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Optimal control for the complication of Type 2 diabetes: the role of awareness programs by media and treatment

Saddam Mollah[1] · Santosh Biswas[1]

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Abstract

T2 diabetes is a silent killer and serious public health issue across the world, though awareness of diabetes allows understanding of the causes and prevention of the disease. With this inspiration, we formulate a deterministic model by incorporating awareness and saturated treatment function of the T2 diabetes model to study the dynamics of the disease. We have carried out thoroughly analysis of the model system, including positivity of solutions, boundedness, equilibrium, and stability analysis. Again, we consider the deterministic model system as an optimal control problem by taking awareness (M) and treatment (u) as time-depended control parameters. The sufficient conditions for optimal control for T2 diabetes are obtained utilizing the *Pontryagin's maximum principle* in time-dependent controls to find optimal strategies for disease control. We intended to assess the efficacy and costs of several strategies to determine which is the best cost-effective strategy with the limited resources for treatment. The parameters incident rate (β), awareness coefficient (p), media (M), and treatment (u) highly influence the dynamics of T2 diabetes. Numerical simulations suggest that both awareness and treatment controls have a significant impact on the optimal system and are economically feasible to reduce the prevalence of T2 diabetes.

Keywords Type-2 diabetes mellitus · Mathematical model · Awareness programs · Optimal control · Cost-effectiveness · Numerical simulation

Mathematics Subject Classification 34D20 · 37M05 · 49K15 · 92D30

1 Introduction

According to global diabetes prevalence figures from 2014, 422 million people were living with T2 diabetes, with the same tendency diabetic patients expected to rise approximately to 642 million by 2035 [1]. The prevalence of T2 diabetes is rising in low- and middle-income countries, although more than 75 percent of adults with the disease live in developed countries [1,2]. South Asia is now dealing with an increase in the prevalence of T2 diabetes and its related complications [3]. Diabetes complications are the fourth leading cause of death worldwide. Diabetes and its related complications kill over three million people per year. Diabetic patients suffer from complications such as stroke, coronary heart disease, and myocardial infarction [4]. Complications like nephropathy, retinopathy, and neuropathy have a depressing impact on the patient and a significant burden on the health sector. Diabetes and its complications cause substantial financial damage to people with diabetes and their families. It also includes the health system and the burden on the national economy. T2 diabetes is primarily associated with many lifestyle factors in humans, including regular smoking, excessive alcohol use, obesity, and insufficient physical exercise. Risk factors related to the behavior of individuals are also responsible for a significant percentage of premature deaths due to coronary disease, which is correlated to diabetes mellitus [5]. T2 diabetes occurs due to insulin insensitivity caused by insulin tolerance. It decreases insulin supply and glucose transfer through to the muscle cells, liver, and fat cells. This causes a rise breakdown in the fat with hyperglycemia. Recently, impaired alpha-cell activity has been identified as a factor in the pathophysiology of T2 diabetes [6]. Improving and maintaining glycemic regulation over time is an effective recommendation for T2 diabetes patients. But, this is not an easy action due to the irreversible

✉ Santosh Biswas
sant_biswas@yahoo.in

1 Department of Mathematics, Centre for Mathematical Biology and Ecology, Jadavpur University, 188, Raja S. C. Mallik Road, Kolkata 700032, India

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disposition of the disease, which necessitates prompt medication optimization. T2 diabetes occurs when insulin release is not enough to compensate for the underlying metabolic disorder. As secretory ability decreases over time, the majority of patients with T2 diabetes are expected will ultimately undergo insulin therapy [7]. Diabetes is becoming a growing burden that is possibly placing a threat on the present healthcare system. Diabetes is related to various health issues that it makes more difficult to manage. Effective measures are needed to address the health condition to postpone the consequences of T2 diabetes.

Diabetes cannot be cured permanently, although knowledge and awareness of the individuals can delay the prevalence of diabetes [8]. People are informed about diabetes prevention through media campaigns that emphasize good nutrition and physical activity to minimize their risk of acquiring the disease. Knowledge of awareness on diabetes and management among the patients remains a challenge for stake holders around the world [4]. Awareness is needed to improve adherence to medical therapy. Awareness on diabetes mellitus can aid in the early diagnosis of the condition and reduce the risk of complications. Diabetes is connected with decreased levels of physical activity and an increase in the incidence of obesity. Physical exercise should be promoted in the population as a top priority to reduce complication of T2 diabetes [9]. Physical activity can help with diabetes control as well as reduce the complications of diabetes [10]. Having metabolic/bariatric surgery is a crucial step in reducing the complications of diabetes, which can also be achieved through lifestyle management. Blood sugar, blood pressure, and cholesterol levels in a reasonable range can reduce the complications such as eye, foot, or heart issues. Recent articles [11,12] state that diabetes reversal is proposed as a standard T2 diabetes treatment and control. There are currently several classes of oral and injectable medications accessible for the treatment of T2 diabetes [11,13]. Complications of diabetes are issues that develop immediately (acute) or gradually (chronic) that affect multiple organ systems in the body. Diabetes complications can have a substantial influence on the quality of life and could lead to long-term impairment. Complications of diabetes can be exacerbated by smoking, obesity, high blood pressure, high cholesterol, and a lack of regular exercise. Thus from the above references, awareness and treatment of diabetes can reduce the complication of diabetes. But without complication of T2 diabetes human are more prone to develop complications by altering the lifestyle factors than the general people.

Due to limitations of resources, the most effective use of available control measures should be prioritized to achieve the most possible benefit. Many research articles have been published recently using control strategies of disease dynamics in optimal control theory [14–17]. Pontryagin et al. first introduced maximum principle on the theory of optimal control, popularly known as *Pontryagin's maximum principle* [18]. Later Fleming and Rishel effectively applied it to various mathematical models to explore the optimal control theory including HIV disease, pandemic influenza, and malaria disease [19]. Okosun et al. studied the effect of treatment and surveillance of unaware infective on the HIV/AIDS epidemic outbreak by using the fundamental function of optimal control theory [20].

Some research articles have been published so far to explore the dynamics of diabetes of mathematical models by utilizing various factors [21–24]. Makanda provided a mathematical model for the impact of drug non-adherence on diabetes management [21]. He showed that nonclinical actions such as anti-smoking initiatives, awareness about unhealthy lifestyles could aid in diabetes management. Kompas et al. developed a mathematical model of diabetes transmission through social interaction. They obtained the behavior of diabetes by taking into account the various risks among susceptible individuals [25]. Boutayeb et al. formulated a mathematical model to study the dynamics of pre-diabetes and diabetes with and without complications [26]. They tried to show how to reduce the prevalence of without and with complications of diabetes. Recently, Kouidere et al. formulated a mathematical modeling with optimal control on the prevalence of diabetes mellitus [23]. They applied four controls in the model system such as awareness program through education and media, treatment, and psychological support. Diabetes patients are known to be more vulnerable to infections including severe covid-19 [27]. Anusha et al. formulated a mathematical model for the co-existence of diabetes and covid-19. They showed that T2 diabetes patients are more likely to get covid-19 if they have come into touch with covid-19 infected individuals [22]. Mollah et al. developed mathematical models by considering the effect of awareness of diabetes mellitus in the general population in both deterministic and stochastic environments [24]. Their finding showed that awareness program on the population may reduce the diabetes mellitus. Mollah et al. also developed a model based on a nonlinear interactions between the number of diabetic patients and the density of diabetes awareness programs [28]. They indicated that diabetes education and awareness campaigns help to reduce the prevalence of diabetes [28]. Kouidere et al. also designed a model to characterize the dynamics of diabetes by emphasizing the negative influence of socio-environmental factors on diabetic patients [29]. They suggest a control strategy for implementing the public awareness programs for diabetes patients from the harmful effects of a lifestyle. It is clear that researchers are interested in modeling diabetes and its related complications. Though only limited mathematical models are developed to characterize the influence of media coverage and treatment function of T2 diabetes transmission dynamics. Diabetes prevention and control strategies are emphasized as health care resources are always limited. However, mathematical methods for studying T2 diabetes transmission patterns that include the media impact and treatment are mostly unexplored in the limited resources of treatment. To address the study gap, further study is needed to determine the optimal methods for reducing the complications T2 diabetes with a cost-effective strategy in the limited treatment environment.

