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An Optimal Control of Vaccination Applied to Whooping Cough Model

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Abstract. Whooping cough is a vaccine preventable public health problem caused by Bordetella Pertussis and Bordetella Parapertussis. It is a highly contagious respiratory disease. In this paper firstly we have incorporated a vaccination rate into whooping cough model. Simulations show that as we go on increasing the vaccination rate, the period of infection decreases. Secondly we have applied an optimal control on a whooping cough model. Our objective is to minimize the infected population. For this we have developed an optimal control strategy. We have constructed an objective functional comprising of Lagrangian and a Hamiltonian. The objective functional along with adjoint equations, transversality conditions, optimality conditions and model equations constitute an optimal control strategy. We have simulated this optimal control problem using the Forward-Backward Sweep Method by incorporating the RK-4 Method. Simulations show that the susceptible and infected populations are reduced under an optimal control where as the recovered individuals are increased with the application of control. At the end we have mentioned some prominent challenges the whole world must address on urgent basis to control this disease.

AMS (MOS) Subject Classification Codes: 92-XX; 92-BXX; 92B05
Key Words: Bordetella Pertussis, Whooping Cough, Vaccination, Epidemiology, Pubic Health.

1. Introduction

Whooping cough or Pertussis is highly contagious respiratory tract disease and remains a major global health problem [1, 2, 3]. It is mainly caused by Bordetella Pertussis which

is an etiological agent that was isolated and identified in 1906 by Bordet and Gengou [2,4]. It is bacterial pathogens [5], or gram-negative coccobacillus [6]. Pertussis has more deaths than measles and polio combined and is still one out of 10 most common causes of deaths from infectious diseases worldwide. Approximately 1 in 10 cases resulted in mortality and it is one of the major causes of infant mortality [3,7]. Despite mass vaccination campaigns for over 50 years, it is still increasing in developing countries [3]. It is both an endemic and epidemic disease [8], responsible for significant morbidity and mortality especially in infants and children [9]. WHO estimates 40-50 million cases of whooping cough and approximately 297,000 to 409,000 deaths annually where ninety percent cases belong to low income countries[4,10]. In third world countries the rate of fatality among infants is about 4%[6].

The first outbreak of whooping cough took in 15th century [7] and the oldest known epidemic is thought to be the Paris Outbreak of 1578 [11]. It was endemic in Europe by the 1600s [10]. The whooping cough outbreak in Ireland, Israel and USA occurred in early months of 2010. The Outbreak of California in 2014 was the most severe than any outbreak since 1947 [2]. In 1947 a major pertussis epidemic occurred in Cape Town causing 107 deaths [12]. The western countries are highly endemic despite high vaccination coverage about 90% [2,7]. In the pre vaccination era whooping cough was most common disease of infants and children and mortality rate was high for infants especially with age less than six months but with passage of time it affected adults as well. Pertussis is human disease and does not have carriers [13]. Children are susceptible to the bacterial infection and in 2008, about 195,000 children died from whooping cough worldwide [14]. Outbreaks of whooping cough are increasing in countries with high vaccination coverage particularly affecting young children [15].

Pertussis is the most common vaccine-preventable disease [5] and whole-cell pertussis vaccine has shown tremendous decrease in its incidence [1]. Vaccination with DTwP(Diphtheria-tetanus-whole cell pertussis) has largely reduced the burden of this disease globally [16]. It affects all age groups especially children [8]. However the number of adult cases have increased over the last decade [17]. Human infection with Bordetella Pertussis depends on age and host immunity. Its clinical signs include hypoglycemia, reduced pulmonary capacity and high leukocytosis [5]. The complications include convulsions, bronchopneumonia and encephalopathy. According to World Health Organization(WHO) it has following three phases: catarrhal, paroxysmal and convalescent [4]. There are two hypothesis to explain the Bordetella Pertussis incidence: either vaccination coverage is too low or vaccinated individuals can still become infected [10]. There is marked increase in teenagers and adults. Its rapid transmission is due to these individuals. In a population with high vaccination coverage and without any booster, there are classes in which Bordetella Pertussis can circulate and from which it can spread infection in infants. There are two hypothesis on which teenagers and adults can spread infection: Firstly, epidemics among children lead to infection among infants and secondly, subclinical adults with infection are responsible for infection of pre-vaccine age individuals[14]. Childhood immunization has tremendously decreased the incidence but this protection is not lifelong. World Health Organization(WHO) says the length of immunity is 10 years, although figures are variable and immunity may range from 6 to 12 months. Severe complications of the disease include apnoea, cyanosis, pneumonia, seizures and encephalopathy[6].

