Abstract—In this paper, we propose the mathematical model to study the endemic of Influenza in Thailand. The aims of the research are to study and analyze the epidemiology of Influenza in Thailand by using the mathematical modeling. The data from the annual number of cases reported to the Division of Epidemiology, Ministry of Public Health during the period 1997-2013 are analyzed. We construct the system of nonlinear differential equations for two models. The first one, we divide the human population into four groups: the susceptible human, infectious human, the recovered human who are totally immune to the strain and the recovered human who are partially immune to that strain classes. For the second model, we enlarge the model by considering the incubation period. The standard dynamical modeling method are applied to determine the behaviors of solutions to each model. The conditions required of the parameters for the disease free and endemic equilibrium states to be local asymptotically stable is obtained. Numerical simulations are seen to support the theoretical predictions. The alternative way to control the outbreak of this disease in Thailand are suggested in our research.

Keywords—Influenza, Mathematical Modeling, Nonlinear Differential Equations, Numerical Simulation.

I. INTRODUCTION

INFLUENZA or the flu is a common respiratory disease caused by influenza virus. Influenza is spread from person to person when droplets of moisture from a person with influenza are spread through the air when that person coughs, sneezes, talks and hands touching eyes, mouth or nose [1]. It caused by influenza virus which are of three types A, B and C [2]. Types A and B being clinically important. Different strains dominate from year to year. The symptoms usually start with sudden onset of chills, shakes, headache, muscle aches, fever and dry cough. The respiratory symptoms then become more prominent. People of all ages are susceptible to the flu.

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Symptoms appear typically 1 to 3 days after exposure to respiratory droplets from an infected person. Usually the diagnosis is based on the appearance of specific signs and symptoms of influenza. Confirmation can be achieved through laboratory testing of throat specimens or blood samples.

Thailand is situated in Southeast Asia, which is bordered to the north by Burma and Laos, to the east by Laos and Cambodia, to the south by the Gulf of Thailand and Malaysia and to the west by the Andaman Sea and the southern extremity of Burma. Thailand is divided into four geographic regions, North, Central, South and Northeast. The country of 513,000 square kilometers. In Thailand, the influenza patients have been reported a total of 809,989 cases between 1997 and 2013. The peak of influenza endemic top in 2009 and the peak in Trang province between 1997 to 2013.

Fig. 1 Geographical distribution of the top ten of provinces by the incidence rate of influenza in 2013, Thailand [18]
Influenza is a seasonal disease in temperate regions. Most cases in Thailand occur during the rainy months between July and September. Fig. 4 shows the time distribution of the influenza outbreak in humans in Thailand [3-18]. The disease activity starts at the beginning of the rainy season (July), peak in August. Most of the influenza outbreaks is in Trang province (average mean from 1997-2013). Trang province is in the south region of Thailand.

Several researchers such as Andreasen et al. [19], in 1997, they develop a model that describes the dynamics of a finite number of strains that confer partial cross-protection among strains. The immunity structure of the host population is captured by an index-set notation where the index specifies the set of strains to which the host has been exposed. In 1999, Lin et al. [20], analyze an epidemiological model consisting of a linear chain of three co-circulating influenza A strains that provide hosts exposed to a given strain with partial immune cross-protection against other strains. In the extreme case where infection with the middle strain prevents further infections from the other two strains. In 2002, Earn et al. [21], they developed mathematical and computational models that elucidate many properties of multi strain systems. The theoretical insights are also required to simplify model structures and facilitate predictions that can be tested with accessible data. In 2004, Alexander et al. [22], they construct a deterministic mathematical model to study the transmission dynamics of influenza. The model is analyzed qualitatively to determine criteria for control of an influenza epidemic and is used to compute the threshold vaccination rate necessary for community-wide control of influenza.

In this paper, we compare the behavior of the transmission of influenza virus by formulating the mathematical models. There is no incubation period condition in the first model. The second model, we take the incubation period into the model.