In this article, we develop a deterministic model to investigate the impact of awareness and saturated treatment in the dynamics of diabetes. According to the literature, this type of work has not been carried out by considering the saturated treatment rate for T2 diabetes. The model system was thoroughly examined, including positivity of solutions, boundedness, equilibrium, and stability analysis. Again, we consider the deterministic model system as an optimal control problem by taking awareness M and treatment u as time depended control parameters. The sufficient conditions for optimal control for T2 diabetes are obtained utilizing the *Pontryagin's maximum principle* in time-dependent controls to find optimal strategies for disease control. We intended to assess the efficacy and costs of several therapies to determine which is the best cost-effective strategy. Thus for this goal, cost-effective analysis is a beneficial tool. Even though numerous cost-effectiveness assessments of diabetes have been published as a systematic review of the literature. We implement a complete set of control actions into a comprehensive mathematical model to improve the severity of the T2 diabetes burden and lower the cost of these efforts. The main goal of this study is to evaluate the role of awareness and treatment of complications of T2 diabetes in struggling against the disease and find out the related cost-effective strategies.

This article is organized as follows. In Sect. 2, we develop a T2-diabetes mathematical model under some basic assumptions and hypotheses. Section 3 contains positivity and boundedness of the solutions, and an analysis of equilibrium and stability of the system. In Sect. 4, we use Pontryagin's principle to solve the optimal control problem and deduce the derivation of the existence of the optimal problem. Numerical simulation of the model with constant controls is carried out in Sect. 5. In Sect. 6, discuss the numerical simulation of the optimal control strategies with time dependent controls. Cost-effectiveness analysis of various optimal control strategies is discussed in Sect. 7. Finally, the article ends with a discussion and conclusion in Sect. 8.

2 Model formulation

We consider a population where human suffering from T2 diabetes. We divide the total population by unaware susceptible S_U, aware susceptible S_A, and T2 diabetes mellitus patients, where T2 diabetes mellitus patients subdivided into with complication X_C and without complication X_W according to their complications. We make the following assumptions regarding T2 diabetes.

(A) We assume that A is the constant rate of immigration at any time and all newly recruited individuals go to the unaware susceptible class. Diabetes mellitus is not an infectious disease and not transmitted from human to human. So, we have taken β is the incident rate of unaware susceptible to diabetes complication and $\beta\beta_1$ $(0 < \beta_1 < 1)$ is the lower incident rate of aware susceptible to T2 diabetes complication [24].

(B) The development of T2 diabetes is a progressive procedure in which the body is not able to produce enough insulin for its and additionally the body cells become resistant to insulin effects. Thus the direct recovery from T2 diabetes to susceptible is not possible, only remission is possible. We consider the treatment function $f_u(X_C) = \frac{buX_C}{1+\gamma u X_C}$ of complication of T2 diabetes to without complication in saturated form, where treatment effect is denoted by u [30,31]. Here $\frac{b}{\gamma}$ denotes the supply of medical resources per unit time and γ denotes the saturation constant related to treatment control. Initially, treatment function f_u increases when complications of diabetes X_C increases and reaches its maximum values, and then it becomes constant for further increasing of X_C. This type of dynamics is seen when resource for treatment is limited in the health care systems. Hence the limited supply of treatment is also involved in the model system by the saturated type treatment function. This is applied to any small or large population and reverse the effect of complication due to delay the treatment.

(C) The media effect is determined by the parameter M that the population being aware and alter their susceptibility. We consider a portion pS_UM of unaware class directly joins the aware class, where p is the awareness rate at which it is implemented [30].

(D) Recovery of T2 diabetes is not permanent. Through diet changes, weight loss, and medication patients may be able to reach and hold normal blood sugar levels. We consider a portion θX_W of without complication of diabetes become complication and join in X_W, where θ is the coefficient of X_W at which without complications of diabetes human joins to the class of complications of diabetes human. We consider d is the natural death rate and e is the additional death rate due to complication of diabetes of all individuals in the different classes, respectively.

Based on the aforementioned assumptions, we derive the following model

$$\frac{\mathrm{d}S_U}{\mathrm{d}t} = A - pS_UM - \beta S_U - \mathrm{d}S_U,$$
$$\frac{\mathrm{d}S_A}{\mathrm{d}t} = pS_UM - \beta\beta_1 S_A - \mathrm{d}S_A,$$

$$\begin{aligned}\frac{dX_C}{dt} &= \beta S_U + \beta\beta_1 S_A - \frac{buX_C}{1+\gamma\, uX_C}\\ &\quad -(d+e)X_C + \theta X_W,\\ \frac{dX_W}{dt} &= \frac{buX_C}{1+\gamma\, uX_C} - \theta X_W - dX_W,\end{aligned} \tag{2.1}$$

with the initial conditions are $S_U(0) > 0$, $S_A(0) >$, $X_C(0) > 0$, $X_W(0) > 0$.

3 Basic properties of the system for fixed controls

In this section, we have treated media control M and treatment control u are as constants. The model system then becomes relatively simple, but this will give the additional potential to draw more biological insights. First, we showed the positivity of solutions and boundedness of the system and subsequently we found the steady state and showed the local stability conditions of the steady state.

3.1 Positivity of solutions

Theorem 1 *Let the initial conditions $S_U(0) > 0$, $S_A(0) > 0$, $X_C(0) > 0$, and $X_W(0) > 0$. Then the solution (S_U, S_A, X_C, X_W) of the system (2.1) remains positive for all $t > 0$.*

Proof From the first equation of the system (2.1), we have

$$\frac{dS_U}{dt} = A - pS_U M - \beta S_U - dS_U \geq -(pM + \beta + d)S_U.$$

This can be written as:

$$\frac{dS_U}{S_U} \geq -(pM + \beta + d)dt.$$

Integrating both sides of the above inequality, we obtain

$$S_U(t) \geq S_U(0)e^{-\int_0^t (pM+\beta+d)ds} > 0, \text{ for all } t > 0.$$

Again, from the second equation of the system (2.1), we have

$$\frac{dS_A}{dt} = pS_U M - \beta\beta_1 S_A - dS_A \geq -(\beta\beta_1 + d)S_A.$$

This can be written as:

$$\frac{dS_A}{S_A} \geq -(\beta\beta_1 + d)dt$$

Integrating both sides of the above inequality, we obtain

$$S_A(t) \geq S_A(0)e^{-\int_0^t (\beta\beta_1+d)ds} > 0, \text{ for all } t > 0.$$

Similarly employing the same approach, it can be shown that

$$X_C(t) > 0 \text{ and } X_W(t) > 0, \text{ for all } t > 0.$$

□

3.2 Boundedness

Proposition 1 *All feasible solutions of the system (2.1) with positive initial conditions are uniformly bounded in the region $\Gamma_\varepsilon = \{(S_U, S_A, X_C, X_W) \in R^4_+ : S_U + S_A + X_C + X_W \leq \frac{A}{d} + \varepsilon\}$.*

Proof Let $W(t)=S_U(t)+S_A(t)+X_C(t)+X_W(t)$, then we have

$$\begin{aligned}&\frac{dW}{dt} = A - dW - eX_C[\text{by using}(2.1)]\\ &\text{or, } \frac{dW}{dt} + dW \leq A.\end{aligned}$$

Now applying the theory of differential inequality we get

$$0 < W(t) \leq \frac{A}{d} + e^{-dt}W(0),$$

which implies

$$limsup_{t\to\infty} W(t) \leq \frac{A}{d}.$$

Thus all the solutions of (2.1) with positive initial values are ultimately bounded in the region $\Gamma_\varepsilon = \{(S_U, S_A, X_C, X_W) \in R^4_+ : S_U + S_A + X_C + X_W \leq \frac{A}{d} + \varepsilon\}$ for any $\varepsilon > 0$. Hence the result is proved. □

3.3 Equilibrium and stability analysis

The model system (2.1) has only one endemic steady state $L^*(S_U^*, S_A^*, X_C^*, X_W^*)$. In steady state $L^*(S_U^*, S_A^*, X_C^*, X_W^*)$, the values of $S_U^*, S_A^*, X_C^*, X_W^*$ are obtained by solving the following algebraic equations:

$$\begin{aligned}&A - pS_U M - \beta S_U - dS_U = 0,\\ &pS_U M - \beta\beta_1 S_A - dS_A = 0,\\ &\beta S_U + \beta\beta_1 S_A - \tfrac{buX_C}{1+\gamma uX_C} - (d+e)X_C + \theta X_W = 0,\\ &\tfrac{buX_C}{1+\gamma uX_C} - \theta X_W - dX_W = 0.\end{aligned} \tag{3.1}$$

