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Program Errors in Taiwan's Mass Immunizations against Pandemic A/H1N1

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Abstract

On November 1, 2009, Taiwan launched a mass vaccination campaign against A/H1N1 pandemic. Because of the large quantity of vaccine doses to be administered, the number of program errors may also increase. We collected reports to the nationwide, voluntary error reporting system from November 1, 2009 through February 24, 2010. We analyzed reports to determine the types of errors and assess critical contributors to the error. From November 1, 2009 through February 24, 2010, 33 incidents of vaccination errors were reported. The reported errors included wrong vaccine (n=22), wrong dose (n=7), repeated vaccinations (n=2), and others (n=2). Inadequate staff competency and education, lack of quality process and risk management, and communication failures were key system elements contributing to reported errors. In the mass pandemic A/H1N1 vaccine campaign, program errors were associated with predictable/correctable human and systemic factors; efforts to decrease errors need to focus on provider education, computer support, and vaccine recipient flow optimization.

Keywords: pandemic H1N1, mass immunization, vaccine administration errors

Introduction

On June 11, 2009, World Health Organization (WHO) raised the level of influenza pandemic alert to highest phase [1]. Although the pandemic appears to be moderate in severity, exposures to a novel virus like 2009 pandemic A/H1N1 (pH1N1) in a population without pre-existing immunity could lead to widespread transmissions. WHO estimated that approximately one-third of the global population would contract pH1N1 in the 2009 influenza season and considered vaccines to be one of the most important strategies to reduce the morbidity and mortality [2]. To protect the integrity of the healthcare system, reduce the morbidity and mortality among high-risk

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population, and reduce pH1N1 transmission within communities, Taiwan's Central Epidemic Command Center (CECC) initiated a pH1N1 vaccination program. Beginning November1, 2009, 15 million doses of pH1N1 vaccine, including an inactivated vaccine without adjuvant (Adimmune Corporation, Taichung, Taiwan) and an MF59®-adjuvanted vaccine (Novartis Vaccines and Diagnostics, Sovicille, Italy), would be administered according to a priority list with target groups, through more than 2,000 public health or contracted clinics/hospitals [3, 4]. Public confidence in vaccine safety could greatly impact an immunization program. Although errors related to vaccine preservation, transportation, or administration occur in routine vaccination programs, the risks are higher in a campaign setting [5]. Therefore it is crucial to monitor and timely investigate program errors and adverse events following immunizations in this mass immunization program.

Material and Methods

Reporting of program errors

Program errors are technical errors and accidents in vaccine preparation, handling, or administration. Public health or contracted clinics/hospitals should directly report such errors to their local health authorities by filling a reporting and investigation form in the Pandemic A/H1N1 Vaccine Manual (Table 1). Local health authorities conducted site visits and process review to identify any potentially correctable causes, and reported the errors to the jurisdictional branch of Taiwan Centers for Diseases Control, which in turn, reported to CECC's H1N1 Vaccine Safety Working Group (The Working Group) [6]. The Working Group reviewed reported incidents and made recommendations to CECC's Risk Management Committees.

Data source

The Influenza Vaccination Information System (IVIS) provided the number of pH1N1 vaccine doses administered. Reports of program errors received from November 1, 2009 through February 24, 2010 (date of CECC dismissal) were reviewed and analyzed by a single investigator [7]. For each report, we classified type of errors by wrong vaccine, wrong dose, repeated vaccinations, wrong time, wrong vaccine recipient, and others. The causes of errors were classified in the context of key system elements identified by the Institute for Safe Medication Practice (ISMP) [8].

Data analyses

We conducted descriptive analyses by types and causes of errors. For each type of errors, we summarized the number of vaccine

Table 1. Report and investigation form for program errors related to pandemic A/H1N1 vaccine

