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FluSiM Simulation for Malaysia: Towards Improved Pandemic Surveillance

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Abstract— **The A H1N1 2009 influenza that started in Mexico in early April 2009 ultimately spread over the entire globe within a matter of a few months. Malaysia reported its first confirmed A H1N1 2009 infection on 15 May 2009. The infection persisted for 23 weeks, peaking at week 12, with a total of about thirteen thousand infections, with residual infections continuing until today. Many countries are concerned over the potential of a more severe second wave of H1N1 and have put in place contingency plan to mitigate this H1N1 threats should they occur. This paper presents the model FluSiM developed to simulate A H1N1 2009 in Malaysia. Simulation results for H1N1 2009 in Malaysia indicate that the basic reproduction number varied between 1.5 and 2.5. The on-going enhancement of FluSiM will improve on its robustness in order to permit integrated surveillance and simulation of future pandemic influenza.**

Index Terms—**FluSiM, H1N1 model, Malaysia.**

I. Introduction

The A H1N1 2009 influenza pandemic occurred some forty years after the most recent Hong Kong Flu pandemic in 1968-1969. This forty year gap is a source of concern to the medical profession. Some are of the view that the next pandemic is imminent. The most severe influenza pandemic known so far is the 1918-1919 Spanish Flu (A-H1N1), which was reported to have caused about 40 to 50 million deaths worldwide [1]. The other two twentieth century pandemics, the 1957-1958 Asian Flu (H2N2) and 1968-69 Hong Kong Flu (H3N2) caused one million deaths. The recorded daily and cumulative numbers of hospital notifications in Geneva, Switzerland for the 1918 pandemic indicated two waves of consecutive infections, each lasting about 70 days or 10 weeks from beginning to end. The more severe form occurred as a second wave during the winter months, soon after the apparent end of the first wave around 10 September 1918. The occurrence of a second more severe pandemic wave in Geneva in 1918 provided the basis to theorize on the possibility of a second wave during the A H1N1 2009 pandemic. The frequency of pandemic has been reported to be about three in one century. The last pandemic occurred in 1968, about 43 years ago. Based upon this statistics it is not surprising that WHO is concerned that the A H1N1 2009 might evolve into the next pandemic.

The A H1N1 2009 influenza that started in Mexico in April 2009 [2] ultimately spread to Malaysia. For Malaysia, Fig. 1 shows the number of H1N1 weekly infections reported in Malaysia from week 22 of 2009 to week 11 of 2010, available from the Malaysian Ministry of Health (MOH), with the first case confirmed on 15 May 2009. The bell-shape infection curve strongly suggests that the A H1N1 infections can be modeled by the well-known SIR model. Details regarding the SIR model will be presented later.

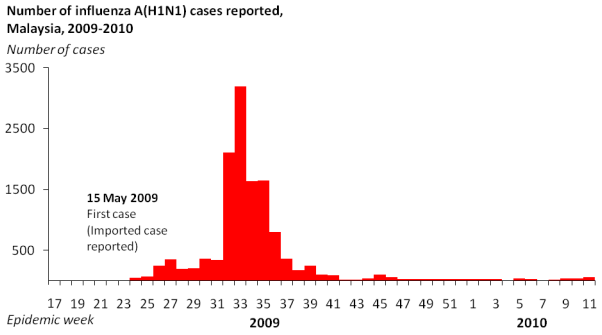

Figure 1. Number of influenxa A(H1N1) infections reported by MOH.

Referring to Fig. 1, the infections began on week 22, peaked on week 34 and ended on week 45 of 2009, with residual cases reported since then till the time of completion of this paper (February 2011). Hence, the infection peaked after 12 weeks or 84 days after the first reported case and lasted 23 weeks. The overall shape of Fig. 1 fits well with influenza infection curves modeled by the SIR models [3], in which S refers to the Susceptible, I the Infected and R the Recovered. In this paper, we model the A H1N1 2009 epidemic in Malaysia by the SIR model, which was also used by the Centers for Disease Control and Prevention (CDC) in USA [4]. A more complex model (SEIR) was used to model influenza in Vietnam, in which the country was divided into 64 provinces and the population was divided into 7 age-classes [5]. The model predicted that H1N1 would spread through half of the 64 provinces in 57 days and peak after 81 days. However, the results for basic reproduction number R_0 obtained were not accurate despite the complexity of the model, or rather because of the complexity, since much of the data required to calibrate the complex model was not available. In lieu of this inaccuracy, the value of $R_0 \in (1.2, 3.1)$ was adopted in [5] by incorporating results obtained from Mexico, USA and Japan. Indeed few complex models have been proven to be superior to the simple SIR. Further,

