MATHEMATICAL MODELING AND COMPUTING, Vol. 10, No. 3, pp. 944–955 (2023)

Mathematical modeling and optimal control strategy for the monkeypox epidemic

El Mansouri A.[1,*], Smouni I.[1], Khajji B.[2], Labzai A.[2], Belam M.[1]

[1] *Laboratory LMACS, Sultan Moulay Slimane University, MATIC research team: Applied Mathematics and Information and Communication Technologies, Department of Mathematics and Computer Science, Khouribga Polydisciplinary Faculty, Morocco*
[2] *Laboratory of Analysis Modeling and Simulation, Department of Mathematics and Computer Science, Faculty of Sciences Ben M'Sik, Hassan II University of Casablanca, Morocco*
[*] *Corresponding author: abdelbar.elmansouri@gmail.com*

(Received 27 October 2022; Revised 25 June 2023; Accepted 27 June 2023)

In this study, we propose a discrete time mathematical model (SEIQR) that describes the dynamics of monkeypox within a human population. The studied population is divided into five compartments: susceptible (S), exposed (E), infected (I), quarantined (Q), and recovered (R). Also, we propose an optimal strategy to fight against the spread of this epidemic. In this sense we use three controls which represent: 1) the awarness of vulnerable people through the media, civil society and education; 2) the quarantine of infected persons at home or, if required, in hospital; 3) encouraging of vaccination of susceptible persons. To characterize these optimal controls, we apply the Pontryagin's maximum principle. The optimality system is solved numerically using Matlab. Therefore, the obtained results confirm the effectiveness of the proposed optimization approach.

Keywords: *discrete mathematical model; monkeypox; optimal control; Pontryagin's Maximum Principle.*

2010 MSC: 26B10, 39A05, 39A10, 39A12, 49J10 **DOI:** 10.23939/mmc2023.03.944

1. Introduction

Monkeypox is a zoonotic viral disease [1, 2] that occurs primarily in tropical rainforest regions of central and western Africa [3, 4], with occasional spread to other regions. It is a virus of the genus Orthopoxvirus, from the family Orthopoxviridae [7]. Monkeypox was first identified in 1970 in a 9-year-old human in the Democratic Republic of Congo in an area where smallpox was uprooted in 1968 [8]. Utmost cases have been reported in pastoral areas of the Congo Basin rainforests and West Africa, and deadly cases of infection are decreasingly being reported across Central and West Africa [5]. Outside Africa, the disease was first reported in the United States of America in 2003 [6]. In May 2022, multiple cases of monkeypox were detected in numerous non-endemic countries [9], with people under 50 years old being most exposed to the threat of monkeypox due to the ceasing of compulsory smallpox vaccination.

Clinical symptoms of monkeypox are analogous to those of smallpox, which was declared defunct worldwide in 1980 [10]. The most important of these symptoms are [6]: fever, rash and enlarged lymph nodes, secondary infections, bronchitis, encephalitis and corneal infection with vision loss [11]. These symptoms can last from 2 to 4 weeks [12–15], and their effect can lead to a range of medical complications and severe health conditions. Recently, the death rate from these various injuries ranged between 3 and 6 percent [16].

To diagnose monkeypox [11, 12, 17, 18] the examining doctor excludes other rash diseases such as chicken pox, hand, foot and mouth syndrome, shingles, measles, bacterial skin infections, scabies, syphilis, and allergic skin reactions [19, 20]. In case of diagnostic doubt, biological diagnosis is resorted to by detecting the genome of monkeypox virus using the DNA amplification test for this virus (NAAT) [21].

One of the most important ways of transmitting the monkeypox virus to humans is to be in close contact with an infected person or animal or with contaminated material [22,23]. Also, the infection is transmitted among humans through close contact with sores, or with body fluids, respiratory droplets and contaminated items such as bedding [14,24–26] and also through the placenta from mother to fetus (congenital smallpox) [27–29]. In a recent study, researchers from the Spalanzani Institute announced the discovery of DNA fragments of the monkeypox virus in the semen of four infected people in Italy [30]. This troubling discovery tilts the balance in favor of the hypothesis that monkeypox virus may be sexually transmitted between spouses.

Among the effective measures to prevent monkeypox is: sensitization and vaccination. These are two important strategies to reduce the severity of this disease. The first one contributes to raising awareness of risk factors and educating people about measures they can take to reduce exposure to the virus. Through several existing studies [31], vaccination has been proven to be approximately 85 percent effective in preventing monkeypox.

Researchers in infectious diseases revealed the important role of mathematics and mathematical models in giving a clear framework for understanding the dynamics of transmission of infectious diseases among people, families, and animals. They developed simplified mathematical models and expressions that include a set of clinical and important biological information to explain the development and spread dynamics of disease [3,32–34]. In this context, numerous studies have examined the dynamics of several epidemic phenomena (alcoholism, smoking, Covid-19, obesity, etc.), for example [35–42]. To understand the dynamics of monkeypox, there are some works based on compartmental models that are widely used in epidemiology, among these contributions, we cite [43–45]. Besides the aforementioned works, we study the dynamics of monkeypox, which contains the following important additions:

- Discrete time mathematical modeling;
- Focused study on disease transmission only between humans;
- Propose control strategies separately and then combinately.

In this paper, we study the dynamics of the discrete time mathematical model of monkeypox. The goal is to reduce the spread of the epidemic, to achieve this, we propose effective strategies to minimize the number of infected people by introducing optimal control in the discrete time SEIQR model. To reach this aim, we propose three controls: the first one represents the media and education awareness and prevention strategy. It can be implemented through campaigns to raise awareness of the severity of the disease and call for preventive measures such as face masks, regular hand washing and physical distancing, etc. The second control involves quarantining people with serious infections in hospitals or health centers. The third control is through encouraging vulnerable populations to get vaccinated. We prove the existence of an optimal control. To characterize the optimal controls, we rely on the principle of Pontryagin maximum in discrete time [46]. The optimal system is solved by the iterative method.

We have organized this article as follows. In Section 2 we present our mathematical model which describes the dynamics of propagation and transmission of monkey pox. In Section 3 we expose the problem of optimal control for the proposed model and characterize the optimal controls using the principle of Pontryagin maximum in discrete time. Section 4 consists of a numerical simulation via MATLAB. The conclusion is displayed in Section 5.