From the first two equations in (3.1), we obtain

$$S_U^* = \frac{A}{pM + \beta + d}, \; S_A^* = \frac{pM}{\beta\beta_1 + d}\frac{A}{pM + \beta + d}.$$

Again, eliminating X_W from the last two equations in (3.1), we obtain a quadratic equation in X_c as:

$$R_1 X_C^2 + R_2 X_C + R_3 = 0, \tag{3.2}$$

where

$$R_1 = d(d+e)\gamma u + \theta\gamma u(d+e) > 0,$$
$$R_2 = \beta ud + \theta(d+e) - \theta\gamma u\beta S_U - \theta\gamma u\beta\beta_1 S_A + d(d+e) - d\gamma u\beta S_U - d\gamma u\beta\beta_1 S_A,$$
$$R_3 = -(\beta\theta S_U + \beta\beta_1\theta S_A + \beta d S_U + \beta\beta_1 d S_A) < 0.$$

Therefore from (3.2), we get

$$X_C = \frac{-R_2 \pm \sqrt{R_2^2 - 4R_1R_3}}{2R_1}.$$

We find that $R_1 > 0$, $R_3 < 0$, and it must have $-4R_1R_3 > 0$. Thus for any values of R_2, we have $(R_2^2 - 4R_1R_3) > R_2^2 > 0$.

Thus the positive root is given by

$$X_C^* = \frac{-R_2 + \sqrt{R_2^2 - 4R_1R_3}}{2R_1}.$$

From the last equation in (3.1), by substituting X_C^*, we obtain $X_W^* = \frac{1}{\theta+d}\frac{\beta u X_C}{1+\gamma u X_C}$.

Finally, we obtained the positive endemic steady state $L^*(S_U^*, S_A^*, X_C^*, X_W^*)$.

The Jacobian matrix to the system (2.1) at the steady state $L^*(S_U^*, S_A^*, X_C^*, X_W^*)$ is given below:

$$J_{L^*} \equiv \begin{bmatrix} -(pM+\beta+d) & 0 & 0 & 0 \\ pM & -\beta\beta_1 - d & 0 & 0 \\ \beta & \beta\beta_1 & -\frac{bu}{(1+\gamma u X_C^*)^2} - (d+e) & \theta \\ 0 & 0 & \frac{bu}{(1+\gamma u X_C^*)^2} & -(\theta+d) \end{bmatrix}.$$

Therefore the characteristic equation is given by

$$|J_{L^*} - \rho I_4| = (pM+\beta+d+\rho)(\beta\beta_1+d+\rho)(\rho^2 + B_1\rho + C_1) = 0,$$

with

$$B_1 = \frac{bu}{(1+\gamma u X_C^*)^2} + 2d + e + \theta,$$
$$C_1 = \frac{bdu}{(1+\gamma u X_C^*)^2} + (d+e)(d+\theta).$$

Now, $\rho^2 + B_1\rho + C_1$=0,
Since

$$B_1^2 - 4C_1 = \{\frac{bu}{(1+\gamma u X_C^*)^2} + 2d + e + \theta\}^2 - 4\{\frac{bdu}{(1+\gamma u X_C^*)^2} + (d+e)(d+\theta)\}$$
$$= \{\frac{bu}{(1+\gamma u X_C^*)^2}\}^2 + \frac{2bu(e+\theta)}{(1+\gamma u X_C^*)^2} + (e-\theta)^2 > 0.$$

Also, $B_1^2 > B_1^2 - 4C_1$ as $C_1 > 0$.

Then, we get two negative roots $\frac{-B_1 \pm \sqrt{B_1^2 - 4C_1}}{2}$. Hence, four eigenvalues of the Jacobian matrix J_{L^*} are given by:

$$\rho_1 = -(pM+\beta+d),\ \rho_2 = -(\beta\beta_1+d),$$
$$\rho_3 = \frac{-B_1 + \sqrt{B_1^2 - 4C_1}}{2}, \text{ and}$$
$$\rho_4 = \frac{-B_1 - \sqrt{B_1^2 - 4C_1}}{2}.$$

Since all the eigenvalues are negative, the system (2.1) is locally asymptotically stable at the steady state $L^*(S_U^*, S_A^*, X_C^*, X_W^*)$.

4 Application of optimal control to the T2 diabetes model

The main objective in this study is to assess both complications of T2 diabetes mellitus patients and financial outcomes by considering time-dependent controls like media control parameter M, and treatment control parameter u into the model system (2.1). Due to the cost of treatment and media awareness, it is always important to find out a strategy in which minimize the prevalence of diabetes patients also associated cost on it and maximize aware susceptible human. Optimal control theory is important and effective to find out such strategies. Hence we consider an objective function as follows:

$$J = \frac{min}{u,M} \int_0^{t_f} (A_1X_C - A_2S_A + A_3u^2 + A_4M^2)e^{-qt}\mathrm{d}t, \tag{4.1}$$

subject to the system of differential Eq. (2.1). Here A_1, A_2 are the measure of the cost of interventions on $[0\ t_f]$ of diabetes patients, aware susceptible, respectively. Also A_3, A_4 are, respectively, taken as weight of the cost of interventions of the square of treatment and media awareness control and q is the relatively discount rate. We choose a quadratic cost on the controls to determine nonlinear interaction arising in the cost at high implementation level. The cost can define the funds needed for treatment including implementation of awareness campaign. Our main aim is to find out an optimal control $(u^*, M^*) = min\{J(u, M); (u, M) \in \mathfrak{U}\}$, where $\mathfrak{U}$={(u, M):$0 \leq u(t), M(t) \leq 1$ for t $\in [0, t_f]$ } is the control set.

Here we applying *Pontryagin's* principle to solve the optimal control problem and the derivation of the existence of the optimal problem is given below.

$$H = A_1X_C - A_2S_A + A_3u^2 + A_4M^2 + \lambda_1\frac{dS_U}{dt} + \lambda_2\frac{dS_A}{dt} + \lambda_3\frac{dX_C}{dt} + \lambda_4\frac{dX_W}{dt} \tag{4.2}$$

where the adjoint variables or co-state variables λ_i, i=1, 2, 3, 4 are the solutions of the following set of differential equations:

$$\begin{aligned}\frac{d\lambda_1}{dt} &= (pM + \beta + d)\lambda_1 - pM\lambda_2 - \beta\lambda_3,\\ \frac{d\lambda_2}{dt} &= A_2 + (\beta\beta_1 + d)\lambda_2 - \beta\beta_1\lambda_3,\\ \frac{d\lambda_3}{dt} &= -A_1 + (d + e + \frac{bu}{(1+\gamma uX_C)^2})\lambda_3 - \frac{bu}{(1+\gamma uX_C)^2}\lambda_4,\\ \frac{d\lambda_4}{dt} &= -\theta\lambda_3 + (\theta + d)\lambda_4,\end{aligned} \tag{4.3}$$

and satisfying the transversality conditions at t_f, i.e., $\lambda_i(t_f)$ =0, i=1, 2, 3, 4.