_____ **County/City Report and Investigation Form for Program Errors Related to Pandemic A/H1N1 Vaccine**	
Date/time of error(s): _____ Facility name: _____ Vaccine administered by: Name: _____ Title: _____ Affiliation name: _____	Reporter Name: _____ Title: _____ Affiliation name:_____ Date/time of notification: _____ Investigated and reviewed by: Name: _____ Title: _____ Date/time form completed: _____
Type of Error	**Details of the Vaccination**
□ Wrong vaccine □ Wrong dose □ Repeated vaccinations □ Wrong time □ Wrong vaccine recipient □ Others, please specify:_____	The correct vaccine to be administered: Vaccine (type): _____ Dose: _____ The administered vaccine: Vaccine (type): _____ Dose: _____ Manufacturer: _____ Lot number: ____ Expiration date: _____ Any coadministered vaccine(s)? □ Yes, please specify: _____ □ No
Describe the Sequence of Error(s)	
Incident Investigation (Complete the following after investigation)	
Date/time of review	Administration facility:
	Public health clinics /local health authorities:
Others	Any adverse events following immunization? □ No, please specify number of vaccine recipients without adverse reaction: _____ □ Yes, please specify number of vaccine recipients affected: ____ Symptoms: _____ Date/time of symptom onset: _____ Medically-attended? □ No □ Yes, please specify: Date of visit: _____ Facility name: _____ Treatment: _____
Process Review	
Having existing plans for vaccine recipient flow optimization? □ No □ Yes (attach the optimization plan) Describe how the “Five Rights” are implemented in the facility: Improvement plan:	
List of Vaccine Recipients Affected	
1. Name: _____ Date of birth: _____ Age at vaccination: ___ years __ months Date of the most recent influenza vaccination: _____ Number of doses received in this influenza season: _____ 2. Name: _____ Date of birth: _____ Age at vaccination: ___ years __ months Date of the most recent influenza vaccination: _____ Number of doses received in this influenza season: _____ 3. Name: _____ Date of birth: _____ Age at vaccination: ___ years __ months Date of the most recent influenza vaccination: _____ Number of doses received in this influenza season: _____ (Use additional pages to list all affected vaccine recipients)	

recipients affected (median, range) and their outcomes. Illustrative incidents were presented as case studies to inform the key system elements implicated in errors.

Results

Descriptive analyses

By February 24, 2010, 5,651,265 pH1N1 vaccine doses had been administered. The Working Group received 33 reports of program errors in association with pH1N1 vaccine, which involved 129 persons (1–32 persons per incident) (Table 2). The most frequently reported errors fell in the category of wrong vaccine (67%), wrong dose (21%), and repeated vaccinations (6%). Among the 129 persons affected, 5 (4%) reported symptoms including malaise, dizziness, fever and skin rash. All these symptoms improved or recovered within days; none was hospitalized.

Table 3 summarized the causes of reported program errors. After excluding two reports with incomplete information, the causes identified included inadequate staff competency and education (24%), lack of quality process and risk management (21%), communication failures (21%), unsupportive environmental factors and staffing patterns (9%), lack of vaccine recipient information (9%), unsafe vaccine standardization, storage and distribution (6%), and flawed delivery devices (3%).

Case studies

A. Incident 1

This incident occurred in a public health clinic. The affected child, 3 years of age, was recommended to receive two doses of pH1N1 vaccines (0.5mL for each dose), with two doses separated for at least 4 weeks [6]. The first dose of pH1N1 vaccine was administered 3 days before this incident. On the date of incident occurred, he was brought by his grandmother to the clinic for seasonal influenza vaccination, along with his younger

Table 2. Program errors in association with pandemic A/H1N1 vaccination in Taiwan, November 1, 2009–February 24, 2010

Type of error	Number of reports (%)	Number of persons affected (%)	Number of persons affected per report (median, range)	Number of persons with adverse events
All	33 (100)	129 (100)[1]	1 (1–32)	5
Wrong vaccine	22 (67)	36 (28)	1 (1–13)	3[2]
Wrong dose	7 (21)	89 (68)	5 (1–32)	1[3]
Repeated vaccinations	2 (6)	2 (2)	1 (1–1)	1[4]
Wrong time	0 (0)	0 (0)	0	0
Wrong vaccine recipient	0 (0)	0 (0)	0	0
Others[5]	2 (6)	2 (2)	1 (1–1)	0

1. Including 64 males, 45 females, and 20 gender unknown
2. Predominant symptoms were malaise, fever, and skin rash
3. Predominant symptom was fever
4. Predominant symptom was dizziness
5. Other types of errors included administering the vaccine using an empty syringe, and having the needle retained at the injection site due to needle-syringe dislocation

Table 3. Causes of program errors in association with pandemic A/H1N1 vaccination in Taiwan, November 1, 2009–February 24, 2010

Cause of error	Number of reports (%)
Inadequate staff competency and education	8 (24)[1]
Lack of quality process and risk management	7 (21)[2]
Communication failures	7 (21)[3]
Unsupportive environmental factors and staffing patterns	3 (9)[4]
Lack of vaccine recipient information	3 (9)[5]
Unsafe vaccine standardization, storage and distribution	2 (6)[6]
Flawed delivery devices	1 (3)[7]
Lack of vaccine information	0 (0)
Unclear or confusing vaccine labels and packages	0 (0)
Inadequate vaccine recipient education	0 (0)
Unclassifiable for incomplete information	2 (6)