2. A discrete mathematical monkeypox model

Description of the model. In this section, we present a compartmental model of the transmission dynamics of monkeypox. The study population is divided at time k into five compartments: susceptible S_k, exposed E_k, infected I_k, isolated Q_k and recovered R_k.

The following graphical representation of the proposed model is shown in Figure 1.

The compartment S: this population of susceptible individuals increases with the rate of the recruitment Λ into the population and decreases by the natural death rate μ and by the rate $\beta\frac{E_k}{N}$, where β is the probability that one susceptible individual becomes genuinely exposed to the disease.

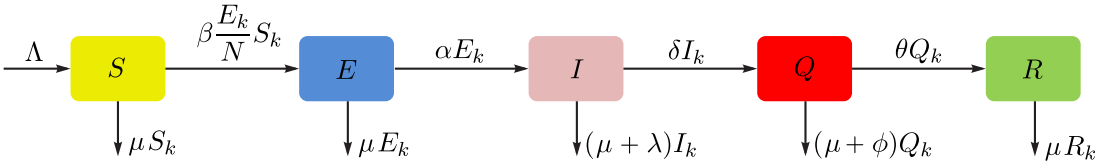


Fig. 1. Schematic representation of the model.

The compartment E: represents the number of humans exposed to the disease. Thus, we have a coming flux equal to $\beta\frac{S_kE_k}{N}$ which designates the individuals entering the exposed class. This population is decreasing because of the natural death μE_k and by the rate αE_k (illustrates the persons who are more likely to become infected).

The compartment I: consists of the individuals infected with monkeypox virus. Their number increases by the rate αE_k. This compartment decreases by natural death μI_k, by death due to the monkeypox infection λI_k and by the rate δI_k which represents the infected persons who become quarantined.

The compartment **Q**: describes confined patients, it decreases by a natural mortality rate μ and by the mortality rate ϕ due to the consequences of monkeypox infection, and it is also decreased by the rate of recovered individuals θ. Q increases by the rate δI_k where δ is the proportion of infected individuals who should be isolated and put under surveillance.

The compartment **R**: recovered patients. It is reduced by a natural mortality rate μ, and it is increased by the θ rate due to people being quarantined who recover.

The total population size at time k is denoted by N_k with $N_k = S_k + E_k + I_k + Q_k + R_k$.

Model equations. We present the monkeypox mathematical model by using the following nonlinear system of difference equations:

$$\begin{cases} S_{k+1} = \Lambda + (1-\mu)S_k - \beta\dfrac{E_k}{N}S_k, \\ E_{k+1} = \beta\dfrac{S_k}{N}E_k + (1-\mu)E_k - \alpha E_k, \\ I_{k+1} = (1-\mu-\delta-\lambda)I_k + \alpha E_k, \\ Q_{k+1} = (1-\mu-\theta-\phi)Q_k + \delta I_k, \\ R_{k+1} = (1-\mu)R_k + \theta Q_k, \end{cases} \tag{1}$$

where $S_0 \geqslant 0$, $E_0 \geqslant 0$, $I_0 \geqslant 0$, $Q_0 \geqslant 0$, and $R_0 \geqslant 0$ are the given initial states.

3. The optimal control problem

In this model, we include three controls u_k, v_k, and w_k, which consecutively represent the awareness program through media and education, encouraging the susceptible people to get vaccinated and inviting infected persons to be isolated at home or if required at the hospital. Thus, the controlled mathematical system is given by using the following system of difference equations:

$$\begin{cases} S_{k+1} = \Lambda + (1-\mu)S_k - \beta(1-u_k)\dfrac{E_k}{N}S_k - v_kS_k, \\ E_{k+1} = \beta(1-u_k)\dfrac{S_k}{N}E_k + (1-\mu)E_k - \alpha E_k, \\ I_{k+1} = (1-\mu-\delta-\lambda)I_k + \alpha E_k - w_kI_k, \\ Q_{k+1} = (1-\mu-\theta-\phi)Q_k + \delta I_k + w_kI_k, \\ R_{k+1} = (1-\mu)R_k + \theta Q_k + v_kS_k, \end{cases} \tag{2}$$

where $S_0 \geqslant 0$, $E_0 \geqslant 0$, $I_0 \geqslant 0$, $Q_0 \geqslant 0$, and $R_0 \geqslant 0$ are the given initial states.

There are three controls $u_k = (u_0, u_1, \ldots, u_{T-1})$, $v_k = (v_0, v_1, \ldots, v_{T-1})$, and $w_k = (w_0, w_1, \ldots, w_{T-1})$. The first control can be interpreted as the proportion to be adopted to awareness programs through media and education, we note that $(1-u_k)\frac{S_kE_k}{N}$ is the proportion of the susceptible people who are protected from contacting exposed people at a time step k. The second control can represent the proportion of individuals who are advised to be vaccinated, we observe that

$v_k S_k$ is the proportion of individuals who recover thanks to the vaccine at a time step k. The third control can be defined as the proportion of individuals to be quarantined. So, we note that $w_k I_k$is the proportion of the individuals move from the class of infected people towards the class of the isolated individuals at a time step k.

The challenge faced here is how to minimize the objective functional:

$$J(u,v,w) = A_T I_T + \sum_{k=0}^{T-1} \left(A_k I_k + \frac{1}{2} a_1 u_k^2 + \frac{1}{2} a_2 v_k^2 + \frac{1}{2} a_3 w_k^2 \right).$$

Where the positive parameters A_k and a_i (for $i = 1, 2, 3$) are the cost coefficients. They are selected to weigh the relative importance of S_k, E_k, I_k, Q_k, u_k, v_k, and w_k at time k. T is the final time.

In other words, we seek the optimal controls u_k^*, v_k^*, and w_k^* such that

$$J(u_k^*, v_k^*, w_k^*) = \min_{(u,v,w)\in U_{ad}^3} J(u_k, v_k, w_k). \tag{3}$$

Where U_{ad} is the set of admissible controls defined by

$$U_{ad} = \{u_k = (u_0, u_1, \ldots, u_{T-1}), v_k = (v_0, v_1, \ldots, v_{T-1}), \text{ and } w_k = (w_0, w_1, \ldots, w_{T-1}); a \leqslant u_k \leqslant b; \\ c \leqslant v_k \leqslant d; \text{ and } e \leqslant w_k \leqslant f \text{ for } k = \{0, 1, 2, \ldots, T-1\}.$$

The sufficient condition for the existence of the optimal controls (u, v, w) for the problem (2), (3) comes from the following theorem.

