



Cost Analysis of the Use of Rapid Influenza Diagnostic Test during H1N1 2009 Influenza Pandemic

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Abstract

In order to evaluate the effect of changes in the proportion of H1N1 2009 influenza among influenza-like illness (ILI) to the direct medical cost associated with different strategies of administering Tamiflu to patients with ILI, a decision tree was constructed to compare the direct cost of two strategies of administering Tamiflu. Baseline parameter values used in the analysis were obtained from literature review and data from Centers for Disease Control and Department of Health, Taiwan. One- and two-way sensitivity analyses were performed to test the effect of changes in parameter values on the outcome of the two strategies.

Administering Tamiflu to patients with ILI according to results of rapid influenza diagnostic test is more economical than to all patients with ILI without performing rapid test based on the current proportion of H1N1 2009 influenza among ILI of 35% in Taiwan. Administering Tamiflu to all patients with ILI is more cost-effective when the fraction of H1N1 2009 influenza among ILI exceeds 54%, or when the average cost of hospitalization due to complications from H1N1 2009 influenza exceeds

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\$218,000. The benefit of administering Tamiflu to all patients with ILI is more evident when the average cost of hospitalization or the probability of hospitalization due to complications is high.

Guidelines for Tamiflu administration should be modified based on the course of H1N1 2009 influenza pandemic. As the proportion of H1N1 2009 influenza among ILI continues to rise, it may be more appropriate to administer Tamiflu to patients with ILI regardless of rapid test results when necessary. To patients with suspected influenza illness who are at increased risk for complications, empirical Tamiflu treatment should be given as early as possible to reduce the risk of developing severe disease.

Keywords: H1N1 2009 influenza, rapid influenza diagnostic test, Tamiflu, cost analysis

Introduction

Rapid influenza diagnostic test is a tool for screening patients with clinical symptoms of influenza-like illness (ILI) in order to provide timely information for clinical decision making. Rapid influenza tests facilitate antiviral drug administration, reduce the use of unnecessary antibiotics, and shorten the duration of hospitalization [1]. However, rapid influenza tests are less accurate than viral culture or RT-PCR [2]. Studies on the sensitivity of rapid influenza tests from various manufacturers showed a wide range of variability from 11% to 69% [3-8]. Because false negative results from rapid influenza test may delay diagnosis and the use of antiviral medication, the relatively low sensitivity of rapid influenza test has become a problem for both clinical practitioners and public health professionals.

According to current guidelines and payment policy of Tamiflu

administration in Taiwan, national health insurance will pay for Tamiflu prescribed to patients under the following conditions: (1) presence of symptoms of ILI and positive rapid test for influenza A; (2) presence of danger signs of severe disease with negative or no rapid test result; (3) clinical symptoms compatible with severe disease [9]. When the proportion of H1N1 2009 influenza among ILI is relatively low, the negative predictive value of rapid test is relatively high, and the number of false negative test results is relatively low. However, when H1N1 2009 influenza epidemic rises, the fraction of H1N1 2009 influenza among ILI may increase, and the negative predictive value of rapid test will decrease, which will in turn increase the number of false negative test results. If we take into account the costs of rapid test and Tamiflu, along with cost associated with hospitalization of patients with severe disease as a result of delayed diagnosis and treatment, the current strategy of Tamiflu administration may require some scrutiny. The purpose of this study is to examine the effect of changes in the proportion of H1N1 2009 influenza among influenza-like illness (ILI) to the direct medical cost associated with different strategies of administering Tamiflu to patients with ILI.

Materials and Methods

Construction of the decision tree

We constructed a decision tree model to compare the direct cost of two strategies of administering Tamiflu (Figure 1). The model was constructed and analyzed using TreeAge Pro 2006 software (Williamstown, MA, U.S.A.). In this model, when patients with ILI sought medical help, they were managed using one of the two strategies: one strategy administered Tamiflu

to patients with ILI according to results of rapid influenza diagnostic test, while the other gave Tamiflu to all patients with ILI without performing rapid test. Patients with H1N1 2009 influenza may develop severe disease which requires hospitalization, whether Tamiflu was given or not. Tamiflu reduces the probability of hospitalization. If patients do not have H1N1 2009 influenza, they will not develop severe disease due to H1N1 2009 influenza. Parameters used in this analysis include the following:

1. The sensitivity and specificity of rapid influenza diagnostic test
2. The proportion of H1N1 2009 influenza among ILI
3. The probability of hospitalization due to severe disease
4. The probability of reduction in hospitalization after taking Tamiflu
5. Cost of Tamiflu
6. Cost of rapid influenza diagnostic test
7. Average cost of hospitalization per case due to severe disease