1. Staff unfamiliar with the correct vaccine brand and dosage for different age groups, or unfamiliar with the use of delivery devices
2. Staff did not confirm vaccine recipient's age, vaccine brand and dosage that the vaccine recipient should receive
3. Wrong vaccination orders, failure to document the brand of prior vaccines, failure to identify vaccine type to be administered
4. Work overload and rushed procedures; flawed vaccine recipient flow resulted in repeated vaccinations
5. Vaccine recipient did not correctly report the age, previous pandemic A/H1N1 vaccine history, and the type of vaccine to be receive
6. Product misidentification due to unlabeled vaccine containers; mixed-up of the prefilled and unused/empty syringes in the same area
7. Dislocation between the needle and syringe

sister who was there to receive the pH1N1 vaccine. The staff member was overloaded by the postvaccination irritable crying of the girl and the vast number of people waiting in line; as a result, she took a rushed procedure to vaccinate the child with another pH1N1 vaccine without double checks. This error was detected soon and the grandmother was informed immediately. The cause of this incident was the unsupportive environmental factors and staffing patterns; vaccine recipient flows for different vaccine types were not separated and vaccinators did not follow the "Five Rights" principle to prevent errors because of task overload.

B. Incident 2

This incident occurred in an elementary school; 32 schoolchildren involved (24 in the 3rd grade and 8 in the 6th grade). Children 3 years of age through the 3rd grade were recommended to receive two doses of pH1N1 vaccine (0.5mL for each dose), whereas students above the 4th grade were recommended to receive a single dose [6]. On the date of incident occurred, staff administering the vaccine was found to deliver wrong dose (0.05mL) to students; they were instructed to administer another 0.45mL of vaccine dose to the non-injection arm. Local health authority and parents were informed.

The cause of this incident was inadequate staff competency and education. Vaccinators did not have the knowledge of the correct vaccine dose that should be administered.

C. Incident 3

This incident occurred in a contracted clinic. The affected infant, 8 months of age, was recommended to receive two doses of the Novartis pH1N1 vaccine (0.25mL for each dose) [6]. On the date of incident occurred, the infant was brought to the clinic by his parents, and the vaccinator administered the Adimmune pH1N1 vaccine. After vaccination, the vaccinator rechecked the vaccine recipient's age, found and reported the error. The cause of this incident was lack of quality process and risk management. The vaccinator fully understood the correct vaccine brand and dosage, but failed to follow the "Five Rights" principle to prevent the error.

Discussion

The pH1N1 vaccination program was the largest influenza immunization program in Taiwan since 1998. With more than 5.65 million doses of vaccines administrated from November 1, 2009 through February 24, 2010, the Working Group received 33 reports of program errors in association with pH1N1 vaccine administration. Inadequate staff competency and education, lack of quality process and risk management, communication failures, and unsupportive environmental factors and staffing patterns all contributed to these errors. Although the immunogenicity and safety of a wrongly administered pH1N1 vaccine was unknown, few (5) of the 129 vaccine recipients involved reported adverse events and none indicated a serious adverse event as an outcome. However, these errors were associated with predictable or correctable human and systemic factors and public health authorities should try the best to avoid their occurrences.

Because of the rapid licensure of pH1N1 vaccines, the appropriate vaccine dosage and schedule for different age groups could not be determined until a month before mass immunization campaign [6]. Two types of vaccines were used: the Adimmune vaccine licensed for use in children aged ≥1 year, and the Novartis vaccine for use in children aged ≥6 months. As a result, infants 6 months to 1 year of age could only receive the Novartis vaccines [9]. These were important but complex details that vaccinators should keep in mind, but because of the urgency of information to be delivered, practitioners were not adequately provided with and learned about these details, which could increase the risk for program errors.

Seasonal influenza vaccine were also available beginning October 1, 2009. After the nationwide campaign started on November 1, 2009, providers might be offering seasonal and pH1N1 vaccines concurrently. As more people might show up simultaneously in the same facility to be vaccinated, inadequate staffing patterns could lead to significant workload and rushed procedures without following the "Five Rights" principle. If providers did not set up separate vaccine recipient flows for different vaccine types, or failed to educate vaccine recipients about the vaccines they should be receiving, program errors such as wrong vaccine or repeated vaccinations could occur.