II. MATHEMATICAL MODELS AND ANALYSIS

A. The First Model

To compare the endemic of Influenza in Thailand for two models, the initial model, we construct a system of nonlinear...
differential equations and divide the human population (no effect of incubation period) into 4 groups: the susceptible human, infectious human, the recovered human who are totally immune to that strain and the recovered human who are partially immune to that strain classes.

Let

\( S \) be the number of susceptible human,
\( I \) be the number of infectious human,
\( R \) be the number of recovered human who are totally immune to that strain,
\( C \) be the number of recovered human who are partially immune to that strain classes.

The dynamics of the model for the pandemic influenza with no effect of incubation period can be described by the following equations

\[
\frac{dS}{dt} = B_n N - (\mu + \beta I) S, \tag{1}
\]

\[
\frac{dI}{dt} = \beta SI - (\mu + \alpha) I, \tag{2}
\]

\[
\frac{dR}{dt} = \alpha I - (\mu + \delta) R, \tag{3}
\]

\[
\frac{dC}{dt} = \delta R - \mu C \tag{4}
\]

with the conditions

\[
N = S + I + R + C
\]

where

\( N \) is the total of human population,
\( B_n \) is the birth rate of human population,
\( \mu \) is the natural death rate of human population,
\( \beta \) is the transmission rate which the susceptible human population become to infectious human,
\( \alpha \) is the transmission rate which the infectious human population become to the recovered human who are totally immune to that strain,
\( \delta \) is the transmission rate which the recovered human who are totally immune to that strain become to the recovered human who are partially immune to that strain classes.

The total number of human population is assumed that constant. So the rates of change for the total human population is equals to zero. Then we obtain \( B_n = \mu \) and we normalize (1) to (4) by letting \( S^* = S/N \), \( I^* = I/N \), \( R^* = R/N \) and \( C^* = C/N \) then our equations become

\[
\frac{dS^*}{dt} = \mu - (\mu + \beta I^*) S^*, \tag{5}
\]

\[
\frac{dI^*}{dt} = \beta S^* I^* - (\mu + \alpha) I^*, \tag{6}
\]

\[
\frac{dR^*}{dt} = \alpha I^* - (\mu + \delta) R^*, \tag{3}
\]

\[
\frac{dC^*}{dt} = \delta R^* - \mu C^* \tag{4}
\]

with the condition \( R^* = 1 - S^* - I^* - C^* \).

**B. Disease free equilibrium and endemic equilibrium states of the first model**

The model (5) to (7) has exactly one disease free equilibrium state \( E^1 = (1,0,0) \) in the region \( \varepsilon \) when \( \varepsilon = \{ (S^*, I^*, C^*) \mid S^*, I^*, C^* \geq 0, S^* + I^* + R^* + C^* = 1 \} \).

We use the next generation matrix approach as described in [23-24] to define the basic reproductive number \( R_{b1} \), \( R_{b1} \) as the number of secondary infections that one infectious individual would create over the duration of the infectious period in the presence of vaccination, provided that everyone else is susceptible. It occur when \( R_{b1} \leq 1 \). From our model, we have the endemic equilibrium state \( E^2 \) when

\[
E^2 = (\hat{S}, \hat{I}, \hat{C}) \text{ which}
\]

\[
\hat{S} = \frac{1}{1 + \hat{h} I}, \tag{8}
\]

\[
\hat{I} = \frac{(h - A)}{Ah}, \tag{9}
\]

\[
\hat{C} = \frac{((\delta I)(h(1 - I) - 1))/((\delta + \mu)(1 + h I))}{(10)}
\]

where \( h = \beta_i N/\mu, A = (\mu + \alpha)/\mu \) and it occur when \( R_{b1} > 1 \).

**C. Stability of the disease free and endemic equilibrium states of the first model**

For the local stability analysis of disease free equilibrium state, the linearized systems of (5) to (7) around \( E^1 \). The Jacobian of linearized is

\[
J_{E^1} = \begin{bmatrix}
-\mu & -\mu h & 0 \\
0 & \mu h - \mu A & 0 \\
-\delta & -\delta & -\delta - \mu
\end{bmatrix}_{(1,0,0)} \tag{11}
\]

The characteristic equation of \( J_{E^1} \) is as follows:

\[
(\mu + \lambda)(\mu A + \lambda - \mu h)(\delta + \mu + \lambda) = 0. \tag{12}
\]

Then we have the negative three roots, \( \lambda_1 = -\mu \), \( \lambda_2 = -\mu - \delta \) and \( \lambda_3 = \mu(h - A) \) when \( R_{b1} = \sqrt{h/A} < 1 \).

