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OPTIMAL CONTROL STRATEGY WITH MULTI-DELAY IN STATE AND CONTROL VARIABLES OF A DISCRETE MATHEMATICAL MODELING FOR THE DYNAMICS OF DIABETIC POPULATION

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Abstract. In order to have realistic model. In this paper, we propose to study an optimal control approach with delay in state and control variables in our discrete mathematical model of kouidere et al [5] talking about the dynamics of a population of diabetics with highlighting the impact of living environment, that time with delay represent the measuring the extent of interaction with the means of treatment or awareness campaigns.

The existence for the optimal control with delay is also provided by Pontryagin's maximum principle is used to characterize these optimal controls. The optimality system is derived and then solved numerically using an algorithm based on the forward and backward difference approximation.

Keywords: diabetes; living environment; optimal control with delay.

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1. INTRODUCTION

According to the World Health Organization (WHO) [1]. Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot use effective insulin or the pancreas does not produce insulin completely. What is Insulin: Insulin is a hormone that regulates blood sugar, which plays a key role in maintaining the normal rate of blood sugar. When a defect in the hormone secretion results in high blood sugar, it is one of the common effects of uncontrolled diabetes.

In 2012, the rise of glucose in blood led to a rise in the number of deaths, which amounted to about 2.2 million people. In 2014, 8.5% of adults aged 18 years and older had diabetes. In 2016, diabetes was a direct cause of death for 1.6 million people, and this number was increase to 4.2 million in 2019.

Nowadays, all the world suffers from the high number of people with diabetes. According to the 9th edition of the International Diabetes Federation (IDF) [2], Diabetes is the fourth leading cause of death, with more than 463 million diabetics, especially those aged over 45, as well as children and adolescents under 20 years of age. It is expected that the number of people with diabetes rises on the horizon of the year 2045 to about 629 million people, Therefore, effective solutions must be sought to reduce the number of diabetics.

According to IDF, diabetes is a costly chronic disease, especially when it is not diagnosed at the time or not treated. It has serious psychological, ethical and behavioral consequences, which can be life-threatening and lead to premature death, in addition to the costs of medical care and treatment expenses, which overburden the concerned community and the family as a whole.

Mathematical modeling of diabetes is not new. Differential equations play an important role in modeling different types of problems. There are different models devoted to mathematical modelling. In a related research work, Boutayeb et al. [3] and Derouich et al [4] proposed a mathematical model for the dynamics of the population of diabetes patients with or without complications using a system of ordinary differential equations, Kouidere et al [5] proposed a discrete mathematical model with highlighting the impact of living environment Also, many researches have focused on this topic and other related topics ($[6]\,,[7]\,,[13]\,,[19-20]\ldots$), But they did not take into account the measuring the extent of interaction with the means of treatment or awareness campaigns. That may cause delays response and this is the objective of this work.

To make the modelling of this phenomena more realistic, we consider an optimal control problem governed by a system of difference equations with time to delay. we study an optimal control problem with time to delay in the state and control variable are described in a descrite PDEC model of kouidere et al [5] and a time delays representing the measuring the extent of interaction with the means of treatment or awareness campaigns. Then we derive first-order necessary conditions for existence of the optimal control and develop a numerical method to solve them.

We note, as mentioned above, that most researchers about diabetes and its complications focus on continuous and discrete time models and describe differential equations. Recently, more and more attention has been paid to the study of optimal control with delay in the state or state and control (see $[8;9;15-18,\cdots]$ and references cited There).

In this paper, in section 2, we represent our discrete *PDEC* mathematical model of kouidere et al[5] , that describes the dynamic of a population of diabetes with highlighting the impact of living environment. In section 3, we present a optimal control problem with delay in our proposed model where we give some results concerning the existence of the optimal control and we caracterize the optimal controls using the Pontryagin's maximum principle in discrete time. Numerical simulations through MATLAB are given in section 4. Finally we conclude the paper in section 5.

2. A Mathematical Model

We consider a discrete mathematical model *PDEC* of kouidere et al [5], that describes the dynamics of a population of diabetics . We divide the population denoted by N into four compartments : People who are likely to have diabetes through genetics P, the individual diabetics without complications D, people who are likely to have diabetes through the effect of living environment or psychological problems E and the individual diabetics with complications C.