This study was subject to at least two

limitations. As with other passive surveillance system, program errors were voluntarily reported to the Working Group. Data collected on the report form were often incomplete and incidents were under-reported. Besides, we were not able to calculate and compare reporting rates of errors in different settings (e.g., public health clinics, contracted clinics/hospitals, schools) due to a lack of the number of doses administered in each facility.

In addition to provide practitioners with ongoing educations and perform independent double checks to verify the prescription using the "Five Rights" principle, the following strategies can be considered to systematically minimize the risk of program errors:

1. *Provide up-to-date, timely vaccine information*. For example, the responsible officer of each facility could update CECC's guidance at the beginning of each workday. The most updated guidance should be made visible in the facility so that vaccinators could be reminded anytime.
2. *Use of an automated verification process to detect and correct errors before reaching vaccine recipient*. For example, vaccination orders with regard to brands and dosages could be generated automatically according to recipient's age (e.g., for infant 6 months to 1 year of age, always prescribe the Novartis vaccine). A nationwide immunization information system (IIS) that keeps individual vaccination records would facilitate information retrievals at any vaccine administration site and therefore, prevent repeated vaccinations or vaccination in advance.
3. *Vaccine recipient flow optimization*. Vaccine information statements, pre-vaccination evaluation forms, and vaccination certificates should be delivered at designed steps. Providers should schedule adequate staffing to have separate vaccine recipient flows for different types of vaccines. People who are already vaccinated should be led to the rest area, instead of staying in the waiting line, to prevent repeated vaccinations.

Although program errors could not be completely avoided, it could be minimized by provider education, computer support, and vaccine recipient flow optimization.

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Analysis of Strategies of the Use of Antiviral Medication in Patients with H1N1 2009 Influenza in Taiwan

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Abstract

Before the start of H1N1 2009 influenza pandemic, Taiwan has stockpiled antiviral medication enough for 10% of the total population. However, because the medication is not covered under the National Health Insurance Program, it was not widely used in the past. In April, 2009, when the pandemic first started, the Central Epidemic Command Center (CECC) adopted the policy of containment, and gave antiviral medication to treat all confirmed H1N1 2009 influenza cases and prophylax their close contacts with government-sponsored medication. However, following the announcement of the mild pandemic phase of H1N1 2009 influenza by the World Health Organization (WHO), the overall prevention and control strategies of H1N1 2009 influenza in Taiwan were shifted to mitigation, where screening with rapid influenza diagnostic test (RIDT) and antiviral treatment were employed as the primary control strategy before vaccines became available. Starting August 15, 2009, antiviral medication against influenza is covered under the National Health Insurance. It is approved for patients with influenza-like illnesses (ILIs) who are tested positive for influenza A with RIDT. Due to the inadequate sensitivity of the RIDT, antiviral medication is also approved in patients with ILIs who present danger signs of developing severe diseases, regardless of test results from RIDT. The cost of antiviral medication and screening is paid for by the government so that these expenses will not affect the maximum quota allocated to each medical provider under the National Health Insurance. Special clinics for ILIs and influenza clinics are also set to improve the

accessibility of medial care for the general public.

Analysis of the first 96 cases of hospitalized H1N1 2009 influenza cases due to pneumonia in Taiwan indicated that the proportion of patients taking Tamiflu within 48 hours from the onset of symptoms showed a statistically significant increase since August 15. In addition, the time from the onset of symptoms to seeking medical help was shortened, and the severity of diseases at the time of physician consultation was also reduced. These results suggest that by providing influenza screening and antiviral medication paid for by the government, as well as increased accessibility to medical care facilities, may have resulted in more rapid diagnosis and treatment for patients with influenza. We believe that as long as the general population has the correct concept about influenza, coupled with effective prevention and control strategies, we will be able to survive this influenza pandemic.

Key words: H1N1 2009 influenza, antiviral medication, Tamiflu, rapid influenza diagnostic test, influenza clinic

Introduction

Influenza is an acute respiratory diseases caused by influenza viruses, primarily during the winter months. Most patients have only mild symptoms, but high-risk patients may develop severe complications which can be fatal. There are two classes of antiviral medication: M2 inhibitors, and neuraminidase inhibitors. The former is only effective against type A influenza, and viral strains resistant to M2 inhibitors have increased rapidly. As a result, the Centers for Disease Control and Prevention of the United States (US CDC) no longer recommend M2 inhibitors for the treatment of influenza. Neuraminidase inhibitors include oseltamivir (Tamiflu) and zanamivir (Relenza). They are effective against both type A and B influenza, have a lower risk of drug resistance, and are the mainstream antiviral treatment of choice [1, 2].