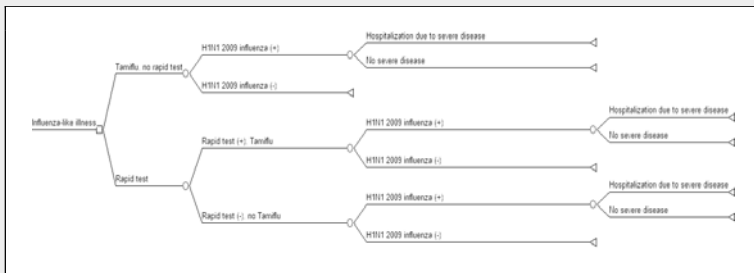


Figure 1. The decision tree to compare the direct medical cost of two strategies of administrating Tamiflu

Estimating probabilities and values used in the analysis

Baseline parameter values used in the analysis, such as the sensitivity and specificity of rapid influenza diagnostic tests from various manufacturers, the probability of hospitalization due to severe disease, and the probability

of reduction in hospitalization after taking Tamiflu were obtained from literature review [3-8,10-16]. Cost of rapid influenza diagnostic test and Tamiflu were obtained from guidelines for application and payment of rapid influenza diagnostic test and Tamiflu provided by Bureau of National Health Insurance, Taiwan [9]. We also estimated the proportion of H1N1 2009 influenza among ILI in Taiwan, and the average cost of hospitalization per case due to severe disease using data from Centers for Disease Control and Department of Health, Taiwan (Table 1).

Table 1. Parameter estimates in decision tree*

Variable	Baseline	Range	Reference
Sensitivity	0.4	0.11-0.69	3-8
Specificity	0.93	0.86-0.99	3-8
Probability of hospitalization due to severe disease	0.013	0.001-0.024	10-13
Probability of reduction in hospitalization after Tamiflu	0.59	0.18-0.87	14-16
Proportion of H1N1 2009 among ILI	0.35	0-1	CDC, Taiwan (2009)
Cost of rapid influenza diagnostic test	\$300		9
Cost of Tamiflu	\$800		9
Average cost of hospitalization	\$120,000	\$10,000-\$300,000	Estimate

*: All values are probabilities unless otherwise noted

When Tamiflu is administered based on the result of rapid test, the total direct medical cost per 1,000 patients with ILI is calculated as follows:

Cost of rapid influenza diagnostic test: \$300,000

Cost of Tamiflu: $\$800 \times 1,000 \times ((1 - \text{proportion of H1N1 2009 influenza among ILI}) \times (1 - \text{specificity}) + \text{proportion of H1N1 2009 influenza among ILI} \times \text{sensitivity})$

Average cost of hospitalization due to severe disease: $\$120,000 \times 1,000 \times \text{proportion of H1N1 2009 influenza among ILI} \times 0.013 \times ((1 - \text{sensitivity}) + \text{sensitivity} \times 0.41)$

When Tamiflu is administered to all patients with ILI, the total direct medical cost per 1,000 patients with ILI is calculated as follows:

Cost of rapid influenza diagnostic test: \$0

Cost of Tamiflu: \$800,000

Average cost of hospitalization due to severe disease: $\$120,000 \times 1,000 \times \text{proportion of H1N1 2009 influenza among ILI} \times 0.013 \times 0.41$

Sensitivity analysis

We used the baseline values listed in Table 1 to compare the direct medical cost associated with the two strategies. One-way sensitivity analysis was used to test the effect of changes in parameter values such as the sensitivity and specificity of rapid influenza diagnostic test, the proportion of H1N1 2009 influenza among ILI, the probability of hospitalization due to severe disease, the probability of reduction in hospitalization after taking Tamiflu, and the average cost of hospitalization per case due to severe disease on the outcome of the two strategies. We also performed two-way sensitivity analysis to explore how changes in the probability and the average cost of hospitalization affect the proportion of H1N1 2009 influenza among ILI at which the cost of the two strategies becomes equal.

Results

When Tamiflu is administered based on the results of rapid influenza diagnostic test, the average direct medical cost per 1,000 patients with ILI is \$868,000. When Tamiflu is given to all patients with ILI, the total direct medical cost per 1,000 patients with ILI is \$1,024,000. As a result, administering Tamiflu to patients with ILI according to results of rapid influenza diagnostic test is more economical than to all patients with ILI without performing rapid test based on the current proportion of H1N1 2009 influenza among ILI of 35% in Taiwan.



Results from one-way sensitivity analysis showed that changes in the sensitivity and specificity of rapid influenza diagnostic test, the probability of hospitalization due to severe disease, and the probability of reduction in hospitalization after taking Tamiflu does not affect the outcome of the analysis. Administering Tamiflu to all patients with ILI is more cost-effective when the fraction of H1N1 2009 influenza among ILI exceeds 54%, or when the average cost of hospitalization per case due to complications from H1N1 2009 influenza exceeds \$218,000.

Two-way sensitivity analysis indicated that when the average cost of hospitalization per case exceeds \$120,000, or when the probability of hospitalization due to severe disease exceeds 1.3%, giving Tamiflu to all patients with ILI may cost less even when the proportion of H1N1 2009 influenza among ILI is less than 54% (Figure 2, 3). The findings suggest that it may be more cost-effective to give Tamiflu to all patients with ILI who are at greater risk of developing severe disease (such as pregnant women, patients with underlying disease or obesity) compared to the general population.