Theorem 1. *There exist the optimal controls (u^*, v^*, w^*) such that:*

$$J(u_k^*, v_k^*, w_k^*) = \min_{(u,v,w)\in U_{ad}^3} J(u_k, v_k, w_k) \tag{4}$$

subject to the control system (2) with initial conditions.

Proof. Since the coefficients of the state equations are bounded and there is a finite number of time steps, $S = (S_0, S_1, \ldots, S_T)$, $E = (E_0, E_1, \ldots, E_T)$, $I = (I_0, I_1, \ldots, I_T)$, $Q = (Q_0, Q_1, \ldots, Q_T)$, and $R = (R_0, R_1, \ldots, R_T)$ are uniformly bounded for all (u, v, w) in the control set U_{ad}; thus $J(u, v, w)$ is bounded for all $(u, v, w) \in U_{ad}^3$. Since $J(u, v, w)$ is bounded, $\inf_{(u,v,w)\in U_{ad}^3} J(u, v, w)$ is finite, and there exists a sequence $(u^j, v^j, w^j) \in U_{ad}^4$ such that $\lim_{j\to+\infty} J(u^j; v^j; w^j) = \inf_{(u,v,w)\in U_{ad}^3} J(u, v, w)$ and corresponding sequences of states S^j, E^j, I^j, Q^{-j}, and R^j. Since there is a finite number of uniformly bounded sequences, there exist $(u^*, v^*, w^*) \in U_{ad}^3$ and S^*, E^*, I^*, Q^* and $R^* \in IR^{T+1}$ such that on a subsequence, $(u^j, v^j, w^j) \to (u^*, v^*, w^*)$, $S^j \to S^*$, $E^j \to E^*$, $I^j \to I^*$, $Q^j \to Q^*$, and $R^j \to R^*$. Finally, due to the finite dimensional structure of system (2) and the objective function $J(u, v, w)$; (u^*, v^*, w^*) is an optimal control with corresponding states S^*, E^*, I^*, Q^*, and R^*. Therefore $\inf_{(u,v,w)\in U_{ad}^3} J(u, v, w)$ is achieved. ∎

We use the discrete version of Pontryagin's Maximum Principle [46–51]. The key trick is to introduce the adjoint function to attach the system of difference equations to the objective functional causing the formation of a function named the Hamiltonian. This principle transforms the problem of finding the control to optimize the objective functional subject to the state of difference equation with initial condition to find the control to optimize the Hamiltonian pointwise. There is the Hamiltonian H_k at time step k, defined by

$$H_k = A_k I_k + \frac{a_1}{2} u_k^2 + \frac{a_2}{2} v_k^2 + \frac{a_3}{2} w_k^2 + \sum_{i=1}^{5} \zeta_{i,k+1} f_{i,k+1}.$$

Where $f_{i,k+1}$ is the right side of the system of difference equations (2) of the i^{th} state variable at time step $k + 1$.

Theorem 2. *Given the optimal controls $(u^*, v^*, w^*) \in U_{ad}^3$ and the solutions S^*, E^*, I^*, Q^*, and R^* of the corresponding state system (2), there exist adjoint functions $\zeta_{1,k}$, $\zeta_{2,k}$, $\zeta_{3,k}$, $\zeta_{4,k}$ and $\zeta_{5,k}$*

satisfying

$$\begin{aligned}
\zeta_{1,k} &= \zeta_{1,k+1}(1-\mu) + \beta(1-u_k)\frac{E_k}{N}(\zeta_{2,k+1}-\zeta_{1,k+1}) + v_k(\zeta_{5,k+1}-\zeta_{1,k+1}),\\
\zeta_{2,k} &= \zeta_{2,k+1}(1-\mu) + (\zeta_{2,k+1}-\zeta_{1,k+1})\,\beta(1-u_k)\frac{S_k}{N} + \alpha(\zeta_{3,k+1}-\zeta_{2,k+1}),\\
\zeta_{3,k} &= A_k + \zeta_{3,k+1}(1-\mu-\lambda) + (\zeta_{4,k+1}-\zeta_{3,k+1})(w_k+\delta),\\
\zeta_{4,k} &= (\zeta_{5,k+1}-\zeta_{4,k+1})\theta + \zeta_{4,k+1}(1-\mu-\phi),\\
\zeta_{5,k} &= \zeta_{5,k+1}(1-\mu).
\end{aligned} \tag{5}$$

With the transversality conditions at time T: $\zeta_{1,T}=\zeta_{2,T}=\zeta_{4,T}=\zeta_{5,T}=0$, and $\zeta_{3,T}=A_T$.

Furthermore, for $k=0,1,2,\ldots,T-1$ the optimal controls u_k^*, v_k^*, and w_k^* are given by

$$\begin{aligned}
u_k^* &= \min\left[b; \max\left(a, \frac{\beta E_k}{a_1 N}\left[(\zeta_{2,k+1}-\zeta_{1,k+1})\,S_k\right]\right)\right],\\
v_k^* &= \min\left[d; \max(c, \frac{1}{a_2}(\zeta_{1,k+1}-\zeta_{5,k+1})S_k)\right],\\
w_k^* &= \min\left[f; \max\left(e, \frac{1}{a_3}\left[\zeta_{3,k+1}-\zeta_{4,k+1})I_k\right]\right)\right].
\end{aligned} \tag{6}$$

Proof. The Hamiltonian at time step k is given by

$$\begin{aligned}
H_k &= A_k I_k + \frac{a_1}{2}u_k^2 + \frac{a_2}{2}v_k^2 + \frac{a_3}{2}w_k^2\\
&\quad + \zeta_{1,k+1}f_{1,k+1} + \zeta_{2,k+1}f_{2,k+1} + \zeta_{3,k+1}f_{3,k+1} + \zeta_{4,k+1}f_{4,k+1} + \zeta_{5,k+1}f_{5,k+1}\\
&= A_k I_k + \frac{a_1}{2}u_k^2 + \frac{a_2}{2}v_k^2 + \frac{a_3}{2}w_k^2 + \zeta_{1,k+1}\left[\Lambda + (1-\mu)S_k - \beta(1-u_k)\frac{E_k}{N}S_k - v_k S_k\right]\\
&\quad + \zeta_{2,k+1}\left[\beta(1-u_k)\frac{E_k}{N}S_k + (1-\mu)E_k - \alpha E_k\right] + \zeta_{3,k+1}\left[(1-\mu-\delta-\lambda)I_k + \alpha E_k - w_k I_k\right]\\
&\quad + \zeta_{4,k+1}\left[(1-\mu-\theta-\phi)Q_k + \delta I_k + w_k I_k\right] + \zeta_{5,k+1}\left[(1-\mu)R_k + \theta Q_k + v_k S_k\right].
\end{aligned} \tag{7}$$

