Applied Mathematical Modelling 37 (2013) 903–915

Contents lists available at SciVerse ScienceDirect

Applied Mathematical Modelling

journal homepage: www.elsevier.com/locate/apm

Uncertainty and sensitivity analysis of the basic reproduction number of a vaccinated epidemic model of influenza

Md. Samsuzzoha *, Manmohan Singh, David Lucy

Mathematics Discipline, Faculty of Engineering and Industrial Sciences, Swinburne University of Technology, Hawthorn, Victoria 3122, Australia

ARTICLE INFO

Article history:
Received 17 November 2011
Received in revised form 2 March 2012
Accepted 12 March 2012
Available online 21 March 2012

Keywords:
Epidemic model
Vaccination
Influenza
Transmission rate
Uncertainty analysis
Sensitivity analysis

ABSTRACT

The basic reproduction number and the point of endemic equilibrium are two very important factors in any deterministic compartmental epidemic model as the basic reproduction number and the point of endemic equilibrium represent the nature of disease transmission and disease prevalence respectively. In this article the sensitivity analysis based on mathematical as well as statistical techniques has been performed to determine the importance of the epidemic model parameters. It is observed that 6 out of the 11 input parameters play a prominent role in determining the magnitude of the basic reproduction number. It is shown that the basic reproduction number is the most sensitive to the transmission rate of disease. It is also shown that control of transmission rate and recovery rate of the clinically ill are crucial to stop the spreading of influenza epidemics.

1. Introduction

Influenza is an infectious disease caused by a virus commonly known as influenza virus and transmitted among humans mainly in three ways: (i) by direct contact with infected individuals; (ii) by contact with contaminated objects and (iii) by inhalation of aerosols that contain virus particles. There are millions of people who suffer or die annually from influenza worldwide. Although different control and prevention strategies are available to control influenza transmission, influenza has been a major cause of morbidity and mortality among humans all over the world. Comparative knowledge of the effectiveness and efficacy of different control strategies is necessary to design useful influenza control programs. Mathematical modeling of the spread of influenza can play an important role in comparing the effects of different control strategies [1–4]. In particular, understanding of the threshold concepts in epidemiology that govern the spread of infection is very important. Among the various threshold concepts, an epidemiologic parameter, R_0 is called the basic reproduction ratio, or basic reproductive rate, or basic reproduction number. It is one of the most important theoretical concepts in theoretical infectious diseases epidemiology.

Sensitivity analysis of model parameters is very important to design control strategies as well as a direction to future research. There are many methods [5] available for conducting sensitivity analysis such as differential analysis, response surface methodology, the Fourier amplitude sensitivity test (FAST) and other variance decomposition procedures, fast probability integration and sampling-based procedures. Chitnis et al. [6] have evaluated the sensitivity indices of the basic reproduction number and the point of endemic equilibrium to the parameters in the model. They have determined the relative importance of different parameters in the transmission and prevalence of malaria. Sanchez and Blower [7] have

* Corresponding author. Tel.: +61 3 9214 4052; fax: +61 3 9214 8264.
E-mail address: MSamsuzzoha@swin.edu.au (Md. Samsuzzoha).

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http://dx.doi.org/10.1016/j.apm.2012.03.029

investigated an uncertainty and sensitivity analysis of the basic reproduction number of tuberculosis. Helton et al. [5] have performed a comparison study of uncertainty and sensitivity analysis using random and Latin hypercube sampling methods.

Uncertainty and sensitivity analysis of influenza epidemic model are not new. Several recent studies [8–13] have performed the uncertainty and sensitivity analysis of influenza epidemic model to the parameters. Lee et al. [9] and Wu et al. [13] have explored the effects of uncertainty in parameter estimation in the final size of influenza epidemic. Nuno et al. [10] and van den Dool et al. [12] have performed uncertainty and sensitivity analysis of the model parameters. They have determined the relative importance of model parameters in influenza transmission. Seaholm et al. [11] have performed a comparison study of sensitivity analysis based on Latin hypercube sampling and full factorial sampling approaches. All of these studies have determined the relative importance of different parameters in influenza transmission based on sampling-based uncertainty/sensitivity analysis.

