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ORIGINAL ARTICLE

Optimal Implementation of Intervention to Control the Self-harm Epidemic

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Abstract

Objectives: Deliberate self-harm (DSH) of a young person has been a matter of growing concern to parents and policymakers. Prevention and early eradication are the main interventional techniques among which prevention through reducing peer pressure has a major role in reducing the DSH epidemic. Our aim is to develop an optimal control strategy for minimizing the DSH epidemic and to assess the efficacy of the controls.

Methods: We considered a deterministic compartmental model of the DSH epidemic and two interventional techniques as the control measures. Pontryagin's Maximum Principle was used to mathematically derive the optimal controls. We also simulated the model using the forward-backward sweep method.

Results: Simulation results showed that the controls needed to be used simultaneously to reduce DSH successfully. An optimal control strategy should be adopted, depending on implementation costs for the controls.

Conclusion: The long-term success of the optimum control depends on the implementation cost. If the cost is very high, the control could be used for a short term, even though it fails in the long run. The control strategy, most importantly, should be implemented as early as possible to attack a comparatively fewer number of addicted individuals.

1. Introduction

Deliberate self-harm (DSH) is an activity of an individual in which the sole intention is to cause self-harm, although not to commit suicide; however, sometimes acute medical situations arise [1]. More scientific definitions of DSH are available in the literature [2—4]. It is associated with the physiology and psychology of the affected individual. In the past decade, it has become a pronounced health concern among adolescents and young adults all over the world [5]. You et al [6] and Whitlock [7] addressed it as a contagious social issue. Deliberate self-harm is associated with depression, anxiety, poor school performance, family conflict [8],

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sexual abuse [9], and other factors. Mathematical modeling of epidemics is a constructive tool to assess the evolution of contagious problems and to discover strategies to reduce or eradicate the epidemic of contagious problems.

The techniques of mathematical modeling have recently been utilized in problems related to human behaviors and social interaction. For example, the theory for social behavior of individuals subjected to the social interaction was developed by Wirl and Feichtinger [10] to address the problem of obesity. Mathematical models have also been used to study the obesity epidemic [11−16]. Such ideas are also used to study smoking dynamics mathematically [17−22]. In addition, Li [23] used Bayesian proportional hazard analysis to deal with school drop-out. Porco et al [24] presented two models for antibiotic abuse. The techniques of mathematical modeling are likewise being exercised to understand contagious social and behavioral epidemics from diverse viewpoints.

Do and Lee [25] proposed a mathematical model for the self-harm epidemic and analyzed it mathematically. By considering self-harm as a contagious disease, they formulated a deterministic compartmental model. In the present study, we introduced time-dependent controls into the Do and Lee model [25], and extend an optimal control problem to understand cost-effective strategies for reducing DSH.

2. Materials and methods

2.1. Basic model

The Lee and Do model [25] without a demographic effect reduces to the following formula:

$$\begin{aligned}
\frac{dS}{dt} &= -\alpha S\frac{A+P}{N}\\
\frac{dA}{dt} &= \alpha S\frac{A+P}{N} + \omega P - \beta\frac{A}{N}(P+R) - \theta A - \eta A\\
\frac{dP}{dt} &= \beta\frac{A}{N}(P+R) + \theta A - \rho P - \omega P\\
\frac{dR}{dt} &= \eta A + \rho P
\end{aligned} \tag{1}$$

In this paper, we note that the whole population $N(t) = S(t)+A(t)+P(t)+R(t)$ is constant. The variable $N(t)$ includes only adolescents and young adults between the ages 12 years and 23 years and is divided into four classes: susceptible, $S(t)$; addicted, $A(t)$; in treatment $P(t)$; and recovered, $R(t)$. Individuals of $S(t)$ who try DSH move to $A(t)$ with the per capita transition rate, α, which is peer pressure on susceptible individuals in $A(t)$ and $P(t)$. Individuals repeating DSH remain in $A(t)$, but individuals who stop DSH move to $R(t)$ at the rate η. This is the rate at which individuals in $A(t)$ stop DSH without any treatment program or individuals who tried DSH only once and transferred to $R(t)$. When individuals in $A(t)$ seek treatment, they go to $P(t)$ at the rate of $\beta(P+R)/N+\theta$. In this equation, β is peer pressure due to individuals in $P(t)$ and $R(t)$ to the individuals in $A(t)$, and θ is the intervention rate at which addicted individuals seek treatment. If the treatment fails, individuals may go back to $A(t)$ from $P(t)$ at the rate ω. Individuals in $P(t)$ recover at rate ρ and move to $R(t)$. The values of α and β may be different, but in this study they are considered the same for homogeneous mixing. Among all of these parameters, the system is most sensitive to α and η [19]. The values of η may also increase or decrease, depending on the positive or negative influence of the Internet [26]. Furthermore, the individual who performs DSH once, seeks more serious injury for the next DSH episode [27]. Therefore, a control strategy should be concerned with prevention through controlling peer pressure α and early intervention η.