Recently mathematical models are considered to be important tools in analyzing the prevalence and control of infectious disease. Several works on epidemics models with theoretical developments include Becker (1978), Dietz (1988), Herbert (2000), Wickwirem (1977), Zhang et al. (2007), Ogren and Martin (2002), where they applied optimal control theory to SIR model using Pontryagin Maximum Principle, Gul Zaman et al(2008), they applied an optimal control theory to SIR model with stability analysis, A. M. Elaiw et al (2013) discussed the optimal treatment on Hepatitis B Virus Dynamics, A. V. Kamyad et al(2014) apllied the two controls vaccination and treatment to hepatitis B virus model, H. S. Rodrigues et al(2010), C. J. Silva et al(2013), H. S. Rodrigues et al(2014) and P. Rodrigues et al(2014). Similarly complex vaccination affects such as boosting, wanning and partial protection have been used by many researchers for measles, rubella, chicken pox, hepatitis and HIV infection [13, 34-40]. In this research work we have applied vaccination control to the whooping cough model. We investigate the impact of vaccination rate on epidemiology of whooping cough model first and then developed optimal control strategy for minimizing the infected individuals and associated cost. Our simulation results show that vaccination rate on whooping cough model decreases the period for infected individuals and optimal control reduces the susceptible and infected pollution but increases the recovered population.

The text is organized as follows. In Section 2 we introduce a mathematical model that describe the dynamics of whooping cough and plotted population behavior versus time. In Section 3 we have extended this model by incorporating vaccination rate and simulated this impact on whooping cough model. In Section 4 we have developed an optimal control strategy to minimize susceptible and infected population by increasing the recovered population. In this section we have explained the Forward-Backward Sweep Method in order to numerically solve our devolved optimal control problem. We have also simulated the population behavior with and without control in this section. Section 5 is devoted to results and discussion. In this section we have also narrated some important measures the whole world must address to control the prevalence of this disease. In section 6 we have commented on the role of vaccination in public health policies. In last section 7 we have concluded our whole work.

2. Material and Methods

We consider the mathematical model for whooping cough which is the transmission model of infectious diseases. It is the classical SIR epidemic model discussed in [18] where W. Piyawong et al developed a converging scheme for this SIR model. Later A. J. Arenas et al. in [19] developed a NSFD scheme for this model. We want to extend the mathematical model of whooping cough used by G. G. Para et al. in [20] by incorporating the external control. In this model the whole population is divided into three populations: S(t), susceptible population, I(t), infected population, and R(t), recovered population. Moreover it is assumed that there is immunity in this class. The complete mathematical model is given by

$$\dot{S(t)} = \mu - \mu S(t) - N\beta S(t)I(t) \tag{2. 1}$$

$$\dot{E(t)} = N\beta S(t)I(t) - (\mu + \nu)I(t) \tag{2. 2}$$

$$\dot{I(t)} = \nu I(t) - \mu R(t) \tag{2. 3}$$

Where μ is death rate which we assume equal to birth rate, β is transmission coefficient, ν is rate of recovery from disease and N is total population. In this model total population N is assumed constant and for convenience normalizing it to unity i.e. $S(t)+I(t)+R(t)=1$. The disease free equilibria(dfe) of this model is $(1,0,0)$ and the endemic equilibria is $(1/R_0, \mu/(\mu+\nu)(1-1/R_0), \nu/(\mu+\nu)(1-1/R_0)$ where $R_0 = N\beta/(\mu+\nu) > 1$ is the basic reproduction number [20]. Population behavior of this model versus time has been demonstrated in Fig. 1, Fig. 2 and Fig. 3. Where we have taken arbitrary initial conditions $S(0) = 0.24, I(0) = 0.007, R(0) = 0.753$ and the values of parameters $\mu = 0.04, \nu = 24, N\beta = 123$ are taken from [19, 20].