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SIR model requires only two parameters to drive the infected population, as compared to more parameters needed in other models. Ultimately it is the availability of quality, timely and reliable data that determines the accuracy and robustness of a model, not the complexity of the model. The three critical parameters that determine the SIR model output are (i) the infective duration or infective period T days, (ii) the disease transmission efficiency β and (iii) the total population that is susceptible P. The product βP is called the contact rate. The product of these three terms $R_0 = \beta PT$ is called the basic reproduction number, which determines whether an infective disease will take hold in a population. An infective disease can sustain in a population only if R_0 is greater than 1. The infective duration or period T for A H1N1 has been reported to vary between 3 to 7 days, with significant variance. As the duration of infection is a crucial parameter for the SIR model, we provide a brief literature review of this infective period in the following section.

II. H1N1 Infective Period

The CDC in USA has stated in their H1N1 Flu Clinical and Public Health Guidance that in general, a person infected with influenza A H1N1 virus might be infectious to another person from the day before the onset of illness to 5-7 days after the onset. Children may remain infectious for a longer duration, up to 10 days. Infective periods have been reported to have a mean value of 4.1 days [6] and to vary between 4 and 8 days [7]. Seasonal influenza A virus shedding after day 7 is commonly reported in some populations such as elderly people, immuno-compromised patients and young children [8, 9, 10]. For seasonal influenza A virus, 54 % remain positive by Polymerase Chain Reaction (PCR) method beyond 7 days after symptoms onset and 29 % were positive by cell culture [11]. Among pandemic H1N1 2009-infected patients, the proportion of patient shedding replicating virus on day 8 vary from 8% to 13 % [12]. Direct estimation of proportion of patients who were culture positive on day 8 has not been conclusively done, however. False negative PCR or cell culture might have underestimated the proportion of patients shedding virus on day 8. Freeze-thaw cycle of culture specimen might have reduced the rate of positive results [13]. In Singapore, among 70 H1N1 2009 infected patients treated with oseltamivir (Tamiflu) and swabbed daily until virus clearance, 37 % were PCR-positive on day 7 of their illness and 9 % on day 10 [14]. This positivity rate by H1N1 PCR on day 7 is similar to the rate of 42 % on day 8 reported in [12]. In China, among 421 patients with serial swabs test by real time PCR, the median time from onset of disease to negative test result by real time PCR was 6 days (range 1-17 days), indicating that 50 % of patients were still shedding virus after 6 days [15]. Hence, for the purpose of SIR simulations, we will adopt 5 days as the median infective period for A H1N1 2009 virus in our SIR model for Malaysia, subject to sensitivity analysis by varying the value of T between 3 to 7 days. We will soon demonstrate that this range of infection duration appears to fit the reported A H1N1 2009 infections in Malaysia as indicated in Fig. 1.

III. FluSiM@USM

Concerned about the potential of A H1N1 evolving into the next pandemic, the authors developed a Flu Simulation Model known as FluSiM@USM to track the evolution of this H1N1 2009 epidemic in Malaysia. This FluSiM model will be further enhanced progressively to permit simulations of other influenza such as H5N1 and SARS. Central to any model of an infectious disease epidemic for a given population is the assumption that new infective persons are generated by the mixing of uninfected susceptible persons with existing infective persons. Epidemic models typically assume that the rate of increase of new infective is proportional to the product of the number of susceptible (S) and the number of infective (I). This is a well known mass action assumption, which has been successfully applied to a wide range of human and wildlife diseases. This assumption implies that each susceptible and each infective are at all times equally accessible and exposed to each other. This fundamental underlying assumption of homogenous mixing is normally not fully satisfied in a population exposed to the influenza, leading to errors between model output and observations. This deviation is particularly true for population that spread over a large geographical area. Further, it is difficult to isolate a particular population or subpopulation for which the SIR model is applied, as the boundary is rather porous. Typically, a large infected population might consist of several separated subpopulations, to each of which the SIR model may be applied with individual characteristics of each subpopulation being used as input. However, the data required for such a detailed spatially explicit approach of SIR application is generally not available. This detailed epidemiological data was not available for the A H1N1 2009 influenza in Malaysia and indeed was not available for most countries in this current A H1N1 2009 influenza pandemic. This underlying deficiency in spatially explicit data should be duly recognized so that better data collection methodology may be implemented in future influenza surveillance.