We present the diabetic model by the following system of difference equations:

$$(1) \quad \begin{cases} P_{k+1} = \Lambda_1 + (1-\mu - \beta_1 - \beta_3)P_k \\ D_{k+1} = \beta_1 P_k + \gamma E_k - \alpha \frac{D_k E_k}{N} + (1-\mu-\beta_2)D_k \\ E_{k+1} = \Lambda_2 + (1-\mu-\gamma)E_k \\ C_{k+1} = \beta_3 P_k + \beta_2 D_k + \alpha \frac{D_k E_k}{N} + (1-\mu-\delta)C_k \end{cases}$$

And $P_0 \geq 0, D_0 \geq 0.E_0 \geq 0$ and $C_0 \geq 0$ are the given initial states.

Where

- Λ_1 : denote the incidence rate of pre-diabetes

- Λ_2 : denote the incidence rate of environment effect

- μ : natural rate mortality

- β_1 : patients who develop diabetes without complications

- β_2 : patients whose complications are cured

- β_3 : patients who develop diabetes with complications

- γ : people who become diabetics without complications because of the effect of the living environment

- α : patients who become diabetic with complication because of the bad contact with the living environment

- δ : mortality rate due to complications

3. The Optimal Control Problem

The strategy of control, we adopt consists of an awareness program in order to minimize the negative the effect of living environment in diabetic people without complication, Our main is to minimize the number of people evolving from the stage of pre-diabetes to the stages of diabetes with and without complications . In this model, we include three control $u = (u_0, u_1, \cdots, u_{T-1})$, $v = (v_0, v_1, \cdots, v_{T-1})$ and $w = (w_0, w_1, \cdots, w_{T-1})$, that represent consecutively the awareness program through media and education, treatment, and psychological support with follow-up at time k. in order to have realistic and logic model, we need to take in consideration that the movement of controlled individuals from the compartment of diabetics without complications (DWC) to diabetics with complications (DC), and transition by the contact between DWC and the effect of the environment E to DC, and the transition of the ordinary people (E) to DWC because of the effect of the environment is subject to a delay. Thus, the time delay is introduced into the system as follows: at the moment,Thus, the delay is introduced into the system as follows: in time, only a percentage of individuals (DWC,DC,E) that have been treated and controlled τ_i time unit ago, that is to say that at the time $k-\tau_i$ with $i \in \{1,2,3\}$, are removed to other compartments.

So the mathematical system with time delay in state and control system of variables is given by the nonlinear retarded system of difference equations :

(2)
$$\begin{cases} P_{k+1} = \Lambda_1 + (1-\ \ \mu -\ \beta_1 -\ \ \beta_3)P_k \\ D_{k+1} = \beta_1 P_k + \gamma(1-w_k)E_k - \alpha\frac{D_k E_k}{N} + \alpha v_{k-\tau_2}\frac{D_{k-\tau_2}E_{k-\tau_2}}{N} + (1-\mu-\beta_2)D_k + u_{k-\tau_1}C_{k-\tau_1} \\ E_{k+1} = \Lambda_2 + (1-\mu)E_k - \gamma E_k + \gamma w_{k-\tau_3}E_{k-\tau_3} \\ C_{k+1} = \beta_3 P_k + \beta_2 D_k + \alpha(1-v_k)\frac{D_k E_k}{N} + (1-\mu-\delta)C_k - u_k C_k \end{cases}$$

In addition, for biological reasons, we assume, for $\varphi \in \{-\tau,...,0\}$, that $P_\varphi, D_{\varphi,} E_\varphi$ and C_φ are nonnegative continuous functions and $u_\varphi = 0, v_\varphi = 0$ and $w_\varphi = 0$.

Our main gaol is to minimize the number of diabetics with complications and maximizethe number of diabetics without complications during the time step $k = 0$ to T, and also minimize the cost spent in this, strategy of control.

