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RESEARCH PAPER

Global dynamics and sensitivity analysis of a diabetic population model with two-time delays

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Abstract

Diabetes is a chronic disease that can cause various long-term complications. This study revisits a four-state model of type-2 diabetic population with a saturating recovery rate of diabetes complications, and its qualitative properties are further analysed. The non-negativity and boundedness of the solution for delay and non-delay models are proved. However, the non-negativity of the solutions of the delay model can only be guaranteed if the model inputs satisfy certain conditions. The stability analysis of the non-delay model is performed, and the numerical simulation is conducted to illustrate and validate the findings. In the presence of two delay parameters, we discuss the characteristic equation of the delay model under the case of the first time delay equal to zero to obtain the stable region of the second time delay. The critical value corresponding to the delay parameter is derived. There are five conditions to characterize the stability properties of the (unique) equilibrium point (either locally asymptotically stable or unstable) and the occurrence of Hopf bifurcation. The delay values affect the stability of the equilibrium point. A locally asymptotically stable equilibrium point can become unstable under certain conditions, and a periodic orbit can arise from the equilibrium point as the model switches its stability. The sensitivity analysis shows that the overall diabetes cases can be reduced significantly by reducing the rate of developing diabetes, and the diabetics with complications will decrease if the parameter measuring the limited medical resources gets smaller.

Keywords: Diabetes; time-delays; Hopf bifurcation; stability analysis; sensitivity analysis

AMS 2020 Classification: 92B05; 34D32; 35B35

1 Introduction

Diabetes mellitus is a life-long disease caused by hyperglycemia (high blood glucose levels) due to defects in either lack of insulin or cells resisting the insulin or both. In 2021, the International

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Diabetes Federation (IDF) [1] estimated that 6.7 million adults died due to diabetes and its complications. and diabetes and its consequences cost the world economy USD966 billion. In Malaysia, the estimated percentage of diabetics among adults aged 18 and above has increased from 11.6% in 2006 to 18.3% in 2019 [2]. In 2021, Malaysia's total diabetes-related health expenditure was estimated at USD4833.5 million, with USD1090.7 per individual with diabetes [3].
Therefore, there is an urgent need to study the population dynamics of diabetes to address the problem. Several population models of non-communicable diseases, such as diabetes [4, 5], hypertension [6], thyroid disorders [7], and anemia [8], have been developed in the literature. In the study, we will revisit the diabetic model in [9]. Although there are a few similarities between the findings of [9] and the present paper, there are some significant differences too, offering valuable insights and further information that were not provided in [9]. The distinctions between [9] and the present paper are as follows: First, [9] did not discuss the non-negativity and boundedness of the solution. This is an important issue in mathematical modeling because we expect the state variables to be non-negative for all time. Secondly, global stability analysis was not addressed in [9]. Third, [9] did not analyze the sensitivity of the model outputs to changes in the model inputs. This aspect is crucial as it helps identify which parameters may become potential targets for further investigation to control the disease in the population. Fourth, the numerical simulations in the present paper involve five sets of parameter values.
In this paper, Section 2 discusses the assumptions of the mathematical model to study the population dynamics of type-2 diabetes. Section 3 mainly focuses on the corresponding model without time delays. The global asymptotic stability is also established by constructing suitable Lyapunov functions. In Section 4, the dynamics of the delay model are studied. The Hopf bifurcation occurs for some parameter values, making the Lyapunov direct method not work due to the appearance of a periodic orbit. In Section 5, we compute the normalized forward sensitivity indices of the model outputs with respect to the changes in the model inputs. We perform the numerical simulation of the model in Section 6.

2 The mathematical model

The progression of diabetes is slow from the stage of non-diabetics to people with diabetes and from the stage of diabetes to the development of complications [5]. In the present paper, we use the model proposed by Nasir [9]. We extend the work of [9] by revising the local stability analysis and adding the global stability analysis and sensitivity analysis. The model assumptions are:

1. The model is used to study the population of type-2 diabetes. The total population is subdivided into four compartments, namely the non-diabetics, diabetics who never had any complications, diabetics with complications, and diabetics with recovered complications. Figure 1 shows the compartmental diagram under study.

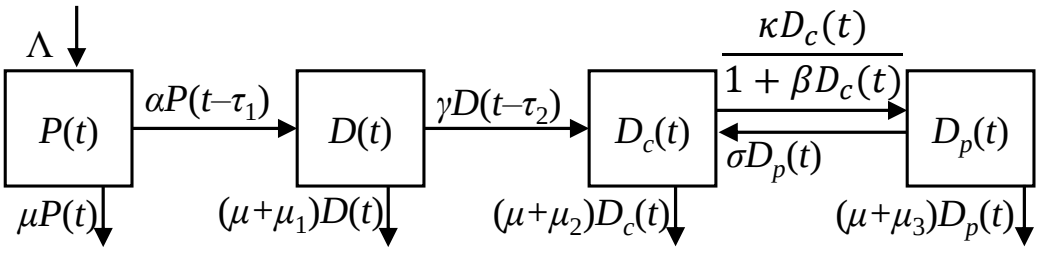

Figure 1. Four-state diabetic population [9]

Table 1. Definition of the symbols in Figure 1

Symbol	Definition	Dimension
$P(t)$	number of non-diabetics at time t	individuals
$D(t)$	number of diabetics who never had any complications at time t	individuals
$D_c(t)$	number of diabetics with complications at time t	individuals
$D_p(t)$	number of diabetics with recovered complications at time t	individuals
Λ	the recruitment rate of non-diabetics	individuals time^{-1}
α	the diabetes incidence rate	time^{-1}
τ_1	the slow progression in developing type-2 diabetes	time
γ	rate of the first incidence of complication	time^{-1}
τ_2	time delay in the first incidence of complication	time
σ	the recurrence rate of complications	time^{-1}
κ	the recovery rate of complications	time^{-1}
β	non-negative parameter measuring the limited medical resources	individuals^{-1}
μ_1	the diabetes-related mortality rate among diabetics without complications	time^{-1}
μ_2	the diabetes-related mortality rate among diabetics with complications	time^{-1}
μ_3	the diabetes-related mortality rate among diabetics with recovered complications	time^{-1}
μ	the mortality rate due to causes other than diabetes	time^{-1}

Every symbol in Figure 1 is defined in Table 1. All parameters are assumed to be positive because they represent human population dynamics.

2. Type 2 diabetes is a slowly progressive disease and degenerative [5]. The type of time delay used in this study is a constant delay. The first delay parameter (τ_1) concerns the stage of non-diabetics to diabetics. This assumption is supported by Khetan and Rajagopalan [10], where nearly all people affected with type 2 diabetes pass through a long phase of pre-diabetes before becoming a full-blown diabetic. The second delay parameter (τ_2) concerns the first incidence of complication after the onset of diabetes. This assumption is introduced by the fact that diabetes is a slowly progressive disease and can be symptomless. After being unrecognized for a long time, people with diabetes may already have complications at the time of diagnosis, such as a foot ulcer, change in vision, or infection that fails to heal [11].