For $k=0,1,\ldots,T-1$ the optimal controls u_k, v_k, and w_k can be solved from the optimality condition,

$$\frac{\partial H_k}{\partial u_k}=0, \quad \frac{\partial H_k}{\partial v_k}=0, \quad \text{and} \quad \frac{\partial H_k}{\partial w_k}=0. \tag{8}$$

That are,

$$\begin{aligned}
\frac{\partial H_k}{\partial u_k} &= a_1 u_k - \beta\frac{E_k}{N}\left(\zeta_{2,k+1}-\zeta_{1,k+1}\right)S_k = 0,\\
\frac{\partial H_k}{\partial v_k} &= a_2 v_k - \left(\zeta_{1,k+1}-\zeta_{5,k+1}\right)S_k = 0,\\
\frac{\partial H_k}{\partial w_k} &= a_3 w_k - \left(\zeta_{3,k+1}-\zeta_{4,k+1}\right)I_k = 0.
\end{aligned}$$

So, we have

$$\begin{aligned}
u_k &= \frac{\beta E_k}{a_1 N}\left(\zeta_{2,k+1}-\zeta_{1,k+1}\right)S_k,\\
v_k &= \frac{1}{a_2}(\zeta_{1,k+1}-\zeta_{5,k+1})S_k,\\
w_k &= \frac{1}{a_3}(\zeta_{3,k+1}-\zeta_{4,k+1})I_k.
\end{aligned} \tag{9}$$

By the bounds in U_{ad} of the controls, it is easy to obtain u_k^*, v_k^* and w_k^* in the form of (6). ∎

4. Numerical simulation

In this section, we present the results obtained by solving numerically the optimality system. This system consists of the state system, adjoint system, initial and final time conditions and the controls characterization. Concerning the numerical method, we apply the forward-backward sweep method to solve our system in an iterative process. We start with an initial guess for the controls at the first iteration and then before the next iteration, we update the controls by using characterization. We continue until convergence of successive iterates is achieved.

The values of the initial states and the parameters used are given in the following Table 1.

In this part, we present numerical simulation to highlight the effect of our control strategy that we have developed within the framework of fight against the spread of the monkeypox.

The numerical solution of model (2) with the following parameter values and initial values of the state variable in Table 1 is executed using MATLAB.

To detect out the best control strategy, we employ and simulate combinations of one, two, and three controls in the optimization system and examine the evolution of each state with the combination of controls applied. Our goal is to precisely specify the optimal controls for each state.

Table 1. The model parameter values and initial system states.

Initial state variable	Value	Source
S_0	4500	Estimated
E_0	3500	Estimated
I_0	500	Estimated
Q_0	80	Estimated
R_0	700	Estimated
Parameter	Value	Source
β	0.25	Estimated
α	0.095	[52]
λ	0.1	[53]
θ	0.83	[53]
δ	0.25	Estimated
Λ	400	Estimated
μ	0.02	[53]
ϕ	0.2	[54]

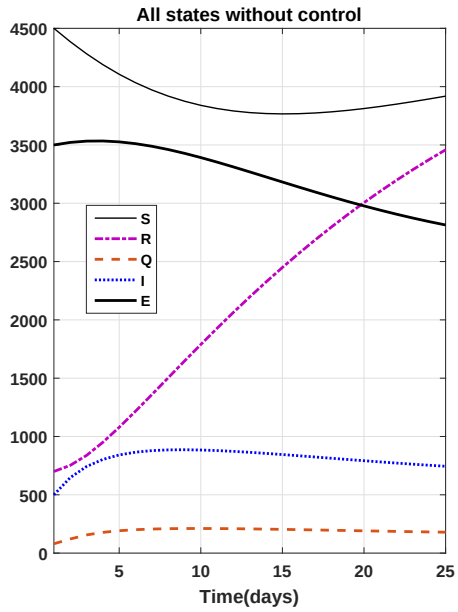
4.1. Comparison of three controls effectiveness

In order to characterize the role of each control in controlling the spread of monkeypox disease, we display the evolution of all the states (S, E, I, Q, and R) before and after the implementation of each of these controls (Figures $2a$–$2d$).

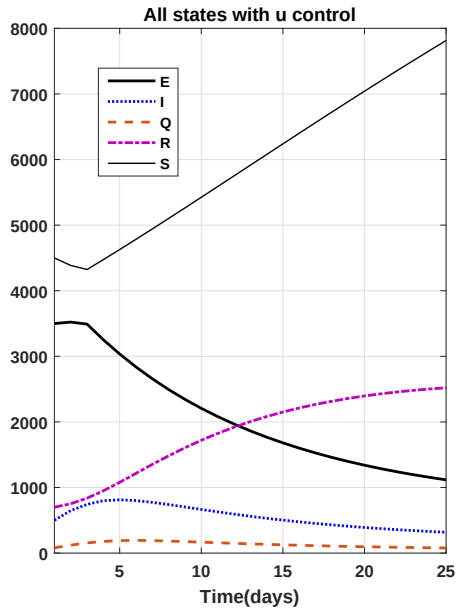
Figures $2a$–$2d$ represent the population's temporal evolution throughout all of the model's compartments (S, E, I, Q, and R).