2.2. Optimal control

To shrink the DSH epidemic, we adopted two control strategies with the intent of increasing prevention [i.e., decreasing α and increasing early intervention (η)]. However, maintaining constant control over time is impractical. Therefore, our aim is to show that it is possible to implement time-dependent control techniques while minimizing the addicted population with minimum cost of implementation of the control measures.

To develop an optimal control problem for the aforementioned purpose, two control terms were introduced into the basic model (1). The model reduces to the following formula:

$$\begin{aligned}
\frac{dS}{dt} &= -\alpha(1-u_1(t))S\frac{A+P}{N}\\
\frac{dA}{dt} &= \alpha(1-u_1(t))S\frac{A+P}{N} + \omega P - \beta\frac{A}{N}(P+R)\\
&\quad -\theta A - (\eta + \mu u_2(t))A\\
\frac{dP}{dt} &= \beta\frac{A}{N}(P+R) + \theta A - \rho P - \omega P\\
\frac{dR}{dt} &= (\eta + \mu u_2(t))A + \rho P
\end{aligned} \tag{2}$$

In this equation $N = S(t)+A(t)+P(t)+R(t)$ is constant.

The control variables, $u_1(t)$ and $u_2(t)$, represent the quantity of intervention associated with the parameters α and η, respectively at time t. The factor of $1-u_1(t)$ reduces the per capita transition rate α from $S(t)$ to $A(t)$. The per capita transition rate η from P to R increases at a rate that is proportional to $u_2(t)$ in which $\mu > 0$ is the proportionality constant.

We define our control set as follows:

$$U := \{(u_1(t), u_2(t)) : u_1(t) \text{ and } u_2(t) \text{ is Lebesgue measurable on } [0,T]; 0 \le u_1(t), u_2(t) \le 1\}$$

An optimal control problem with the objective cost functional can be given by

$$J(u_1, u_2) = \int_0^T \left(A_c A(t) + \frac{B_1}{2} u_1^2(t) + \frac{B_2}{2} u_2^2(t) \right) dt, \quad 0 \le u_1(t), u_2(t) \le 1 \tag{3}$$

which is subject to the state equation (2). In the objective cost functional, the quantities A_c, B_1 and B_2 represent the weight constants. The costs associated with the controls of the transition rates are described by the terms $B_1 u_1^2(t)$ and $B_2 u_2^2(t)$. The variable A_c represents the degree of negative influence on the society by each addicted individual. The goal is to minimize the population $A(t)$ of addicted individuals and the implementation cost of the controls. Therefore, we looked for optimal control functions (u_1^*, u_2^*) so that:

$$J\left(u_1^*, u_2^*\right) = \min\{J(u_1, u_2) : (u_1, u_2) \in U\}, \tag{4}$$

which is subject to the system (2). To approach an optimal solution, we first defined the Hamiltonian function H for problems (2) and (3), and then used Pontryagin's Maximum Principle [28] to derive the characterization for the optimal control. The principle converts problems (2) and (3) into a problem of minimizing pointwise a Hamiltonian, H, with respect to u_1 and u_2. The integrand of the objective functional along with the four right hand sides of the state equations constitutes the Hamiltonian for our problem. So the Hamiltonian is given by,

$$\mathsf{H}(\mathbf{X}(t), \mathbf{u}(t), \boldsymbol{\Lambda}(t)) = A_c A(t) + \frac{B_1}{2} u_1^2(t) + \frac{B_2}{2} u_2^2(t) + \boldsymbol{\Lambda}(t) \left(\frac{d\mathbf{X}(t)}{dt} \right)^T, \tag{5}$$

in which $\mathbf{X}(t) = (S(t), A(t), P(t), R(t))$, $\mathbf{u}(t) = (u_1(t), u_2(t))$ and $\boldsymbol{\Lambda}(t) = (\lambda_1(t), \lambda_2(t), \lambda_3(t), \lambda_4(t))$.

Therefore, $\mathsf{H}(\mathbf{X}(t), \mathbf{u}(t), \boldsymbol{\Lambda}(t))$ becomes:.

$$\begin{aligned}
\mathsf{H}(\mathbf{X}(t), \mathbf{u}(t), \boldsymbol{\Lambda}(t)) = {} & A_c A(t) + \frac{B_1}{2} u_1^2(t) + \frac{B_2}{2} u_2^2(t) \\
& + \lambda_1(t) \left(-\alpha(1 - u_1(t)) S(t) \frac{A(t) + P(t)}{N} \right) \\
& + \lambda_2(t) \begin{pmatrix} \alpha(1 - u_1(t)) S(t) \dfrac{A(t) + P(t)}{N} + \omega P(t) \\ -\beta \dfrac{A(t)}{N} (P(t) + R(t)) - \theta A(t) - (\eta + \mu u_2(t)) A(t) \end{pmatrix} \\
& + \lambda_3(t) \left(\beta \frac{A(t)}{N} (P(t) + R(t)) + \theta A(t) - \rho P(t) - \omega P(t) \right) + \lambda_4(t) ((\eta + \mu u_2(t)) A(t) + \rho P(t))
\end{aligned} \tag{6}$$