3. The time delays are ignored for the other processes in Figure 1 because they do not require as much time as developing type-2 diabetes and the first incidence of complication. For example, complications related to the small blood vessels may range from 6 to 13 years after developing diabetes [12]. In addition, type-2 diabetes is usually diagnosed at an old age. The average age of diabetes that is diagnosed among Malaysians is 53 [13]. Hence, the delay in the recurrence rate of complications (at rate $\sigma D_p(t)$) is ignored because the diabetics with recovered complications are assumed no longer in the early stage of diabetes and are vulnerable to repeated complications [13].

4. For the treatment of complications, a saturating rate of recovery of complications of the form $h(D_c) = \dfrac{\kappa D_c}{1+\beta D_c}$. In reality, $\dfrac{1}{1+\beta D_c}$ can be described as the reverse effect of the diabetics with complications being postponed for treatment. If $\beta = 0$, this saturating recovery rate reverts to the linear one: $\kappa D_c(t)$, representing the unlimited medical resources [14]. The term

$h(D_c) = \dfrac{\kappa D_c}{1+\beta D_c}$ is also widely known as the Holling type-2 functional response [15]. Note that in our model, we employed different functional responses to represent the dynamics of recovery and recurrence. For recovery (cessation of symptoms), we used a Holling Type 2 functional response between D_c and D_p. This choice is biologically motivated by the fact that recovery rates often exhibit saturation effects observed in diabetes recovery. This saturation can be attributed to factors such as limitations in treatment resources and efficacy, which cause the rate of recovery of individuals with complications to plateau as the population of individuals with complications increases. Such saturation is well captured by a Holling Type 2 response. On the other hand, Holling Type 1 is utilized to model the recurrence of symptoms. This assumes a linear relationship between D_p and $\dfrac{dD_c}{dt}$. The rationale behind this choice is that symptom recurrence often depends primarily on individual risk factors such as lifestyle choices (diet, physical activity), medication adherence, and disease progression, rather than being constrained by saturation mechanisms. While this simplification may not capture all potential influences on recurrence, it provides a reasonable approximation for the purpose of our model. A Holling Type 2 response would be inappropriate in this case because the recurrence of symptoms does not exhibit resource-limited behavior in the same way that recovery does. This distinction ensures that the model accurately captures the underlying mechanisms of disease progression and treatment effects. However, if empirical data suggests otherwise, alternative functional forms could be considered in future extensions of this study.

The dynamics in Figure 1 are governed as follows:

$$\frac{dP(t)}{dt} = \Lambda - \alpha P(t-\tau_1) - \mu P(t), \tag{1a}$$

$$\frac{dD(t)}{dt} = \alpha P(t-\tau_1) - \gamma D(t-\tau_2) - (\mu+\mu_1)D(t), \tag{1b}$$

$$\frac{dD_c(t)}{dt} = \gamma D(t-\tau_2) - \frac{\kappa D_c(t)}{1+\beta D_c(t)} + \sigma D_p(t) - (\mu+\mu_2)D_c(t), \tag{1c}$$

$$\frac{dD_p(t)}{dt} = \frac{\kappa D_c(t)}{1+\beta D_c(t)} - (\sigma+\mu+\mu_3)D_p(t), \tag{1d}$$

where the initial conditions are defined as follows:

$$P(\theta) = \phi_1(\theta) > 0,\ D(\theta) = \phi_2(\theta) > 0,\ \theta \in [-\tau_{\max}, 0],$$
$$\tau_{\max} = \max\{\tau_1, \tau_2\},\ D_c(0) = D_{c0} > 0,\ D_p(0) = D_{p0} > 0,$$

where $\phi_i(\theta)$ $(i = 1, 2)$ are continuous functions on $\theta \in [-\tau_{\max}, 0]$. The total population size with respect to model (1) is denoted as $N(t) = P(t) + D(t) + D_c(t) + D_p(t)$.
Note that the case where $\alpha P(t-\tau_1)$ is assumed to be a constant incidence rate I will be addressed in another paper (see [16]). In [16], three variables will be discussed because the variable $P(t)$ is excluded. Consequently, the model in [16] contains one time-delay parameter only. Nasir et al. [16] also pay special attention to the limited availability of medical resources for the treatment of the complications of diabetes.

3 Qualitative analysis of the corresponding non-delay model

In this section, we study model (1) with no time delays $(\tau_1 = \tau_2 = 0)$. For simplifying the notations, the variables P, D, D_c, D_p, and N_2 are evaluated at time t, unless the argument is

other than t (for example, $D_c(0)$ and $P(t-\tau_1)$). Model (1) under the assumption of instantaneous dynamics is written as:

$$\frac{dP}{dt} = \Lambda - (\alpha + \mu)P, \tag{2a}$$

$$\frac{dD}{dt} = \alpha P - (\gamma + \mu + \mu_1)D, \tag{2b}$$

$$\frac{dD_c}{dt} = \gamma D - \frac{\kappa D_c}{1 + \beta D_c} + \sigma D_p - (\mu + \mu_2)D_c, \tag{2c}$$

$$\frac{dD_p}{dt} = \frac{\kappa D_c}{1 + \beta D_c} - (\sigma + \mu + \mu_3)D_p, \tag{2d}$$

with the initial conditions:

$$P(0) = P_0 > 0,\ D(0) = D_0 > 0,\ D_c(0) = D_{c0} > 0,\ D_p(0) = D_{p0} > 0.$$

In the following sections, we study the non-negativity and boundedness of the solution and the stability properties of the equilibrium point of the non-delay model (2).

Basic properties of non-delay model (2)

Non-negativity and boundedness of the solution of non-delay model (2)

Proposition 1 *The solutions P, D, D_c, and D_p of the non-delay model (2) remain non-negative and bounded for all $t > 0$. Furthermore, the region:*

$$\Omega = \left\{ \left(P, D, D_c, D_p\right) \in \mathbb{R}^4_+ \middle| P + D + D_c + D_p \leq \frac{\Lambda}{\mu} \right\},$$

is a positively-invariant region with respect to the non-delay model (2).