Theorem 2 *There exist an optimal control $(u^*, M^*) \in \mathfrak{U}$ on a fixed interval $[0, t_f]$ such that $J(u^*, M^*)=\underset{u,M}{min}\{J(u(t), M(t))\}$.*

Proof Since the solutions of the system (2.1) are bounded then there always exist a solution to the optimal control system [19]. Thus the set of all controls and corresponding state variables are nonempty. From definition, the control set is closed and convex. The integrand of the cost functional is $A_1X_C - A_2S_A + A_3u^2 + A_4M^2$, which is convex on the control set $\mathfrak{U}$. Also there exist p_i, q_i, i=1, 2, and $b > 1$ such that $A_1X_C - A_2S_A + A_3u^2 + A_4M^2 \geq p_1 + q_1|u(t)|^b$, and $A_1X_C - A_2S_A + A_3u^2 + A_4M^2 \geq p_2 + q_2|M(t)|^b$, where p_1, p_2 depend on the upper bound of X_C, S_A, respectively, and $q_i = A_i$, i=1, 2. Hence, there exists an optimal control to the optimal system. □

Theorem 3 *If $\lambda_3 > \lambda_4$, then there is an optimal control (u^*, M^*) that minimizes the objective function J over $\mathfrak{U}$ is given by $u^*=max\{0,min(\overline{u}, 1)\}$ and $M^*=max\{0,min(\overline{M}, 1)\}$, where $\overline{u}=\frac{1}{3}\frac{2^{\frac{4}{3}}A_3}{(B+\sqrt{B^2-C})^{\frac{1}{3}}} + \frac{(B+\sqrt{B^2-C})^{\frac{1}{3}}}{2^{\frac{4}{3}}A_3\gamma^2X_C^2} - \frac{2}{\gamma X_C}$, $\overline{M}=\frac{(\lambda_2-\lambda_1)pS_U}{2A_4}$ with $B=16A_3^3\gamma^3X_C^3+108A_3^2b\gamma^4X_C^5\lambda_3 -108A_3^2b\gamma^4X_C^5\lambda_4$ and $C=256A_3^6\gamma^6X_C^6$.*

Proof Equating to zero to the derivatives of the Hamiltonian function with the controls, we get $\frac{\partial H}{\partial u}$=0 and $\frac{\partial H}{\partial M}$=0. Now $\frac{\partial H}{\partial u}$=0, gives $u(1+\gamma uX_C)^2 = \frac{(\lambda_3-\lambda_4)bX_C}{2A_3}$. Then one real root of the equation is given by $\overline{u}=\frac{1}{3}\frac{2^{\frac{4}{3}}A_3}{(B+\sqrt{B^2-C})^{\frac{1}{3}}} + \frac{(B+\sqrt{B^2-C})^{\frac{1}{3}}}{2^{\frac{4}{3}}A_3\gamma^2X_C^2} - \frac{2}{\gamma X_C}$, where B, C have given in statement of the theorem [30].

Now,

$$\begin{aligned}B^2 - C &= (16A_3^3\gamma^3X_C^3 + 108A_3^2b\gamma^4X_C^5\lambda_3\\ &\quad -108A_3^2b\gamma^4X_C^5\lambda_4)^2 - 256A_3^6\gamma^6X_C^6,\\ &= \{108A_3^2b\gamma^4X_C^5(\lambda_3 - \lambda_4) + 32A_3^3\gamma^3X_C^3\}\\ &\quad \{108A_3^2b\gamma^4X_C^5(\lambda_3 - \lambda_4)\},\\ &= \{108A_3^2b\gamma^4X_C^5(\lambda_3 - \lambda_4)\}^2\\ &\quad +32 \times 108A_3^5\gamma^7bX_C^8(\lambda_3 - \lambda_4).\end{aligned}$$

Thus, $B^2 - C > 0$ if $\lambda_3 > \lambda_4$.

Again $\frac{\partial H}{\partial M}$=0, gives

$$\overline{M} = \frac{(\lambda_2 - \lambda_1)pS_U}{2A_4}.$$

Since the controls are bounded by 0 and 1. We set u^*=0 when $\overline{u} \leq 0$, $u^* = 1$ when $\overline{u} \geq 1$, and $u^* = \overline{u}$ when $0 < \overline{u} < 1$. Similar conditions are also hold for M^*. □

5 Numerical simulation with constant control

To find out a better understanding of the complication of T2 diabetes in the population and corresponding health care cost, we first investigated the dynamics of the model system with different vital parameter values and then analyzed the system with various control strategies. We have taken the biologically relevant parameter values in the following:

$A = 12000$; $p = 0.5$; $\beta = 0.001$; $d = 0.00001$; $\beta_1 = 0.000007$; $\gamma = 0.000004$; $e = 0.0007$; $\theta = 0.0000002$; $b = 0.003$; $M = 0.2$; $u = 0.8$; $A_1 = 1$; $A_2 = 10$; $A_3 = 1$; $A_4 = 10000000$;
and the initial population size $S_U(0) = 500000$; $S_A(0) = 476858$; $X_C(0) = 118283$; $X_W(0) = 35485$; to corroborate our analytical finding by using MATLAB software.

Figure 1 represents the behavior of the variables unaware susceptible S_U, aware susceptible S_A, complications of diabetes X_C, and without complications of diabetes X_W of the model (2.1) with constant control values and they eventually approach to the endemic steady state $L^*(118800, 1.18717 \times 10^9, 176542, 1.34491 \times 10^9)$. From Fig. 1, it also demonstrates that both media and treatment control have the ability to reduce the prevalence of complications of T2 diabetes. Moreover, the eigenvalues of the model (2.1) at L^* are ρ_1=-0.10101, ρ_2=-0.00099, ρ_3=-0.00001, and ρ_4 =-0.00001. Thus the model (2.1) is locally asymptotically stable at the steady state L^*.

Now we discuss the dynamics for wide range of different significant parameters M, u, β, and p of the model system

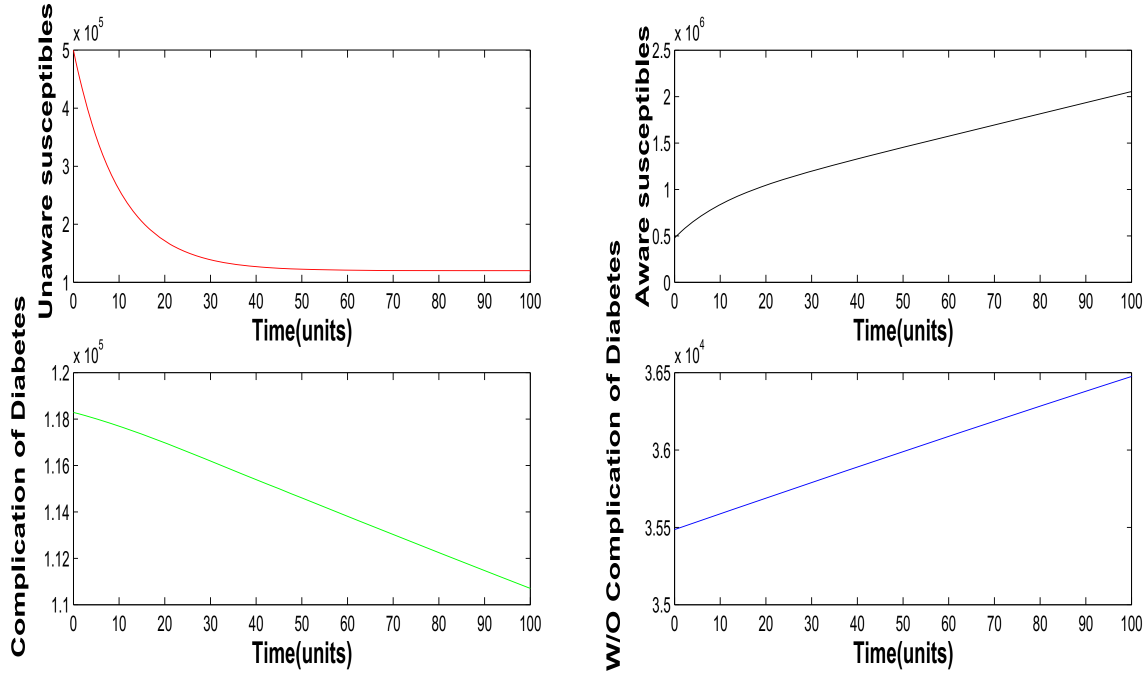


Fig. 1 The figure depicts the solution of the model system (2.1) of the variables S_U, S_A, X_C, and X_W for parameter values $A = 12000$, $p = 0.5$, $\beta = 0.001$, $d = 0.00001$, $\beta_1 = 0.000007$, $\gamma = 0.000004$, $e = 0.0007$, $\theta = 0.0000002$, $b = 0.003$, $M = 0.2$, $u = 0.8$

(2.1) to explore the relationship of T2 diabetes with different parameter values.

5.1 Impact of the media control parameter *M* of T2 diabetes on the model system

The dissemination of awareness not only reduces diabetes prevalence but in some cases can even prevent the onset of diabetes, meaning that awareness can be an effective disease prevention measure [32]. Knowledge and awareness about diabetes of how to monitor and treat diabetes at the right time will reduce complications of diabetes and thus decrease death in diabetes [33]. From Fig. 2a, we see that if we increase the media control parameter M, the number of complications of diabetes X_C decreases for any particular time t. Thus awareness via media control plays an effective role in fighting against complications of T2 diabetes and effectively decreasing diabetes patients.