At the start of the influenza pandemic, antiviral medication was used not only for early treatment of patients, but also for prophylaxis of close contacts in order to prevent the spread of diseases. One of the four strategies for combating the influenza pandemic developed by the Centers for Disease Control, Taiwan (Taiwan CDC) include stockpiling and production of antiviral medication according to the recommendation by the World Health Organization (WHO) [3]. The strategy of stockpiling adopted the principle of diversification in order to prevent widespread drug resistance as a result of monotherapy with only a single type of agent [4]. Through April, 2009, before the start of the H1N1 2009 influenza pandemic, Taiwan has already stockpiled antiviral medication enough for 2,284,000 courses of treatment, which accounted for the need for 10 percent of the total population. This includes 515,000 course of Tamiflu capsules, 1,700,000 courses of Tamiflu powder (API), and 69,000 courses of Relenza. Qualified use of the stockpiled antiviral medication includes suspected cases of H5N1 influenza and their close contacts, workers on animal farms where cases of animals with influenza are reported, and is later expanded to reported cases of severe

complicated influenza [5].

There were relatively few confirmed cases of severe complicated influenza during the past two influenza seasons in Taiwan (26 in 2007, 22 in 2008). The occurrence was mainly during the winter months, and there has been no confirmed human case of H5N1. Antiviral medication such as Tamiflu, as well as rapid influenza diagnostic test (RIDT), was not covered by the National Health Insurance Program. Stockpiled antiviral medication can only be used in patients with certain diseases reportable to the notifiable disease system as specified by Taiwan CDC. The stockpiled medication is allocated according to the population and characteristics of each city and county, and is stored at the local health departments or designated contract hospitals. As a result, antiviral medication was not widely used before the pandemic, and the knowledge towards the use of antiviral medication is also very limited in both medical care professionals and the general public.

Strategies of the Use of Antiviral Medication in Patients with H1N1 2009 Influenza

Outbreaks of the H1N1 2009 influenza epidemic started to emerge in Mexico and the southwest region of the United States since April, 2009. WHO gradually raised the level of influenza pandemic alert to phase 6 from April to June. In Taiwan, the Central Epidemic Command Center (CECC) was enacted on April 28 according to the Communicable Diseases Control Act. H1N1 2009 influenza was also listed as category 1 communicable diseases. Containment was initially adopted as the control strategy in order to block the disease from entering Taiwan. Border control was the primary control measure. All reported cases were immediately admitted to the negative-pressure isolation unit in designated hospitals and treated with antiviral medication. Thorough epidemiologic investigations of all cases were conducted and prophylactic antiviral medication was given to close contacts of reported cases when necessary.

WHO announced the start of the 2009 influenza pandemic of moderate severity on June 12, with the severity of symptoms comparable to seasonal influenza. As the situation of the global influenza pandemic became clear by the day, the prevention and control strategies in Taiwan were also shifted from containment to mitigation. Screening with RIDT and antiviral treatment were employed as the primary control tools before influenza vaccines were made available. On June 19, the CECC removed H1N1 2009 influenza from the list of category 1 communicable diseases. Instead of reporting H1N1 2009 influenza, severe complicated influenza was listed as category 4 communicable diseases, and qualified use of the stockpiled antiviral medication was also expanded to these reported cases of severe complicated influenza. On July 17, the first case of confirmed severe complicated influenza due to H1N1 2009 influenza virus was announced by the CECC. Since then, the number of reported severe complicated influenza cases increased gradually, and questions regarding the diagnosis and timing of medical treatment also surfaced as the number of severe cases increased. As a result, the chief commander of the CECC ordered the formation of clinical working group to

collaborate with medical societies to study issues in the medical care of patients with severe illnesses, the availability of hospital beds, and use of medication. It was also planned that antiviral medication should be covered under the National Health Insurance on the premises of avoiding abuse in order to improve the availability of antiviral medication and prevent patients from more severe illnesses.