Let $S^*(t)$, $A^*(t)$, $P^*(t)$, $R^*(t)$ be optimal state solutions with associated optimal control variables $u_1^*(t)$ and $u_2^*(t)$ for the optimal control problems (2) and (3). Adjoint variables $\lambda_1(t)$, $\lambda_2(t)$, $\lambda_3(t)$, $\lambda_4(t)$ would then exist that satisfy

$$\begin{aligned}
\lambda_1'(t) &= (\lambda_1(t) - \lambda_2(t)) \alpha \left(1 - u_1^*(t)\right) \frac{A^*(t) + P^*(t)}{N} \\
\lambda_2'(t) &= -A_c + (\lambda_1(t) - \lambda_2(t)) \alpha \left(1 - u_1^*(t)\right) \frac{S^*(t)}{N^*} + (\lambda_2(t) - \lambda_3(t)) \left(\beta \frac{P^*(t) + R^*(t)}{N^*} + \theta \right) + (\lambda_2(t) - \lambda_4(t)) \left(\eta + \mu u_2^*(t)\right) \\
\lambda_3'(t) &= (\lambda_1(t) - \lambda_2(t)) \alpha \left(1 - u_1^*(t)\right) \frac{S^*(t)}{N^*} + (\lambda_2(t) - \lambda_3(t)) \left(\beta \frac{A^*(t)}{N^*} - \omega \right) + (\lambda_3(t) - \lambda_4(t)) \rho \\
\lambda_4'(t) &= (\lambda_2(t) - \lambda_3(t)) \beta \frac{A^*(t)}{N^*}
\end{aligned}$$

with the transversality condition (or the boundary condition)

$$\lambda_j(T)=0, j=1,2,3,4. \tag{7}$$

Furthermore, the optimal controls $u_1^*(t)$ and $u_2^*(t)$ are given by

$$u_1^*(t)=\min\left\{1,\max\left\{0,\frac{1}{B_1}\left(\frac{\alpha S^*(A^*+P^*)(\lambda_2-\lambda_1)}{N}\right)\right\}\right\}$$
$$u_2^*(t)=\min\left\{1,\max\left\{0,\frac{\mu A^*(\lambda_2-\lambda_4)}{B_2}\right\}\right\} \tag{8}$$

(Please refer to Appendix 1 for the formulation in detail.)

3. Results

To find the optimal control strategy for controlling the self-harm epidemic of adolescents and young adults in institutional settings, an optimal control problem has been established, based on the model proposed by Do and Lee [25]. The optimal control problem consists of eight ordinary differential equations describing states and adjoint variables with two control variables. The state variables are “susceptible”, S; “addicted”, A; “in treatment”, P; and “recovered”, R; the control u_1 is associated with reducing peer pressure and the control u_2 is associated with early intervention. As a general shortcoming, full efficiency of the controls is unfeasible. To choose an upper bound for the controls, we considered the study of Dunlop et al [29] in which they found that 79% of young people learned about suicide from the newspaper or from friends and family, and 59% of them learned from an online source. We assumed the upper bound of each of the controls was 0.6. The rate constant μ is chosen to be 0.01 in accordance with the value of η. Using the parameter values summarized in Table 1, the problem is solved numerically by the forward-backward sweep method [30], along with the fourth order Runge-Kutta algorithm, which is subject to a wide range of plausible values of weight factors A_c, B_1 and B_2 because the weights should vary from group to group. For an institutional setting, we considered that the total population is $N(0) = 10000$ with $S(0) = 8700$, $A(0) = 900$, $P(0) = 100$, $R(0) = 300$. Time span for the simulation is [0, T], in which T = 60 months (i.e., 5 years).

Figure 1 depicts the dynamics of states with and without the controls when the weight factors are $A_c = 1$, $B_1 = 500$, $B_2 = 500$. The rightmost graphs in Figure 1 show the time-dependent control strategy in which we see that the controls u_1 and u_2 should be implemented at maximum for a long period and then gradually decreased to zero. The controls work fairly well for reducing the number of addicted population.