From Figures 2, we draw the following remarks:

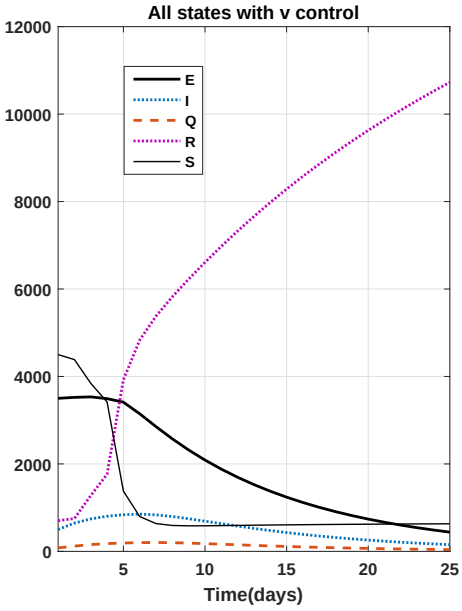
— Generally, the adoption of three control measures resulted in both a decrease in susceptible (S), exposed (E) and infected (I) cases and an increase in cured cases (R).
— The reduction in the number of people quarantined (Q) is mainly due to vaccination (Figure $2c$), because this strategy reduces the number of infected people.
— Early in the initiation of control, sensitization (w) can rapidly reduce the number of exposed cases and slowly diminish infected cases (Figure $2b$). In the first three days, the number of infections dropped by 50% thanks to quarantine (Figure $2d$).
— Vaccination is a more advantageous strategy than awareness or isolation. Indeed Figure $2c$ shows that after 25 days the disease has almost disappeared (no infected cases: $I \approx 0$), and the number of healings goes from $R = 700$ at check out to $R \approx 4000$ for five days.
— Figure $2d$ shows the effectiveness of the quarantine, especially at the onset of the disease, as the number of infected people decreased significantly on the fourth day.



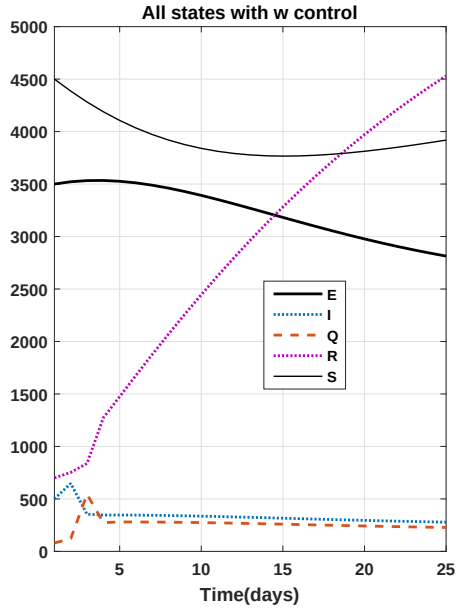
a (The evolution without any control)



b (The evolution under control u)



c (The evolution with control v)



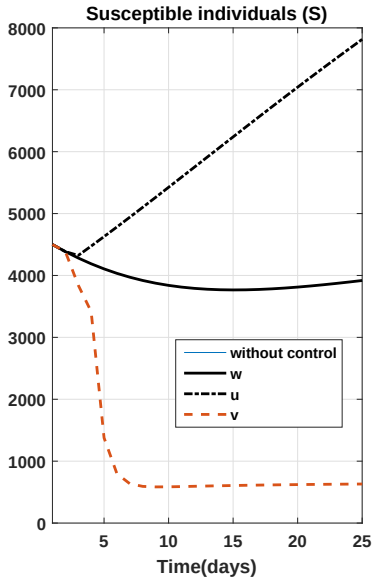
d (The evolution with control w)

Fig. 2. The evolution of all states with and without controls.

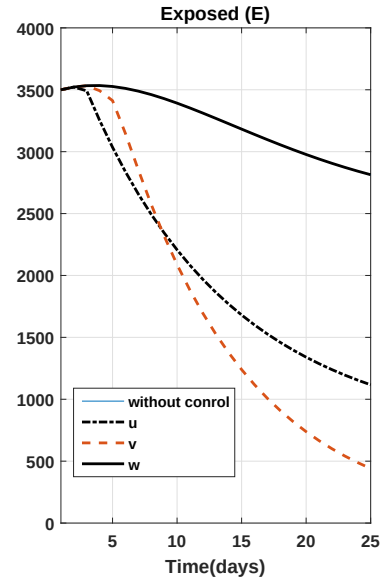
4.2. Effect of applying three controls separately

In this section, we apply three controls separately and we track the dynamics for each state when only one control (u, v or w) is applied. The simulation results are given in the following Figures $3a$–$3d$.

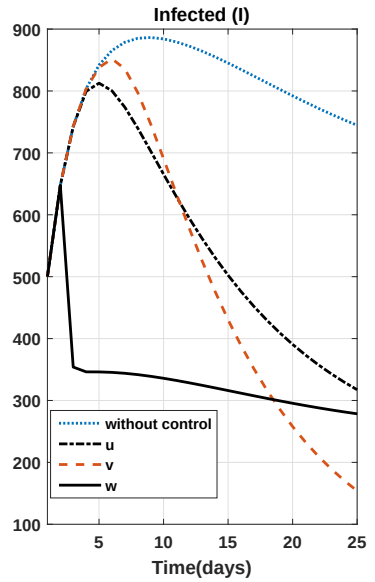
Analysis of the simulation results indicates that quarantine (w) is a control that has no effect on the development of sensitive (S) and exposed (E) cases (Figures $3a$, $3b$), however (w) represents a very effective strategy to limit infected cases number (Figure $3c$). Two controls: vaccination (v) and sensitization (u) reduce the number of exposed and infected more quickly (around the fifth day of control: Figures $3b$, $3c$). On the other hand, Figure $3d$ shows that quarantine ranks second after vaccination in terms of contribution to the increase in recovered cases (R).



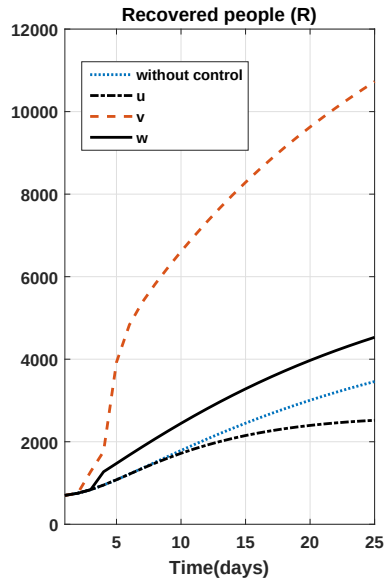
a (The evolution of susceptible cases (S) without control and with three controls u, v and w separately)



b (The development of exposed cases (E) without control and with three controls u, v and w separately)



c (The evolution of infected cases (I) without control and with three controls u, v and w separately)



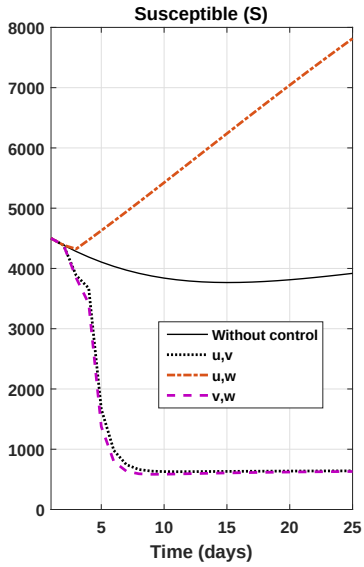
d (The progression of recovered cases (R) without control and with three controls u, v and w separately)

Fig. 3. The effect of applying three controls separately.