3. Whooping Cough Model Dynamics under Vaccination

Infectious diseases have great influence on human lives. Recently controlling infectious diseases has become a hot issue. One important strategy to control infectious diseases is through vaccination. We want to vaccinate the dynamics of whooping cough model. The improved model (1) with vaccination becomes

$$\dot{S(t)} = \mu - \mu S(t) - N\beta S(t)I(t) - V_{vac}S(t) \tag{3. 4}$$

$$\dot{E(t)} = N\beta S(t)I(t) - (\mu+\nu)I(t) \tag{3. 5}$$

$$\dot{I(t)} = \nu I(t) - \mu R(t) + V_{vac}S(t) \tag{3. 6}$$

We simulate the model (2) in order to study the behavior of infected individuals under several vaccination rates. This behavior has been demonstrated in Fig. 4. Where we have taken initial conditions $S(0) = 0.24, I(0) = 0.007, R(0) = 0.753$ and the values of parameters are taken as $S(0) = 0.04, I(0) = 24, R(0) = 123$. V_{vac} is a vaccination rate parameter. From simulations we observe as we increase the rate of vaccination the peak value of infected population decreases. The time dependent curve of infected individuals shows that when the percentage of the vaccinated infected individuals increases, the peak of the curve of infected individuals is less important and the period of infection (the corresponding number of days) is shorter. In fact in case of infection without vaccination the curve of infected individuals go to zero in about 1 years where in the presence of vaccination the curve of infected group go to zero in about 0.5 years. This shows the efficiency of using vaccination in controlling whooping cough.

4. Optimal Control of the System

Optimal control has been recently used with success in a series of biological models [21-24]. In this section we have developed an optimal control problem by incorporating a control $u(t)$ at t time. The control $u(t)$ is the fraction of susceptible individuals. We assume that all susceptible population that is vaccinated is directly transferred to recovered class. We investigate the effective optimal control technique for model [20]. We analyzed the behavior of this extended model using this control. We have considered this control as time dependent. Our objective is to minimize infected individuals and increase recovered individuals. So we want an optimal control strategy that minimizes the susceptible and infected populations and also accounts for the cost associated with vaccination. We also want to increase recovered population. Our optimal control

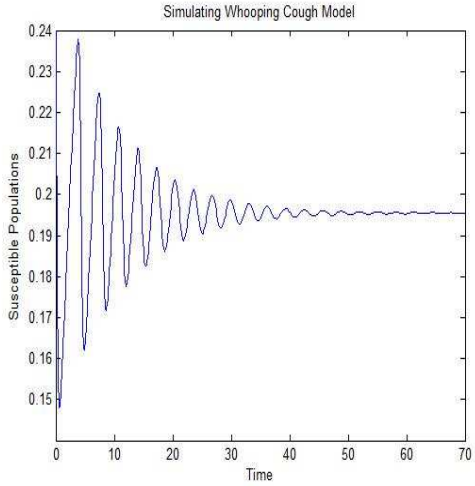

FIGURE 1. Plot shows the behavior of the susceptible population for the whooping cough model

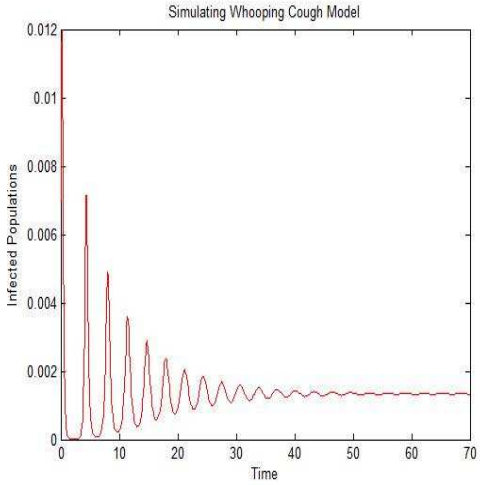

FIGURE 2. Plot shows the behavior of the infected population for the whooping cough model

problem take the control variables $u(t) \in \prod$ where control is bounded and measured with $\prod = (u(t), 0 \leq u \leq 1, t \in [0, t = T_f])$. The controls are restricted to take values between zero and one so that it may not be addressed limitations from financial, technical support and resources available. With no control infections spread faster or reproduction

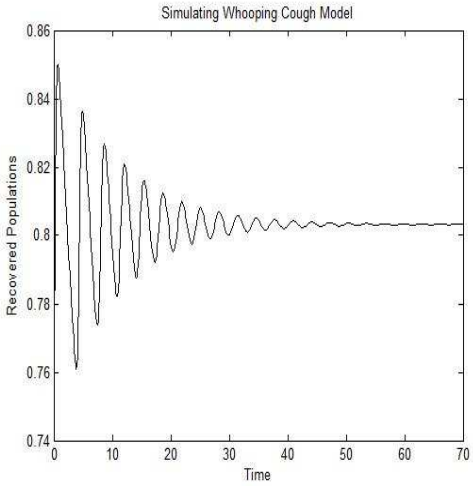

FIGURE 3. Plot shows the behavior of the recovered population for the whooping cough model