Proof For the non-negativity of the solution P of the non-delay model (2), from Eq. (2a), we obtain:

$$\frac{dP}{dt} + (\alpha + \mu)P = \Lambda. \tag{3}$$

Since $\Lambda \geq 0$, Eq. (3) becomes:

$$\frac{dP}{dt} + (\alpha + \mu)P \geq 0. \tag{4}$$

The integrating factor is given as $e^{(\alpha+\mu)t}$. By multiplying inequality (4) with the integrating factor and changing the variable t to variable ε, we obtain:

$$\frac{d}{d\varepsilon}\left[P(\varepsilon)e^{(\alpha+\mu)\varepsilon}\right] \geq 0. \tag{5}$$

Integrating both sides of inequality (5) from $\varepsilon = 0$ to $\varepsilon = t$ gives:

$$P \geq P(0)e^{-(\alpha+\mu)t}.$$

Therefore, the solution P remains non-negative for all $t > 0$.

For the non-negativity of the solution D of the non-delay model (2), from Eq. (2b), we obtain:

$$\frac{dD}{dt} + (\gamma + \mu + \mu_1)D = \alpha P. \tag{6}$$

Since the term $\alpha P \geq 0$, Eq. (6) becomes:

$$\frac{dD}{dt} + (\gamma + \mu + \mu_1)D \geq 0,$$
$$D \geq D(0)e^{-(\gamma+\mu+\mu_1)t}.$$

Therefore, the solution D remains non-negative for all $t > 0$.
Since the solution is assumed to be a continuous and differentiable function, the functions $D_c(t)$, $D_p(t)$ cannot become negative without crossing the axes $D_c = 0, D_p = 0$. Let $t^* = \min\{t_c, t_p\}$ where $D_c(t_c) = 0, D_p(t_p) = 0$ and $(t_c, t_p) \geq (0, 0)$. If $t^* = t_c$ then $D_c(t_c) = 0$ and the functions $D_p(t_c) > 0$ at $t = t_c$, yields

$$\frac{dD_c}{dt}(t^* = t_c) = \gamma D(t) + \sigma D_p(t) \geq 0.$$

Therefore, when the function $D_c(t)$ touches the axis $D_c = 0$, $\frac{dD_c}{dt}$ is always non-negative, and the function $D_c(t)$ will not decrease and will never cross to the negative part. Using a similar argument, it can be shown that

$$\frac{dD_p}{dt}(t^* = t_p) = \frac{\kappa D_c(t)}{1 + \beta D_c(t)} \geq 0.$$

Thus, all solutions $D_c(t), D_p(t)$ are always non-negative for all $t > 0$.
For the boundedness of the solutions P, D, D_c, and D_p of the non-delay model (2), adding all equations of the non-delay model (2) yields:

$$\frac{dN}{dt} = \Lambda - \mu N - \mu_1 D - \mu_2 D_c - \mu_3 D_p. \tag{7}$$

Since the terms $\mu_1 D \geq 0$, $\mu_2 D_c \geq 0$, and $\mu_3 D_p \geq 0$, Eq. (7) becomes:

$$\frac{dN}{dt} + \mu N \leq \Lambda,$$
$$N(t) \leq \frac{\Lambda}{\mu} + \left(N(0) - \frac{\Lambda}{\mu}\right)e^{-\mu t}.$$

If $N(0) \leq \frac{\Lambda}{\mu}$, then we have $N(t) \leq \frac{\Lambda}{\mu}$. This implies that the upper bound of the total population size is $\frac{\Lambda}{\mu}$. If $N(0) > \frac{\Lambda}{\mu}$, then $N_2(t)$ will decrease to $\frac{\Lambda}{\mu}$ because $\lim_{t\to\infty} N(t) = \frac{\Lambda}{\mu}$.
The region Ω is a positively-invariant region with respect to the non-delay model (2).

Stability of the equilibrium point of non-delay model (2)

Equilibrium point of non-delay model (2)

Let $T^* = (P^*, D^*, D_c^*, D_p^*)$ be the equilibrium point of the non-delay model (2), where $P = P^*$, $D = D^*$, $D_c = D_c^*$, and $D_p = D_p^*$. Substituting these into the right-hand-side equations of the non-delay model (2) and letting them equal to zero yields:

$$\Lambda - (\alpha + \mu)P^* = 0, \tag{8a}$$

$$\alpha P^* - (\gamma + \mu + \mu_1)D^* = 0, \tag{8b}$$

$$\gamma D^* - \frac{\kappa D_c^*}{1 + \beta D_c^*} + \sigma D_p^* - (\mu + \mu_2)D_c^* = 0, \tag{8c}$$

$$\frac{\kappa D_c^*}{1 + \beta D_c^*} - (\sigma + \mu + \mu_3)D_p^* = 0. \tag{8d}$$

From Eq. (8a), we have $P^* = \dfrac{\Lambda}{\alpha + \mu}$. From Eq. (8b), we have $D^* = \dfrac{\alpha P^*}{\gamma + \mu + \mu_1}$. From Eq. (8d), we have $D_p^* = \dfrac{\kappa D_c^*}{(1 + \beta D_c^*)(\sigma + \mu + \mu_3)}$. By substituting the expressions of D^* and D_p^* into Eq. (8c), we obtain:

$$z_1 (D_c^*)^2 + z_2 D_c^* + z_3 = 0, \tag{9}$$

where $z_1 = \beta(\mu + \mu_2)(\sigma + \mu + \mu_3)$, $z_2 = (\mu + \mu_2)(\mu + \mu_3 + \sigma) + \kappa(\mu + \mu_3) - \beta\gamma(\sigma + \mu + \mu_3)D^*$, and $z_3 = -\gamma(\sigma + \mu + \mu_3)D^*$. The roots of Eq. (9) are as follows:

$$\frac{-z_2 + \sqrt{z_2^2 - 4z_1 z_3}}{2z_1}, \tag{10}$$

and

$$\frac{-z_2 - \sqrt{z_2^2 - 4z_1 z_3}}{2z_1}. \tag{11}$$

Notice that z_1 and z_3 are opposite signs. Then, we have $\sqrt{z_2^2 - 4z_1 z_3} > \sqrt{z_2^2} = |z_2|$. This indicates that the root in (10) is positive while the root in (11) is negative.