With the approval of the medication working group of the National Health Insurance Bureau, antiviral medication against influenza is covered by the National Health Insurance from August 15, 2009 to March 31, 2010. Patients who are diagnosed by certain specialty physicians with ILIs or tested positive for influenza A by RIDT may obtain prescriptions for antiviral medications paid for by the National Health Insurance. The cost of RIDT is also paid for by the government [6]. The purpose of using RIDT is to prevent the abuse of antiviral medication and reduce the associated risk of developing drug resistance. However, due to the inadequate sensitivity of the RIDT, in order to avoid delays in antiviral treatment due to false negative test results, following the recommendation from the WHO and the expert advice from the H1N1 Novel Influenza Advisory Group convened by the Executive Yuan, on September 8, 2009, the CECC determined that antiviral medication is also approved in patients with ILIs who present one of the danger signs of developing severe diseases, such as tachypnea, respiratory distress, cyanosis, hemoptysis, chest pain, change of consciousness, and hypotension, regardless of test results from RIDT [7]. The cost of Tamiflu prescribed to the above mentioned patients is covered by the government and does not count toward the maximum quota allocated under the National Health Insurance. As a result, patients with danger signs may start antiviral treatment without waiting for results of further influenza confirmatory tests in order to shorten the time between disease onset and the start of antiviral treatment, and to reduce the chance of developing complications. In addition, restrictions on the type of specialists and clinics allowed to prescribe antiviral medications were also lifted so that more primary care physicians were able to provide patients with ILI with timely treatment. To avoid interference with the maximum quota allocated under the National Health Insurance, on September 16, the CECC approved that the cost of Tamiflu prescribed to patients tested positive for influenza A by RIDT will be paid for by the government through the National Health Insurance. On October 2, prescription of government-paid Tamiflu was expanded to individuals not covered under the National Health Insurance. For all citizens of the Republic of China and foreign nationals with Alien Resident Certificates, antiviral medications will be provided when medically necessary following physician consultations. These measures removed the economic barriers of the general population when seeking medical care, and provided more coverage to the underprivileged groups. Government-paid antiviral medication and RIDT kits also relieved the worry of many physicians and hospitals that such cost may affect the maximum quota allocated under the National Health Insurance.

Since antiviral medication was covered

under the National Health Insurance, the demand of medication from medical care facilities increased significantly, which resulted in inadequate supply of antiviral mediation from the manufacturers. On August 29, 2009, the CECC decided to release the Tamiflu stockpiled by the Taiwan CDC and offered them to medical care providers at a reasonable price. In addition to the existing sites where the reserved antiviral medication was provided, stockpiled antiviral medication was also distributed to more primary care providers. Due to the rapidly increasing number of patients with ILI visiting the emergency department at all major hospitals, ILI special clinics were established at all major hospitals since September in order to alleviate the pressure of the emergency rooms. All city and county health departments also started providing lists of primary care providers offering RIDT and antiviral medication with clearly marked “flu clinics” for the convenience of patients seeking medical care. All local medical associations and health centers also voluntarily made coordinated efforts to extend office hours during weekends and holidays in order to reduce the number of emergency room visits due to ILIs during these periods. These measures aimed at increasing the availability of convenient clinic sites for patients with ILI and diverting some patients with milder symptoms from hospitals to local health care providers. This should lessen the burden and preserve the capacity of medical centers and prevent hospital-acquired infection. In addition to the added purchase of 900,000 doses of Relenza, the CECC also increased the purchase of Tamiflu in order to avoid shortage and price gouging of antiviral medications.

Previous research on seasonal influenza indicated that antiviral treatment with Tamiflu is effective when it is administered within 48 hours from the onset of symptoms. However, some studies suggested that patients hospitalized due to influenza can still benefit from antiviral treatment even when initiated after 48 hours from the onset of symptoms [8]. Despite the fact that there is no sufficient scientific evidence on the effectiveness of Tamiflu treatment in patients with H1N1 2009 influenza, preliminary data from studies in the United States suggested that Tamiflu treatment initiated within 48 hours from the onset of symptoms is associated with better patient prognosis [9]. In addition, studies form Mexico pointed out that excluding severe cases of H1N1 2009 influenza who died within 72 hours from the onset of symptoms, the proportion of patients treated with Tamiflu was higher in those who survived [10]. As a result, the WHO and US CDC both recommend that all patients hospitalized due to H1N1 2009 influenza and high risk groups should receive Tamiflu treatment [11, 12]. The policy of government-paid antiviral medication in Taiwan adopted recommendation from the above-referenced studies and further included all ILI patients with positive RIDT results. Theoretically, patients with positive RIDT carry higher viral loads, and early initiation of antiviral treatment may reduce the viral loads more rapidly. Early treatment not only reduces the probability of further transmission, but also prevents invasion of vital organs by the influenza virus which may result in severe diseases. Patients with danger signs should

start antiviral treatment immediately without performing RIDT in order to reduce the chance of developing complications or even deaths.