Let t_1 and t_2 be the period of time for maximum implementation of the optimal controls u_1 and u_2, respectively. The time t_1 and t_2 may depend on the weights A_c, B_1, B_2 and the initial conditions as well. Figure 2 depicts the changes of t_1 and t_2 with $B_1 = 100-1000$ and $A_c = 1-100$ while keeping $B_2 = 200$ fixed. Figure 2A shows that for $A_c > 60$, the time t_1 is the same for all B_1; however, for smaller A_c; the effect of B_1 to the change of t_1 is more pronounced. A smaller B_1 results in a higher t_1 and vice versa. Figure 2B shows that t_2 increases with A_c but it is not affected by B_1. Figure 3 depicts the changes of t_1 and t_2 with $B_2 = 100-1000$ and $A_c = 1-100$ while keeping $B_1 = 200$ fixed. The change of weight B_2 does not affect the change of t_1 for all A_c and also does not affect the change of t_2 for $A_c > 40$. Figure 4 depicts the changes of t_1 and t_2 with $B_1 = 100-1000$ and $B_2 = 100-1000$ while keeping $A_c = 1$ fixed. Figure 4A illustrates that changes in B_1 and B_2 negatively affect changes in t_1 and t_2, as we have already seen in Figures 2 and 3. In addition, for $B_1 > 100$ t_1 increases with B_2. However, B_1 has no noticeable effect in the change of t_2. Figure 5 depicts the changes of t_1 and t_2 with $B_1 = 100-1000$ and $B_2 = 100-1000$ while keeping $A_c = 10$ fixed. In this case, B_1, and B_2 have no effect on changes in t_2 and t_1, respectively.

The optimal control aims at reducing the number of addicted individuals while ensuring the least implementation cost of the two controls mentioned previously. Let ${A_{with\_control}}^t_{B1,B2}$ and ${A_{without\_control}}^t_{B1,B2}$ be the number of addicted people with and without optimal control, respectively, for specific values of the parameters at time $t\in[0,T]$, and define $\Delta A^t_{B1,B2} := A_{without\_control^t_{B1,B2}} - A_{with\_control^t_{B1,B2}}$ as the number of reductions in the addicted population because of optimal control. From the previous results, it is clear that higher values of B_1 and B_2 reduce the implementation of the controls and consequently $\Delta A^t_{B1,B2}$. For successful implementation of the controls, the condition $\Delta A^t_{B1,B2} > 0$ is needed for all $t\in[0,T]$. However, Figure 6A shows that $\Delta A^T_{B1,B2} < 0$ for some combinations of B_1, B_2 which

Table 1. The parameter values for the model.

Parameters	α	ω	β	θ	η	ρ	μ
Value (per mo.)	0.17	0.018	0.024	0.0042	0.03	0.08	0.01

*All values of the parameters are adopted from the results of parameter estimation in [25].

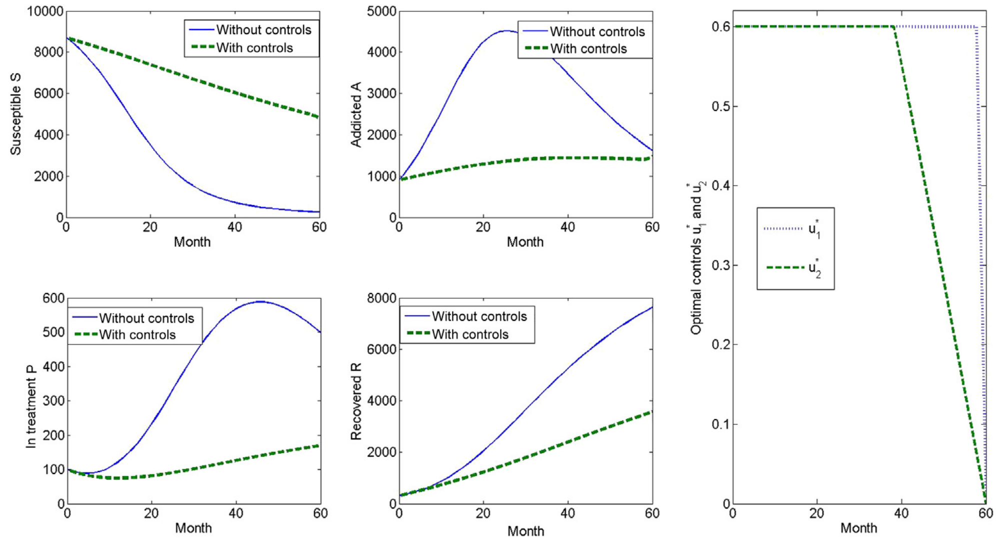

Figure 1. The dynamics of states with and without controls when the weight factors are $A_c = 1$, $B_1 = 500$, $B_2 = 500$.

include higher values for both. Figure 6B shows the same phenomena for different initial conditions $S(0) = 7400$, $A(0) = 1800$, $P(0) = 200$, $R(0) = 600$. In this case $\Delta A^T_{B1,B2} < 0$ for comparatively lower and more values of B_1, B_2.