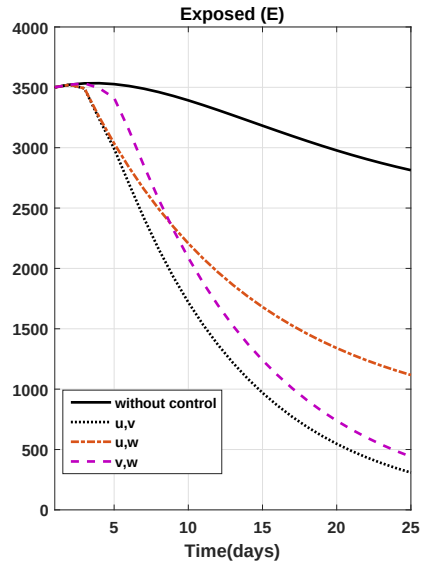
4.3. Applying the combination of two controls

In the present scenario we apply the combination of two controls each time.

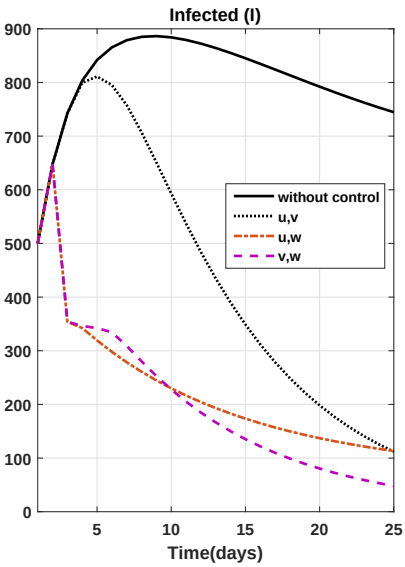
The adoption of two combined controls: vaccination and sensitization (u, v) or quarantine and vaccination (w, v) leads to almost the same results, the application of these two controls reduces the number of susceptible people (Figure 4a), exposed (Figure 4b) and the number of people infected (Figure 4c). The doublet of combined controls (u, w) effectively contributes to decreases in the number of infected persons (Figure 4b). Figure 4d shows the increase in recovered cases with these two controls. Thus, it is concluded that the control doublets (u, v) and (w, v) are effective strategies to reduce the spread of monkeypox.



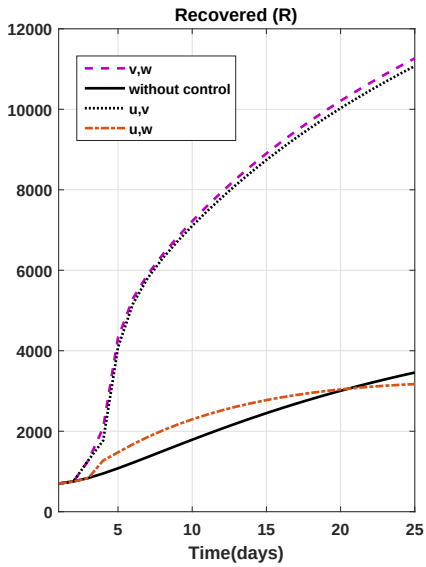
a (The evolution of sensitive cases (S) without control and with three pairs of controls (u, v); (u, w) and (v, w))



b (The development of exposed cases (E) without control and with three pairs of controls (u, v); (u, w) and (v, w))



c (The evolution of infected cases (I) without control and with three pairs of controls (u, v); (u, w) and (v, w))



d (The progression of recovered cases (R) without control and with three pairs of controls (u, v); (u, w) and (v, w))

Fig. 4. Two control strategies.

5. Conclusion

In this article, we propose a mathematical model to study the dynamics of monkeypox in human populations. We tie our model to three control measures: vaccination, awareness through media and civil society, and isolation. The optimal control problem is formulated and analyzed, and thus best control strategies are found by minimizing the number of susceptible, exposed and infected individuals, using the Pontryagin's Maximum Principle. A comparison of evolution of all states with and without controls is presented. Also, we try to study all the possible combinations between the controls and analyze all the scenarios. All strategies are effective in limiting the spread of monkeypox disease, and the choice of one over another depends on the desired goal of model control.

[1] Durski K. N., McCollum A. M., Nakazawa Y., Petersen B. W., et al. Emergence of Monkeypox — West and Central Africa, 1970–2017. Morbidity and Mortality Weekly Report. **67** (10), 306 (2018).

[2] World Health Organization (WHO). Mpox (monkeypox). `https://www.who.int/news-room/fact-sheets/detail/monkeypox` (2022).

[3] Yan X., Zou Y. Optimal and sub-optimal quarantine and isolation control in SARS epidemics. Mathematical and Computer Modelling. **47** (1–2), 235–245 (2008).

[4] Likos A. M., Sammons S. A., Olson V. A., Frace A. M., Li Y., Olsen-Rasmussen M., Davidson W., et al. A tale of two clades: monkeypox viruses. Journal of General Virology. **86** (10), 2661–2672 (2005).

[5] Yinka-Ogunleye A., Aruna O., Ogoina D., Aworabhi N., Eteng W., Badaru S., Mohammed A., et al. Reemergence of Human Monkeypox in Nigeria, 2017. Emerging Infectious Diseases. **24** (6), 1149 (2018).

[6] Centers for Disease Control and Prevention (CDC). Multistate outbreak of monkeypox – Illinois, Indiana, and Wisconsin, 2003. Morbidity and Mortality Weekly Report. **52** (23), 537–540 (2003).

[7] Sklenovská N., Van Ranst M. Emergence of monkeypox as the most important orthopoxvirus infection in humans. Frontiers in Public Health. **6**, 241 (2018).