number has higher values. Our control strategy carries the following features

4.1. **Construction of Objective Functional. Step 1.**In order to keep balance in the size of each population we use A as positive constant. [25, 26] i.e. $AS(t)$.
Step 2. Take B as weight corresponding to u control. Weight factors act as cost associated with control. They may be human effort and material resources. Thus $Bu^2(t)$ represents the cost associated with vaccination control. Here square of the control is used to eradicate severity of side effects and over doses of control [25, 26].
Step 3. Combining Step 1 and Step 2 we get $AI(t) + \frac{1}{2}Bu^2(t)$.
Step 4. Taking T_f as final time and minimize the integral with respect to u.Thus the objective functional to be minimized is

$$J = min_{(u)} \int_0^{T_f} AI(t) + \frac{1}{2}Bu^2(t)dt \tag{4. 7}$$

Subject to

$$\dot{S(t)} = \mu - \mu S(t) - N\beta S(t)I(t) - uS(t) \tag{4. 8}$$

$$\dot{E(t)} = N\beta S(t)I(t) - (\mu + \nu)I(t) \tag{4. 9}$$

$$\dot{I(t)} = \nu I(t) - \mu R(t) + uS(t) \tag{4. 10}$$

With ICs $S(0) \geq 0, L(0) \geq 0, I(0) \geq 0, C(0) \geq 0$

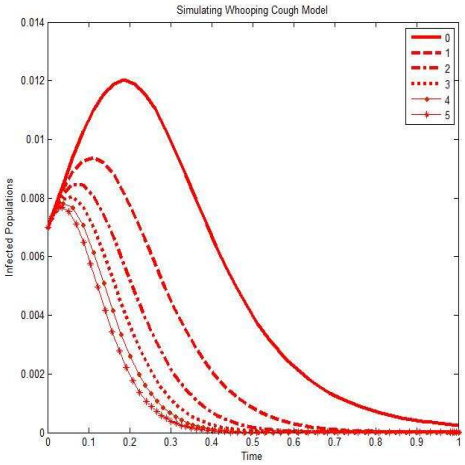

FIGURE 4. Plot shows the behavior of infected population under the impact of several vaccination rates. With the increase amount of rate of vaccination the infected period becomes shorter. Here vaccination rate is the amount of vaccination dose per time. We have taken only arbitrary values 1, 2, 3, 4, 5 for vaccination rates in order to show the decrease of the infected population with the increase of dose amount inserted into patient's body instead of going into details in clinical perspectives

4.2. **Constructing Lagrangian and Hamiltonian for Optimal Control Problem.** To find the optimal control pair we first find Lagrangian

$$L(I,u) = AI(t) + \frac{1}{2}Bu^2(t) \tag{4. 11}$$

In order to optimize Lagrangian we need Hamiltonian of the system which is given by

$$H(I,u,\lambda_1,\lambda_2,\lambda_3,\lambda_4) = L + \lambda_1(t)\dot{S}(t) + \lambda_2(t)\dot{I}(t) + \lambda_3(t)\dot{R}(t) \tag{4. 12}$$

Where $\lambda_i, i = 0,1,2,...$ are adjoint variables

$$H(I,u,\lambda_1,\lambda_2,\lambda_3,\lambda_4) = AI(t) + \frac{1}{2}Bu^2(t) + \lambda_1(t)\dot{S}(t) + \lambda_2(t)\dot{I}(t) + \lambda_3(t)\dot{R}(t) \tag{4. 13}$$

$$H(I,u,\lambda_1,\lambda_2,\lambda_3,\lambda_4) = AI(t) + \frac{1}{2}Bu^2(t) + F_1 + F_2 + F_3 \tag{4. 14}$$

$$F_1 = \lambda_1(t)(\mu - \mu S(t) - N\beta S(t)I(t) - uS(t)) \tag{4. 15}$$

$$F_2 = \lambda_2(t)(N\beta S(t)I(t) - (\mu + \nu)I(t)) \tag{4. 16}$$

$$F_3 = \lambda_3(t)(\nu I(t) - \mu R(t) + uS(t)) \tag{4. 17}$$

4.3. **Adjoint Equations.** The associated adjoint equations are

$$\dot{\lambda_1}(t) = -(\frac{\partial H}{\partial S}) = -((\mu + N\beta I + u)(-\lambda_1) + \lambda_2 N\beta I + \lambda_3 u) \tag{4. 18}$$

