Existence and characterization of optimal control in mathematics model of diabetics population

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Abstract. Diabetes is a chronic disease with a huge burden affecting individuals and the whole society. In this paper, we constructed the optimal control mathematical model by applying a strategy to control the development of diabetic population. The constructed mathematical model considers the dynamics of disabled people due to diabetes. Moreover, an optimal control approach is proposed in order to reduce the burden of pre-diabetes. Implementation of control is done by preventing the pre-diabetes develop into diabetics with and without complications. The existence of optimal control and characterization of optimal control is discussed in this paper. Optimal control is characterized by applying the Pontryagin minimum principle. The results indicate that there is an optimal control in optimization problem in mathematics model of diabetic population. The effect of the optimal control variable (prevention) is strongly affected by the number of healthy people.

1. Introduction
Diabetes is a chronic disease caused by the lack of responsiveness of cells to insulin. Generally, level of fasting plasma glucose concentration (FPGC) is used to diagnose diabetes. Someone is said to be healthy if he has normal glucose levels i.e less than 6.1 mmol/L by FPGC [1]. Pre-diabetes is defined as a state which places individuals at high risk of developing diabetes and its complications. Pre-diabetes and diabetes are defined by a FPGC between 6.1-6.9 mmol/L and greater than 7.0 mmol/L, respectively [2]. Diabetes is a disease that the number of sufferers increase continously. More than 370 million people are living with diabetes worldwide (8.5% of adult population) and nearly 300 million people are in the pre-diabetic stage (6.5% of adult population) [3]. Due to its chronic nature, diabetes can cause complications and disabilities due to these complications. For example, retinopathy can cause blindness, gangrene diabetic can cause lower leg amputation, and stroke can cause mute. Treatment and care for diabetes with its complications cost a lot. In order to prevent adults from this disease, efficient and optimal strategies are needed to reduce the burden of diabetes and its complications. Following previous mathematical models on diabetes [3-5], in this paper we present an optimal control model of diabetic population by considering the stage of disabled due to complications. The main purpose are to investigate the existence and characterization of the optimal control of the model.

2. Methods
The method used in this study is literature review and reference collection of theories that support the completion of this research. We collect references about the characteristics of diabetes, the causes of
diabetes, diabetes complications, the treatments such as prevention, dynamical model of diabetes, and optimal control problem. We consider a population of diabetics, divided into five subcategories i.e. healthy people, pre-diabetics, diabetics without complications, diabetics with complications, and diabetics become disabled. From the diabetics population, we establish an optimal control problem. Moreover, the optimal control problem consist of five states and a variable control for which necessary conditions of an optimal control are well known. We can prove the existence and positivity of solutions, existence of optimal control, and also we can characterize the optimal control as it has been done in [6-13]. Therefore, the literature review aims to determine the use of the Pontryagin minimum principle to characterize the optimal control problem based on functional objectives and the transversality conditions. Transversality conditions for the optimal control problem is free and point-fixed final time. In addition, we can understand the theorems used to investigate the existence and positivity of solutions and the existence of optimal control.

3. Result and Discussion

3.1. Optimal Control Model

In this paper, the mathematical model constructed on the population of diabetics. This model is modified from mathematical models that have been developed by [5]. Let $P=P(t), E=E(t), D=D(t), C=C(t)$ and $B=B(t)$ be respectively the numbers of healthy people, pre-diabetics and diabetics without complications, diabetics with complications and diabetics become disabled. This population evolves continuously in the time interval $[0, t_f]$. Figure 1 illustrates the dynamics of an adult population with related settings.

