



REVIEW OF MATHEMATICAL MODELS OF MALARIA

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ABSTRACT

Epidemiologists have widely used various mathematical models as tools to predict the occurrence of infectious diseases epidemics. Mathematical models have also been utilised as a tool for guiding research for eradication of malaria.

Mosquito density (m), biting rate (a) and mosquito mortality rate (μ_2) are the various parameters which are of prime importance in determining the fraction of human population that will enter into the exposed (E) and infected (I) classes. R_0 is the measure of the intensity of transmission.

Dietz et al pioneered a model considering seven compartments of human. Chitnis et al incorporated another important parameter of constant immigration of susceptible human population. The effects of migration and visitation on malaria transmission were demonstrated by Torres-Sorando and Rodriguez.

In this review, the workers have made an attempt to group the various epidemiological models of malaria in terms of the complexity of infection processes included in its description, with a view to make them more realistic.

The workers would like to strongly recommend to develop connections between mathematical analysis and their real world implications. Such analyses may help us to comprehend the effect of temperature, seasonal forcing, excessive rainfall; and correlation between different variables and parameter changes.

KEYWORDS :

In this article, the workers aim to develop various mathematical models. The workers propose to commence from the very basic models, and progress to a hierarchical structure of more complex models. The workers hope to describe malaria incidence by including the critical features of host-vector-parasite interactions. In our survey, we have summarized the modeling activity in this field, in order to help reach a wider range of workers working on epidemiology, transmission, and various other aspects of malaria.

Several known clinical and biological information are included in any mathematical expression or a model. Only features that appear to be important to the question being investigated in disease progression and dynamics are selected in the mathematical model. Epidemiologists have widely used mathematical models as tools in order to predict the occurrence of epidemics of infectious disease. Besides, they have also been used as a tool for guiding research for eradication of malaria.

MODEL BASICS

Whenever a pathogen appears in a host community, individuals in the community are categorized into different categories. This categorization depends on parasite density inside the hosts and the type of infection. Kermack and McKendrick were the pioneers in this field. Thus, these categories or compartments are represented by standard notation of S (Susceptible)-E (Exposed)-I (Infectious)-R (Recovered). To put it in simple words, these categories can be easily described as follows. The first group comprises of the fraction of host population that is Susceptible (S) to infection; followed by the Exposed (E) class. The third category is I or Infectious individuals; and the fourth and last category comprises of those individuals who have recovered from the infection; and make up the R class. Sir Ronald Ross used a deterministic differential equation model. With the help of this model it was deduced that reduction of mosquito numbers "below a certain figure" was sufficient to control malaria transmission. This figure was called "Transmission threshold". The Ross model was modified by George Macdonald in the 1950s. In this model the factor of malaria parasite development in the mosquito leading to latency has been incorporated. The survival of adult female mosquito was implicated to be the weakest link in the malaria transmission

cycle. Therefore, this model divides the mosquito population into three categories or compartments viz, (SEI). The World Health Organization (WHO) coordinated campaign, followed this model. The campaign focused on using the adulticide dichlorodiphenyltrichloroethane (DDT) in order to eliminate malaria transmission among 500 million people in Africa.

The ~21 days incubation period of the parasite in humans, was considered by Anderson and May. They introduced the Exposed (Eh) class in human population in their model. Thus the host population has three compartments (Sh, Eh, Ih), along with that in the mosquito population (Sm, Em, Im). (Figure 1).

Predicting The Effects Of Interventions In The Basic Models

Mosquito density (m), biting rate (a) and mosquito mortality rate (μ_2) are the various parameters which are of prime importance in determining the proportion of human population that will enter into the exposed (E) and infected (I) classes or categories. R_0 is the measure of the intensity of transmission. Given the expressions of R_0 in all the three models it is obvious that the square dependence of the biting rate 'a' implies that halving the biting rate is more effective than halving the coefficients 'b' or 'c' in all three models. Therefore, a more effective method of transmission control will be reduction of the biting rate (by use of bed nets, or any other method of personal protection)

COMPLEX MODELS

Dietz et al were the pioneers in proposing a model considering seven compartments of human. They introduced the effect of vectorial capacity of mosquito. This model conceptualizes that, a person may either recover from the infected class (Ih) and directly return to the susceptible class (Sh). Alternatively he may become re-infected through a temporary immune class (Rh).

Ngwa and Shu proposed an immunity model with a significantly high disease related death rate. This model also assumes that the total population is not constant. This model consists of four human compartments viz Susceptible (Sh), Exposed (Eh), Infected (Ih) and Immune (Rh). However, this model proposes three compartments in mosquitoes – Susceptible (Sm), Exposed (Em), and Infected (Im) akin to the

Anderson and May model. (Figure 2). The role of inclusion of demographic effects in predicting the number of fatalities due to the disease is aptly demonstrated by this model. Chitnis et al considered another important parameter of constant immigration of susceptible human population. In their SEI model for the human host Filipe et al divided the infected humans into three classes –severe disease (Ih1), asymptomatic patent infection (Ih2), and undetectable parasite density (Ih3).