Hence by Hurwitz’s criteria we have established the following result.

For the endemic equilibrium state, we analyze the local stability by linearizing systems (5) to (7) around \( E^2 \), then we have the Jacobian

\[
J_{E^2} = \begin{bmatrix}
-(\mu + \mu h I) & -\mu h \hat{S} & 0 \\
\mu h \hat{I} & \mu h \hat{S} - \mu A & 0 \\
-\delta & -\delta & -\delta - \mu
\end{bmatrix}_{(\hat{S}, \hat{I}, \hat{C})} \tag{13}
\]

The characteristic equation for the endemic state is given by
\[(\lambda + \delta + \mu)(\lambda^2 + a_1\lambda + a_2) = 0 \]  \hspace{1cm} (14)
when
\[a_1 = (1 + A + h\hat{I} - h\hat{S})\mu \text{ and } a_2 = (A + Ah\hat{I} - h\hat{S})\mu^2.\]
The eigenvalues of (14) are \(\lambda_1 = -\delta - \mu\), \(\lambda_2 = -a_1 - \sqrt{a_1^2 - 4a_2} \) and \(\lambda_3 = -a_1 + \sqrt{a_1^2 - 4a_2} / 2\).
\(\lambda_3 < 0\) when \(h > A\). So that the stability of the endemic equilibrium point by using Routh-Hurwitz criteria, we found that the endemic equilibrium state is locally stable when \(R_{\text{bi}} = \sqrt{h/A} > 1\).

**D. The Second Model**

For the second mathematical model, we consider the time of incubation period when the susceptible human become to exposed human population and we consider the re-infection in recovered human population. The dynamic of human population can be described by the following equations

\[
\frac{dS}{dt} = B_nN + \gamma C - (\mu + \beta_2 I)S, \hspace{1cm} (15)
\]
\[
\frac{dE}{dt} = \beta_2 SI - (\mu + \phi)E, \hspace{1cm} (16)
\]
\[
\frac{dI}{dt} = \phi E - (\mu + \alpha)I, \hspace{1cm} (16)
\]
\[
\frac{dR}{dt} = \alpha I - (\mu + \delta)R, \hspace{1cm} (17)
\]
\[
\frac{dC}{dt} = \delta R - (\mu + \gamma)C. \hspace{1cm} (18)
\]

where
- \(S\) be the number of susceptible human,
- \(E\) be the number of infectious human which in the incubation period (exposed human population),
- \(I\) be the number of infectious human,
- \(R\) be the number of recovered human who are totally immune to that strain,
- \(C\) be the number of recovered human who are partially immune to that strain classes,
- \(N\) is the total of human population,
- \(B_n\) is the birth rate of human population,
- \(\mu\) is the natural death rate of human population,
- \(\beta_2\) is the transmission rate which the susceptible human population become to exposed human,
- \(\phi\) is the transmission rate which the exposed human population become to infectious human,
- \(\alpha\) is the transmission rate which the infectious human population become to the recovered human who are totally immune to that strain,
- \(\delta\) is the transmission rate which the recovered human who are totally immune to that strain become to the recovered human who are partially immune to that strain classes.
- \(\gamma\) is the transmission rate which the recovered human population become to re-infection again (in susceptible human population).