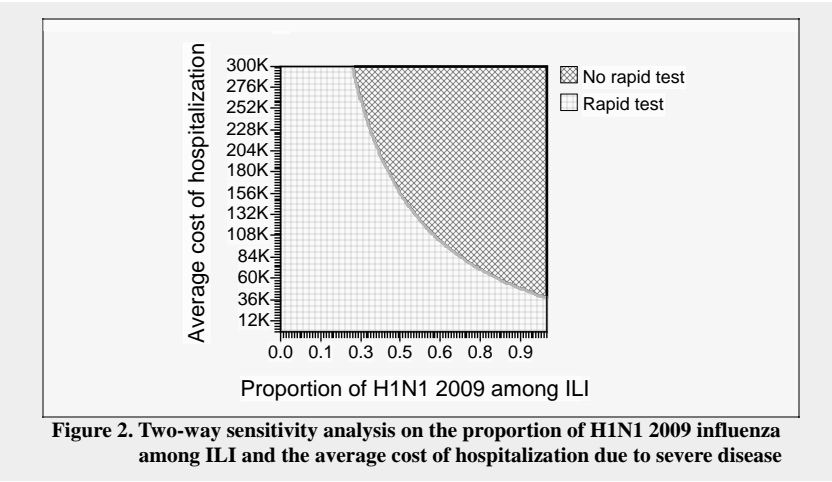


Figure 2. Two-way sensitivity analysis on the proportion of H1N1 2009 influenza among ILI and the average cost of hospitalization due to severe disease

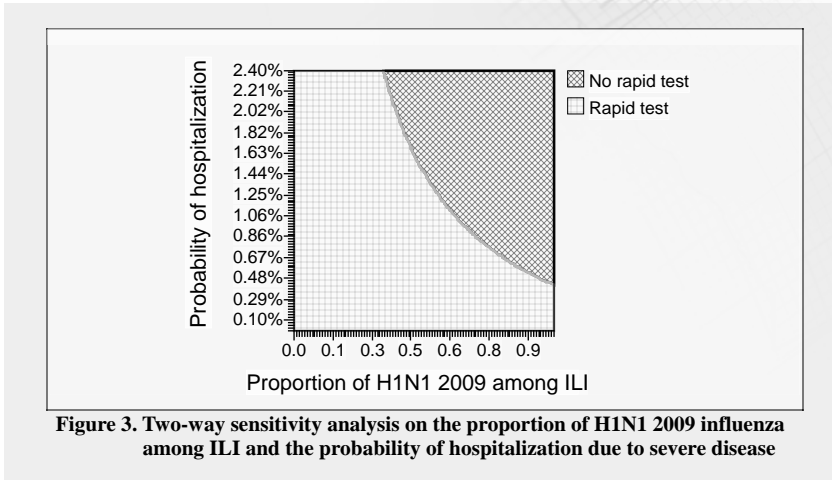


Figure 3. Two-way sensitivity analysis on the proportion of H1N1 2009 influenza among ILI and the probability of hospitalization due to severe disease

Discussion

Our cost analysis includes direct medical cost only. It does not take into account costs associated with possible Tamiflu resistance, loss in productivity, and the impact on society. When the proportion of H1N1 2009 influenza among ILI is greater than 54%, the total direct cost of administering Tamiflu to patients with ILI based on the result of rapid test is greater than to all patients with ILI without performing rapid test. As the H1N1 2009 pandemic continues to rise, giving Tamiflu to all patients with ILI without rapid test may be more appropriate on a cost basis.

The average cost of hospitalization due to severe disease plays an important role in determining which strategy is more economical. The benefit of administering Tamiflu to all patients with ILI is more evident when the cost of hospitalization is relative high compared to the cost of Tamiflu. As a result, in countries where the cost of hospitalization is high relative to the cost of medicine (such as United States), the use of Tamiflu depends more on



clinical symptoms rather than results of rapid test alone. In Taiwan, due to more limited medical resources and relatively low cost of hospitalization, the use of antiviral medical medication is more restrictive. In fact, the main consideration in antiviral treatment is to give Tamiflu to as many patients with ILI as possible in order to minimize complications due to severe disease whenever resources allow. The primary benefit of administering Tamiflu to all patients with ILI is to reduce the number of H1N1 2009 influenza patients whose diagnoses may be delayed due to false negative rapid test results. United States Centers for Disease Control and Prevention also recommended that patients with suspected influenza illness who are at increased risk for complications, empirical Tamiflu treatment should be given as early as possible to reduce the risk of developing severe disease [17].

We recommend that guidelines for Tamiflu administration should be modified based on the course of H1N1 2009 influenza pandemic. As the proportion of H1N1 2009 influenza among ILI continues to rise, it may be more appropriate to administer Tamiflu to patients with ILI regardless of rapid test results when necessary. In addition, Tamiflu should be administered to all patients with ILI who are at greater risk of developing severe disease to facilitate better utilization of available resources and reduce the probability of developing complications.

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