![Figure 1. The dynamics of the development of the diabetic population](image)

Following the description and illustration above, the proposed model can be written as:

\[
\begin{align*}
\dot{P} &= \rho - \sigma_1 (1 - u) P - (\sigma_2 + \sigma_3 + \mu) P + \gamma_1 E \\
\dot{E} &= \sigma_1 (1 - u) P - (\gamma_1 + \mu + \beta_1 + \beta_3) E + \gamma_2 D \\
\dot{D} &= \sigma_2 P + \beta_1 E - (\mu + \beta_2 + \gamma_2 + \gamma_3) D + \gamma_3 C \\
\dot{C} &= \gamma_3 D + \nu_1 C - (\mu + \tau) B \\
\dot{B} &= \nu_2 D + \nu_1 C - (\mu + \tau) B
\end{align*}
\]

where $\rho$ is the incidence of healthy adult population. The rate of healthy persons to become diabetic without complication and diabetic with complication, is described by the parameters $\sigma_2$ and $\sigma_3$, respectively. Parameter $\mu$ is natural mortality rate. Parameter $\gamma_1$ and $\sigma_1$ are related to the rate at which a pre-diabetic person becomes healthy and vice versa. We denote $\gamma_2$ as the rate of a diabetic person to become pre-diabetic, and $\gamma_3$ as the rate at which a diabetic with complications become...
diabetic without complications. Parameter $v_1$ is related to the rate at which a diabetic person become disabled and $v_2$ is the rate at which a diabetic with complication person become disabled. The probability of a pre-diabetic person to become diabetic is denoted by $\beta_1$. Parameter $\beta_2$ representsthe probability of a diabetic person developing a complications. The probability of a pre-diabetic person developing a complication is denoted by $\beta_3$. By $\tau$ and $\delta$ we denote themortality rate due to disabled and mortality rate due to complications, respectively.

The optimal control approach is used to reduce the number of pre-diabetics in order to prevent adults from diabetes and its complications and also minimizing controlling costs. We consider the control variable $u = u(t)$ to be the percentage of healthy people being prevented from pre-diabetes per unit of time. The problem is then to minimize the objective functional defined as:

$$ J(u) = \int_0^{t_f} (E(t) + Au^2(t))dt $$

(2)

In equation (2), the term $E(t)$ represents the result of performance pre-diabetics who want to be minimized. The term $Au^2(t)$ represents the systematic cost of control. The constant $A$ is a positive weight that balances the size of the term $u$, $t = 0$ is initial time, $t_f$ is final time, and $u$ is control through prevention. $U$ is the control set defined as:

$$ U = \{u : 0 \leq u \leq 1, t \in \left[0, t_f\right]\} $$

Control $u^*$ represents the severity of the side effects of control. The optimal control $u^* \in U$ satisfies

$$ J(u^*) = \min_{u \in U} J(u) $$

and system (1) would be a constraint to optimal control optimization problems.

3.2. Existence and Positivity of Solutions

Theorem 1. The set $\Omega = \{(P, E, D, C, B) \in \mathbb{R}^4 \mid 0 \leq P, E, D, C, B \leq \frac{P}{\mu}\}$ is positively invariant under system (1).

Proof: We assume that there exists $t^* > 0$ such that $P(t^*) = 0$, other variables are positive and $P(t) > 0$, for $t \in \left[0, t^*\right]$, we have

$$ \frac{dP(t)}{dt} + (\sigma_1 + \sigma_2 + \sigma_3 + \mu)P = \rho + \sigma_1 uP + \gamma_1 E $$

(3)

Both sides in equation (3) are multiplied with $e^{(\sigma_1 + \sigma_2 + \sigma_3 + \mu)t}$ obtained

$$ \frac{d(Pe^{(\sigma_1 + \sigma_2 + \sigma_3 + \mu)t})}{dt} = e^{(\sigma_1 + \sigma_2 + \sigma_3 + \mu)t} (\rho + \sigma_1 uP + \gamma_1 E) $$

(4)

After integrating the equation (4) from 0 to $t^*$, we obtain:

$$ P(t^*) = e^{-(\sigma_1 + \sigma_2 + \sigma_3 + \mu)t} \left( P(0) + \int_0^{t^*} e^{(\sigma_1 + \sigma_2 + \sigma_3 + \mu)t} (\rho + \sigma_1 uP + \gamma_1 E) dt \right) $$

Therefore $P(t^*) > 0$ which contradict with $P(t^*) = 0$, thus $P(t) > 0, \forall t \in \left[0, t_f\right]$. Similarly, we prove that $E(t) > 0, D(t) > 0, C(t) > 0, B(t) > 0$. Also, one assumes that:
\[
\frac{dN(t)}{dt} = \rho - \mu N(t) - \delta C(t) - \tau B(t)
\]
\[
\Leftrightarrow N(t) \leq \frac{\rho}{\mu} e^{-\mu t} + N(0) e^{-\mu t}
\]

If we take limit \( t \to \infty \) then \( N(t) \leq \frac{\rho}{\mu} \).