Introducing the proportion \(S^* = S/N\), \(E^* = E/N\), \(I^* = I/N\), \(R^* = R/N\) and \(C^* = C/N\) and with the conditions \(R^* = 1 - S^* - E^* - I^* - C^*\). The previous (15)-18 become

\[
\frac{dS^*}{dt} = \mu + \gamma C^* - (\mu + \beta_2 I^*)N, \hspace{1cm} (19)
\]
\[
\frac{dE^*}{dt} = \beta_2 NS^*I^* - (\mu + \phi)E^*, \hspace{1cm} (20)
\]
\[
\frac{dI^*}{dt} = \phi E^* - (\mu + \alpha)I^*, \hspace{1cm} (21)
\]
\[
\frac{dC^*}{dt} = \delta (1 - S^* - E^* - I^* - C^*) - (\mu + \gamma)C^*. \hspace{1cm} (22)
\]

**E. Disease free equilibrium and endemic equilibrium states of the second model**

The model (19) to (22) has two equilibrium states. This gives the disease free equilibrium state \(E^1 = (1, 0, 0, 0)\) and the endemic disease equilibrium state \(E^2 = (\hat{S}, \hat{E}, \hat{I}, \hat{C})\) where

\[
\hat{S} = \frac{1 + j\hat{C}}{1 + h\hat{I}}, \hspace{1cm} (23)
\]
\[
\hat{E} = \frac{h\hat{I}(1 + j\hat{C})}{(1 + k)(1 + h\hat{I})}, \hspace{1cm} (24)
\]
\[
\hat{I} = \frac{\phi(1 + j\hat{C})}{(\mu + \alpha)(1 + k)} - \frac{1}{h}, \hspace{1cm} (25)
\]
\[
\hat{C} = \frac{\delta}{(\delta + \mu + \gamma)}(1 - \hat{S} - \hat{E} - \hat{I}), \hspace{1cm} (26)
\]

which \(h = \frac{\beta_2 N}{\mu}, j = \frac{\gamma}{\mu}, k = \frac{\phi}{\mu}\).

**F. Stability of the disease free and endemic equilibrium states of the second model**

The local stability of disease free equilibrium solutions can be examined by linearizing (19) to (22) around \(E^1\). This gives the Jacobian matrix as follow

\[
J_{E^1} = \begin{bmatrix}
-\mu & 0 & -\mu h & \mu j \\
0 & -(\mu + k\mu) & \mu h & 0 \\
0 & k\mu & -(\mu + \alpha) & 0 \\
-\delta & -\delta & -\delta & -(\mu - \mu j)
\end{bmatrix}_{(1,0,0,0)}
\]

The characteristic equation for the disease free is given by
\[
(\lambda + \mu + \delta)(\lambda + \mu + j\mu)(\lambda^2 + b_1\lambda + b_2) = 0 
\]  
(28) 

when \( b_1 = \alpha + (2 + k)\mu \) and  
\( b_2 = \alpha\mu(1 + k) + \mu^2(1 + k - h\mu) \).  

The eigenvalues of \( E_1 \) are \( \lambda_1 = -\mu - \delta \), \( \lambda_2 = -\mu - j\mu \),  
\( \lambda_3 = \frac{-b_1 - \sqrt{b_1^2 - 4b_2}}{2} \) and \( \lambda_4 = \frac{-b_1 + \sqrt{b_1^2 - 4b_2}}{2} \).  

\( \lambda_4 < 0 \) when \( R_{b_2} = \frac{\sqrt{(\mu h k)}/((\alpha + \mu)(1 + k))}{1} < 1 \). So that the stability of the disease free equilibrium state is locally stable by using Routh-Hurwitz criteria.  

For the endemic equilibrium state of second model, we analyze the local stability by linearizing systems (19) to (22) around \( E^2 \), then we have the Jacobian  
\[
J_{E^2} = \begin{bmatrix}
-(\mu + \mu h) & 0 & -\mu h S & \mu j \\
\mu h I & -(\mu + k\mu) & \mu h S & 0 \\
0 & k\mu & -(\mu + \alpha) & 0 \\
-\delta & -\delta & -\delta & -\delta - \mu - \mu j \\
\end{bmatrix}_{(\hat{S}, \hat{I}, \hat{C})}
\]  
(29) 