A susceptible individual (S) may become infected by contact with an infected individual (I). An infective person either dies or recovers after several days, after which he is no longer infective and is removed from the Infective Compartment I to the Recovered Compartment R, and is no longer considered as Susceptible. This constitutes the basic concept in the SIR model (Fig. 2), which will be briefly described below. Several extensions and enhancements of this basic SIR model to cover other scenarios such as vaccination, treatment and social interventions will be developed later. An infected person is considered infective. Susceptible individuals who become infected proceed from class S to class I, at a rate that depends on the infectiousness of the virus and the prevalence of infection.

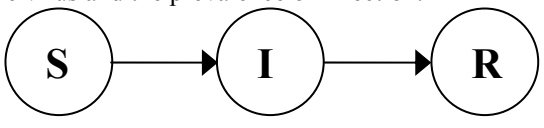

Figure 2. Compartmental SIR model of disease transmission.

IV. Mathematics of the Basic SIR Model

Early detection of epidemic of infectious disease requires both real time data and real time simulation of disease evolution. The data compilation and model simulation will provide the scientific basic for early detection of infectious diseases with the potential of evolving into a pandemic. However, some data is observable, while others are not observable. Observable variables are infected persons but hidden unobservable variables include the susceptible, for example. Simulation models are helpful in the understanding of the disease evolution, and in making possible the discussion of data requirement and data interpretation to permit optimal management of disease. In particular the importance of certain critical parameters such as infection duration T and contact rate βP can be better appreciated. This improved understanding of disease spread, assisted by model simulations, may lead to better surveillance system in the future. We adopt the approach of the SIR model to develop the flu simulation model FluSiM. The authors have conducted several national workshops on disease modeling in Malaysia. Based upon the response and request of the workshop participants, we have redeveloped FluSiM on C# programming language in order to render it more user-friendly. Fig. 3 shows the FluSiM log-in interface while Fig. 4 shows the input window, indicating the input parameters required by the model.

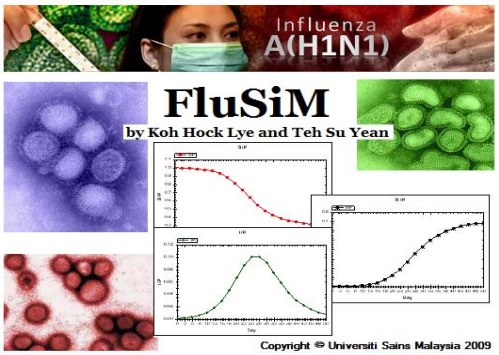

Figure 3. Flu simulation model FluSiM.interface

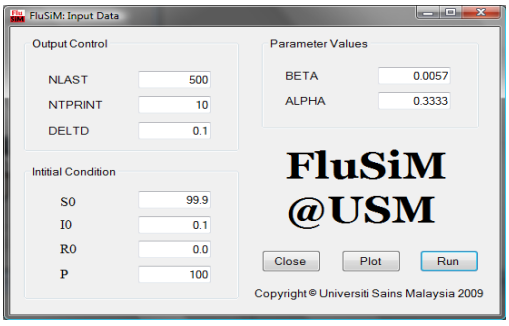

Figure 4. FluSiM window indicating input values.

Let S = number of susceptible, I = number of infective, R = number of Recovered (Removed), and P = S + I + R, the total model susceptible population. Define the following variables.

$$s = \frac{S}{P},\ i = \frac{I}{P},\ r = \frac{R}{P},\ P = \text{Total population.} \quad (1)$$

Then the basic SIR model consists of the following ordinary differential equations.

$$\frac{ds}{dt} = -\beta Psi;\ \frac{di}{dt} = \beta Psi - \alpha i;\ \frac{dr}{dt} = \alpha i. \quad (2)$$