Since the state variables represent individuals in the population, the only biologically meaningful equilibrium point is as follows:

$$T^* = \left(\frac{\Lambda}{\alpha + \mu}, \frac{\alpha P^*}{\gamma + \mu + \mu_1}, \frac{-z_2 + \sqrt{z_2^2 - 4z_1 z_3}}{2z_1}, \frac{\kappa D_c^*}{(1 + \beta D_c^*)(\sigma + \mu + \mu_3)} \right). \tag{12}$$

Local stability

Theorem 1 *The equilibrium point T^* of the non-delay model (2) is locally asymptotically stable.*

Proof The characteristic equation with respect to the equilibrium point T^* of the non-delay model

(2) is obtained by computing:

$$\det[\lambda_3 \mathbf{I}_4 - \mathbf{B}_1] = 0, \tag{13}$$

where λ_3 represents the eigenvalues, $\mathbf{I}_4$ is an identity matrix of dimension 4,

$$\mathbf{B}_1 = \begin{bmatrix} -(\alpha+\mu) & 0 & 0 & 0 \\ \alpha & -(\gamma+b_1) & 0 & 0 \\ 0 & \gamma & -b_2 & \sigma \\ 0 & 0 & b_3 & -b_4 \end{bmatrix},$$

and

$$b_1 = \mu + \mu_1,\ b_2 = b_3 + \mu + \mu_2,\ b_3 = \frac{\kappa}{(1+\beta D_c^*)^2},\ b_4 = \sigma + \mu + \mu_3. \tag{14}$$

After expanding Eq. (13), we obtain:

$$\chi_1(\lambda_3)(\lambda_3 + \alpha + \mu)(\lambda_3 + \gamma + b_1) = 0, \tag{15}$$

where $\chi_1(\lambda_3) = \lambda_3^2 + (b_2 + b_4)\lambda_3 + b_3(\mu + \mu_3) + b_4(\mu + \mu_2)$. Two of the roots of Eq. (15) are $-(\alpha+\mu)$ and $-(\gamma+b_1)$, which is negative because $\alpha + \mu > 0$ and $\gamma + b_1 > 0$. The other two roots of Eq. (15) are determined by $\chi_1(\lambda_3) = 0$ or:

$$\lambda_3^2 + (b_2 + b_4)\lambda_3 + b_3(\mu + \mu_3) + b_4(\mu + \mu_2) = 0. \tag{16}$$

By the Routh-Hurwitz criteria of a polynomial of degree two [17], all roots of Eq. (16) are negative or have negative real parts because $b_2 + b_4 > 0$ and $b_3(\mu + \mu_3) + b_4(\mu + \mu_2) > 0$. As a result, Theorem 1 is established.

Theorem 1 tells us that the small displacement from the equilibrium point T^* will decrease to zero regardless of the parameter values.

Global stability

In this section, we use the Lyapunov direct method to prove the non-existence of periodic orbits for the non-delay model (2) [18]. Constructing an appropriate Lyapunov function to investigate global stability is known to be a difficult problem in general. In the following, we discuss two remarks, where Remark 1 is an example of an attempt to find a Lyapunov function and Remark 2 is the numerical simulation to indicate the global stability of the equilibrium point T^*.

Remark 1 A function is suggested as follows:

$$\begin{aligned} \tilde{L}(P, D, D_c, D_p) =& (2\mu + \gamma + \mu_1)(D - D^*)^2 + \alpha[(P - P^*) + (D - D^*)]^2 \\ &+ (2\mu + \mu_2 + \mu_3)(D_c - D_c^*)^2 + \sigma[(D_c - D_c^*) + (D_p - D_p^*)]^2, \end{aligned} \tag{17}$$

where $\tilde{L}(P, D, D_c, D_p) \geq 0$ for all $(P, D, D_c, D_p) \geq (0, 0, 0, 0)$ with equality if and only if $(P, D, D_c, D_p) = (P^*, D^*, D_c^*, D_p^*)$. The time derivative of $\tilde{L}$ computed along the solution of non-delay model (2) is

given by:

$$\begin{aligned}\frac{d\tilde{L}}{dt} &= \frac{\partial \tilde{L}}{\partial P}\frac{dP}{dt} + \frac{\partial \tilde{L}}{\partial D}\frac{dD}{dt} + \frac{\partial \tilde{L}}{\partial D_c}\frac{dD_c}{dt} + \frac{\partial \tilde{L}}{\partial D_p}\frac{dD_p}{dt} \\ &= \Big(2\alpha(P-P^*) + 2\alpha(D-D^*)\Big)\Big(\Lambda - (\alpha+\mu)P\Big) \\ &\quad + \Big(2\alpha(P-P^*) + 2(2\mu+\gamma+\mu_1+\alpha)(D-D^*)\Big)\Big(\alpha P - (\gamma+\mu+\mu_1)D\Big) \\ &\quad + \Big(2(2\mu+\mu_2+\mu_3+\sigma)(D_c-D_c^*) + 2\sigma(D_p-D_p^*)\Big)\Big(\gamma D - \frac{\kappa D_c}{1+\beta D_c} + \sigma D_p \\ &\quad - (\mu+\mu_2)D_c\Big) + \Big(2\sigma(D_c-D_c^*) + 2\sigma(D_p-D_p^*)\Big)\Big(\frac{\kappa D_c}{1+\beta D_c} - (\sigma+\mu+\mu_3)D_p\Big). \end{aligned} \tag{18}$$

Note that we have:

$$\begin{aligned}\Lambda &= (\alpha+\mu)P^*, \\ 0 &= -\alpha P^* + (\gamma+\mu+\mu_1)D^*, \\ 0 &= -\gamma D^* + \frac{\kappa D_c^*}{1+\beta D_c^*} - \sigma D_p^* + (\mu+\mu_2)D_c^*, \\ 0 &= -\frac{\kappa D_c^*}{1+\beta D_c^*} + (\sigma+\mu+\mu_3)D_p^*. \end{aligned}$$

Therefore, Eq. (18) becomes:

$$\begin{aligned}\frac{d\tilde{L}}{dt} &= \Big(2\alpha(P-P^*) + 2\alpha(D-D^*)\Big)\Big((\alpha+\mu)P^* - (\alpha+\mu)P\Big) \\ &\quad + \Big(2\alpha(P-P^*) + 2(2\mu+\gamma+\mu_1+\alpha)(D-D^*)\Big)\Big(\alpha P - (\gamma+\mu+\mu_1)D \\ &\quad - \alpha P^* + (\gamma+\mu+\mu_1)D^*\Big) + \Big(2(2\mu+\mu_2+\mu_3+\sigma)(D_c-D_c^*) + 2\sigma(D_p-D_p^*)\Big) \\ &\quad \times \Big(\gamma D - \frac{\kappa D_c}{1+\beta D_c} + \sigma D_p - (\mu+\mu_2)D_c - \gamma D^* + \frac{\kappa D_c^*}{1+\beta D_c^*} - \sigma D_p^* + (\mu+\mu_2)D_c^*\Big) \\ &\quad + \Big(2\sigma(D_c-D_c^*) + 2\sigma(D_p-D_p^*)\Big)\Big(\frac{\kappa D_c}{1+\beta D_c} - (\sigma+\mu+\mu_3)D_p \\ &\quad - \frac{\kappa D_c^*}{1+\beta D_c^*} + (\sigma+\mu+\mu_3)D_p^*\Big) \\ &= -2\alpha\mu(P-P^*)^2 - 2(2\mu+\gamma+\mu_1+\alpha)(\gamma+\mu+\mu_1)(D-D^*)^2 \\ &\quad - \frac{2\kappa(2\mu+\mu_2+\mu_3)(D_c-D_c^*)^2}{(1+\beta D_c)(1+\beta D_c^*)} - 2(2\mu+\mu_2+\mu_3+\sigma)(\mu+\mu_2)(D_c-D_c^*)^2 \\ &\quad - 2\sigma(\mu+\mu_3)(D_p-D_p^*)^2 + 2\gamma(2\mu+\mu_2+\mu_3+\sigma)(D-D^*)(D_c-D_c^*) \\ &\quad + 2\sigma\gamma(D-D^*)(D_p-D_p^*). \end{aligned}$$