5.2 Impact of the treatment control parameter *u* of T2 diabetes on the model system

The prevalence of T2 diabetes is increasing, so finding an effective treatment is becoming a top priority for fighting against the disease [34]. Different types of treatment are available for the remission of the complications of T2 diabetes such as bariatric surgery, low-calorie diets, and carbohydrate-restricted diets [11,12]. From Fig. 2b, it shows that if we increase the treatment control parameter u, the number of complications of diabetes X_C decrease for any specified time t. Thus treatment is an important priority to tackle the prevalence of T2 diabetes.

5.3 Effect of the incidence rate β of T2 diabetes on the model system

Sedentary behavior, lack of exercise, smoking, and alcohol consumption are all lead to the rapid increases in the incidence of T2 diabetes [34]. It is critical to improve prevention measures for recognizing high-risk individuals and identifying possibly modifiable risk factors to decrease the incidence of T2 diabetes. From Fig. 3a, its demonstrated that if we increase incident rate β then number of diabetes complication X_C also increase for any specified time t. Sedentary behavior, lack of exercise, smoking, and alcohol consumption are risk factors to the rising incidence of T2 diabetes in individuals.

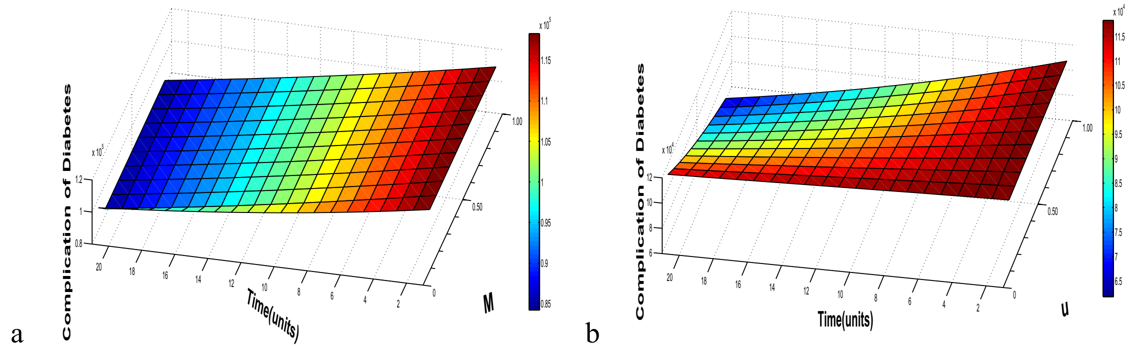


Fig. 2 The figures depict the role of the complications of diabetes X_C with respect to time for different values of u and M, respectively, and other values of parameters are kept same as Fig. 1

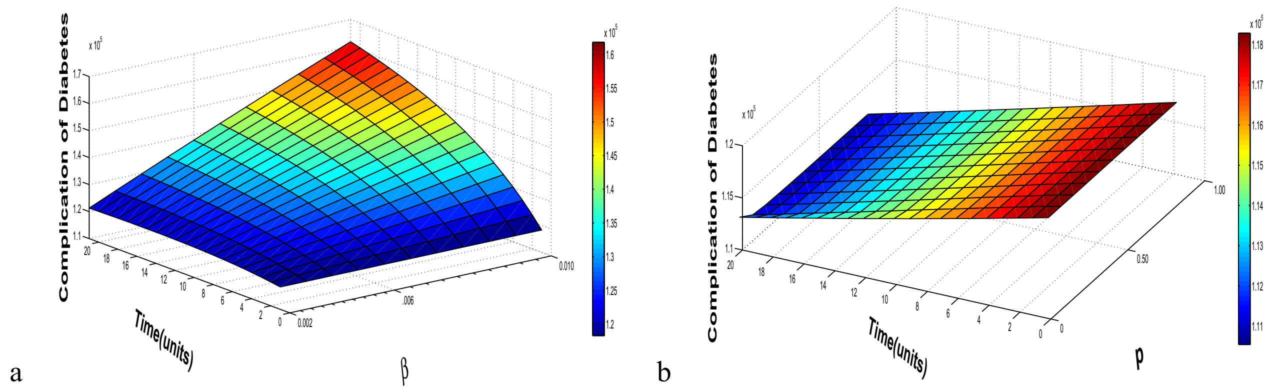


Fig. 3 The figures depict the role of the complications of diabetes X_C with respect to time for different values of β and p, respectively, and other values of parameters are kept same as Fig. 1

5.4 Role of awareness coefficient *p* of T2 diabetes on the model system

Awareness about the complications of diabetes and sequential rise in dietary knowledge, attitude, and practices can manage better control diabetes. Some articles have shown that awareness of diabetes will significantly increase the quality of life of patients and reduce the burden of the disease on their family [4,35]. From Fig. 3b, it shows that if we increase awareness coefficient p, the number of complications of T2 diabetes X_C is also slightly decreased with any particular time t.

6 Numerical simulation with optimal control

In this section, we carried out numerical simulations to show the effect of the control strategies on the T2 diabetes mathematical model. Solving the optimality system (2.1) and (4.3) and corresponding their initial conditions, we obtained solutions of the optimal system. At first, we take an initial guess of the control variables, then state variables of the model system (2.1) are solved using the RK4 method forward in time. Next, using initial control guess and state variables corresponding adjoint system (4.3) is solved by using RK4 method backward in time. This iterative method ends when the current state, adjoint, and control values are converged sufficiently [36–38]. In addition, different types of strategies are taken with the combination of control profiles as strategy 1 (only media control), strategy 2 (only treatment control), and strategy 3 (together with the media and treatment controls) to figure out the effects of media and treatment controls in the system.

First of all, we solve the control system (4.1) in different types of control strategies with the same initial population size and parameters values are used in the previous section. The corresponding outcomes of the control system have been displayed in Fig. 4. It is clear that in the absence of control, the complication of T2 diabetes increases gradually and resulting in a massive disease prevalence in the population. In addition, aware susceptible and without complication of T2 diabetes remain low due to the rapid increase of complication of T2 diabetes.

Again from strategy 1, it is clear that the slope of the line of complications of T2 diabetes decreases and delays the prevalence of T2 diabetes compared to the absence of