Result

In order to investigate the effect of insurance-paid antiviral medication and rapid test on the medical care-seeking behavior and treatment of patients with ILI, we studied the first 96 cases of hospitalized H1N1 2009 influenza patients with pneumonia with onset date between July 2 and August 29. Patients were divided into two groups based on the date of disease onset. We chose August 15, the date when National Health Insurance started coverage of antiviral medication, as the cut-off date. Chi-square test for discrete variables and Wilcoxon rank sum test for continuous variables were used as the methods of analysis. All analyses were performed using SAS statistical software. As shown in table 1, there were 34 patients with disease onset date prior to August 15, and 62 patients after August 15. Nine patients (26%) with onset date prior to August 15 progressed into respiratory failure. Five patients (15%) died. Thirteen patients (21%) with onset date after August 15 progressed into respiratory failure, and eight patients (8%) died. Although the difference did not reach statistical significance, the incidence and death rate seem to decline after August 15. The proportion of patients taking Tamiflu within 48 hours of disease onset increased significantly after August 15 (52% vs. 15%, p=0.004). From the course of patients seeking medical care, the median number of days from disease onset to admission (2 vs. 5 days), disease onset to rapid test (2 vs. 5 days), and disease onset to antiviral treatment (2 vs. 6days) all decreased significantly after August 15. When we used the Sequential Organ Failure Assessment Score (SOFA score) as an indicator for disease severity of patients, the SOFA scores of patients with disease onset date after August 15 were lower than those prior to August 15. These findings may be explained by the fact that after RIDT and antiviral medication were covered under the National Health Insurance, patients with ILI were able to access faster and more convenient medical care, receive RIDT, and start timely antiviral treatment before developing severe diseases. In addition,

Table 1. Comparison of the first 96 severe influenza patients with pneumonia by date of disease onset－Taiwan, 2009

	Onset before Aug 15 (n=34)	Onset after Aug 15 (n=62)	p-value
Number of respiratory failure (%)	9 (26)	13 (21)	0.7191
Number of deaths (%)	5 (15)	8 (8)	0.5032
Number of patients taking Tamiflu within 48 hours (%)	5 (15)	32 (52)	0.0004
Median days from onset to antiviral treatment (IQR)	5 (2-7)	2 (1-4)	0.0001
Median days from onset to rapid test (IQR)	5 (3-7)	2 (1-4)	0.0006
Median days from onset to admission (IQR)	6 (4-8)	2 (1-5)	<0.0001
Median SOFA score (IQR)	2 (1-3)	0 (0-1)	0.0013

effective dissemination of influenza-related information, broad establishment of ILI special clinics and influenza clinics by many hospitals, increased availability of convenient medical care facilities, and increased awareness of influenza by the general population and medical care professionals may also contribute these results. All the strategies together resulted in the decreased number of deaths and respiratory failure in hospitalized influenza patients with pneumonia.

On September 15, the chief commander of the CECC emphasized "conveniently accessible medical care facilities, timely administration of antiviral medication, and assurance of holistic medical care" as the current main objectives of CECC. After interventions such as government-paid antiviral medications and RIDT, broad establishment of influenza clinics, and consistent communication with the general population and medical care professionals, the number of patients with ILI seeking medical consultation and reported severe cases both reduced after the 38th week of 2009 [13] (Figures 1, 2). The results indicated that with the coordinated effort by the CECC, the medical community, and the general population, we have successfully passed the first wave of influenza pandemic. In order to prevent the severe damage by the possible second wave of pandemic, important measures including H1N1 2009 influenza vaccination, establishment of surge capacities of medical care facilities, and persistent health education to the general population need to be well executed. As long as all citizens possess the correct understanding about influenza, coupled with effective prevention and control strategies, we are confident that Taiwan should be able to pass this influenza pandemic safely.