4. Discussion

An optimal control problem has been established that takes into consideration self-harm as a contagious disease. We considered two control strategies: (1) reducing peer pressure and (2) accelerating early intervention with their associated costs (i.e., B_1 and B_2, respectively). The control problem is solved using Pontryagin's Maximum Principle. In this circumstance, the negative effect of an addicted individual is parameterized by A_c. The simultaneous use of both controls reduces the self-harm epidemic by increasing susceptible individuals and reducing the addicted individuals remarkably. But the costs associated with control strategies and the weight A_c may not be the same in all groups of young people. Depending on the groups, the costs and the weight may be varied so that different control strategies are needed. For a higher weight of addicted individuals, we used nearly the same control strategy for the groups, even

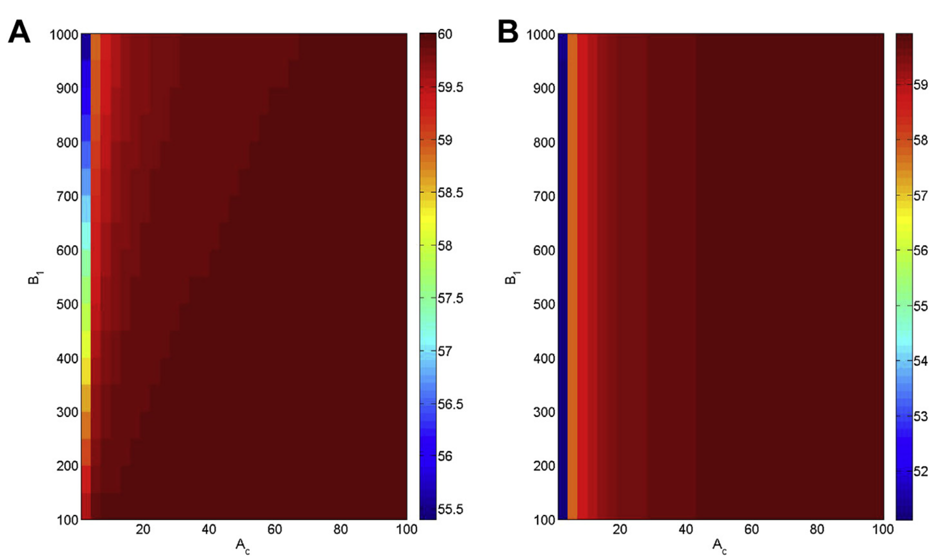

Figure 2. (A) The duration of maximum implementation for the optimal control u_1. In this equation, $A_c = 1-100$, $B_1 = 100-1000$, and $B_2 = 200$. (B) The duration of maximum implementation for the optimal control u_2. In this equation, $A_c = 1-100$, $B_1 = 100-1000$, and $B_2 = 200$.

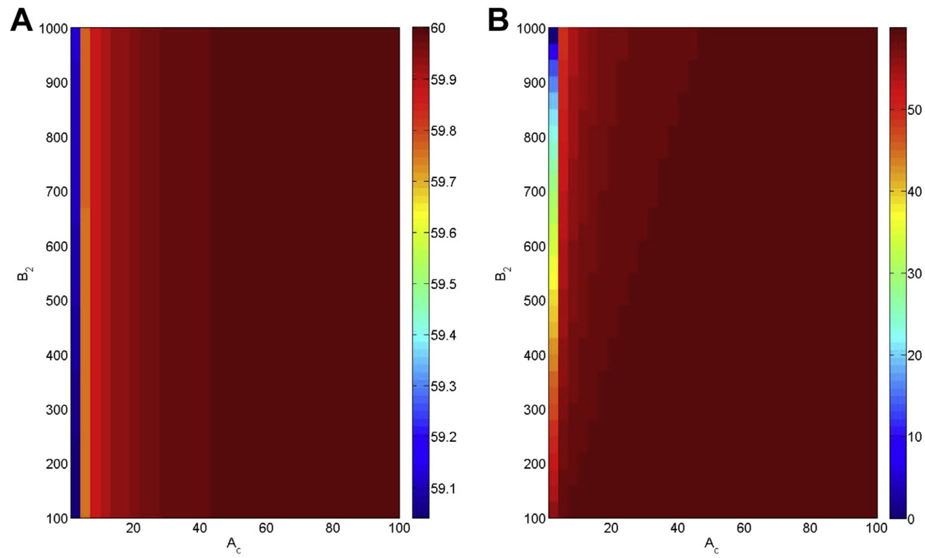

Figure 3. (A). The duration of maximum implementation for the optimal control U_1. In this equation, $A_c = 1-100$, $B_2 = 100-1000$, and $B_1 = 200$. (B). The duration of maximum implementation for the optimal control U_2. In this equation, $A_c = 1-100$, $B_2 = 100-1000$, and $B_1 = 200$.

with different control costs, which agrees with our intuition that a greater weight requires greater effort from the controls, irrespective of the control cost. However, if the weight is low, a great effort by the controls is no longer necessary. As a result, the strategy varies from group to group, depending on the control costs associated with the groups. Controls are implemented in smaller numbers in groups with a high control cost and vice versa.

In the case of low weight, the strategy for early intervention is not affected by the cost associated with reducing peer pressure. However, if the cost of reducing peer pressure is high in some groups, it affects the reduction of peer pressure. As a result, the number of addicted individuals increase, which requires more effort for early intervention, even though it is expensive. Furthermore, the control strategies have no interdependency, resulting from the associated costs.