The characteristic equation for the endemic state is given by  
\[
\lambda^4 + a_1\lambda^3 + a_2\lambda^2 + a_3\lambda + a_4 = 0
\]  
(30) 

when  
\[
a_1 = \mu^2((1 + j + k + jk + h\hat{I}(1 + j + k))(\alpha\delta + (1 + h\hat{I})(1 + j)(1 + k)\alpha\mu + (1 + j)(1 + k + h(\hat{I} + k\hat{I} - k\hat{S}))\mu(\delta + \mu)),
\]
a_2 = \mu((2 + h\hat{I} + j + k))\alpha\delta + (3 + 2j + 92 + jk) + h\hat{I}(2 + j + k))\alpha\mu + \mu((3 + 2j + (2 + j)k + h\hat{I}(2 + j + k) - h\hat{k}(3 + 2j + (2 + j)k) - h(2 + j)k\hat{S})\mu),
\]
a_3 = \alpha\delta + (3 + h\hat{I} + j + k)(\alpha + \delta)\mu + (jk + 3(2 + j + k) + h\hat{I}(3 + j + k) - h\hat{k}(3 + j + k) - h(2 + j)k\hat{S})\mu^2,
\]
a_4 = \alpha + \delta + (4 + h\hat{I} + j + k)\mu.

The stability of the endemic equilibrium state can be determined without solving the actual values of eigenvalues by using the Routh-Hurwitz criteria. So the four conditions of Routh-Hurwitz criteria for local asymptotical stability in 4th order characteristic polynomial equation are  

i) \( a_1 > 0 \),  
(31)  
ii) \( a_2 > 0 \),  
(32)  
iii) \( a_3 > 0 \),  
(33)  
iv) \( a_1a_2a_3 > a_3^2 + a_2^3a_4 \).  
(34)  

After we check the stability of the endemic equilibrium state, we found that the endemic equilibrium state is locally stable when \( R_{b_2} = \sqrt{(\mu h k)/((\alpha + \mu)(1 + k))} > 1 \).
Fig. 6 Numerical solution of (19) to (22) yield the time series solutions of the proportion susceptible, exposed, infectious and recovered human populations. Values of parameters are 
\[ \mu = \frac{1}{70}, \quad \beta_2 = 0.00005, \quad \gamma = 0.5, \quad \phi = 0.5 \]
\[ \alpha = 117.32 \quad \text{and} \quad \delta = 0.75. \quad (\hat{S}, \hat{E}, \hat{I}, \hat{C}) = (0.0385304, 0.041905, 0.000178, 0.545425) \]

IV. DISCUSSION AND CONCLUSION

In our paper, we analyze the endemic influenza in Thailand by using the real data between 1997 and 2013. The numerical simulations for two mathematical models have different behaviors. Fig. 5 shows time series solution when there is no the effect of incubation period and re-infection in human population. Fig. 6 shows time series solutions when there is the effect of incubation period and re-infection. The values of parameters are satisfied Routh-Hurwitz criterions for the endemic equilibrium states.

Moreover, we consider the basic reproductive number in each model. For the first model which no effect of incubation period

\[ R_{bt} = \sqrt{\frac{\beta_1 N}{\mu + \alpha}} \]  

which shows that the number of secondary case from infectious human with influenza no effect of incubation period depend on the transmission rate which the susceptible human population become to infectious human, the total of human population and the transmission rate which the infectious human population become to the recovered human who are totally immune to that strain. Because of the natural death rate of human population is constant (almost unchanged) . For the second model, we consider the time of incubation period when the susceptible human become to exposed human population and we consider the re-infection in recovered human population. Then we have the basic reproductive number

\[ R_{b2} = \sqrt{(\mu h k) / ((\alpha + \mu)(1 + k))} \]  

\[ = \sqrt{\frac{\beta_2 \phi N}{(\mu + \alpha)(\mu + \phi)}} \]  

which its value depend on the transmission rate which the susceptible human population become to exposed human, the transmission rate which the exposed human population become to infectious human, the total human population and the transmission rate which the infectious human population become to the recovered human who are totally immune to that strain. In the second model has the proportions of the susceptible human and infectious human are higher than the first model which no effect the incubation period.

The most important thing in mathematical models in this study is to understand how influenza spreads in the real world and how various complexities affect the dynamics for searching the method to prevention and control the endemic of influenza in Thailand.

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