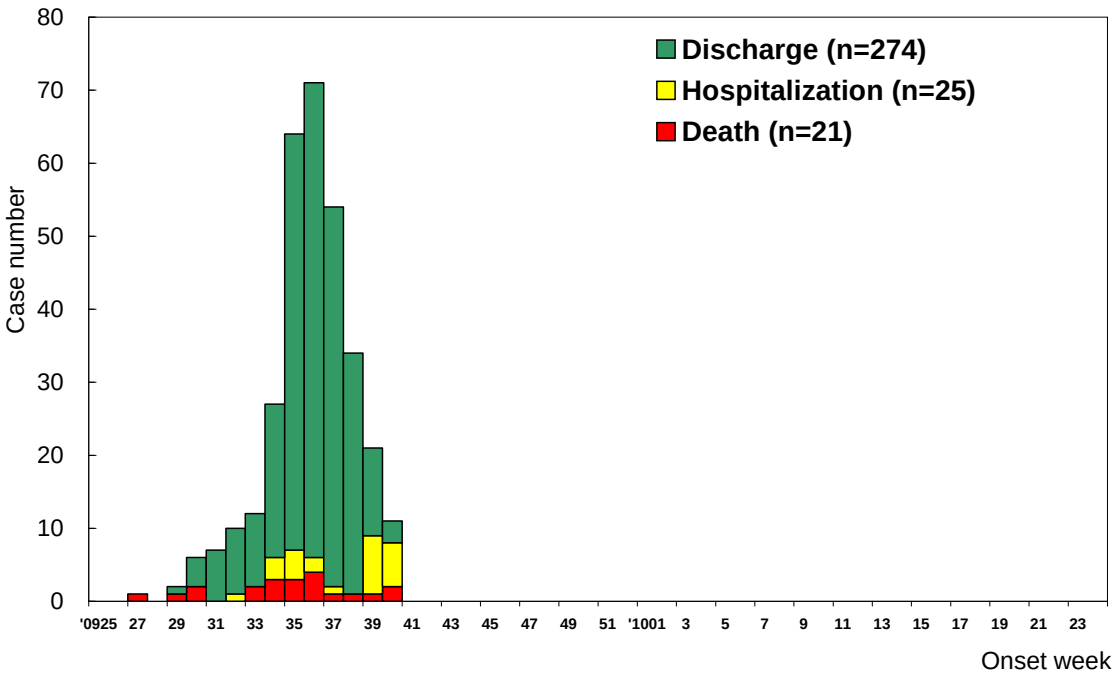

Figure 1. Epidemic curve of patients with severe complicated influenza, week 26 and beyond－Taiwan, 2009

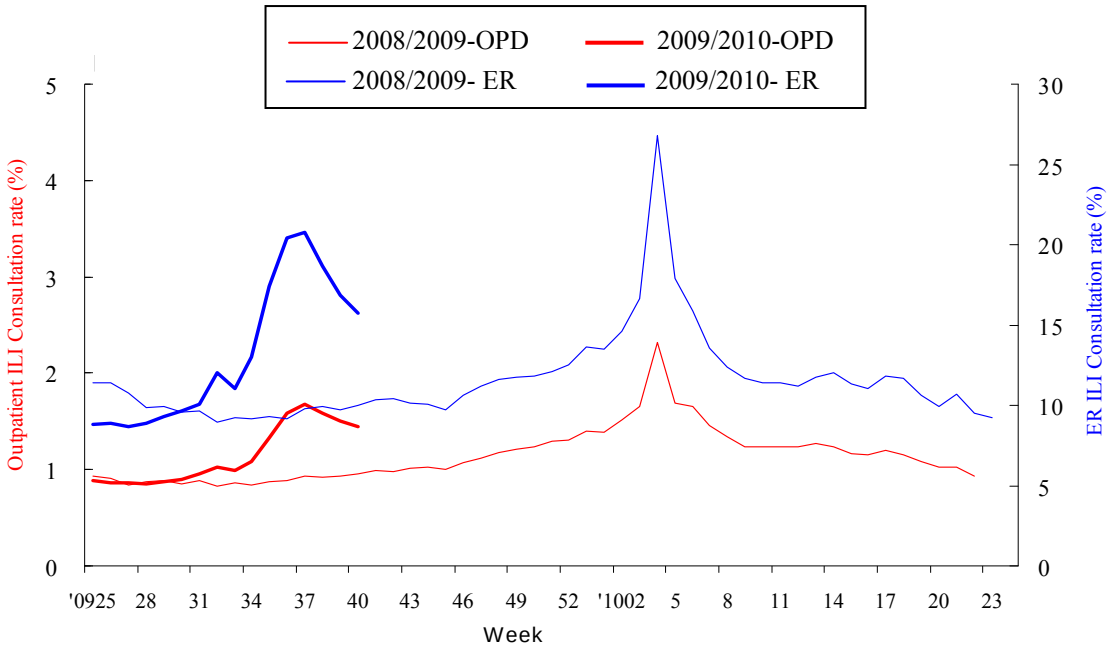

Figure 2. Trend of the number of outpatient and emergency room visits of patients with influenza-like illnesses－Taiwan, 2008-2009

Note: Data on National Health Insurance outpatient visit as of September 30, 2009
Data on RODS emergency room visit as of October 3, 2009

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