The term $\frac{d\tilde{L}}{dt} \leq 0$ for all $(P, D, D_c, D_p) \geq (0,0,0,0)$ is not satisfied because the terms $2\gamma(2\mu+\mu_2+\mu_3+\sigma)(D-D^*)(D_c-D_c^*)$ and $2\sigma\gamma(D-D^*)(D_p-D_p^*)$ are not less than or equal to zero for all $(P, D, D_c, D_p) \geq (0,0,0,0)$. Therefore, Eq. (17) in this Remark 1 is not the Lyapunov function that we are looking for.

Remark 2 As shown in Remark 1, it is difficult to show the global stability by the Lyapunov direct method because we have to go through trial and error and it requires a lot of guessing. We will use numerical simulations to display the global stability of the equilibrium point T^* of the non-delay model (2). Consider the following particular case of the non-delay model (2):

$$\frac{dP}{dt} = 35 - 0.015P, \tag{19a}$$

$$\frac{dD}{dt} = 0.005P - 0.135D, \tag{19b}$$

$$\frac{dD_c}{dt} = 0.05D - \frac{0.5D_c}{1 + 0.0005D_c} + 0.4D_p - 0.26D_c, \tag{19c}$$

$$\frac{dD_p}{dt} = \frac{0.5D_c}{1 + 0.0005D_c} - 0.51D_p. \tag{19d}$$

We obtain the equilibrium point $T^* = (2333.3333, 86.4198, 11.7670, 11.4688)$. Figure 2 shows the numerical simulations of system (19) with four sets of initial conditions $(P_0, D_0, D_{c0}, D_{p0})$: $(3000, 200, 15, 80)$, $(1500, 150, 30, 30)$, $(500, 10, 50, 5)$, and $(100, 100, 5, 50)$. This figure shows the

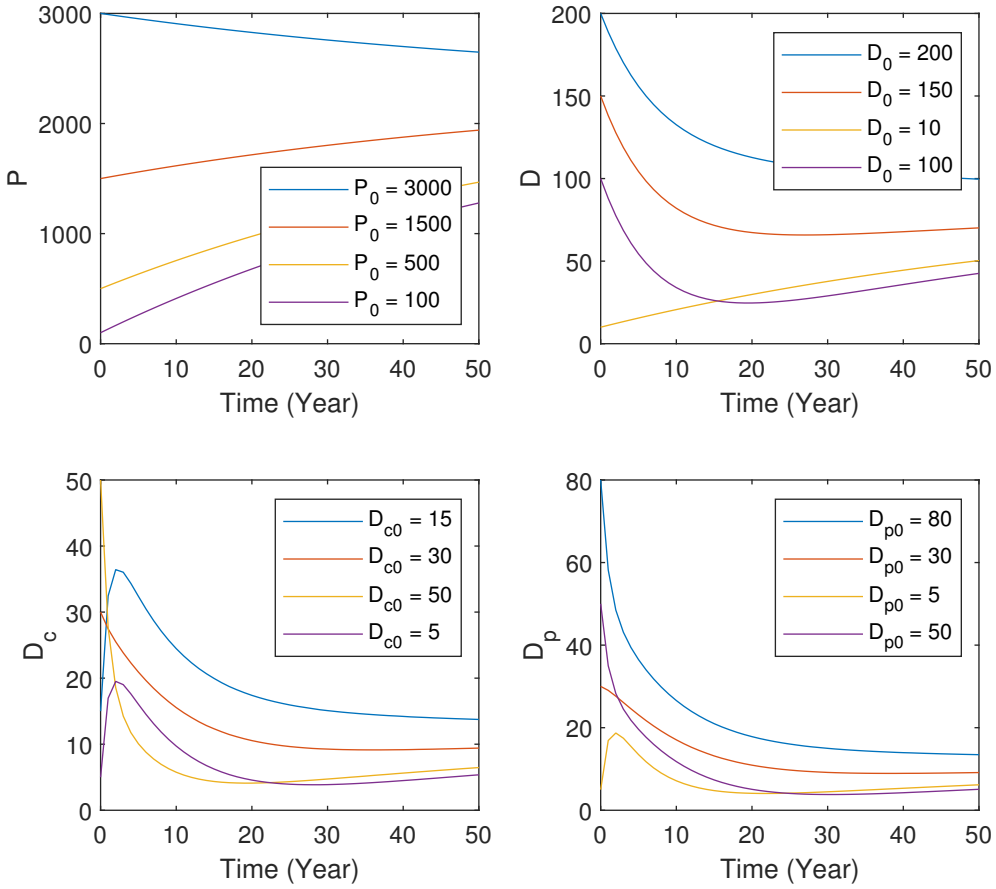

Figure 2. Numerical simulations of system (19)

global stability of T^* where the solutions P, D, D_c, and D_p of model (19) converge to T^* as time t increases, regardless of any positive initial conditions. The numerical simulations indicate that the

equilibrium point T^* of the non-delay model (2) may be globally asymptotically stable.

4 Qualitative analysis of the delay model

In this section, we study the non-negativity and boundedness of the solution, and the stability properties of the equilibrium point of the delay model (1).

Basic properties of delay model (1)

Non-negativity and boundedness of the solution of delay model (1)

Proposition 2 *If conditions:*

(H1) $\Lambda > \alpha P(t_1 - \tau_1)$ *at the boundary* $P(t_1) = 0$ *for any time* t_1,

and

(H2) $\alpha P(t_2 - \tau_1) > \gamma D(t_2 - \tau_2)$ *at the boundary* $D(t_2) = 0$ *for any time* t_2,

are satisfied, then the solutions P, D, D_c, *and* D_p *of the delay model* (1) *remain non-negative and bounded for all* $t > 0$. *Furthermore, the region:*

$$\Omega = \left\{ \left(P, D, D_c, D_p\right) \in \mathbb{R}^4_+ \middle| P + D + D_c + D_p \leq \frac{\Lambda}{\mu} \right\},$$

is a positively-invariant region with respect to the delay model (1).