We note that the mean duration of infection T days is related to α by $T = 1/\alpha$. Hence T is an important parameter that governs the evolution of disease. Hopefully in the future, this T value can be reliably compiled during the disease evolution. However, the dynamics of disease transmission (represented by βP) is poorly understood. Large uncertainties are often embedded in this unobservable parameter. For example, βP was adopted to vary seasonally in the form of $\beta P = \gamma = \gamma_0 + \gamma_1 \cos(2\pi t)$, where $\gamma_0 \in (0.92\alpha, 2.52\alpha)$ and $\gamma_1 \in (0.05\alpha, 0.80\alpha)$ in [4]. The value of α was chosen to be 1/3, corresponding to infective period $T = 3$ days. Once $T = 3$ days was adopted, the values of γ_0 and γ_1 were then obtained by best fit between simulation results and real infection data to arrive at the value of $\gamma_0 = 1.56$ and $\gamma_1 = 0.54$. This implies that γ varies between 1.02 and 2.10 and that R_0 varies between 3.06 and 6.30. The above model simulation parameters used provides an initial basis for selecting model input values for calibrating our SIR Model for Malaysia. Seasonality is not important for tropical countries, hence for Malaysia, the seasonality amplitude is set to $\gamma_1 = 0.0$. To facilitate discussion regarding the input of parameter values used in FluSiM, the following illustration is provided.

V. An Illustrative Example

For illustration purpose we choose the parameter values as indicated in Fig. 4. Following [4] we choose the infectious period $T = 3$ days. Then ALPHA = $\alpha = 1/T = 0.3333$ per day. The value βP (known as the contact rate), is related to the basic reproduction number R_0 by the relationship $R_0 = \beta PT = \beta P/\alpha$. In this case, $R_0 = 1.72$, since $\beta P = 0.57$, or BETA = β = 0.0057 and P = 100. Hence, BETA = 0.0057 per day; ALPHA = 0.3333 per day and P = 100 in Fig. 4. To run a typical FluSiM simulation as shown in Fig. 4, we may choose the following run-time parameter values:

NLAST = 500; NTPRINT = 25; DELTD = 0.1 day.

The above set of input run-time parameter values implies that we run the disease simulation for (500 x 0.1) days = 50 days. We output the results for every 25 iterations or every (25 x 0.1) = 2.5 days for a duration of 50 days. Further we assume that the total population is P = 100, scaled for convenience, with 0.1 person initially infected (or 0.1 % infected initially to initiate the simulation). Hence we have: $S_0 = 99.9$; $I_0 = 0.1$; $R_0 = 0.0$; $P = 100$.

VI. Sensitivity Analysis

Following the earlier discussion regarding infectious periods reported, the infective period to be used in our SIR Model is chosen to vary between 3 and 7 days, with mean value of 5 days. The contact rate βP is related to the basic reproduction number R_0 by the relation $R_0 = \beta PT = \beta P/\alpha$.

Before we calibrate the SIR Model with infection curve given in Fig. 1, we first perform sensitivity analysis to gain critical insights regarding the evolution of infection based upon the SIR concept.

Fig. 5 shows the ratio I/P, indicating the proportion of infective to total susceptible population, as functions of T and βP. It is obvious that the infective proportion I/P increases with increasing values of contact rate βP. Further I/P also increases with increasing values of infective duration T. For example, with $\beta P = 0.9$ and $T = 7$ days ($R_0 = \beta PT = 6.3$), the infective proportion is 55 %, implying that 55 % of susceptible population will be infected. If the infective duration T is increased to 10 days, keeping $\beta P = 0.9$ ($R_0 = 9.0$), then the infective proportion will increase to 65 % of the susceptible population. On the other hand, reducing the contact rate to $\beta P = 0.2$ and $T = 7$ days ($R_0 = 1.4$) will reduce the infective proportion to only 4 % of susceptible population. When T is decreased to 5 days, keeping $\beta P = 0.2$ ($R_0 = 1.0$), then the infective proportion is 0.0 and the disease will not develop in the susceptible population.

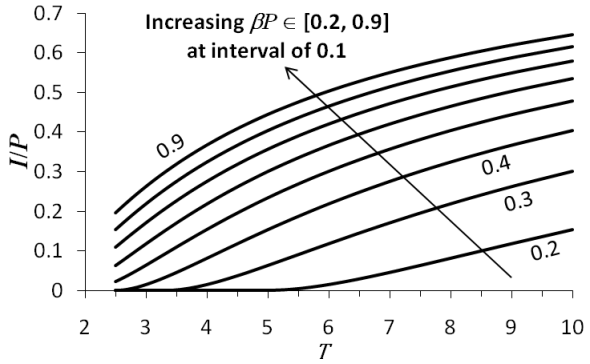

Figure 5. Dependency of FluSiM simulation results on T and βP.