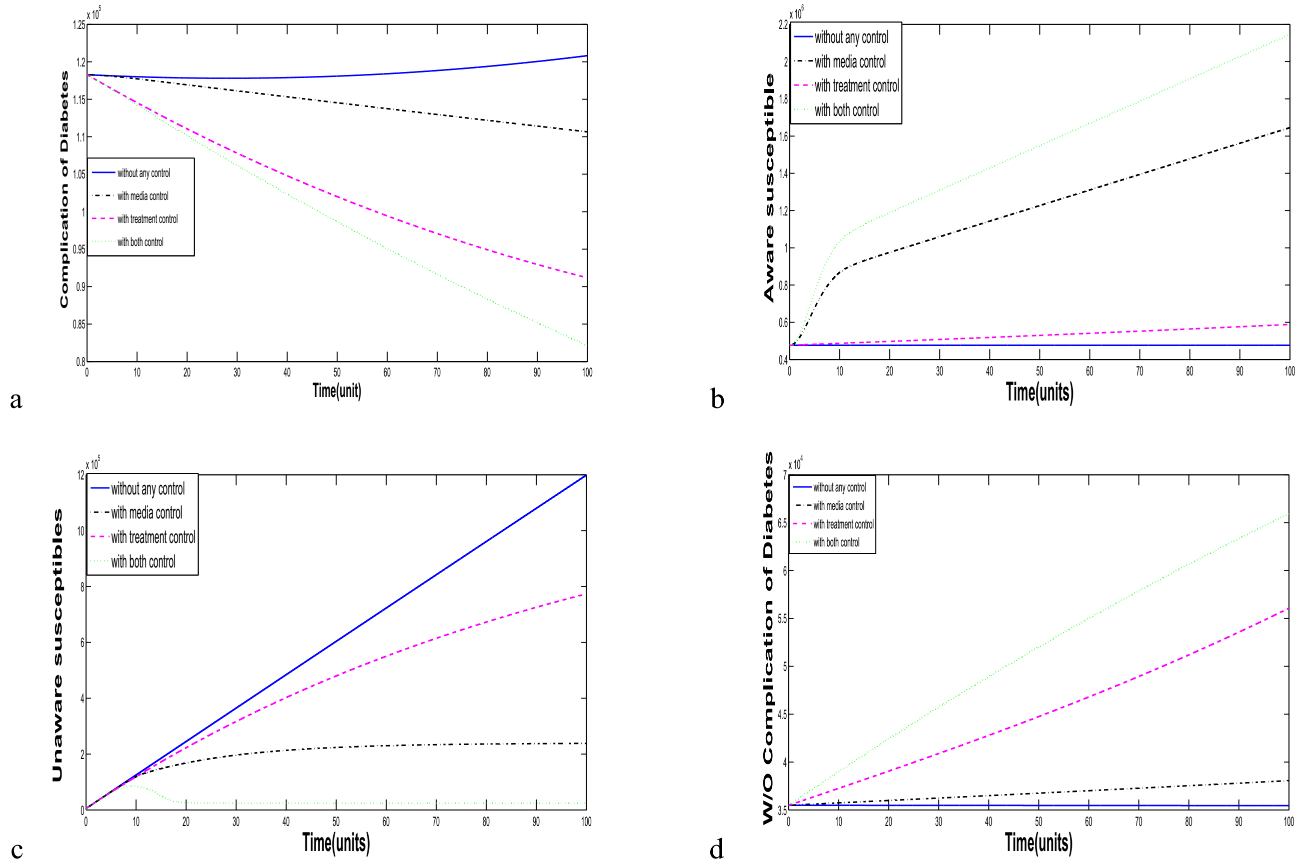


Fig. 4 The figure depicts the role of **a** complications of diabetic human, **b** aware susceptible, **c** unaware susceptible, and **d** without complications of diabetes with different types of optimal control for any time *t*

control. Consequently, strategy-1 plays a prominent role in reducing the prevalence of T2 diabetes over time. The optimal path of M for strategy 1 is displayed in Fig. 5a and found that awareness program M executing over the entire period with full potential.

Next, in strategy 2, it is clear that the slope of the line of complications of T2 diabetes decreases, and the graph lies below from strategy 1. Thus strategy 2 has a significant impact on the prevalence of T2 diabetes to minimize the disease. The optimal path of u in this strategy is displayed in Fig. 5b and found that recovery u has been executing over time with full potential. Finally, in strategy 3, it is clear that the graph of complications of T2 diabetes is at a minimal level over time compared to earlier cases. Thus, in this case, there is no rapid prevalence of T2 diabetes. Consequently, it significantly minimizes the complication of T2 diabetes. Also, rapid growth is observed in aware susceptible humans and without the complication of diabetes under strategy 3. In addition, the curve of unaware susceptible human rapid growth is happening initially after that, it gradually decays and stays at a lower level than any other earlier cases. The optimal path of the controls M and u for strategy 3 is displayed in Fig. 5c and found that awareness program M and recovery control u executing over the entire period but relatively lower than the previous strategies, whereas Fig. 6 represents the role of the corresponding adjoint variables when both optimal controls are applied. Here it is noted that λ_1 and λ_3 are increasing over time, but λ_2 and λ_4 are decreasing over time. These findings are consistent with the results of the earlier research studies [15,30,38].

7 Cost-effectiveness analysis

Controlling and reducing T2 diabetes in a population can be time-consuming and costly. As a result, cost-effectiveness analysis is needed to decide the most cost-effective approach to use for strategy 1 (only media control), strategy 2 (only treatment control), and strategy 3 (together with the media and treatment controls). In this segment, we use cost-effectiveness analysis to look at the cost-effectiveness of treatment and personal safety management measures (e.g., physical activity and dietary choices), as well as the benefits that come with them. We have used three different methods

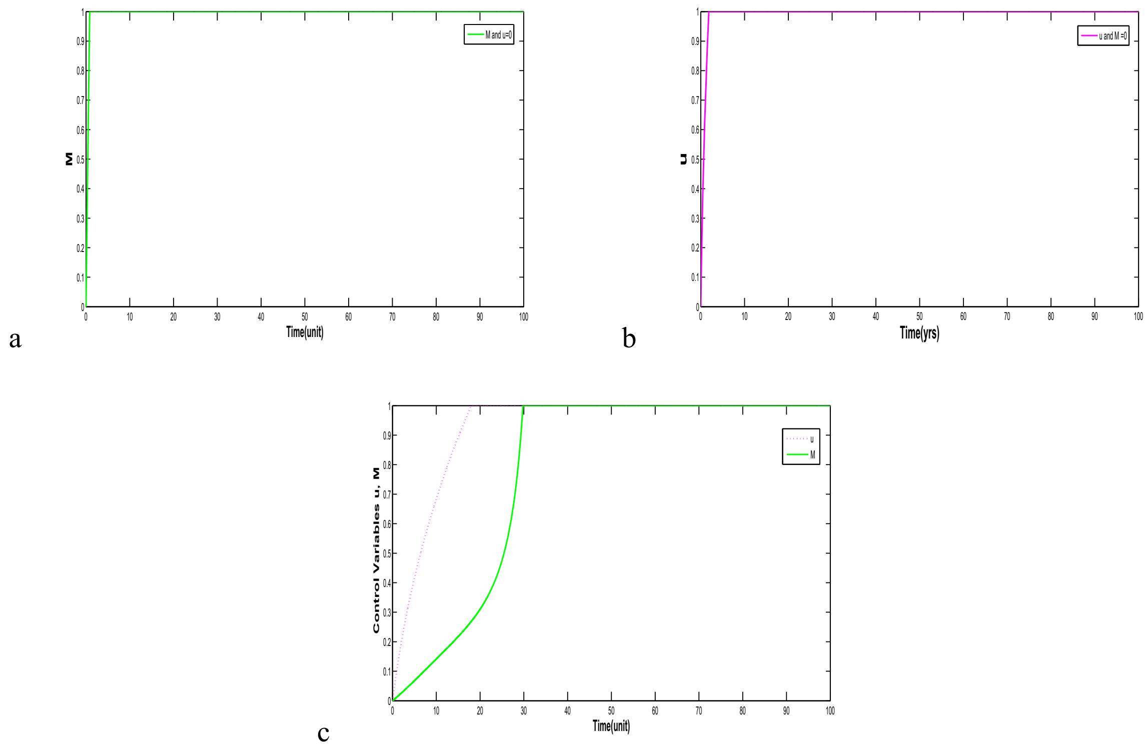


Fig. 5 The figures depict the role of **a** only media control parameter M, **b** only recovery control parameter u, **c** both media control parameter M and recovery control parameter u at any time

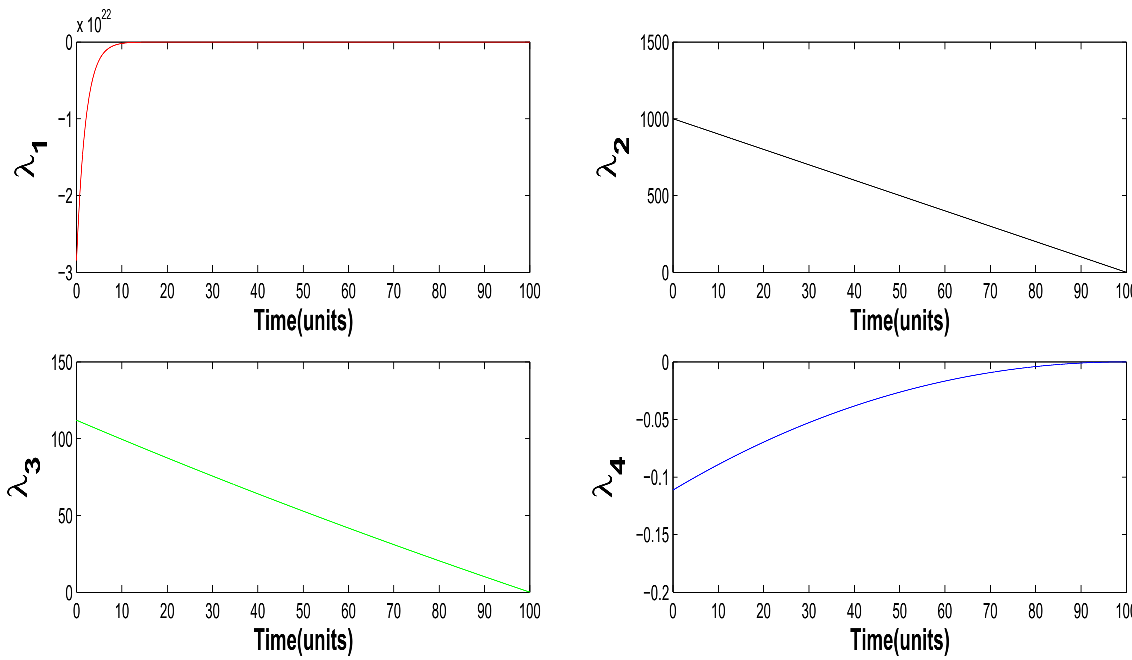


Fig. 6 The figure depicts the role of the adjoint variables when both optimal controls are applied