The simulations presented above also shows that the control strategy is affected by the initial condition and the control costs. In groups with a high control cost, the control strategy is unsuitable for the long run. If the

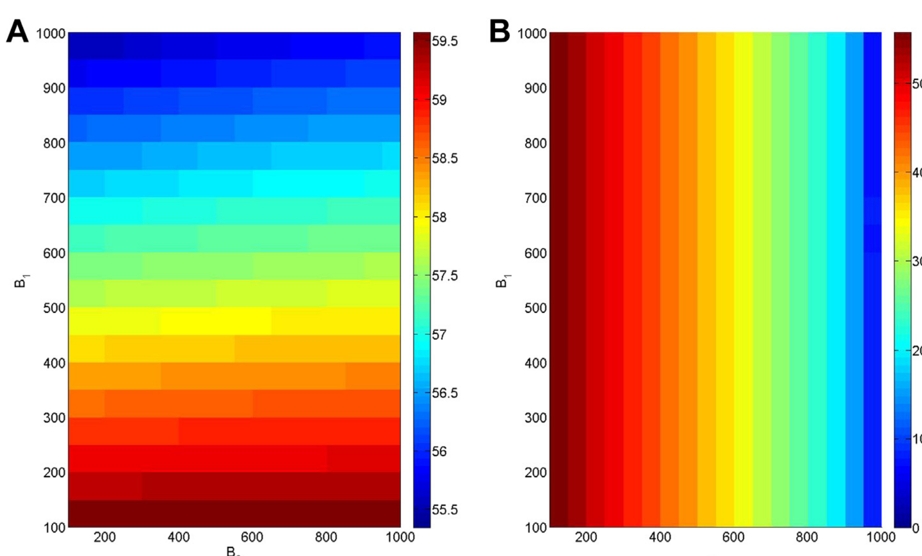

Figure 4. (A). The duration of maximum implementation for the optimal control U_1. In this equation, $A_c = 1$, $B_1 = 100-1000$, and $B_2 = 100-1000$. (B). The duration of maximum implementation for the optimal control U_2. In this equation, $A_c = 1$, $B_1 = 100-1000$, and $B_2 = 100-1000$.

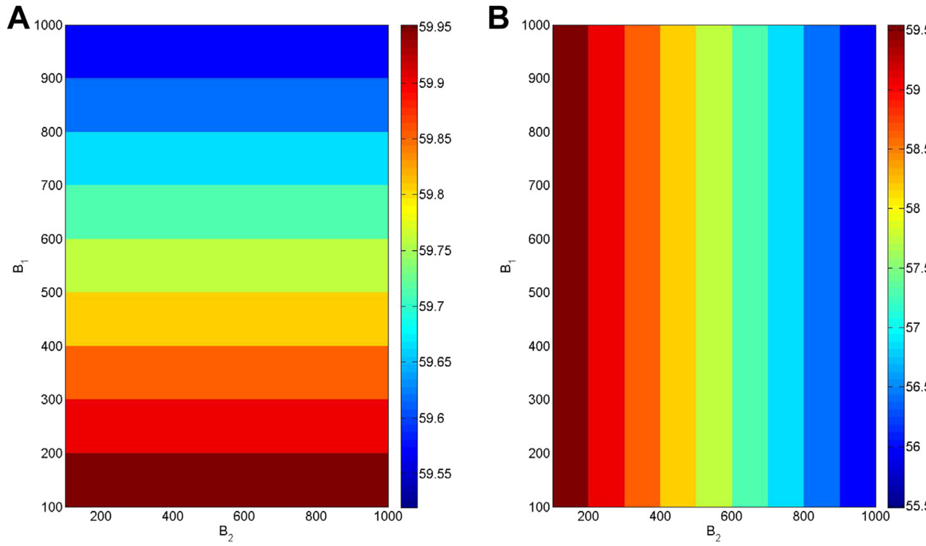

Figure 5. (A). The duration of the maximum implementation for the optimal control u1. In this equation, $A_c = 10$, $B_1 = 100-1000$, and $B_2 = 100-1000$. (B). The duration of the maximum implementation for the optimal control u2. In this equation, $A_c = 10$, $B_1 = 100-1000$, and $B_2 = 100-1000$.