**Theorem 2.** The controlled system (1) that satisfies a given initial condition \((P(0), E(0), D(0), C(0), B(0)) \in \Omega\) has a unique solution.

Proof: Let

\[
X = \begin{bmatrix} P(t) \\ E(t) \\ D(t) \\ C(t) \\ B(t) \end{bmatrix}, \quad \phi(X) = \begin{bmatrix} \dot{P} \\ \dot{E} \\ \dot{D} \\ \dot{C} \\ \dot{B} \end{bmatrix}
\]

We can write the system (1) as

\[
\phi(X) = AX + B
\]

where

\[
A = \begin{bmatrix}
\omega_1 & \gamma_1 & 0 & 0 & 0 \\
\sigma_1(1-u) & \omega_2 & \gamma_2 & 0 & 0 \\
\sigma_2 & \beta_1 & \omega_3 & \gamma_3 & 0 \\
\sigma_3 & \beta_3 & \beta_2 & \omega_4 & 0 \\
0 & 0 & \nu_2 & \nu_1 & \omega_2 \\
\end{bmatrix}, \quad B = \begin{bmatrix} \rho \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}
\]

then,

\[
\|\phi(X_1) - \phi(X_2)\| \leq \|M\| \|X_1 - X_2\|
\]

Thus, it follows that the function \( u \) is uniformly Lipschitz continuous. So from the definition of the control \( u(t) \) and the restriction on \( P(t) > 0, E(t) > 0, D(t) > 0, C(t) > 0, \) and \( B(t) > 0 \), we conclude that a solution of the system (1) exists.

**3.3. Existence of an Optimal Control**

**Theorem 3.** Consider the control problem with system (1). There exists an optimal control \( u^* \in U \) such that

\[
J(u^*) = \min_{u \in U} J(u)
\]

Proof: We can prove the existence of the optimal control checking the following points:

- The Theorems 2 and 3 indicate that the set of controls and corresponding state variables is not empty.
- The control space \( U = \{u : 0 \leq u \leq 1, t \in [0, t_f]\} \) is convex and closed by definition.
- All the right hand sides of equations of system (2) are continuous, bounded above by a sum of bounded control and state, and can be written as a linear function of \( u \) with coefficients depending on time and state.
- The integrand in the objective functional, \( E(t) + Au^2(t) \) is clearly convex in \( U \).
• There exist constants \( \alpha_1, \alpha_2 > 0 \) and \( \alpha > 1 \) such that \( E(t) + Au^2(t) \) satisfies
\[
E(t) + Au^2(t) \geq \alpha_1 + \alpha \|u\|^2
\]
The state variables being bounded, let \( \alpha_1 = \frac{1}{2} \inf_{\tau(0,1)} E(t), \alpha_2 = A, \alpha = 2 \) then it follows that
\[
E(t) + Au^2(t) \geq A\|u\|^2
\]
then we conclude that there exists an optimal control.

3.4. Characterization of the Optimal Control

In order to derive the necessary conditions for the optimal control, we apply Pontryagin’s maximum principle to the Hamiltonian \( H \).

