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#### Research paper

## Vaccination and treatment as control interventions in an infectious disease model with their cost optimization

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#### ABSTRACT

In this work, an optimal control problem with vaccination and treatment as control policies is proposed and analysed for an SVIR model. We choose vaccination and treatment as control policies because both these interventions have their own practical advantage and ease in implementation. Also, they are widely applied to control or curtail a disease. The corresponding total cost incurred is considered as weighted combination of costs because of opportunity loss due to infected individuals and costs incurred in providing vaccination and treatment. The existence of optimal control paths for the problem is established and guaranteed. Further, these optimal paths are obtained analytically using Pontryagin's Maximum Principle. We analyse our results numerically to compare three important strategies of proposed controls, viz.: vaccination only; with both treatment and vaccination; and treatment only. We note that first strategy (vaccination only) is less effective as well as expensive. Though, for a highly effective vaccine, vaccination alone may also work well in comparison with treatment only strategy. Among all the strategies, we observe that implementation of both treatment and vaccination is most effective and less expensive. Moreover, in this case the infective population is found to be relatively very low. Thus, we conclude that the comprehensive effect of vaccination and treatment not only minimizes cost burden due to opportunity loss and applied control policies but also keeps a tab on infective population.

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#### 1. Introduction

Diseases cause mortality and morbidity that lead to loss in productive capacity of individuals and financial loss in terms of health care, medical diagnosis, vaccination, treatment etc. [17,29]. Thus diseases affect the social well being as well as economy of a society or a country. It is reported in global status report of WHO that infectious diseases contribute to around 1/6th of total deaths worldwide and are second leading cause of deaths [3]. In particular, for example, various types of hepatitides (Hepatitis A-E) affect millions of people worldwide and cause around 1.4 million deaths every year [5]. Moreover, diseases have consequences related to health care, employment and travel etc. which affect economy. For example, total worldwide impact of 50 billion dollars was estimated related to SARS in 2003 [1,4]. Further, there are direct and indirect costs involved when a disease transpires in a population. The direct costs include costs incurred in treatment, diagnosis, travelling expenses to get treatment and care, special food etc. for patients. Indirect costs may include productivity loss, effective man hour loss due to illness, time loss in caring and attending patient and mortality loss with burden of

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dependents on society such as orphan etc. Thus, we may conclude that in totality several costs are involved in illness of an individual [2,29].

Therefore, it becomes utmost important to understand the disease progression dynamics and to develop adequate preventive or control interventions for the disease and also to estimate the cost effectiveness of these preventive or control interventions. One of the popular preventive intervention used is vaccination which prevents an estimated 2–3 million deaths every year. Due to immunization, about 78% reduction in measles deaths were observed between 2000 and 2012 worldwide [6]. Almost 25 diseases can be prevented by WHO approved available vaccination [6]. In last few decades, vaccination and several other control interventions such as treatment, screening, quarantine, isolation, educational campaigns etc. were also considered and their effect on the disease prevalence in population was studied by many researchers [8,10,14,19,21,32].

Mathematical modeling has been successfully used in constructing control strategies with suitable interventions for various diseases [9,14,18,24,32]. Though, there is always a trade-off among the interventions for implementation of suitable control strategy to reduce the disease prevalence [11,14,23,27]. Researchers have considered different combinations of relevant control interventions and their impact on the disease progression with cost optimization of these interventions. We present here a brief survey on recent works related to control strategies and corresponding costs.

In 2007, Armbruster et al. proposed an infectious disease model to study the combined effect of screening and contact tracing [7] as well as the effect of walk-ins programs in detection of new infective. They performed the cost-effective analysis of the corresponding control strategy. In 2009, Gaff et al. studied the effect of vaccination and treatment on a set of SIR, SIRS and SEIR models [14]. They analysed these epidemiological models and explored the expensiveness of vaccination in absence of treatment and vice-versa. Optimal control theory has also been used to study the control in spread of SARS, Influenza, HIV and other sexually transmitted diseases etc. (see for example [7,16,20,27,31]). In [16] Gumel et al. proposed a model and studied the impact of quarantine and isolation for SARS outbreaks in GTA, Hong Kong, Singapore and Beijing. Further, Yan et al. in 2008 formulated an optimal control problem corresponding to the model of Gumel et al. by taking quarantine and isolation as control and obtained optimal cost corresponding to these interventions [31]. In 2013, Okosun et al. investigated the impact of combined control policies such as using condom, screening and treatment on the control of HIV/AIDS and also performed cost-effective analysis [27]. Recently, Moualeu et al. proposed and studied the dynamics of tuberculosis in Cameroon as a control problem by considering education, diagnosis campaigns and chemoprophylaxis of latently infected individuals as interventions [26]. Their aim was to minimize undiagnosed infectious with help of education and diagnosis campaigns as a control along with eradication of latently infected individuals through treatment. They numerically obtained framework for designing cost-effective strategies for diseases with multiple intervention methods. They observed that combining chemoprophylaxis and education the burden of TB can be reduced by 80% in 10 years.

From economic point of view, we know that a large sum of money is needed to deal with the disease burden as well as to apply any control intervention. But health agencies or governments have limitation in funding for applying control interventions during and after the course of epidemic. At the same time it is also important to maintain quality of life of population. Thus in this paper we tried to address the problem with cost optimization of applied interventions and disease burden. Cost optimization problems related to epidemiology have also been studied in reference to health care expenditures (see [8,10,14,15] and references therein). Behncke in 2000 focused on various control policies such as vaccination, quarantine, screening and health promotional campaigns [8] and analysed the control models using these policies. He quantified the crucial role of funds on disease dynamics in case of health campaigns. In 2002, Goldman et al. emphasized on the interconnection between the economy of medical treatment and infectious diseases with stress on limitation of constant recovery in model dynamics [15].

In this paper we consider an SVIR model proposed by Liu et al. [25]. The nonlinear model system is given as follows:

$$\frac{dS}{dt} = \mu - \beta SI - \mu S - \alpha S, 
\frac{dV}{dt} = \alpha S - \beta_1 VI - \gamma_1 V - \mu V, 
\frac{dI}{dt} = \beta SI + \beta_1 VI - \gamma I - \mu I, 
\frac{dR}{dt} = \gamma_1 V + \gamma I - \mu R,$$
(1)

with initial conditions  $S(0) \ge 0$ ,  $V(0) \ge 0$ ,  $I(0) \ge 0$  and  $R(0) \ge 0$ . Here, all the parameters are taken to be non-negative. Parameter  $\mu$  represents growth rate of susceptible population and natural mortality rate,  $\gamma$  is recovery rate of infected population and  $\alpha$  denotes constant vaccination rate of susceptible population.  $\beta$  and  $\beta_1$  are the transmission rate of disease when infected individuals make contact with susceptible and vaccinated individuals respectively. Parameter  $\gamma_1$  is vaccineinduced immunity rate from vaccinated to recovered populations during or after the vaccination process *i.e.*  $1/\gamma_1$  is average period to obtain immunity after vaccination. For the detailed description of parameters refer to [25]. Liu et al. [25] studied the model for both continuous and impulsive vaccination. They observed that if the basic reproduction number of the model system is below one then disease dies out otherwise it persists in both cases. Vaccination is found to be helpful in reducing the disease burden and also the basic reproduction number under certain condition.

In model (1) Liu et al. [25] considered only natural recovery of infected individuals. We modify the model of Liu et al. to include the treatment of the infective individuals. Let  $\gamma_T$  be the treatment rate in infective class. Thus we get following

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