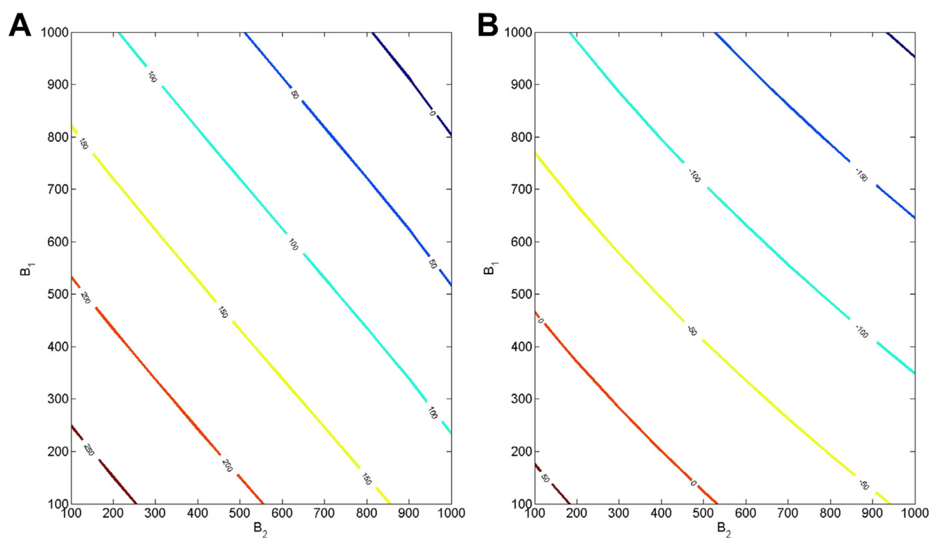

Figure 6. (A) The contour plot of $\Delta A^T_{B1,B2}$ for the initial conditions$S(0) = 8700$, $A(0) = 900$, $P(0) = 100$, $R(0) = 300$. (B) The contour plot of $\Delta A^T_{B1,B2}$ for initial conditions $S(0) = 7400$, $A(0) = 1800$, $P(0) = 200$, $R(0) = 600$.

initial number of addicted people in a population is high, the control fails for lower costs of the controls. Therefore, even if the control costs are high, early implementation gives better results rather than waiting and allowing the number of addicted individuals to increase.

Therefore, we conclude that the simultaneous use of the controls gives the desired outcome. In groups in which associated costs are high, the controls may fail after a long period. What is most important is that the control strategy should be implemented as early as possible to attack a comparatively fewer number of addicted individuals. To make the model more realistic, further efforts should be focused on including age-dependent peer pressure [31], which remains for our future work.

Conflicts of interest

The authors declare no conflicts of interest.

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Appendix 1.

Theorem 1. Let $S^*(t)$, $A^*(t)$, $P^*(t)$, $R^*(t)$ be the optimal state solutions with associated optimal control variables $u_1^*(t)$ and $u_2^*(t)$ for the optimal control problems (2) and (3). There then exist the adjoint variables $\lambda_1(t)$, $\lambda_2(t)$, $\lambda_3(t)$, $\lambda_4(t)$ that satisfy:

$$
\begin{aligned}
\lambda_1'(t) &= (\lambda_1(t)-\lambda_2(t))\alpha(1-u_1^*(t))\frac{A^*(t)+P^*(t)}{N} \\
\lambda_2'(t) &= -A_c+(\lambda_1(t)-\lambda_2(t))\alpha(1-u_1^*(t))\frac{S^*(t)}{N^*}+(\lambda_2(t)-\lambda_3(t))\left(\beta\frac{P^*(t)+R^*(t)}{N^*}+\theta\right)+(\lambda_2(t)-\lambda_4(t))(\eta+\mu u_2^*(t)) \\
\lambda_3'(t) &= (\lambda_1(t)-\lambda_2(t))\alpha(1-u_1^*(t))\frac{S^*(t)}{N^*}+(\lambda_2(t)-\lambda_3(t))\left(\beta\frac{A^*(t)}{N^*}-\omega\right)+(\lambda_3(t)-\lambda_4(t))\rho \\
\lambda_4'(t) &= (\lambda_2(t)-\lambda_3(t))\beta\frac{A^*(t)}{N^*}
\end{aligned}
\tag{9}
$$

with transversality condition (or boundary condition):

$\lambda_j(T)=0, j=1,2,3,4.$

Furthermore, the optimal controls $u_1^*(t)$ and $u_2^*(t)$ are given by:

$$
\begin{aligned}
u_1^*(t) &= \min\left\{1, \max\left\{0, \frac{1}{B_1}\left(\frac{\alpha S^*(A^*+P^*)(\lambda_2-\lambda_1)}{N}\right)\right\}\right\} \\
u_2^*(t) &= \min\left\{1, \max\left\{0, \frac{\mu A^*(\lambda_2-\lambda_4)}{B_2}\right\}\right\}
\end{aligned}
\tag{10}
$$