[8] Eteng W. E., Mandra A., Doty J., Yinka-Ogunleye A., Aruna S., Reynolds M. G., McCollum A. M., Davidson W., Wilkins K., et al. Notes from the field: responding to an outbreak of monkeypox using the one health approach — Nigeria, 2017–2018. Morbidity and Mortality Weekly Report. **67** (37), 1040 (2018).

[9] Organisation panaméricaine de la Santé. VIIIe réunion ad hoc du Groupe consultatif technique (GCT) de l'OPS sur les maladies évitables par la vaccination. Briefing technique sur l'épidémie multi-pays de variole du singe, 31 mai 2022 (virtual).

[10] Grant R., Nguyen L. B., Breban R. Modelling human-to-human transmission of monkeypox. Bulletin of the World Health Organization. **98** (9), 638 (2020).

[11] Weinstein R. A., Nalca A., Rimoin A. W., Bavari S., Whitehouse C. A. Reemergence of monkeypox: prevalence, diagnostics, and countermeasures. Clinical Infectious Diseases. **41** (12), 1765–1771 (2005).

[12] Jezek Z., Szczeniowski M., Paluku K. M., Mutombo M., Grab B. Human monkeypox: confusion with chickenpox. Acta Tropica. **45** (4), 297–307 (1988).

[13] Jezek Z., Marennikova S. S., Mutumbo M., Nakano J. H., Paluku K. M., Szczeniowski M. Human monkeypox: a study of 2,510 contacts of 214 patients. Journal of Infectious Diseases. **154** (4), 551–555 (1986).

[14] Lai C.-C., Hsu C.-K., Yen M.-Y., Lee P.-I., Ko W.-C., Hsueh P.-R. Monkeypox: an emerging global threat during the COVID-19 pandemic. Journal of Microbiology, Immunology and Infection. **55** (5), 787–794 (2022).

[15] Samaranayake L., Anil S. The monkeypox outbreak and implications for dental practice. International Dental Journal. **72** (5), 589–596 (2022).

[16] Yinka-Ogunleye A., Aruna O., Dalhat M., Ogoina D., McCollum A., Disu Y., Mamadu I., Akinpelu A., et al. Outbreak of human monkeypox in Nigeria in 2017–18: a clinical and epidemiological report. The Lancet Infectious Diseases. **19** (8), 872–879 (2019).

[17] Petersen E., Kantele A., Koopmans M., Asogun D., Yinka-Ogunleye A., Ihekweazu C., Zumla A. Human monkeypox: epidemiologic and clinical characteristics, diagnosis, and prevention. Infectious Disease Clinics of North America. **33** (4), 1027–1043 (2019).

[18] Thornhill J. P., Barkati S., Walmsley S., Rockstroh J., et al. Monkeypox virus infection in humans across 16 countries — April – June 2022. New England Journal of Medicine. **387** (8), 679–691 (2022).

[19] Foster S. O., Brink E. W., Hutchins D. L., Pifer J. M., Lourie B., Moser C. R., Cummings E. C., et al. Human monkeypox. Bulletin of the World Health Organization. **46** (5), 569–576 (1972).

[20] Ježek Z., Szczeniowski M., Paluku K. M., Mutombo M. Human monkeypox: clinical features of 282 patients. Journal of Infectious Diseases. **156** (2), 293–298 (1987).

[21] Cheema A. Y., Ogedegbe O. J., Munir M., Alugba G., Ojo T. K. Monkeypox: A Review of Clinical Features, Diagnosis, and Treatment. Cureus. **14** (7), e26756 (2022).

[22] Desenclos J.-C., De Valk H. Emergent infectious diseases: importance for public health, epidemiology, promoting factors, and prevention. Médecine et Maladies Infectieuses. **35** (2), 49–61 (2005).

[23] Artois M., Caron A., Leighton F. A., Bunn C., Vallat B. La faune sauvage et les maladies émergentes. Rev. sci. tech. Off. int. Epiz. **25** (3), 897–912 (2006).

[24] Vaughan A., Aarons E., Astbury J., Balasegaram S., Beadsworth M., Beck C. R., Chand M., O'Connor C., Dunning J., Ghebrehewet S., Harper N. et al. Two cases of monkeypox imported to the United Kingdom, September 2018. Eurosurveillance. **23** (38), 1800509 (2018).

[25] Uwishema O., Adekunbi O., Peñamante C. A., Bekele B. K., Khoury C., Mhanna M., Nicholas A., Adanur I., Dost B., Onyeaka H. The burden of monkeypox virus amidst the Covid-19 pandemic in Africa: A double battle for Africa. Annals of Medicine and Surgery. **80**, 104197 (2022).

[26] Koenig K. L., Beÿ C. K., Marty A. M. Monkeypox 2022 Identify-Isolate-Inform: A 3I Tool for frontline clinicians for a zoonosis with escalating human community transmission. One Health. **15**, 100410 (2022).

[27] Dashraath P., Nielsen-Saines K., Mattar C., Musso D., Tambyah P., Baud D. Guidelines for pregnant individuals with monkeypox virus exposure. The Lancet. **400** (10345), 21–22 (2022).

[28] George L. A., Regi A. Monkey Pox: An Upcoming Threat in World; A Systematic Review. International Journal of Research Publication and Reviews. **3** (7), 2202–2206 (2022).

[29] Mbala P. K., Huggins J. W., Riu-Rovira T., Ahuka S. M., Mulembakani P., Rimoin A. W., Martin J. W., Muyembe J. J. Maternal and fetal outcomes among pregnant women with human monkeypox infection in the Democratic Republic of Congo. Journal of Infectious Diseases. **216** (7), 824–828 (2017).

[30] Antinori A., Mazzotta V., Vita S., Carletti F., Tacconi D., Lapini L. E., D'Abramo A., Cicalini S., Lapa D., Pittalis S., Puro V. Epidemiological, clinical and virological characteristics of four cases of monkeypox support transmission through sexual contact, Italy, May 2022. Eurosurveillance. **27** (22), 2200421 (2022).

[31] Islam Q. T. Monkeypox – A New Threat for the Globe! Journal of Medicine. **23** (2), 104–105 (2022).

[32] Kermack W. O., McKendrick A. G. A contribution to the mathematical theory of epidemics. Proceedings of the Royal Society of London. Series A. **115** (772), 700–721 (1927).