$$\dot{\lambda_1}(t) = (\lambda_1(\mu + N\beta I + u) - \lambda_2 N\beta I - \lambda_3 u) \tag{4. 19}$$

$$\dot{\lambda_2}(t) = -(\frac{\partial H}{\partial I}) = -(A - \lambda_1 N\beta S + \lambda_2(N\beta S - (\mu + \nu)) - \lambda_3\nu) \tag{4. 20}$$

$$\dot{\lambda_3}(t) = -(\frac{\partial H}{\partial R}) = \lambda_3(t)\mu \tag{4. 21}$$

4.4. **Transversality Conditions.**

$$\lambda_1(T_f) = \lambda_2(T_f) = \lambda_3(T_f) = 0 \tag{4. 22}$$

4.5. **Optimality Conditions.**

$$\frac{\partial H}{\partial u_1(= u^*)} = 0 \tag{4. 23}$$

$$Bu^* - \lambda_1 S + \lambda_3 S = 0 \tag{4. 24}$$

$$u^* = \frac{(\lambda_1 - \lambda_3)S}{B} \tag{4. 25}$$

4.6. **Optimal Pair and Bounded Control.** Thus (X^*, u^*) is an optimal solution of the optimal control problem for $X = (S, I, R)$. The property of control space with bounded controls that is upper bound is 1 and lower bound is 0 implies
$u^* = 0$ if $u \leq 0$
$u^* = u$ if $0 < u < 1$
$u^* = 1$ if $u \geq 1$
Or in compact form it can be written as $u_1^* = max[0, T][0, min(u(t), 1)]$ The control pair (u^*, X^*) give the optimal value of the objective functional J.

4.7. **Forward-Backward Sweep Method.** In order to numerically solve the optimal control problem

$$J = min_{(u)} \int_{t_0}^{t_1} f(t, x(t), u(t))dt \tag{4. 26}$$

Subject to

$$\dot{x}(t) = g(t, x(t), u(t)) \tag{4. 27}$$

and $x(t_0) = a$

$$\dot{\lambda_t} = -(\frac{\partial H}{\partial x}) = -(f_x(t, x, u) + \lambda(t)(g_x(t, x, u))) \tag{4. 28}$$

$$\lambda(t_1) = 0 \tag{4. 29}$$

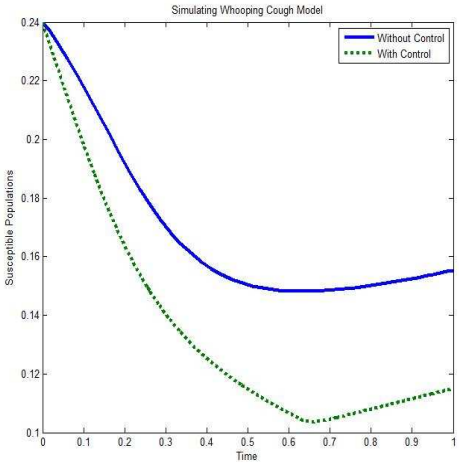

FIGURE 5. Simulations show the susceptible populations both with control and without control

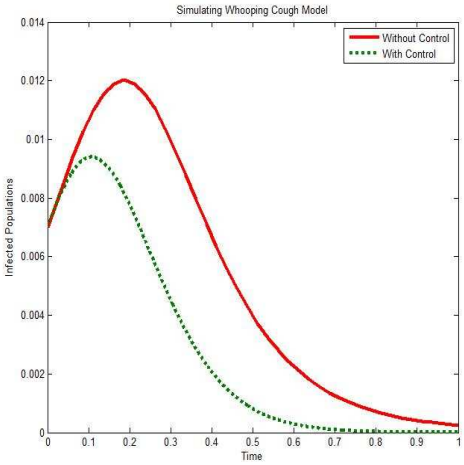

FIGURE 6. Simulations show the infected population both with control and without control

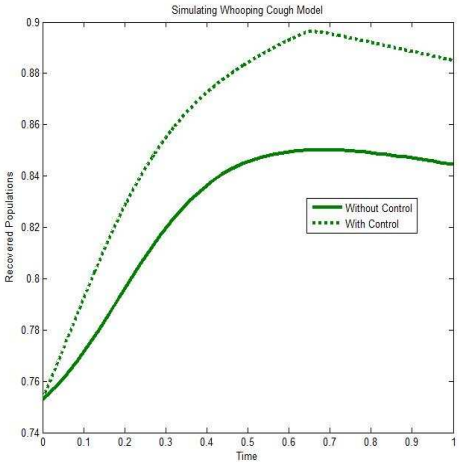

FIGURE 7. Simulations show the recovered population both with control and without control

$$0 = \frac{\partial H}{\partial u} = (f_{u=u^*}(t,x,u)) + \lambda(t)(g_{u=u^*}(t,x,u))) \tag{4. 30}$$