Then, the problem is to minimize the objective functional

$$L(u,v,w) = C_T - D_T + \sum_{k=0}^{T-1}\left[C_k - D_k + \frac{A_k}{2}u_k^2 + \frac{B_k}{2}v_k^2 + \frac{G_k}{2}w_k^2\right] \tag{3}$$

Where A_k, B_k and G_k are the cost coefficients. They are selected to weigh the relative importance of u_k, v_k and w_k at time k, T is the final time.

In other words, we seek the optimal controls u^*,v^* and w^* such that

$$L(u^*,v^*,w^*) = \min_{u,v,w\in U} L(u,v,w) \tag{4}$$

Where U is the set of admissible controls defined by

$U = \{(u,v,w)/\ 0 \leq u_{\min} \leq u_k \leq u_{\max} \leq 1,\ 0 \leq v_{\min} \leq v_k \leq v_{\max} \leq 1$ and $0 \leq w_{\min} \leq w_k \leq w_{\max} \leq 1, k \in \{0,1,...,T-1\}\}$

3.1. The optimal control: Existence.

We first show the existence of solutions of the system, after that we will prove the existence of optimal control.

Theorem 1. *Consider the control problem with the system. There are three optimal controls* $(u^*,v^*,w^*) \in U^3$ *such that*

$$L(u^*,v^*,w^*) = \min_{u,v,w \in U} L(u,v,w) \tag{5}$$

Proof. Since the coefficients of the state equations are bounded and there are a finite number of time steps, $P = (P_0,P_1,...,P_T)$, $D = (D_0,D_1,...,D_T)$, $E = (E_0,E_1,...,E_T)$ and $C = (C_0,C_1,...,C_T)$ are uniformly bounded for all (u,v,w) in the control set U, thus $L(u,v,w)$ is bounded for all $(u,v,w) \in U^3$. Since $L(u,v,w)$ is bounded, $\inf\limits_{(u,v,w)\in U} L(u,v,w)$ is finite, and there exists a sequence $(u^i,v^i,w^i) \in U^3$ such that $\lim\limits_{i\to+\infty} L(u^i,v^i,w^i) = \inf\limits_{(u,v,w)\in U^3} L(u,v,w)$ and corresponding sequences of states P^i,D^i,E^i and C^i. Since there is a finite number of uniformly bounded sequences, there exist $(u^*,v^*,w^*) \in U^3$ and P^*,D^*,E^* and $C^* \in \mathbb{R}^{T+1}$ such that, on a subsequence, $(u^i,v^i,w^i) \mapsto (u^*,v^*,w^*)$, $P^i \mapsto P^*$, $D^i \mapsto D^*$, $E^i \mapsto E^*$, and $C^i \mapsto C^*$. Finally, due to the finite dimensional structure of system (2) and the objective function $L(u,v,w)$ and also (u^*,v^*,w^*) is an optimal control with corresponding states P^*,D^*,E^* and C^*. Therefore $\inf\limits_{(u,v,w)\in U^3} L(u,v,w)$ is achieved. □

3.2. Characterization of the Optimal Control.

In order to derive the necessary condition for optimal control, the pontryagins maximum principle, in discrete time, given in was used. This principle converts into a problem of minimizing a Hamiltonian, H_k at time step k defined by

$$H_k = C_k - D_k + \frac{A_k}{2}u_k^2 + \frac{B_k}{2}v_k^2 + \frac{G_k}{2}w_k^2 + \sum_{i=1}^{4} \lambda_{i,k+1} f_{i,k+1}(P_k,D_k,E_k,C_k) \tag{6}$$

where $f_{i,k+1}$ is the right side of the difference equation of the i^{th} state variable at time step $k+1$.