The host population infected by drug-sensitive strain was divided into two groups viz treated and untreated by Koella and Antia. Thus, this model proposes five compartments of the human host viz, Susceptible (Sh), Sensitive, Infected, and Treated (Ih1), Sensitive, Infected, and Untreated (Ih2), Infected with the resistant strain (Ih3), and the Recovered (Rh).

ENVIRONMENTAL FACTORS

Influence of global warming besides local social and economic conditions on R0 of malaria transmission is demonstrated by the Yang model. This model takes into account good, intermediate and poor economic conditions in the human population. Further, this model divides each condition into three temperature zones. Thus, this model takes into account, differential immunity, endemicity, resistance, economic conditions and temperature dependence of mosquito development. The results of this model indicate the requirement of proper environmental management, besides a robust health care system, in transmission dynamics.

MIGRATION AND VISITATION

The role of migration and visitation on malaria transmission were demonstrated by Torres-Sorando and Rodriguez. The basic Ross model was modified so as to include a number of patches into which space is fragmented. This model works on the assumption that only humans move among the patches, mosquitoes being evenly distributed.

Data Based Statistical Modeling

Fitting of past data and predicting the future trend is one of the important uses of a model. This capability of a model improves the credibility of the underlying hypothesis of the model.

SUMMARY AND OUTLOOK

A model is nothing but a mathematical abstraction of reality. Inter-host transmission models or epidemiological models of infectious diseases do not take into account, most molecular events in host-pathogen interactions. These events include types of immune cells involved, parasite development inside the host; and signaling pathways. Intra-host models, study how the quantum of the infective agent or related molecules changes in an individual.

In this review, the workers have made an attempt to group the various epidemiological models of malaria in terms of the complexity of infection processes included in its description, with a view to make them more realistic. It is assumed that with more realistic models being devised, it would enhance the understanding of the transmission cycle at the level of the population. This would lead to better prediction of intervention strategies.

The various models discussed by the workers are only indicative and not exhaustive. The workers would like to strongly recommend to develop connections between mathematical analysis and their real world implications. Such analyses may help us to comprehend the effect of temperature, seasonal forcing, excessive rainfall; and correlation between different variables and parameter changes. An ideal combination would be to devise/utilize

models which consider the dynamics of host-parasite-vector interaction, proper clinical population subdivisions for disease transmission and also describe multiple data sets from different ecological regions. This comparative analysis carried out by the workers of various mathematical models of malaria will contribute to augment our understanding about the evolution of these models. It may also help in developing new models by taking into account various features which have been discussed above so as to improve predictions and decide realistic control measures.

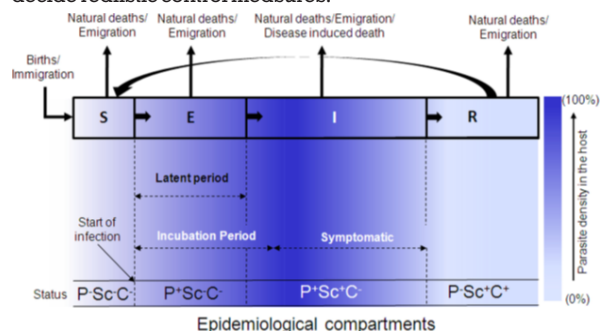


Figure 1 Epidemiological Compartments separating different stages of infection and parasite density in a population. S, E, I and R represent Susceptible, Exposed, Infected and Recovered fraction of the population respectively. Arrows on the top indicate different ways of population loss and transfer of population from one compartment to another. Different periods (Latent, Incubation, Symptomatic) characteristic of infection are shown by dotted arrows. The bottom panel shows the status of clinical markers for each compartment - PCR (P), Seroconversion (Sc) and Cellular immunity (C) (positive or negative). Colour Bar indicates the density of parasites in host in different compartments (0-100%).

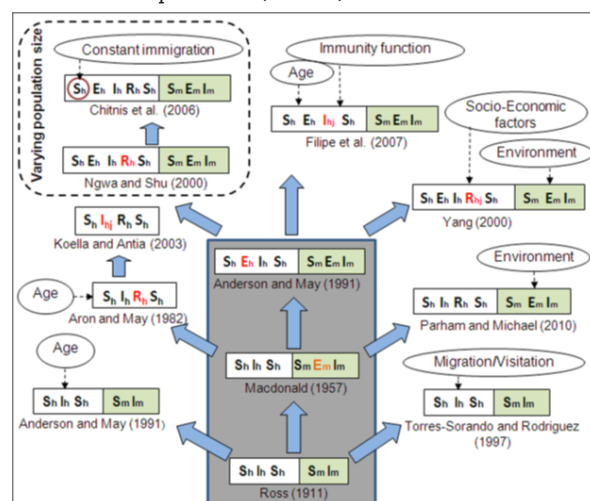


Figure 2 Evolution and grouping of different types of SEIR malaria models. Subscripts 'h' and 'm' stands for human and mosquito. Double folded boxes are for both human & mosquito population, and single fold boxes are only for human. First time addition of a new compartment is shown in red. The subscript 'j' (= 1, 2, 3) indicates further subdivision of the corresponding compartment. Three models inside the big grey box are considered as the Basic malaria models in this paper. Dotted arrows show the incorporation of complex factors in different models or specific compartment (red circle). Total population size is constant for all models, except the ones inside the dashed box.

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