Condition (H1) means that, in any event, if the number of non-diabetics drops to zero, the number of non-diabetics who will develop diabetes should be less than the number of newly recruited non-diabetics. On the other hand, condition (H2) means that if the number of diabetics who never had any complications drops to zero, the number of diabetics who will develop the first complication should be less than the number of non-diabetics who will develop diabetes. The proof of Proposition 2 is as follows.

Proof We prove the non-negativity of variable P of the delay model (1) as follows. $P(t) > 0$ for all $t > 0$. If this is not the case, suppose that there exists $t_1 > 0$ such that $P(t) > 0$ for $t \in [0, t_1)$, $P(t_1) = 0$, and $\frac{dP(t_1)}{dt} \leq 0$. From Eq. (1a), we obtain:

$$\frac{dP(t_1)}{dt} = \Lambda - \alpha P(t_1 - \tau_1).$$

We have $\frac{dP(t_1)}{dt} \leq 0$ for $\Lambda \leq \alpha P(t_1 - \tau_1)$, which agrees to the supposition that $\frac{dP(t_1)}{dt} \leq 0$. Therefore, if $\Lambda \leq \alpha P(t_1 - \tau_1)$ at the boundary $P(t_1) = 0$ for any time t_1, the solution P may enter the negative region. Condition (H1) indicates that the solution P remains non-negative for all $t > 0$.

Next, we prove the non-negativity of the solution D of the delay model (1) as follows. $D(t) > 0$ for all $t > 0$. If this be not the case, suppose that there exists $t_2 > 0$ such that $D(t) > 0$ for $t \in [0, t_2)$, $D(t_2) = 0$, and $\frac{dD(t_2)}{dt} \leq 0$. From Eq. (1b), we obtain:

$$\frac{dD(t_2)}{dt} = \alpha P(t_2 - \tau_1) - \gamma D(t_2 - \tau_2).$$

We have $\frac{dD(t_2)}{dt} \leq 0$ for $\alpha P(t_2-\tau_1) \leq \gamma D(t_2-\tau_2)$, which agrees to the supposition that $\frac{dD(t_2)}{dt} \leq 0$. Therefore, if $\alpha P(t_2-\tau_1) \leq \gamma D(t_2-\tau_2)$ at the boundary $D(t_2) = 0$ for any time t_2, the solution D may enter the negative region. Condition (H2) indicates that the solution D remains non-negative for all $t > 0$.
In the following, conditions (H1) and (H2) are satisfied.
Since variables D_c and D_p of delay model (1) depend on each other, we prove the non-negativity as follows: $D_c(t) > 0$ for all $t > 0$. If this is not the case, suppose that there exists $t_3 > 0$ such that $D_c(t) > 0$ for $t \in [0, t_3)$, $D_c(t_3) = 0$, and $\frac{dD_c(t_3)}{dt} \leq 0$. We first find the integration of Eq. (1d). From Eq. (1d), we obtain:

$$D_p(t) = D_p(0)e^{-(\sigma+\mu+\mu_3)t} + e^{-(\sigma+\mu+\mu_3)t}\int_0^t \frac{\kappa D_c(\varepsilon)}{1+\beta D_c(\varepsilon)} e^{(\sigma+\mu+\mu_3)\varepsilon}\, d\varepsilon. \tag{20}$$

From Eq. (20), we have $D_p(t) > 0$ for $t \in [0, t_3]$. Then, from Eq. (1c), we have:

$$\frac{dD_c(t_3)}{dt} = \gamma D(t_3-\tau_2) + \sigma D_p(t_3) > 0,$$

but this leads to a contradiction to the supposition that $\frac{dD_c(t_3)}{dt} \leq 0$. We can conclude that the solution D_c remains non-negative for all $t > 0$. Consequently, from Eq. (20), the solution D_p also remains non-negative for all $t > 0$.
For the boundedness of the solutions P, D, D_c, and D_p of the delay model (1), adding all equations of the delay model (1) yields:

$$\frac{dN}{dt} = \Lambda - \mu N_2 - \mu_1 D - \mu_2 D_c - \mu_3 D_p. \tag{21}$$

Since the terms $\mu_1 D \geq 0$, $\mu_2 D_c \geq 0$, and $\mu_3 D_p \geq 0$, Eq. (21) becomes:

$$\frac{dN}{dt} + \mu N \leq \Lambda.$$
$$N(t) \leq \frac{\Lambda}{\mu} + \left(N(0) - \frac{\Lambda}{\mu}\right)e^{-\mu t}.$$

If $N(0) \leq \frac{\Lambda}{\mu}$, then we have $N(t) \leq \frac{\Lambda}{\mu}$. This implies that the upper bound of the total population size is $\frac{\Lambda}{\mu}$. If $N(0) > \frac{\Lambda}{\mu}$, then $N(t)$ will decrease to $\frac{\Lambda}{\mu}$ because $\lim_{t\to\infty} N(t) = \frac{\Lambda}{\mu}$.
As a result, conditions (H1) and (H2) are required to be true so that the region Ω becomes a positively-invariant region with respect to the delay model (1). The proposition is proposed.

Stability of the equilibrium point of delay model (1)

Equilibrium point of delay model (1)

The equilibrium point $T^* = (P^*, D^*, D_c^*, D_p^*)$ given in (12) is also the equilibrium point of the delay model (1) because when the delay model (1) reaches its equilibrium state, we have:

$$P = P(t-\tau_1) = P^*,\ D = D(t-\tau_2) = D^*,\ D_c = D_c^*,\ D_p = D_p^*. \tag{22}$$

Upon substituting (22) into the right-hand-side equations of the delay model (1) and letting them equal to zero, we obtain the same set of equations as given in (8).

Local stability and the occurrence of Hopf bifurcation

In the following sections, we will separate the local stability discussion into two parts. First, in section "Stable region of τ_2 when $\tau_1 = 0$", we identify the stable region of τ_2 when $\tau_1 = 0$. Then, for τ_2 is within its stable region, we identify the critical value for τ_1 in section "$\tau_1 > 0$ and τ_2 is within its stable region".

Stable region of τ_2 when $\tau_1 = 0$

For $\tau_1 = 0$ and $\tau_2 > 0$, we have the following theorem.

Theorem 2 *For the delay model (1) with $\tau_1 = 0$:*

(i) If condition:

(H3) $b_1 \geq \gamma$,

holds, then T^* is locally asymptotically stable for $\tau_2 \geq 0$.