Theorem 2. *Given the optimal controls (u^*, v^*, w^*) and the solutions P^*, D^*, E^* and C^* of the corresponding state system (2), there exists adjoint variables $\lambda_{1,k}$, $\lambda_{2,k}$, $\lambda_{3,k}$ and $\lambda_{4,k}$ satisfying:*

$$\lambda_{1,k} = \frac{\partial H_k}{\partial P_k} = \lambda_{1,k+1}\left[1-\mu-\beta_1-\beta_3\right] + \lambda_{2,k+1}\beta_1 + \lambda_{4,k+1}\beta_3$$

$$\begin{aligned}\lambda_{2,k} &= \frac{\partial H_k}{\partial D_k} + \chi_{\{0,\ldots,T-\tau_2\}}(k)\frac{\partial H_{k+\tau_2}}{\partial D_{k-\tau_2}} = -1 + \lambda_{2,k+1}\left[-\alpha\frac{E_k}{N} + (1-\mu-\beta_2)\right] \\ &\quad + \lambda_{4,k+1}\left[\alpha(1-v_k)\frac{E_k}{N} + \beta_2\right] + \chi_{\{0,\ldots,T-\tau_2\}}(k) \times \alpha\lambda_{2,k+\tau_2+1}v_{k+\tau_2}\frac{E_{k+\tau_2}}{N}\end{aligned}$$

$$\begin{aligned}\lambda_{3,k} &= \frac{\partial H_k}{\partial E_k} + \chi_{\{0,\ldots,T-\tau_3\}}(k)\frac{\partial H_{k+\tau_3}}{\partial E_{k-\tau_3}} = \lambda_{2,k+1}\left[\gamma(1-w_k) - \alpha(1-v_k)\frac{D_k}{N}\right] \\ &\quad + \lambda_{3,k+1}\left[1-\mu-\gamma\right] + \lambda_{4,k+1}(\alpha(1-v_k)\frac{D_k}{N}) + \chi_{\{0,\ldots,T-\tau_3\}}(k)\lambda_{3,k+\tau_3+1}\gamma w_{k+\tau_3}\end{aligned}$$

$$\lambda_{4,k} = \frac{\partial H_k}{\partial C_k} + \chi_{\{0,\ldots,T-\tau_1\}}(k)\frac{\partial H_{k+\tau_1}}{\partial C_{k-\tau_1}} = 1 + \chi_{\{0,\ldots,T-\tau_1\}}(k) \times \lambda_{2,k+\tau_1+1}u_{k+\tau_1} + \lambda_{4,k+1}(1-\mu-\gamma-u_k)$$

with

$$\chi_{\{0,\ldots,T-\tau_i\}=I}(k) = \begin{cases} 1 & if \quad k \in I \\ 0 & if \quad k \notin I \end{cases}$$

With the transversality conditions at time T : $\lambda_{1,T} = 0$, $\lambda_{2,T} = -1$, $\lambda_{3,T} = 0$ and $\lambda_{4,T} = 1$. Furthermore, for $k = 0,1,2\ldots T$, the optimal controls u^*, v^* and w^* are given by

$$u^* = \min\left(1, \max\left(0, \frac{\lambda_{4,k+1}C_k - \chi_{\{0,\ldots,T-\tau_1\}}(k)\lambda_{2,k+\tau_1+1}C_{k+\tau_1}}{A_k}\right)\right)$$

$$v^* = \min\left(1, \max\left(0, \frac{\alpha(\lambda_{4,k+1}D_kE_k - \chi_{\{0,\ldots,T-\tau_2\}}(k)\lambda_{2,k+\tau_2+1}D_{k+\tau_2}E_{k+\tau_2})}{NB_k}\right)\right)$$

$$w^* = \min\left(1, \max\left(0, \frac{\gamma(\lambda_{2,k+1}E_k - \chi_{\{0,\ldots,T-\tau_3\}}(k)\lambda_{3,k+\tau_3+1}E_{k+\tau_3})}{G_k}\right)\right)$$

Proof. In order to derive the necessary condition for optimal control, the pontryagins maximum principle in discrete time given in $[10-12,13,14]$ was used. This principle converts into a problem of minimizing a Hamiltonian H_k at time step k defined by