Where last equation is employed to find u^* in terms of t and x and λ and when this representation is substituted back into the ODEs for $x$and λ the above two equations form a two-point boundary value problem, we partition the time interval $[t_0, t_1]$ into usually equally spaced points $t_0 = b_1, b_2, , b_N, b_{N+1} = t_1$. The approximation will be a vector $\vec{u} = (u_1, u_2, u_3, , u_{N+1})$, where $u_i \approx u(b_i)$.
We outline the following algorithm of Forward-Backward Sweep Method [31] for this problem where $\vec{x} = (x_1, x_2, x_3, , x_{N+1})$ and $\vec{\lambda} = (\lambda_1, \lambda_2, \lambda_3, , \lambda_{N+1})$ are vector approximations for the state and adjoint.
Step 1. Make initial guess for $\vec{u}$ over the interval.
Step 2. Using the initial condition $x_1 = x(t_0) = a$ and values for $\vec{u}$, solve $\vec{x}$ forward in time according to the differential equation in the optimality system.
Step 3. Use the Transversality condition $\lambda_{N+1} = \lambda(t_1) = 0$ and the values of $\vec{u}$and $\vec{x}$, solve $\vec{\lambda}$ backward in time according to its differential equation in the optimality system.
Step 4. Update $\vec{u}$ by entering the new $\vec{x}$ and $\vec{\lambda}$ values into the characterization of the optimal control.
For the step 2 and 3 we have used ODE solver Runge-Kutta 4. Which for step size h and ODE $\dot{x}(t) = f(t, x(t))$. The approximation $x(t+h)$ given $x(t)$ is

$$x(t+h) \approx x(t) + \frac{h}{6}(k_1 + 2k_2 + 2k_3 + k_4) \tag{4. 31}$$

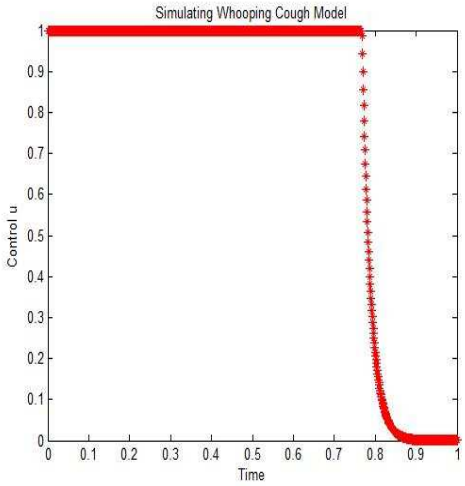

FIGURE 8. Simulation of control versus time

Where

$$k_1 = f(t, x(t)) \tag{4. 32}$$

$$k_2 = f(t + \frac{h}{2}, x(t) + \frac{h}{2}k_1) \tag{4. 33}$$

$$k_3 = f(t + \frac{h}{2}, x(t) + \frac{h}{2}k_2) \tag{4. 34}$$

$$k_4 = f(t + h, x(t) + hk_3) \tag{4. 35}$$

4.8. **Results and discussion.** Whooping cough infected millions and killed hundreds of thousands globally[27]. In 2012, the United States had 48,000 whooping cough cases. This number dropped between 2014 and 2015 to 29,000 yearly. Between 1965 and 2002, there were about 10,000 cases annually. In the United States, whooping cough steadily declined by the end of 1970s [15]. Vaccination has been one of the most successful and cost effective public health invention in the last century that saved millions of lives [28]. Control through mass vaccination had initially appeared to be very successful in Canada, Australia and Taiwan and most European countries [15]. The Whooping cough vaccine was made by South African Institute of Medical Research. Potency test of this vaccine was performed on mouse sample. Furthermore little is known about locally produced vaccines [12]. Doctors started vaccinating people against whooping cough in the 1940s with whole-cell vaccine (DTwP) made of dead bacteria. "This vaccine can boost immune response but not cause the disease" said by Manoj Ghambir an associate professor of Epidemiology at Monash University at Melbourne, Australia. This vaccine has dramatic impact on the infection reduction and the number of infected people reduced to average of 0.5 percent cases yearly. According to Manoj this vaccine carries side effect like convulsions which induce fever. Therefore in 1991 researchers developed Acellular Vaccine which does not