(ii) If condition:

(H4) $b_1 < \gamma$,

holds, then there exists a critical value:

$$\tau_{20} = \frac{1}{\omega_{20}} \cos^{-1}\left\{-\frac{b_1}{\gamma}\right\}, \tag{23}$$

where

$$\omega_{20} = \sqrt{-(b_1+\gamma)(b_1-\gamma)}, \tag{24}$$

such that T^* is locally asymptotically stable for $\tau_2 \in [0, \tau_{20})$ and becomes unstable for $\tau_2 > \tau_{20}$. Furthermore, a Hopf bifurcation occurs at $\tau_2 = \tau_{20}$ and a family of periodic orbits arises from T^*.

Condition (H3) means that the rate of the first incidence of complication does not exceed the total death rate of diabetics who never had any complications. While condition (H4) means that the rate of the first incidence of complication is greater than the total death rate of diabetics who never had any complications. The proof of Theorem 2 is as follows:

Proof The characteristic equation with respect to the equilibrium point T^* of the delay model (1) with $\tau_1 = 0$ is obtained by computing:

$$\det\left[\lambda_4 \mathbf{I}_4 - \mathbf{B}_2 - e^{-\lambda_4 \tau_2}\mathbf{B}_3\right] = 0, \tag{25}$$

where λ_4 represents the eigenvalues, $\mathbf{I}_4$ is an identity matrix of dimension 4,

$$\mathbf{B}_2 = \begin{bmatrix} -(\alpha+\mu) & 0 & 0 & 0 \\ \alpha & -b_1 & 0 & 0 \\ 0 & 0 & -b_2 & \sigma \\ 0 & 0 & b_3 & -b_4 \end{bmatrix}, \ \mathbf{B}_3 = \begin{bmatrix} 0 & 0 & 0 & 0 \\ 0 & -\gamma & 0 & 0 \\ 0 & \gamma & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix},$$

and b_1, b_2, b_3, and b_4 are as given in Eqs. (14). After expanding Eq. (25), we obtain:

$$(\lambda_4 + \mu + \alpha)\chi_1(\lambda_4)\chi_2(\lambda_4) = 0, \tag{26}$$

where

$$\chi_1(\lambda_4) = \lambda_4^2 + (b_2 + b_4)\lambda_4 + b_3(\mu + \mu_3) + b_4(\mu + \mu_2),$$
$$\chi_2(\lambda_4) = (\lambda_4 + b_1 + e^{-\lambda_4\tau_2}\gamma).$$

One of the roots of Eq. (26) is $-(\mu + \alpha)$, which is negative because $\mu + \alpha > 0$. The other two roots of Eq. (26) are determined by equation $\chi_1(\lambda_4) = 0$ and by the Routh-Hurwitz criteria [17], they are all negative or have negative real parts because $b_2 + b_4 > 0$ and $b_3(\mu + \mu_3) + b_4(\mu + \mu_2) > 0$. Lastly, the other roots of Eq. (26) are determined by equation $\chi_2(\lambda_4) = 0$ or

$$(\lambda_4 + b_1 + e^{-\lambda_4\tau_2}\gamma) = 0. \tag{27}$$

Assume that for some $\tau_2 > 0$, $\lambda_4 = i\omega_2$ ($i = \sqrt{-1}$ and $\omega_2 > 0$) is one of the roots of Eq. (27). Then, we can obtain

$$\omega_2^2 + (b_1 + \gamma)(b_1 - \gamma) = 0. \tag{28}$$

Eq. (28) can be written into a polynomial of degree one in $\varpi_2 = \omega_2^2$, as follows:

$$\varpi_2 + (b_1 + \gamma)(b_1 - \gamma) = 0. \tag{29}$$

The root of Eq. (29) is negative if condition (H3) is satisfied. Condition (H3) implies that $\varpi_2 = \omega_2^2 \leq 0$, which is a contradiction because we initially assumed $\omega_2 > 0$. The characteristic Eq. (27) cannot have $\lambda_4 = i\omega_2$ as one of the roots. Therefore, the equilibrium point T^* is locally asymptotically stable for $\tau_2 \geq 0$ with $\tau_1 = 0$. This proves Theorem 2(i).
For the second proof, suppose that condition (H4) is satisfied. Condition (H4) implies that Eq. (28) has one positive root, that is, Eq. (24). Then, the corresponding critical delays are given by:

$$\tau_2^{(j)} = \frac{1}{\omega_{20}}\cos^{-1}\left\{-\frac{b_1}{\gamma}\right\} + \frac{2j\pi}{\omega_{20}}, \quad j = 0, 1, 2, \ldots.$$

Let $\tau_{20} = \tau_2^{(0)}$ be the first critical value at which Eq. (27) has roots on the imaginary axis and $\lambda_4 = \pm i\omega_{20}$ are the corresponding roots. Then, the equilibrium point T^* is locally asymptotically stable for $\tau_2 \in [0, \tau_{20})$ with $\tau_1 = 0$. Moreover, the transversality condition for the establishment of Hopf bifurcation at $\tau_2 = \tau_{20}$ is satisfied [19], as follows:

$$\text{sign}\left\{\Re\left[\frac{d\lambda_4}{d\tau_2}\right]\Big|_{\lambda_4(\tau_{20})=i\omega_{20}}\right\} = \text{sign}\left\{\Re\left[\frac{d\lambda_4}{d\tau_2}\right]^{-1}\Big|_{\lambda_4(\tau_{20})=i\omega_{20}}\right\} > 0,$$

where

$$\Re\left[\frac{d\lambda_4}{d\tau_2}\right]^{-1}\Big|_{\lambda_4(\tau_{20})=i\omega_{20}} = \frac{1}{\gamma^2}.$$

This completes the proof of Theorem 2(ii).

$\tau_1 > 0$ and τ_2 is within its stable region

For $\tau_1 > 0$ and τ_2 is within its stable region, we have the following theorem.

Theorem 3 *For delay model (1) with $(\tau_1, \tau_2) > (0, 0)$, given τ_2 is within its stable region (τ_2 can be any non-negative value if condition (H3) holds, or $\tau_2 \in [0, \tau_{20})$ if condition (H4) holds). Given an equation with respect to ω_1 as follows:*

$$\begin{aligned}&\omega_1^4 + (b_1^2 + \gamma^2 + \mu^2 - \alpha^2)\omega_1^2 + (b_1^2 + \gamma^2)(\mu^2 - \alpha^2)\\ &+ 2b_1\gamma(\omega_1^2 + \mu^2 - \alpha^2)\cos\omega_1\tau_2 - 2\gamma\omega_1(\omega_1^2 + \mu^2 - \alpha^2)\sin\omega_1\tau_2 = 0.\end{aligned} \tag{30}$$

We have:

(i) If condition:

(H5) *Eq. (30) has no root,*

holds, then the equilibrium point T^* is locally asymptotically stable for $\tau_1 \geq 0$.