$$\begin{aligned}
H_k &= C_k - D_k + \frac{A_k}{2}u_k^2 + \frac{B_k}{2}v_k^2 + \frac{G_k}{2}w_k^2 + \lambda_{1,k+1}\left[\Lambda_1 + (1-\ \mu-\ \beta_1-\ \beta_3)P_k\right] \\
&+\lambda_{2,k+1}\left[\beta_1 P_k + \gamma(1-w_k)E_k - \alpha\frac{D_kE_k}{N} + \alpha v_{k-\tau_2}\frac{D_{k-\tau_2}E_{k-\tau_2}}{N}\right. \\
&\left. + (1-\mu-\beta_2)D_k + u_{k-\tau_1}C_{k-\tau_1}\right] \\
&+\lambda_{3,k+1}\left[\Lambda_2 + (1-\mu)E_k - \gamma E_k + \gamma w_{k-\tau_3}E_{k-\tau_3}\right] \\
&+\lambda_{4,k+1}\left[\beta_3 P_k + \beta_2 D_k + \alpha(1-v_k)\frac{D_kE_k}{N} + (1-\mu-\delta)C_k - u_kC_k\right]
\end{aligned}$$

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

$$\frac{\partial H_k}{\partial u_k} + \chi_{\{0,\ldots,T-\tau_1\}}(k)\frac{\partial H_{k+\tau_1}}{\partial u_{k-\tau_1}} = 0$$
$$\frac{\partial H_k}{\partial v_k} + \chi_{\{0,\ldots,T-\tau_2\}}(k)\frac{\partial H_{k+\tau_2}}{\partial v_{k-\tau_2}} = 0$$
$$\frac{\partial H_k}{\partial w_k} + \chi_{\{0,\ldots,T-\tau_3\}}(k)\frac{\partial H_{k+\tau_3}}{\partial w_{k-\tau_3}} = 0$$

That are

$$\begin{aligned}
\frac{\partial H_k}{\partial u_k} + \chi_{\{0,\ldots,T-\tau_1\}}(k)\frac{\partial H_{k+\tau_1}}{\partial u_{k-\tau_1}} &= A_ku_k + \lambda_{4,k+1}C_k - \chi_{\{0,\ldots,T-\tau_1\}}(k)\lambda_{2,k+\tau_1+1}C_{k+\tau_1} = 0 \\
\frac{\partial H_k}{\partial v_k} + \chi_{\{0,\ldots,T-\tau_2\}}(k)\frac{\partial H_{k+\tau_2}}{\partial v_{k-\tau_2}} &= B_kv_k + \lambda_{4,k+1}\frac{\alpha D_kE_k}{N} - \chi_{\{0,\ldots,T-\tau_2\}}(k)\lambda_{2,k+\tau_2+1}\frac{\alpha D_{k+\tau_2}E_{k+\tau_2}}{N} = 0 \\
\frac{\partial H_k}{\partial w_k} + \chi_{\{0,\ldots,T-\tau_3\}}(k)\frac{\partial H_{k+\tau_3}}{\partial w_{k-\tau_3}} &= G_kw_k + \chi_{\{0,\ldots,T-\tau_3\}}(k)\lambda_{3,k+\tau_3+1}\gamma E_{k+\tau_3} - \lambda_{2,k+1}\gamma E_k = 0
\end{aligned}$$

we have

$$u_k = \frac{\lambda_{4,T-k+1}C_k - \chi_{\{0,\ldots,T-\tau_1\}}(k)\lambda_{2,T-k+\tau_1+1}C_{k+\tau_1}}{A_k}$$
$$v_k = \frac{\alpha(\lambda_{4,T-k+1}D_kE_k - \chi_{\{0,\ldots,T-\tau_2\}}(k)\lambda_{2,T-k+\tau_2+1}D_{k+\tau_2}E_{k+\tau_2})}{NB_k}$$
$$w_k = \frac{\gamma(\lambda_{2,T-k+1}E_k - \chi_{\{0,\ldots,T-\tau_3\}}(k)\lambda_{3,T-k+\tau_3+1}E_{k+\tau_3})}{G_k}$$

By the bounds in U of the controls, it is easy to obtain u_k^*, v_k^* and w_k^* in the form of system.

□

4. Numerical Simulation

In this section, we shall solve numerically the optimal control problem for our *PDEC* model. Here, we obtain the optimality system from the state and adjoint equations.