Proof. To determine the adjoint equations and the transversality conditions, use the Hamiltonian (7). By Pontryagin's Maximum Principle, setting $S(t) = S^*(t)$, $A(t) = A^*(t)$, $P(t) = P^*(t)$, $R(t) = R^*(t)$ and differentiating the Hamiltonian (6) with respect to $S(t)$, $A(t)$, $P(t)$, $R(t)$, the following is obtained:

$$
\begin{aligned}
\lambda_1'(t) &= -\frac{\partial H}{\partial S} = \lambda_1(t)\alpha(1-u_1^*(t))\frac{A^*(t)+P^*(t)}{N(t)}-\lambda_2(t)\alpha(1-u_1^*(t))\frac{A^*(t)+P^*(t)}{N(t)} \\
\lambda_2'(t) &= -\frac{\partial H}{\partial A} = -A_c+\lambda_1(t)\alpha(1-u_1^*(t))\frac{S^*(t)}{N^*(t)}-\lambda_2(t)\alpha(1-u_1^*(t))\frac{S^*(t)}{N^*(t)}+\lambda_2(t)\left(\beta\frac{P^*(t)+R^*(t)}{N^*(t)}+\theta\right) \\
&\quad +\lambda_2(t)(\eta+\mu u_2^*(t))-\lambda_3(t)\left(\beta\frac{P^*(t)+R^*(t)}{N^*(t)}+\theta\right)-\lambda_4(t)(\eta+\mu u_2^*(t)) \\
\lambda_3'(t) &= -\frac{\partial H}{\partial P} = \lambda_1(t)\alpha(1-u_1^*(t))\frac{S^*(t)}{N^*(t)}-\lambda_2(t)\alpha(1-u_1^*(t))\frac{S^*(t)}{N^*(t)}+\lambda_2(t)\beta\frac{A^*(t)}{N^*(t)}-\lambda_2(t)\omega-\lambda_3(t)\beta\frac{A^*(t)}{N^*(t)} \\
&\quad +\lambda_3(t)\omega+\lambda_3(t)\rho-\lambda_4(t)\rho \\
\lambda_4'(t) &= -\frac{\partial H}{\partial H} = \lambda_2(t)\beta\frac{A^*(t)}{N^*(t)}-\lambda_3(t)\beta\frac{A^*(t)}{N^*(t)}
\end{aligned}
$$

which reduces to (9).To obtain the optimality conditions (10), the Hamiltonian, H, is differentiated with respect to $u_1(t)$, $u_2(t)$. It is set equal to zero.

$$
\begin{aligned}
0 &= \frac{\partial H}{\partial u_1} = B_1u_1^*(t)+\lambda_1(t)\alpha S^*(t)\frac{A^*(t)+P^*(t)}{N(t)} \\
&\quad -\lambda_2(t)\alpha S^*(t)\frac{A^*(t)+P^*(t)}{N(t)} \\
0 &= \frac{\partial H}{\partial u_2} = B_2u_2^*(t)-\lambda_2(t)\mu A^*(t)+\lambda_4(t)\mu A^*(t)
\end{aligned}
$$

Solving for the optimal controls obtains:

$$
\begin{aligned}
u_1^*(t) &= \frac{\alpha S^*(t)(A^*(t)+P^*(t))(\lambda_2(t)-\lambda_1(t))}{B_1N} \\
u_2^*(t) &= \frac{\mu A^*(t)(\lambda_2(t)-\lambda_4(t))}{B_2}
\end{aligned}
$$

To determine an explicit expression for the optimal controls for $0 \le u_1^*(t), u_2^*(t) \le 1$, a standard optimality technique is utilized. We considered the following three cases.On the set: $\{t : 0 < u_1^*(t) < 1\}$, $\frac{\partial H}{\partial u_1}=0$. Hence, the optimal control is:

$$u_1^*(t) = \frac{\alpha S^*(t)(A^*(t)+P^*(t))(\lambda_2(t)-\lambda_1(t))}{B_1 N}$$

In the set: $\{t : u_1^*(t) = 0\}$, $\frac{\partial H}{\partial u_1} \geq 0$. This implies that:

$$\lambda_1(t)\alpha S^*(t)\frac{A^*(t)+P^*(t)}{N} - \lambda_2(t)\alpha S^*(t)\frac{A^*(t)+P^*(t)}{N} \geq 0$$

in which: $\frac{\alpha S^*(t)(A^*(t)+P^*(t))(\lambda_2(t)-\lambda_1(t))}{B_1 N} \leq 0 = u_1^*(t)$In the set: $\{t : u_1^*(t) = 1\}$, $\frac{\partial H}{\partial u_1} \leq 0$. This implies that:

$$\lambda_1(t)\alpha S^*(t)\frac{A^*(t)+P^*(t)}{N} - \lambda_2(t)\alpha S^*(t)\frac{A^*(t)+P^*(t)}{N} \leq -B_1$$

in which: $\frac{\alpha S^*(t)(A^*(t)+P^*(t))(\lambda_2(t)-\lambda_1(t))}{B_1 N} \geq 1 = u_1^*(t)$Combining these three equations, results in the characterization of u_1^*:

$$u_1^*(t) = \min\left\{1, \max\left\{0, \frac{1}{B_1}\left(\frac{\alpha S^*(A^*+P^*)(\lambda_2-\lambda_1)}{N}\right)\right\}\right\}$$

Using similar arguments, a second optimal control function is obtained:

$$u_2^*(t) = min\left\{1, \max\left\{0, \frac{\mu A^*(\lambda_2-\lambda_4)}{B_2}\right\}\right\}.$$

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