In this article we analyze an influenza epidemic model proposed by Samsuzzoha et al. [14] based on the sensitivity indices of the basic reproduction number, $(\Re_{vac})$ and the endemic point of equilibrium, (E^*) to the parameters. Sensitivity analysis of the basic reproduction number $(\Re_{vac})$ is performed using two different approaches based on: (i) the local derivative and (ii) sampling. In turn, the sampling-based approach consists of two different methods: (i) random and (ii) Latin hypercube sampling. Thus results are compared using (i) local derivative, (ii) random and (iii) Latin hypercube sampling methods. We then numerically calculate the sensitivity indices of the endemic point of equilibrium (E^*). This analysis makes this work different to others as it will provide a comprehensive insight into a difficult problem. This will help us to determine the relative importance of different parameters in transmission and prevalence of influenza.

2. Model

The model for influenza [14] consists of a system of nonlinear ordinary differential equations, where population is divided into five subgroups: susceptible, S, vaccinated, V, exposed, E, infective, I and recovered, R. The total population size is denoted by $N = S + V + E + I + R$.

The model is represented by the following system of ordinary differential equations:

$$\frac{dS}{dt} = -\beta\beta_E\frac{ES}{N} - \beta\beta_I\frac{IS}{N} - \phi S - \mu S + \delta R + \theta V + rN, \quad (1)$$
$$\frac{dV}{dt} = -\beta\beta_E\beta_V\frac{EV}{N} - \beta\beta_I\beta_V\frac{IV}{N} - \mu V - \theta V + \phi S, \quad (2)$$
$$\frac{dE}{dt} = \beta\beta_E\frac{ES}{N} + \beta\beta_I\frac{IS}{N} + \beta\beta_E\beta_V\frac{EV}{N} + \beta\beta_I\beta_V\frac{IV}{N} - (\mu + \kappa + \sigma)E, \quad (3)$$
$$\frac{dI}{dt} = \sigma E - (\mu + \alpha + \gamma)I, \quad (4)$$
$$\frac{dR}{dt} = \kappa E + \gamma I - \mu R - \delta R. \quad (5)$$

In terms of the dimensionless proportions of susceptible, vaccinated, exposed, infectious and recovered individuals it is assumed that $s = \frac{S}{N},\ v = \frac{V}{N},\ e = \frac{E}{N},\ i = \frac{I}{N}$ and $r_1 = \frac{R}{N}$. After some manipulations and replacing s by S, v by V, e by E, i by I and r_1 by R, Eqs. (1)–(5) can be written as

$$\frac{dS}{dt} = -\beta\beta_E ES - \beta\beta_I IS + \alpha IS - \phi S - rS + \delta R + \theta V + r, \quad (6)$$
$$\frac{dV}{dt} = -\beta\beta_E\beta_V EV - \beta\beta_I\beta_V IV + \alpha IV - rV - \theta V + \phi S, \quad (7)$$
$$\frac{dE}{dt} = \beta\beta_E ES + \beta\beta_I IS + \beta\beta_E\beta_V EV + \beta\beta_I\beta_V IV + \alpha IE - (r + \kappa + \sigma)E, \quad (8)$$
$$\frac{dI}{dt} = \sigma E - (r + \alpha + \gamma)I + \alpha I^2, \quad (9)$$
$$\frac{dR}{dt} = \kappa E + \gamma I - rR - \delta R + \alpha IR. \quad (10)$$

The biological meaning of the parameters and chosen values of these parameters are specified in the Table 1.

The main objective is to perform sensitivity analysis in order to determine the most influential parameters affecting prevalence as well as transmission of disease. In view of that the following two methods have been used.

- Evaluation of sensitivity indices of the point of endemic equilibrium using specific estimated input parameters' values.
- Evaluation of sensitivity indices of the basic reproduction number using specific estimated input parameters' values as well as considering the uncertainties involved in estimating the parameters's values of the model.