Fig. 6 shows the time to disease peak (in days) as functions of T and βP. The time to peak decreases with increasing values of βP; and also decreases with increasing values of T. For example, with $\beta P = 0.3$ and $T = 5$ days ($R_0 = 1.5$), the time to peak is about 60 days. Increasing βP and T to $\beta P = 0.4$ and $T = 6$ days ($R_0 = 2.4$), the time to peak is reduced to only 30 days. In this case it takes only 30 days for the disease to reach its peak. The shorter time to disease peak will reduce the time available to implement disease control measures effectively.

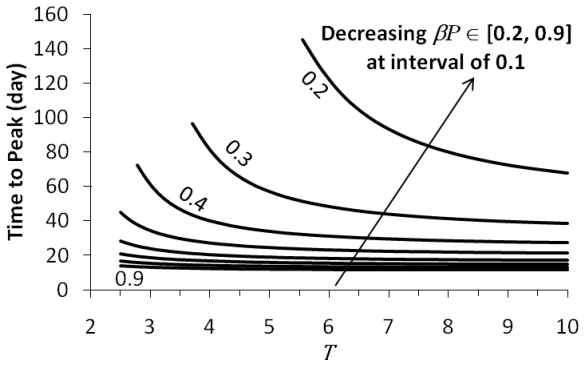

Figure 6. Dependency of FluSiM simulation results on T and βP.

Having gained some insight regarding FluSiM simulation response to input parameter values βP and T, we now proceed to present nine simulated H1N1 scenarios by selecting three values of βP (contact rate) and three values of infective duration T days. We recall that T and α are related by $T\alpha = 1$. Hence, we choose the infection duration $T = 3$, 5 and 7 days, corresponding to $\alpha = 0.3333$, 0.2 and 0.1428 respectively. For each choice of T, we select $\beta P = 0.57$, 0.77 and 0.97, representing increasing contact rates. The value of P is normalized to 100, for convenience of theoretical analysis. The initial proportion of infected is 0.1 %. With $R_0 = \beta PT = \beta P/\alpha$, this set of choices implies that $R_0 \in$ (1.71, 6.79), which is comparable to the range used by CDC [4]. We plot the time series of the Infective Proportion I/P in Fig. 7 and Fig. 8 and provide tabulation of Infective Proportion, Time to Peak and R_0 in Tables I and II to gain insights.

With $\beta P = 0.57$ and $T = 3$ days ($R_0 = 1.71$), the infection time series peaks at day 26 and the percentage of infection is 10 %. The time to peak is longer if the initial proportion of infected is reduced to 0.01 % from 0.1 %. Increasing values of T (corresponding to decreasing values of α) decreases the time to peak but increases the percentage of infective as shown in Table I and Fig. 7. Increasing values of βP (corresponding to increasing contact rate) decreases the time to peak but increases the percentage of infective as shown in Table II and Fig. 8. This implies that during the heights of disease transmission, efforts must be taken to reduce the contact rate βP (by social distancing for example) in order to reduce the percentage of infective. Reducing contact rate will increase the time to peak, which will allow additional time to prepare for emergency response.

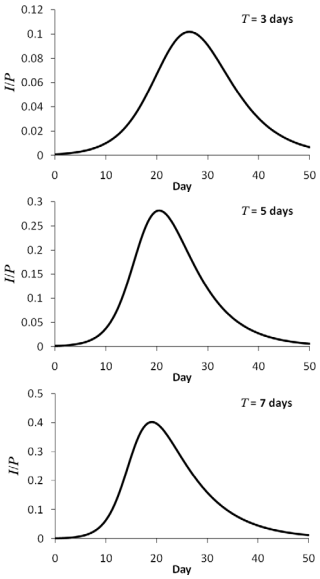

Figure 7. Infective ratio for $\beta P = 0.57$, $T = 3, 5, 7$ days.