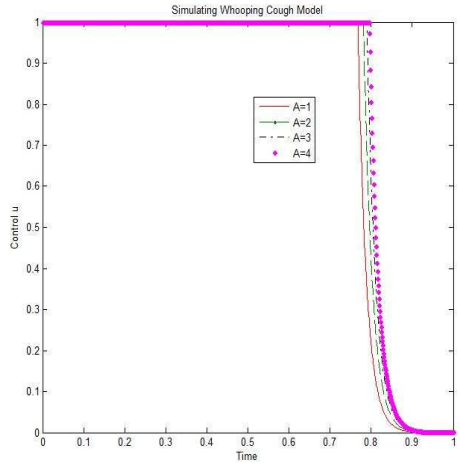

FIGURE 9. Simulation of control versus time by varying the values of A

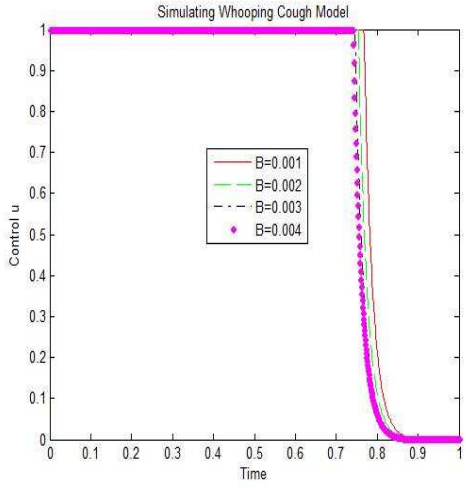

FIGURE 10. Simulation of control versus time by varying the values of B

comprises of dead bacteria but its application in 1990 in US proved it less effective than the original vaccine [29].

The worldwide incidence of Bordetella Pertussis has increased dramatically over the past

20 years. Last year in the United States alone, there were more cases diagonized of Bordetella Pertussis than any year since 1955 despite high vaccination coverage [10]. Pertussis epidemics in the pre vaccination era (before mid 1940s) occurred at two to five year intervals. Although immunization played a good role to reduce it but could not fully control its spread and transmission. Vaccination can prevent Bordetella Pertussis [30]. Common complications of pertussis include pneumonia, otitis media, seizures and encephalopathy. The most common symptoms we fond in patients positive for Bordetella Pertussis were similar to those found in other studies including paroxysm of coughing, cyanosis and respiratory disease [9].

Mathematical modeling technique is an effective control technique to study the underlying ideas and key parameters responsible for spread of this disease. We have considered the mathematical model of whooping cough developed by G. G. Parra in [20]. In Fig. 1, Fig. 2, and Fig. 3 we have simply simulated the susceptible, infected and recovered populations versus time (in years). We have then extended the mathematical model of whooping cough by incorporating vaccination rate through parameter V_{vac}. In Fig. 4 we have simulated the impact of vaccination rate on the whooping cough model which shows that in the absence of vaccination infected individuals are zero in one year but with the application of vaccination the same infected population reduced to zero in 0.5 years. Therefore, the period of infection becomes shorter with the application of vaccine. In section 4 we have developed optimal control strategy for this model. We have constructed the objective functional to minimize the infected population and associated costs. We have also constructed the Lagrangian and Hamiltonian for optimal control problem. We developed associated adjoint equations, transversality conditions and optimality equation for the optimal problem. We simulated this optimal control problem consisting of six ordinary differential equations having three state equations and three adjoint equations along with boundary conditions. We have simulated this optimal control problem using Forward-Backward Sweep Method discussed in [31] and in section 4.7. In Fig. 5 we have simulated the susceptible population versus time (in years). Susceptible population without control is represented by dashed blue line and with control represented by green dotted line. Simulations demonstrate that susceptible population is decreased with the application of control. In Fig. 6 we have simulated infected population versus time (in years). Infected population without control is represented by red dashed line and with control represented by green dotted line. Infected population is also significantly reduced with the application of control. In Fig. 7 we have simulated the recovered population versus time(in years). Recovered population without control is represented by green dashed line and with control represented by green dotted line. Recovered population with control is increased. In Fig. 8 we have simulated the control versus time and the graph shows that we must control the disease at the beginning in order to reduce its spread. In Fig. 9 we have simulated the same scenario but varied the weight factor A through values 1,2,3 and 4. Graph shows as we increase the values of A, the amount of control increases. In Fig. 10 we have again simulated the control versus time but at this time we have varied values of weight factor B through the values 0.001, 0.002, 0.003 and 0.004. Simulations reveal that when we increase the weight factor B the amount of the control u decreases. The control variable u for the associated weight factor B=0.001 is much larger than the other three weight factors. Thus simulations of our optimal control problem agree with theoretical interpretations. We wind up our discussion by narrating