The proposed optimal control strategy is obtained by solving the optimal system which consists of six difference equations and boundary conditions. The optimality system can be solved by using an iterative method. Using an initial guess for the control variables, u_k, v_k and w_k, the state variables, PDE and C are solved forward and the adjoint variables λ_i for $i = 1;2;3;4$ are solved backwards at times step $k = 0$ and $k = T$. If the new values of the state and adjoint variables differ from the previous values, the new values are used to update u_k, v_k and w_k, and the process is repeated until the system converges.

Different simulations can be carried out using various values of parameters. In the present numerical approach, we use the following parameters values taken from [5]:

paramter	value in mth^{-1}
μ	0.02
δ	0.001
β_1	0.2
β_2	0.5
β_3	0.1
α	0.8
γ	0.8
Λ_1	2000000
Λ_2	2000000

Table 1: Parameter values used in numerical simulation

$P(0) = 6660000,\ D(0) = 10200000,\ E(0) = 10000000,\ C(0) = 5500000,\ n = 120,\ \lambda_1(n) = 0,\ \lambda_2(n) = -1,\ \lambda_3(n) = 0$ and $\lambda_4(n) = 1$.

Since control and state functions are on different scales, the weight constant value is chosen as follows: $A = 100$, $B = 100$ and $G = 100$.

That is, we use the value parameter in table 1,the optimality system is a two-point boundary value problem with separated boundary conditions at time steps $k = 0$ and $k = T$. We solve the optimality system by an iterative method with forward solving of the state system followed by backward solving of the adjoint system. 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 the characterization.

We continue until convergence of successive iterates is achieved.

We proposed control strategy in this work helps to achieve several objectives.

4.1. **Strategy A: Education.** Awareness program

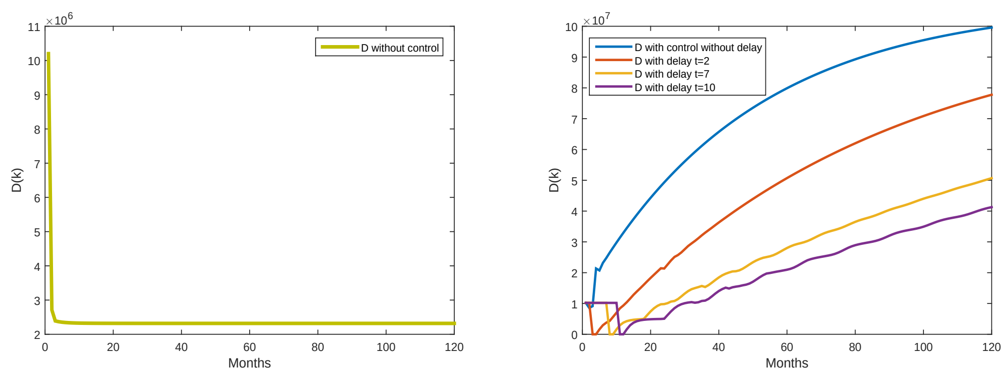

FIGURE 1. The evolution of the number of diabetics without complications with controls with delay

From figure 1,and we use the value parameter in table 1, which represents the evolution of the number of diabetics without complications, Note that if any delay in dealing positive interaction with the awareness-raising campaign targeted for diabetic patients, which raise the awareness of the dangers of diabetes, is by adopting a structured diet program as well as to stay away as much as possible from work and family problems, With an awareness campaign targeting the surrounding environment, the family should take some precautions to spare the patient's family and work problems, and not taking these things seriously will lead to serious complications, for example: $\tau = 2$ rose to about 7.03×10^7, while at $\tau = 7$ rose to 4.18×10^7 and at $\tau = 10$ the value reached 3.49×10^7.