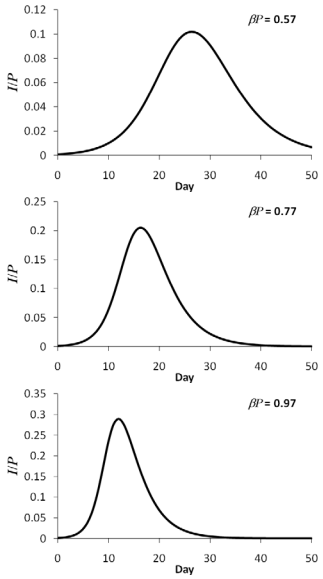

Figure 8. Infective ratio for $T = 3$ days, $\beta P = 0.57, 0.77, 0.97$.

TABLE I. INFECTIVE AND PEAK TIME: $\beta P = 0.57$, $T = 3, 5, 7$ DAYS

$\beta = 0.0057$	$\alpha = 0.3333$	$\alpha = 0.2$	$\alpha = 0.1428$
Time to Peak, Days	26	20	19
% Infective	10	28	40
R_0	1.71	2.85	3.99

TABLE II. INFECTIVE AND PEAK TIME: $T = 3$ DAYS, $\beta P = 0.57, 0.77, 0.97$

$\alpha = 0.3333$	$\beta = 0.0057$	$\beta = 0.0077$	$\beta = 0.0097$
Time to Peak, Days	26	16	12
% Infective	10	20	29
R_0	1.71	2.31	2.91

I. RESULTS AND DISCUSSION

The basic reproduction number $R_0 = \beta PT = \beta P/\alpha$ is defined as the average number of new infections that one infected individual generates in the entirely susceptible population during the time that person is infective. If R_0 is greater than 1, an epidemic will develop; if R_0 is less than 1, the outbreak will die down. The basic reproduction number R_0 has been estimated to be between 1.4 and 1.6 for the recent Mexican A H1N1 in 2009. For the 1918-1919 pandemic strain, R_0 is approximately 2 to 6. The value of $T = 3$ days chosen by CDC is the lower end for the range of $T \in (3, 7)$ days. With good medical care and Tamiflu application in USA, $T = 3$ days may be appropriate for USA. For developing countries in the tropic, $T = 3$ days appears too short, based upon clinical and hospital observations.

For our first SIR Model 1, we choose $T = 5$ days ($\alpha = 0.2$ per day), and best fit Fig. 1 by choosing the best value of βP. The best fit value of βP is 0.40, resulting in $R_0 = 2.0$ with $T = 5$ days or $\alpha = 0.2$. This is slightly higher than the R_0 values of between 1.4 and 1.6 estimated by the SIR model for La Gloria in Mexico. This value is also slightly higher than the R_0 value of approximately 1.3 estimated for regular seasonal strain of influenza. The SIR Model 1 simulation results are plotted in Fig. 9, together with the infection figure provided by MOH, indicating a reasonable fit. The total number of susceptible persons P in the SIR Model 1 population works out to be about one tenth of a million or less than one percent of the entire Malaysian population. This low percentage of population exposed and susceptible to the infection may have been a consequence of various preventive measures taken during the infection period to isolate the infective persons from infecting the general population. This success of the prevention measures taken is the consequence of wisdom learned from the previous infectious disease SARS in 2003.

The second scenario SIR Model 2 is simulated by choosing $T = 3$ days (with Tamiflu), following the value used by CDC. The comparison of MOH data with SIR Model 2 results by best fit was demonstrated in Fig. 10. The best fit value for βP is 0.50, resulting in $R_0 = 1.5$. The final scenario SIR Model 3 is simulated by choosing $T = 7$ days. The comparison of MOH data with SIR Model 3 results by best fit was shown in Fig. 11. The best fit value for βP is 0.35, implying $R_0 = 2.45$. Fitting simulation results to MOH data with a two-parameter SIR Model has resulted in several possible sets of parameters (α, βP), each of which appears to fit MOH data well by adjusting the unknown parameters βP and T. The basic reproduction number R_0 for the A H1N1 2009 in Malaysia hovers around 2.0. For the 1918-1919 pandemic strain in Geneva, R_0 has been estimated to be between 1.2 and 3.0 for community-based settling, and between 2.1 and 7.3 for confined settling.