[33] Kumar A., Srivastava P. K. Vaccination and treatment as control interventions in an infectious disease model with their cost optimization. Communications in Nonlinear Science and Numerical Simulation. **44**, 334–343 (2017).

[34] Sari R. A., Habibah U., Widodo A. Optimal control on model of SARS disease spread with vaccination and treatment. Journal of Experimental Life Science. **7** (2), 61–68 (2017).

[35] El Mansouri A., Labzai A., Belam M., Rachik M. Mathematical modeling and optimal control strategy for the obesity epidemic. Communications in Mathematical Biology and Neuroscience. **2022**, 20 (2022).

[36] Essounaini A., Labzai A., Laarabi H., Rachik M. Mathematical modeling and optimal control strategy for a discrete time model of COVID-19 variants. Communications in Mathematical Biology and Neuroscience. **2022**, 25 (2022).

[37] Khajji B., Kada D., Balatif O., Rachik M. A multi-region discrete time mathematical modeling of the dynamics of Covid-19 virus propagation using optimal control. Journal of Applied Mathematics and Computing. **64**, 255–281 (2020).

[38] Labzai A., Kouidere A., Balatif O., Rachik M. Stability analysis of mathematical model new corona virus (COVID-19) disease spread in population. Communications in Mathematical Biology and Neuroscience. **2020**, 41 (2020).

[39] Khajji B., Boujallal L., Elhia M., Balatif O., Rachik M. A fractional-order model for drinking alcohol behaviour leading to road accidents and violence. Mathematical Modeling and Computing. **9** (3), 501–518 (2022).

[40] Sadki M., Harroudi S., Allali K. Dynamical analysis of an HCV model with cell-to-cell transmission and cure rate in the presence of adaptive immunity. Mathematical Modeling and Computing. **9** (3), 579–593 (2022).

[41] Bounkaicha C., Allali K., Tabit Y., Danane J. Global dynamic of spatio-temporal fractional order SEIR model. Mathematical Modeling and Computing. **10** (2), 299–310 (2023).

[42] Elkaf M., Allali K. Fractional derivative model for tumor cells and immune system competition. Mathematical Modeling and Computing. **10** (2), 288-298 (2023).

[43] Peter O. J., Kumar S., Kumari N., Oguntolu F. A., et al. Transmission dynamics of Monkeypox virus: a mathematical modelling approach. Modeling Earth Systems and Environment. **8**, 3423–3434 (2022).

[44] Yuan P., Tan Y., Yang L., Aruffo E., Ogden N. H., Bélair J., Heffernan J., Arino J., Watmough J., Carabin H., Zhu H. Assessing transmission risks and control strategy for monkeypox as an emerging zoonosis in a metropolitan area. Journal of Medical Virology. **95** (1), e28137 (2023).

[45] Usman S., Adamu I. I. Modeling the transmission dynamics of the monkeypox virus infection with treatment and vaccination interventions. Journal of Applied Mathematics and Physics. **5** (12), 2335 (2017).

[46] Hwang C. L., Fan L. T. A discrete version of Pontryagin's maximum principle. Operations Research. **15** (1), 139–146 (1967).

[47] Zeb A., Zaman G., Momani S. Square-root dynamics of a giving up smoking model. Applied Mathematical Modelling. **37** (7), 5326–5334 (2013).

[48] Zhang D. C., Shi B. Oscillation and global asymptotic stability in a discrete epidemic model. Journal of Mathematical Analysis and Applications. **278** (1), 194–202 (2003).

[49] Ding W., Hendon R., Cathey B., Lancaster E., Germick R. Discrete time optimal control applied to pest control problems. Involve, a Journal of Mathematics. **7** (4), 479–489 (2014).

[50] Pontryagin L. S., Boltyanskii V. G., Gamkrelidze R. V., Mishchenko E. F. The Mathematical Theory of Optimal Processes. Wiley, New York (1962).

[51] Rafal M. D., Stevens W. F. Discrete dynamic optimization applied to on-line optimal control. AIChE Journal. **14** (1), 85–91 (1968).

[52] Von Magnus P., Andersen E. K., Petersen K. B., Birch-Andersen A. A pox-like disease in cynomolgus monkeys. Acta Pathologica Microbiologica Scandinavica. **46**, 156–176 (1959).

[53] The Eagle Online. Breaking: Monkey pox: FG confirms only four cases. `https://theeagleonline.com.ng/breaking-monkey-pox-fg-confirms-only-four-cases/` (2017).

[54] Odom M. R., Hendrickson R. C., Lefkowitz E. J. Poxvirus protein evolution: Family wide assessment of possible horizontal gene transfer events. Virus Research. **144** (1–2), 233–249 (2009).

Математичне моделювання та оптимальна стратегія боротьби з епідемією віспи мавп

Ель Мансурі А.[1], Смуні І.[1], Хаджі Б.[2], Лабзай А.[2], Белам М.[1]

[1] *Лабораторія LMACS, Університет Султана Мулая Слімана, дослідницька група MATIC: прикладна математика та інформаційно-комунікаційні технології, кафедра математики та інформатики, полідисциплінарний факультет Хурібга, Марокко*
[2] *Лабораторія аналізу, моделювання та симуляції, кафедра математики та інформатики, факультет наук Бен М'Сік, Університет Хасана II Касабланки, Марокко*

У цьому дослідженні запропоновано математичну модель з дискретним часом (SEIQR), яка описує динаміку віспи мавп у людській популяції. Досліджувана популяція поділяється на п'ять компартментів: чутливі (S), заражені (E), інфіковані (I), карантиновані (Q) та одужалі (R). Також запропоновано оптимальну стратегію боротьби з поширенням цієї епідемії. У цьому сенсі використовується три елементи керування, які представляють: 1) інформованість вразливих груп через ЗМІ, громадянське суспільство та освіту; 2) карантин інфікованих осіб вдома або, якщо потрібно, у лікарні; 3) заохочення до вакцинації сприйнятливих осіб. Щоб охарактеризувати ці оптимальні керування, застосовано принцип максимуму Понтрягіна. Система оптимальності розв'язана чисельно за допомогою Matlab. Отримані результати підтверджують ефективність запропонованого оптимізаційного підходу.

Ключові слова: *дискретна математична модель; віспа мавп; оптимальний контроль; принцип максимуму Понтрягіна.*