Table 1 DAR and ACER of all strategies

Strategies	Total infection averted	Total recovered	DAR	ACER
Strategy 1	3.5012×10^7	8.8679×10^4	394.82	0.022042
Strategy 2	9.5097×10^7	4.8757×10^7	1.9504	0.010210
Strategy 3	1.3008×10^8	4.8743×10^7	2.6687	0.024642

Table 2 ICER of all strategies

Strategies	Total infection averted	Total costs	ICER
Strategy 1	3.5012×10^7	8.8679×10^4	4.427×10^{-4}
Strategy 2	9.5097×10^7	4.8757×10^7	6.66×10^{-5}
Strategy 3	1.3008×10^8	4.8743×10^7	-5.72×10^{-5}

Table 3 ICER of all strategies

Strategies	Total infection averted	Total costs	ICER
Strategy 2	9.5097×10^7	4.8757×10^7	2.06×10^{-4}
Strategy 3	1.3008×10^8	4.8743×10^7	0.23×10^{-4}

like DAR, ACER, and ICER given in one by one in the following subsections to evaluate the most cost-effective strategy.

7.1 Disease averted ratio (DAR)

The disease averted ratio (DAR) is calculated as follows:

$$\text{DAR} = \frac{\text{Number of disease averted}}{\text{Number of recovered}},$$

The *number of disease averted* is termed by the difference between the total diabetic individuals without control and the total disease individuals with control over the same period of time. The strategy with the highest DAR values is the least cost-effective. From Table 1, we see that strategy 2 is the least cost-effective strategy.

7.2 Average cost-effectiveness ratio (ACER)

A single intervention's average cost-effectiveness ratio (ACER) is compared to the no-intervention baseline alternative. ACER is determined as

$$\text{ACER} = \frac{\text{Total cost produced by the intervention}}{\text{Total number of disease averted}},$$

where the total cost is evaluated from the objective function given in Eq. (4.1). From this cost-effectiveness approach strategy 2 is the least cost-effective strategy (see Table 1).

7.3 Incremental cost-effectiveness ratio (ICER)

The incremental cost-effectiveness ratio (ICER) measures the extra cost per added health result and the costs of different control measures are assumed to be proportional to the number of controls deployed. One intervention is compared to the next-less-effective alternative in order to equate two or more opposing intervention methods incrementally. Then the ICER can be calculated as follows:

$$\text{ICER} = \frac{\text{Difference in disease averted costs in strategies } i \text{ and } j}{\text{Difference in total number of disease averted in strategies } i \text{ and } j}.$$

The variations in the costs of disease averted or cases avoided, the costs of intervention(s), and the costs of averting production losses, among other things, are included in the ICER numerator (where applicable). On the other hand, the ICER numerator is the difference in health effects, which may include the total number of disease averted or the number of susceptibility cases avoided. Therefore,

$$\begin{aligned}
\text{ICER(Strategy 1)} &= \frac{1.5501\times10^4}{3.5012\times10^7} = 0.000443,\\
\text{ICER(Strategy 2)} &= \frac{1.9501\times10^4 - 1.5501\times10^4}{9.5097\times10^7 - 3.5012\times10^7}\\
&= 0.0000066,\\
\text{ICER(Strategy 3)} &= \frac{1.7551\times10^4 - 1.9501\times10^4}{1.3008\times10^7 - 9.5097\times10^7}\\
&= 0.000024.
\end{aligned}$$

From Table 2, comparing ICER (strategy 1), and ICER(strategy 2), shows a cost saving of 0.4427 for strategy 2 over strategy 1. The minimum ICER from strategy 2 is indicated that strategy 1 is strongly dominated. This means that strategy 1 is comparatively much costly and less effective to implement than the strategy 2. Thus we can exclude strategy 1 from the other set of two strategies as it will not be effective on the limited resource.

Again similarly strategy 2 is compared with strategy 3 to obtain alternative intervention. Computation of ICER as follows:

$$\begin{aligned} \text{ICER(Strategy 2)} &= \frac{1.9501 \times 10^4 - 1.5501 \times 10^4}{9.5097 \times 10^7} \\ &= 0.0004206, \\ \text{ICER(Strategy 3)} &= \frac{1.7551 \times 10^4 - 1.9501 \times 10^4}{1.3008 \times 10^7 - 9.5097 \times 10^7} \\ &= 0.000024. \end{aligned}$$

From Table 3 it is clear that strategy 3 is strongly dominated by strategy 2. This means that strategy 2 is much costly compared to strategy 3. Thus strategy 3 is more cost-effective compared to strategy 2.

Remark The results of DAR, ACER, and ICER are not same although they demand that strategy 1 is not cost-effective. Health policy maker should decide which control will be least cost- effective to tackle the disease.

7.4 Cost design analysis

We undertake a cost design analysis and comparison research to determine the appropriateness and cost-effectiveness of these strategies (1, 2, and 3). Figure 7 represents the temporal profile of the cost under different types of control profile. In the absence of controls, the produced cost is solely attributable to complications of diabetes (productivity loss), which is extremely high (as indicated in the black color dashed curve in Fig. 7) since the count of T2 diabetes patients is maximum in this case. Thus disease outbreak not only produces a large epidemic but also imposes a significant financial burden on communities. From Fig. 7, it also demonstrates that when both the controls are applied, the total corresponding cost is minimal. Also further noticed that cost induced by only treatment control is less than in either case of media control. Thus from this cost design analysis, strategy 2 is economically effective than strategy 1, whereas strategy 3 is highly economically better than all other strategies during the epidemic.

7.5 Effect of saturation on the optimal controls and cost function

We vary the saturation constant γ to see how limitations in medical resources affect the optimal control and the cost function. When γ=0 in Fig. 8a (i.e., recovery of T2 diabetes is sufficiently large), then the number of complications of T2 diabetes is relatively lower than all other values of X_C for positive values of γ. Also Fig. 8b demonstrates that by increasing the higher values of γ the corresponding cost is found to be higher under the strategy. To avoid an excessive number of figures we just left the figures under strategy 3 for different values of γ. Consequently, if the treatment is not limited (i.e., if γ=0), then not only disease but also economic burden can be minimized using both the control profiles. Next, Fig. 9 represents optimal controls for different values of γ. It is clear that when saturation constant γ increases then a higher potential of the optimal control u is needed to minimize the disease. In addition, there is no significant impact of the control M by changing the value of γ.

8 Discussion and conclusion

Mathematical modeling has become an important theoretical tool for understanding fundamental features of a wide range of medical-biological processes. Dynamics of mathematical modeling of T2 diabetes under appropriate diagnosis, prevention, awareness, and recovery of individuals allowing understanding to control the disease. Now researchers have been formulating mathematical models on diabetes mellitus to simulate, analyze, and understand the dynamics of diabetes. Earlier Mollah et al. [24] formulated mathematical models under deterministic as well as the stochastic environment and tried to investigate the dynamics of diabetes mellitus under the effect of awareness. Their results reflect that awareness can prevent diabetes mellitus in the community. A related work Kouidere et al. proposed a mathematical model with optimal control strategy highlighting the impact of behavioral factors on the complication of diabetes [23]. They showed only the effectiveness of the control techniques but did not evaluate the best possible strategy for controlling the disease. In this regard, the novelty of our proposed model is that effect of media and saturated treatment function are taken as control measures to find out the most cost-effective strategy with the limited resources.