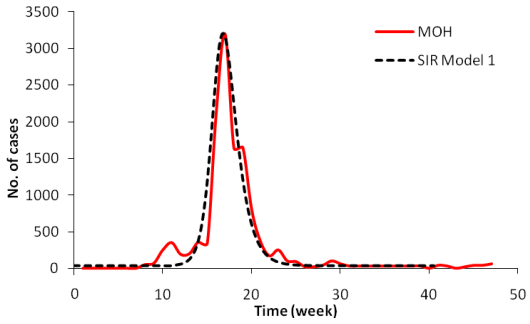

Figure 9. Comparison of MOH data and SIR Model 1, $T = 5$ days.

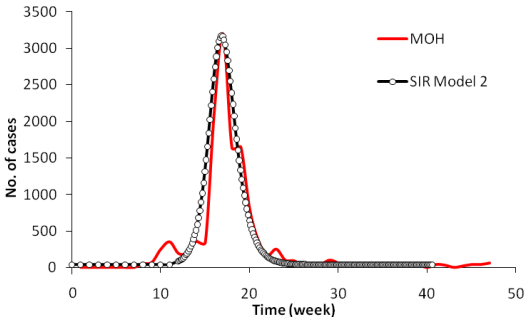

Figure 10. Comparison of MOH data and SIR Model 2, $T = 3$ days.

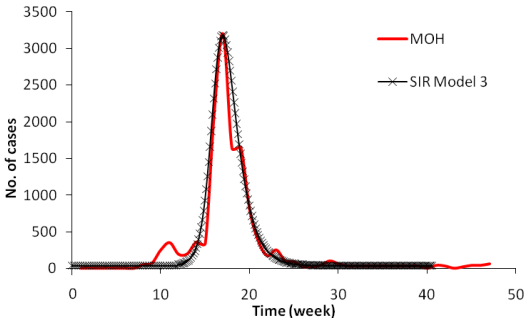

Figure 11. Comparison of MOH data and SIR Model 3, $T = 7$ days.

II. Hypothetical Worst-Case Scenarios

The choice of $T = 7$ days adopted in SIR Model 3 might represent a scenario close to the 1918-1919 pandemic. We therefore venture to simulate two hypothetical worst-case scenarios for Malaysia in which $T = 7$ days, but with higher values of $\beta P = 0.7$ and 0.9, corresponding to $R_0 = 4.9$ and $R_0 = 6.3$ respectively. These higher values of βP may result from a combination of higher number of people susceptible (P) and higher transmission rate (β), which might result from recombination of swine, avian and human strains. The recent strain of A H1N1 2009 might subsequently evolve into a strain that are highly transmissible (high value of β) and to which more people are susceptible (higher value of P). Based upon the data from Fig. 5, we deduce that the total number of persons infected under this hypothetical worst-case scenario could well be many times more than what was witnessed so far in Malaysia in 2009. This high number of people potentially infected might render existing medical facilities grossly inadequate. Further, Fig. 6 suggests that the time to disease peak might be significantly reduced by higher values of βP. This shortened time to peak would reduce valuable time that is needed to plan and implement disease control measures. In view of the fact that the last pandemic occurred 43 years ago, this long gestation period might just lay the foundation for the next pandemic that possesses the characteristics mentioned above to evolve into a severe pandemic. Hence, vigilance is absolutely essential. In the following section, FluSiM simulation results will be presented for the two hypothetical worst-case scenarios mentioned earlier.

A. *Worst-case scenario 1: $T = 7$ days, $\beta P = 0.7$, $R_0 = 4.9$*

The worst-case scenario 1 represents a scenario for which $T = 7$ days, $\beta P = 0.7$, $R_0 = 4.9$. As shown in Fig. 12, the new weekly infective cases peak several days earlier, compared to the scenario with $\beta P = 0.35$ (fitted to MOH data). This earlier time to peak can also be deduced from Fig. 6. The peak weekly cases simulated increases from around 3200 (MOH data) to 6700 cases.

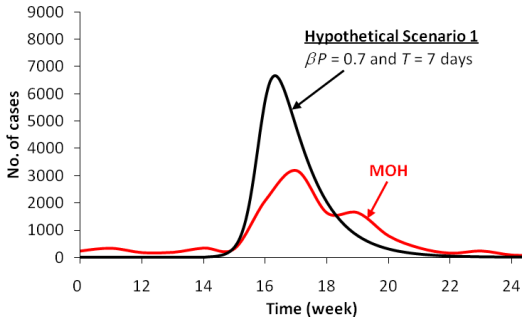

Figure 12. Worst-case scenario 1: $T = 7$ days, $\beta P = 0.7$, $R_0 = 4.9$

B. *Worst-case scenario 2: $T = 7$ days, $\beta P = 0.7$, $R_0 = 4.9$*

The worst-case scenario 2 represents a scenario for which $T = 7$ days, $\beta P = 0.9$, $R_0 = 6.3$. Fig 13 shows the number of new weekly cases simulated, indicating a peak weekly infective of around 8000 cases. This almost triples the peak weekly cases reported by MOH for the 2009 epidemic in Malaysia.

