during seasons with a good match between vaccine and circulating strains.<sup>13</sup> Large outbreaks of influenza B have occurred with high attack rates (35.9%) despite high resident vaccination rates (93%), even when the vaccine strain was matched to the circulating strain.<sup>15</sup> It would not have been possible to ascertain if there was a mismatch between the vaccine and circulating strain without the appropriate genetic studies.

In this outbreak, the clinical attack rate of less than 10% was lower than what have been reported by some others. It could be due to the fact that the majority (82.4%) of the

Fig. 2. Phylogenetic relationship of influenza B virus isolates from the outbreak.



infected residents were aged below 65 years (median 55 years, range 23 to 75 years), which was lower than the average age in nursing home populations. However, the outbreak was not without its consequences. While some of the residents who were admitted could probably have been managed as outpatients, most were discharged within a couple of days. Two patients developed serious complications. This raises the question of whether timely empirical administration of oseltamivir to residents presenting with acute respiratory illness would have been useful in this outbreak and similar situations. The data showed that 80% of cases had presented 48 hours after onset of symptoms, hence, oseltamivir could not be administered within the accepted window period of efficacy.<sup>23</sup>

It could be argued that oseltamivir could be used more liberally in influenza seasons where there was a vaccine and circulating strain mismatch, particularly in institutionalised populations. However, we would like to point out that, in the tropics, influenza seasons are far less predictable in timing than in temperate countries. Vaccination thus remains the most important strategy for minimising the burden of influenza disease in institutionalised populations in Singapore. One limitation of this study is that not all symptomatic residents were tested for Influenza B. Nevertheless, in an outbreak setting like this, it can be assumed that all patients presenting with acute respiratory illness have been infected with the outbreak strain, and the response measures would not have been any different.

In Singapore, an outbreak of influenza B was reported among residents of a mental hospital during the SARS epidemic in 2003.<sup>24</sup> Subsequently, from September 2003, the Ministry of Health recommended annual influenza vaccination for high-risk patients including residents of LTCFs. This explains the high immunisation coverage in the population of this home. Influenza vaccines have been recommended to be administered on an annual basis using either the Northern or Southern Hemisphere formulation. However, in tropical Singapore, there is a bimodal increase in influenza incidence in April to July and November to January.<sup>25</sup> There has been a suggestion that vaccination should

be increased to twice a year for tropical and subtropical regions whenever a significant drift in circulating strain from current vaccine strain is detected by the National Influenza Surveillance programme. This outbreak strengthens the case for such measures.

## Conclusions

In conclusion, the failure of influenza vaccination to prevent infection in this outbreak does not imply that vaccination is not effective as a strategy for minimising the burden of disease from influenza. Rather, this outbreak underscores the importance of continual surveillance including laboratory diagnosis of new viral infections, even in highly vaccinated populations. In the event of any mismatch between vaccine and circulating strains, antigenic drift, like this outbreak, there should be the flexibility to issue revised guidelines to re-vaccinate populations, as and when the need arises. Active surveillance for acute respiratory illness in LTCFs could also be implemented to detect circulating pathogens quickly, so that pharmacologic measures (such as oseltamivir for influenza), and non-pharmacologic measures like enhanced infection control measures can be deployed in a timely manner to mitigate the effect of any outbreaks.

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