4.2. **Strategy B.** Control with Treatment and Psychological

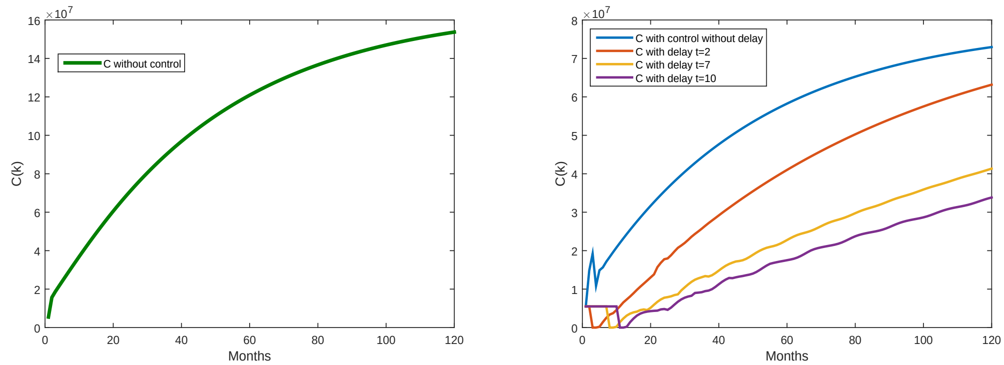

FIGURE 2. The evolution of the number of diabetics with complications with control with delay

We note from the figure 2 that represents the evolution of the number of diabetics with complications,we use the value parameter in table 1, was at $\tau = 2$ rose to about 6.52×10^7, while at $\tau = 7$ rose to 4.08×10^7 and in the $\tau = 10$ and reached the value to 3.3×10^7, We show this decrease in these values, that there is a decrease in the number of diabetics suffering from complications, the longer the effect of the drug, the greater the positive results for the patient, This treatment is accompanied by psychosocial follow-up, by raising the patient's morale as well as his positive thinking and optimistic vision of life, while sensitizing the risks of developing diabetes in critical stages that directly target the eye, kidneys, feet and heart, etc., which have had very excellent results, Reverse the previous figure 1 and figure 3.

4.3. **Strategy C: Prevention and protection E from diabetes.**

We note from the figure 3, this decrease can be explained by the fact that the longer the delay in the positive response to the awareness and awareness campaigns carried out by the government and specialists as well as civil society associations. lead to a negative reaction as mentioned above, we will not get the desired results, and the number of diabetic patients will increase due to negative convergence with the effect of the living medium, for example, when $\tau = 2$ the value was 1.42×10^7, And when $\tau = 7$ the value decreased to 1.38×10^7, and , the devaluation $\tau = 10$ increased to 1.31×10^7 after 120 months.

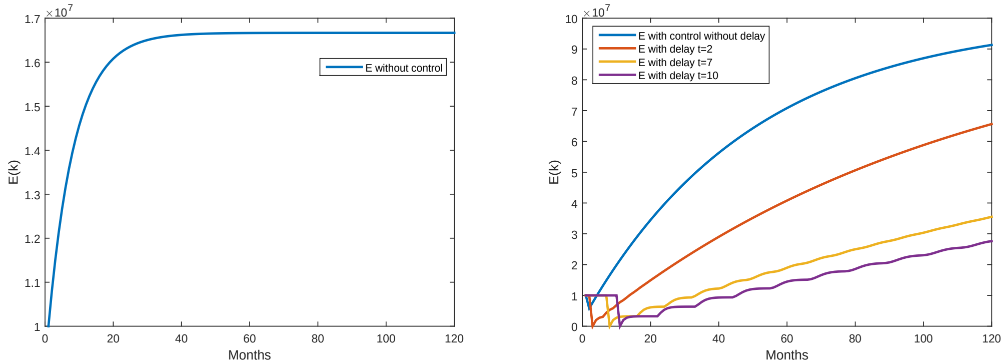

FIGURE 3. The evolution of the number of pre-diabetics people by the bad contact of effect environment.

4.4. Conclusion. In this paper, we introduced a discrete modeling of populations diabetics of kouidere et al [5] , in order to minimize the number of diabetics with complications.

We also introduced three controls which, respectively,represent awareness program through education and media, treatment, and psychological support with follow up.

We also study the optimal control with delay, that represent the measuring the extent of interaction with the means of treatment or awareness campaigns.

We applied the results of the control theory and we managed to obtain the characterizations of the optimal controls. Pontryagin's Maximum Principle, in discrete time, is used to characterize the optimal controls and the optimality system is solved by an iterative method.

The numerical simulation of the obtained results showed the effectiveness of the proposed control strategies.

CONFLICT OF INTERESTS

The author(s) declare that there is no conflict of interests.

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