In the present article, we propose a mathematical model of T2 diabetes by considering awareness M and treatment u are constant parameters. The complete analysis of the model system (2.1) including the positivity of solutions, boundedness, stability is carried out, and Fig. 2 plots for varying values of M and u to verify their effectiveness in the system (2.1). It is observed that both awareness and treatment have a significant impact on the prevalence of complication of T2 diabetes mellitus. Again, we have considered the model system (2.1) as an optimal control problem by taking awareness M and saturated treatment u as time depended control parameters to assess the complication of T2 diabetes and financial cost over a finite time. Existence conditions for the optimal solution of the control problem (2.1) are discussed and some effective strategies for controlling the disease are identified. We used numerical simulation to verify the control problem (2.1) and encountered optimal control solution for the problem, which can minimize the objective functional outcome (4.1). From numerical simulations, optimal control strategies have a sig-

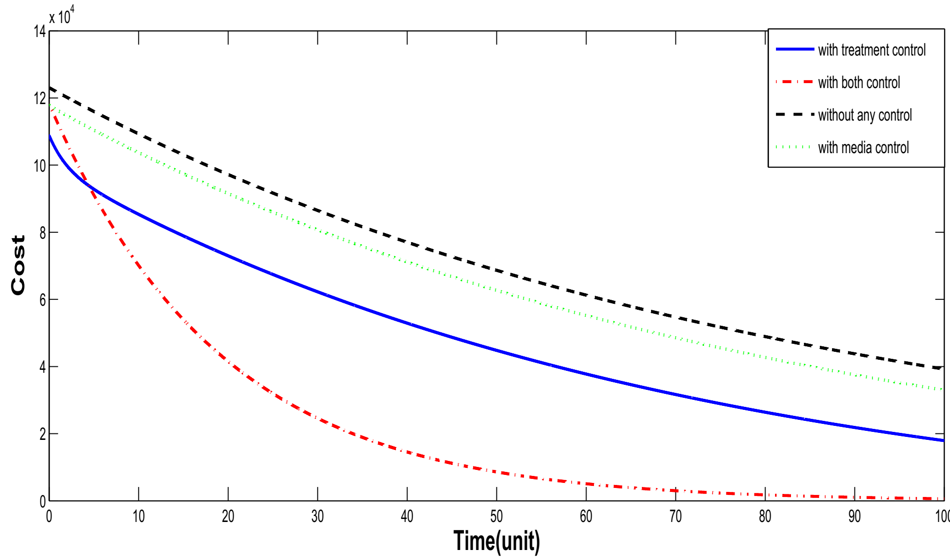
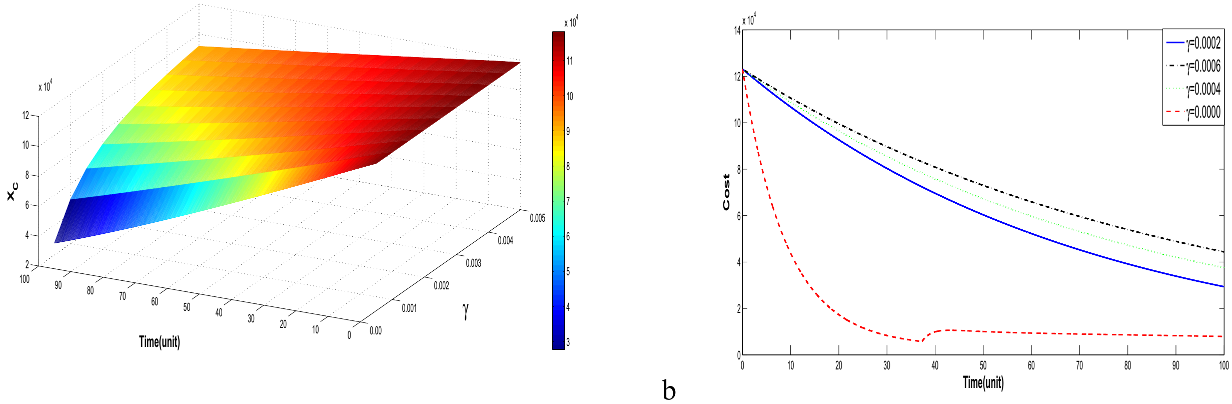
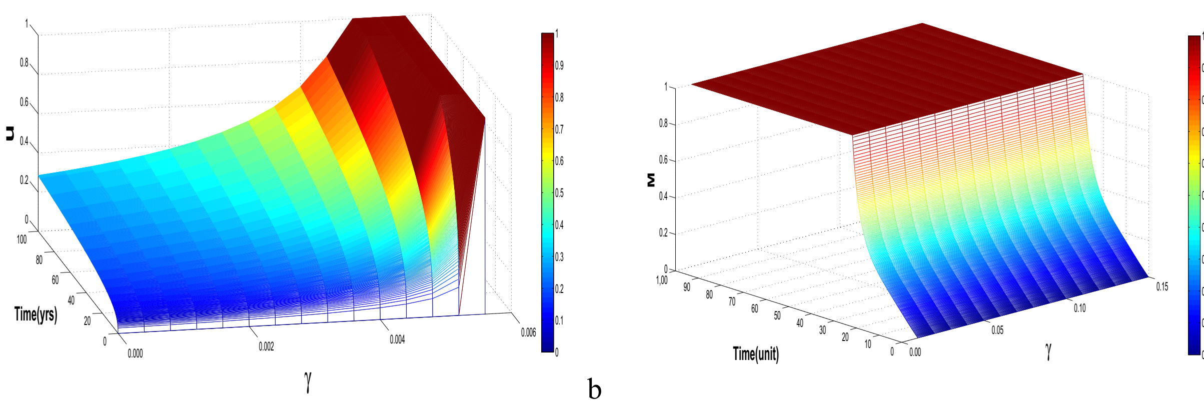


Fig. 7 The figure depicts the related costs under various control strategies



a b

Fig. 8 The figures depict the role of the a) complications of diabetes X_C with respect to time for different values of γ and b) related costs with respect to for different values of γ



a b

Fig. 9 The figures depict the role of the a) optimal control profiles u with respect to time for different values of γ and b) optimal control profiles M with respect to time for different values of γ and other values of parameters are kept same as Fig. 1

nificant impact on reducing the complication of diabetes in the population has displayed in Fig. 4. When different types of control strategies are applied in the system (2.1) then the complication of diabetes decrease and without complications of diabetes increase. In strategy 3, the graph of complications of diabetes is the least, and the graph of without complications of diabetes is the highest at any time when compared to the other strategies. Thus the result emphasizes that awareness and treatment reduce the complication of diabetes and turn them into without complication of diabetes. Overall in strategy 3, significantly minimizes the prevalence of T2 diabetes than strategy 1 or strategy 2. Also, awareness control M and treatment control u in strategy 3 execute over the entire period but their values are relatively lower than strategy 1 and strategy 2 (See Fig. 5). Thus in strategy 3, optimal control functions are needed relatively lower potential than strategy 1 and strategy 2 to obtain the least prevalence of the disease. In addition, the results of DAR, ACER, and ICER agreed that strategy 1 is not a cost-effective strategy other than strategy 2 and strategy 3. Also, cost design analysis is performed and the related cost is displayed in Fig. 9 to establish the most cost-effective disease-control strategy with the limited resource. The results showed that if the treatment is not limited, then not only disease prevalence but also economic burden can be minimized using both the control profiles (i.e., in strategy 3). Thus, it is very effective for the policymakers to follow the strategy 3. Again, findings of the numerical simulation show that if the treatment is not limited (i.e., if γ=0), then complication of diabetes is remain least for all time in Fig. 8, a). Also, from Fig. 9 when saturation constant γ increases then a higher potential of the optimal control u is needed to minimize the disease. Thus from the above substantial outcomes, it is evident that the model is biologically well motivated [30].

This article represents a snapshot against the rising prevalence of T2 diabetes and its related cost on aspects of awareness and treatment. There are several directions in which the modeling of diabetes can be generalized. The issue of T2 diabetes is the long lag time between disease causes and outcomes. Furthermore, a delay-induced mathematical model will be more efficient in evaluating time-lag characteristics throughout the awareness period as non-instantaneous responses to awareness programs of an individual. From our mathematical perspective, a time delay is needed for accurate modeling of T2 diabetes models. Again, T2 diabetes is more likely to develop as a result of certain infectious infections such as hepatitis B virus (HBV) and human papillomavirus (HPV). Considering the co-infection of HBV and HPV on the assumptions, a highly nonlinear mathematical model can be generated.

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Declaration

Conflict of Interest The authors have declared that they have no conflicts of interest that are relevant to the content of this work.

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