**Theorem 4.** Given an optimal control \( u^* \) and solutions \( P^*, E^*, D^*, C^* \), and \( B^* \) of the corresponding state system (1), there exist adjoint variables \( \lambda_1, \lambda_2, \lambda_3, \lambda_4 \), and \( \lambda_5 \) satisfying
\[
\begin{align*}
\dot{\lambda}_1 &= \lambda_1 \mu + (\lambda_1 - \lambda_2)(1-u)\sigma_1 + (\lambda_2 - \lambda_3)\sigma_2 + (\lambda_4 - \lambda_5)\sigma_3 \\
\dot{\lambda}_2 &= -1 - \lambda_2\gamma_1 + \lambda_2(\mu + \gamma_1) + (\lambda_2 - \lambda_3)\beta_1 + (\lambda_3 - \lambda_4)\beta_1 \\
\dot{\lambda}_3 &= -\lambda_2\gamma_1 + \lambda_3(\mu + \gamma_1) + (\lambda_3 - \lambda_4)\beta_2 + (\lambda_4 - \lambda_5)\beta_2 \\
\dot{\lambda}_4 &= (\lambda_4 - \lambda_5)\gamma_1 + \lambda_4(\mu + \delta) + (\lambda_4 - \lambda_5)v_1 \\
\dot{\lambda}_5 &= -\lambda_5(\mu + \tau)
\end{align*}
\]
with transversality conditions \( \lambda_1(t_f) = \lambda_4(t_f) = \lambda_3(t_f) = \lambda_2(t_f) = \lambda_5(t_f) = 0 \). Moreover, the optimal control is given by
\[
u^* = \min \left( 1, \max \left( 0, \frac{1}{2A} \left[ \sigma_1P(\lambda_2 - \lambda_1) \right] \right) \right)
\]

Proof: The Hamiltonian is defined as follows:
\[
H = E + Au^2 + \lambda_1P + \lambda_2E + \lambda_3D + \lambda_4C + \lambda_5B
\]
The adjoint variables \( \lambda_1, \lambda_2, \lambda_3, \lambda_4, \), and \( \lambda_5 \) are obtained by the following system:
\[
\begin{align*}
\dot{\lambda}_1 &= -\frac{\partial H}{\partial P}, \quad \dot{\lambda}_2 = -\frac{\partial H}{\partial E}, \quad \dot{\lambda}_3 = -\frac{\partial H}{\partial D}, \quad \dot{\lambda}_4 = -\frac{\partial H}{\partial C}, \quad \dot{\lambda}_5 = -\frac{\partial H}{\partial B}
\end{align*}
\] (5)

The optimal control \( u^* \), derived from the stationary condition \( \frac{\partial H}{\partial u} = 0 \), and considering the properties from the control space, is given by
\[
u^* = \begin{cases} 
0, & \frac{1}{2A} \left[ \sigma_1P(\lambda_2 - \lambda_1) \right] \leq 0 \\
\frac{1}{2A} \left[ \sigma_1P(\lambda_2 - \lambda_1) \right], & 0 < u < 1 \\
\frac{1}{2A} \left[ \sigma_1P(\lambda_2 - \lambda_1) \right] \geq 1
\end{cases}
\]

Thus, the optimal control of the optimization problem (1) – (2) can be characterized as
\[
u^* = \min \left( 1, \max \left( 0, \frac{1}{2A} \left[ \sigma_1P(\lambda_2 - \lambda_1) \right] \right) \right)
\]

Control \( u \) is linear against the number of healthy people. That is, the larger the number of healthy people then the greater the control \( u \). An optimal system of control optimal optimization problems consists of state of the system which is paired with the adjoint system with the initial condition and the
transversal condition along the characterization of optimal control. By substituting the optimal control \( u^* \) into the state system (1) and the adjoint system (5) we obtain the corresponding \( P^*, E^*, D^*, C^*, B^* \) and \( \lambda^*_i, i = 1, \ldots, 5 \) with the help of the transversality conditions \( \lambda^*_i(t_f) = 0, \ i = 1, \ldots, 5 \).

4. Conclusion

Based on the description and explanation of the chapter of results and discussion can be concluded that there is an optimal control for optimization problem (1) and to determine the optimal control used the minimum Pontryagin principles on Hamiltonian formed. The effect of the optimal control variable (prevention) is strongly affected by the number of healthy people. Optimal control that has been obtained also found state of the differential equations system (PEDCB model) and a vector Langrange multiplier appropriate for the fulfillment of the objective functional of minimizing the number of pre-diabetics so that automatically minimize the number of diabetics with and without complications, besides also minimizing relative cost of preventive control, so that in the end will find the optimal system of optimization problem (1).

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