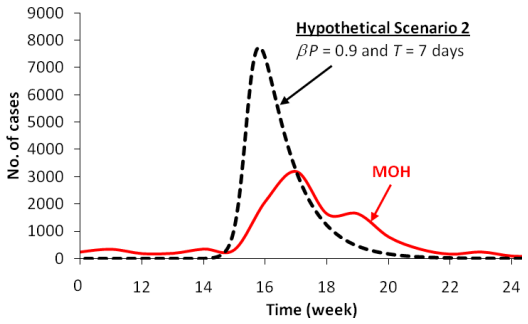

Figure 13. Worst-case scenario 2: $T = 7$ days, $\beta P = 0.9$, $R_0 = 6.3$.

III. Conclusion

In this concluding section we will discuss the direction in which FluSiM may be enhanced for integration into a national influenza surveillance system. First, it is noted that the MOH data presented in Fig. 1 refers to the aggregate of infections reported over the whole country. A critical assumption inherent in SIR is that each susceptible and each infective are at all times equally accessible and exposed to each other. This assumption is no longer valid for a large population spread over a large geographical area, such as the whole of Malaysia. To improve model accuracy, we therefore need to segregate the model population that spread over large geographic area into smaller local homogenous subpopulations. The individual subpopulations are linked to each other by a network of movement or diffusion, to be parameterized in SIR model. However, the calibration of this spatially-explicit SIR model would require spatially-explicit medical surveillance data. Compilation of such data presents

a challenge. The enhanced SIR model should incorporate several control measures such as household quarantine, school closure and other social distancing measures.

Several studies have suggested that household quarantine could be more effective than closing schools. This hypothesis can be tested by SIR based models to identify the optimal strategy of quarantine choices. Analysis on age-specific targeting strategies has surmised that vaccinating 80 % of children (less than 19 years old) would be almost as effective as vaccinating 80 % of the entire population, but demanding much less resources. Some simulation studies indicate that when R_0 is less than 1.9, the epidemic could be significantly reduced if enough antiviral is available to treat only 2 to 6 % of the population. A combination of targeted antiviral prophylaxis and pre-epidemic vaccination would be necessary to contain a severe epidemic ($R_0 > 2.5$). A combination of high levels of targeted antiviral prophylaxis, pre-vaccination and quarantine is needed to contain a very severe epidemic ($R_0 > 4.0$). For a given population, simulations by SIR models would provide useful insights regarding the efficacy of various mitigating policies, if MOH compiles such quality data, and release them real time.

The A H1N1 influenza emerged through cross species transmission and has been shown to have arisen due to recombination of swine, avian and human strains [16, 17]. Avian influenza is already endemic particularly in Asian poultry [18, 19]. New strains can emerge through co-infection and genetic recombination in intermediate hosts. Wild ducks and wading birds are considered to be a reservoir for influenza because they can carry all sub-types and the virus is avirulent to the wild avian hosts. Highly virulent virus can kill 50 to 70 % of infected humans. More complex biologically based SIR models are needed in these cases in order to track influenza transmission dynamics among multi-species (birds, pigs and humans).

During the 1918-1919 pandemic, the mortality rate of A H1N1 in the city of Sao Paolo was about 1 % of the population. The total number of deaths recorded was 5331 out of 523,194 inhabitants. For the Spanish Flu pandemic in Geneva, Switzerland, the basic reproduction number for the first wave was estimated to be about 1.5 while that for the second wave was 3.75. The overall fatality was reported to be 4.2 %. These figures may be used as guide to assess the severity of any impeding H1N1 second wave infections. The possibility of co-infections as a source of multiple pandemic waves has been suggested in [20]. To what extent this possibility may actually lead to real multiple pandemic waves may be tested in part by model simulations. This modeling research is therefore essential and timely.

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