some important measures that must be taken urgently in order to control this disease.
Major challenges around the world to control pertussis include:
1. Awareness of whooping cough disease in medical community is low. A few laboratories perform routine diagnostics tests for Bordetella Pertussis [12]. Accurate laboratory tests are needed for diagnosis of pertussis patients. Currently available diagnosing methods include culture, direct fluorescent antigen (DFA) tests, serology and nucleic acid amplification assays such as polymerase chain reaction(PCR). Culture is specific but insensitive and time consuming. PCR assays are faster and highly sensitive. PCR is included in the Center for Disease Control and Prevention(CDC) and World Health Organization(WHO) laboratory definition of confirmed cases. Recently its usage in epidemiological surveillance has increased due to better capacity to measure the impact of disease on community and to improve studies of vaccine efficacy [9].
2. To enhance the vaccine coverage over 90% worldwide provide first booster and primary vaccination on time.
3. To introduce a hospitalized surveillance that include specific clinical and biological diagnoses such as culture and specific $RT - PCR$. The surveillance is a key part of the public health response to control whooping cough. Comprehensive notification is needed to assess the efficacy of vaccination programmes. Notification is necessary to monitor the incidence of disease so that future vaccination policy such as need for preschool booster can take into account any changes in the epidemiology of the disease [32].
4. To perform the microbiological surveillance and proficiency tests we should establish national centers.
5. To evaluate the duration of protection on regular bases induced by the vaccine.
6. In order to analyze precisely the evolution of epidemiology, continue basic research [33].

4.9. **Health Policies.** Vaccination has been one of the most successful and cost effective public health interventions in the last century and has saved millions of people from different diseases. In 1974, the World Health Organization (WHO) established the Expanded Program on Immunization (EPI) to ensure that all children have access to routinely recommended vaccines. In 1984, the EPI was launched in Iran as one of the main components of Primary Health Care (PHC). The coverage of vaccination in Iran at the beginning of the EPI was less than 40% which increased to 99% by 2011. Iran has achieved considerable success in the health sector including vaccination against communicable diseases during the past decades. Between 1990 and 2010, the life expectancy has increased from 64.6 to 71.6 years for males and from 71 to 77.8 years, for females. According to WHO estimation in 2008, 1.5 million deaths among children under 5 years were due to diseases that could be prevented by vaccines recommended through the EPI. This group is the cause of 17% of global mortality in under aged 5. Worldwide under 5 mortality has dropped from 11.9 million deaths in 1990 to 7.7 million deaths in 2010. In the Eastern Mediterranean Region, about 1.24 million children under five years of age died in 2008. Approximately 20% of these deaths are attributed to diseases for which potent vaccines are available. Under 5 mortality rate in Iran has reduced about 83%, from 183.1 to 31.1 per 1000 from 1970 to 2010. Infant mortality rate has also fallen by 49% (53.1 to 27.1 per 1000) during this period. Since the public health importance of different diseases cannot be sufficiently compared

only based on their morbidity and mortality data, it is recommended to calculate all health effects, duration and severity of diseases to estimate their total impact, namely the burden of a disease. In this regard, the Institute for Health Metrics and Evaluation (IHME) has performed a series of comprehensive systematic reviews and calculated the Global Burden of Disease (GBD) for the years 1990, 1995, 2000, 2005 and 2010[28].

4.10. **Conclusion.** We have extended the whooping cough model by incorporating vaccination rate as an external control and an increase in the amount of this vaccination rate reduced the infected population. This shows that the vaccination is very efficient factor in reducing whooping cough cases. In order to minimize infected population and cost associated with vaccination we have developed optimal control strategy. Simulations of our optimal control problem demonstrate that under the impact of external control susceptible and infected populations are decreased but recovered population is increased. Thus our developed optimal control strategy works well to control the pertussis disease. In future we need to adopt new vaccination strategies to reduce pertussis incidence in all age groups.

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