(ii) If condition:

(H6) *Eq. (30) has at least one positive root,*

holds, then there exists a critical value:

$$\tau_{10} = \min_{k\in\{1,2,\ldots,n\}}\{\tau_{1k}^{(0)}\}, \tag{31}$$

where

$$\tau_{1k}^{(0)} = \frac{1}{\omega_{1k}}\cos^{-1}\left\{-\frac{\mu}{\alpha}\right\},$$

where ω_{1k} $(k = 1, 2, \ldots, n)$ are any positive roots of Eq. (30), such that the equilibrium point T^* is locally asymptotically stable for $\tau_1 \in [0, \tau_{10})$ and becomes unstable for $\tau_1 > \tau_{10}$. Furthermore, if the following condition is satisfied:

(H7) $V_0V_2 + V_1V_3 > 0$,

where

$$\begin{aligned}V_0 &= (b_1 + \mu) + \alpha\cos\omega_{10}\tau_{10} + (\gamma - \mu\gamma\tau_2)\cos\omega_{10}\tau_2\\ &\quad - \gamma\tau_2\omega_{10}\sin\omega_{10}\tau_2 - \alpha\gamma\tau_2\cos\omega_{10}(\tau_{10} + \tau_2),\end{aligned} \tag{32a}$$

$$\begin{aligned}V_1 &= 2\omega_{10} - \alpha\sin\omega_{10}\tau_{10} - (\gamma - \mu\gamma\tau_2)\sin\omega_{10}\tau_2\\ &\quad - \gamma\tau_2\omega_{10}\cos\omega_{10}\tau_2 + \alpha\gamma\tau_2\sin\omega_{10}(\tau_{10} + \tau_2),\end{aligned} \tag{32b}$$

$$V_2 = b_1\alpha\omega_{10}\sin\omega_{10}\tau_{10} - \alpha\omega_{10}^2\cos\omega_{10}\tau_{10} + \alpha\gamma\omega_{10}\sin\omega_{10}(\tau_{10} + \tau_2), \tag{32c}$$

$$V_3 = \alpha\omega_{10}^2\sin\omega_{10}\tau_{10} + b_1\alpha\omega_{10}\cos\omega_{10}\tau_{10} + \alpha\gamma\omega_{10}\cos\omega_{10}(\tau_{10} + \tau_2), \tag{32d}$$

where ω_{10} is the corresponding positive root of Eq. (30) when $\tau_1 = \tau_{10}$, then a Hopf bifurcation occurs at $\tau_1 = \tau_{10}$ and a family of periodic orbits arises from T^*.

Proof The characteristic equation with respect to the equilibrium point T^* of the delay model (1) is obtained by computing:

$$\det\left[\lambda_5 \mathbf{I}_4 - \mathbf{B}_4 - e^{-\lambda_5\tau_1}\mathbf{B}_5 - e^{-\lambda_5\tau_2}\mathbf{B}_3\right] = 0, \tag{33}$$

where λ_5 represents the eigenvalues, $\mathbf{I}_4$ is an identity matrix of dimension 4,

$$\mathbf{B}_4 = \begin{bmatrix} -\mu & 0 & 0 & 0 \\ 0 & -b_1 & 0 & 0 \\ 0 & 0 & -b_2 & \sigma \\ 0 & 0 & b_3 & -b_4 \end{bmatrix}, \mathbf{B}_5 = \begin{bmatrix} -\alpha & 0 & 0 & 0 \\ \alpha & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}, \mathbf{B}_3 = \begin{bmatrix} 0 & 0 & 0 & 0 \\ 0 & -\gamma & 0 & 0 \\ 0 & \gamma & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix},$$

and b_1, b_2, b_3, and b_4 are given in Eqs. (14). After expanding Eq. (33), we obtain:

$$\chi_1(\lambda_5)\chi_3(\lambda_5) = 0, \tag{34}$$

where

$$\begin{aligned} \chi_1(\lambda_5) &= \lambda_5^2 + (b_2 + b_4)\lambda_5 + b_3(\mu + \mu_3) + b_4(\mu + \mu_2), \\ \chi_3(\lambda_5) &= (\lambda_5 + \mu + e^{-\lambda_5\tau_1}\alpha)(\lambda_5 + b_1 + e^{-\lambda_5\tau_2}\gamma). \end{aligned}$$

Two of the roots of Eq. (34) are determined by $\chi_1(\lambda_5) = 0$ and by the Routh-Hurwitz criteria [17], they are all negative or have negative real parts because $b_2 + b_4 > 0$ and $b_3(\mu + \mu_3) + b_4(\mu + \mu_2) > 0$. The other roots of Eq. (34) are determined by $\chi_3(\lambda_5) = 0$ or:

$$\lambda_5^2 + (b_1 + \mu)\lambda_5 + b_1\mu + e^{-\lambda_5\tau_1}(\alpha\lambda_5 + b_1\alpha) + e^{-\lambda_5\tau_2}(\gamma\lambda_5 + \mu\gamma) + e^{-\lambda_5(\tau_1+\tau_2)}\alpha\gamma = 0. \tag{35}$$

For τ_2 within its stable region (either condition (H3) or (H4) holds), we assume that for some $\tau_1 > 0$, $\lambda_5 = i\omega_1$ ($i = \sqrt{-1}$ and $\omega_1 > 0$) is one of the roots of Eq. (35). Substituting $\lambda_5 = i\omega_1$ into Eq. (35) and separating the real and imaginary parts yields:

$$\begin{aligned} (b_1\alpha + \alpha\gamma\cos\omega_1\tau_2)\cos\omega_1\tau_1 + (\alpha\omega_1 - \alpha\gamma\sin\omega_1\tau_2)\sin\omega_1\tau_2 & \\ = (\omega_1^2 - b_1\mu) - \gamma\omega_1\sin\omega_1\tau_2 - \mu\gamma\cos\omega_1\tau_2, & \quad (36a) \\ (b_1\alpha + \alpha\gamma\cos\omega_1\tau_2)\sin\omega_1\tau_1 - (\alpha\omega_1 - \alpha\gamma\sin\omega_1\tau_2)\cos\omega_1\tau_2 & \\ = (b_1 + \mu)\sin\omega_1\tau_1 + \gamma\omega_1\cos\omega_1\tau_2 - \mu\gamma\sin\omega_1\tau_2. & \quad (36b) \end{aligned}$$

We eliminate τ_1 by squaring and adding both Eqs. (36). Then, we can obtain Eq. (30). Suppose that condition (H5) is satisfied. Condition (H5) implies that the characteristic Eq. (35) cannot have $\lambda_5 = i\omega_1$ as one of the roots. Therefore, the equilibrium point T^* is locally asymptotically stable for $\tau_1 \geq 0$. This proves Theorem 3(i).

For the second proof, suppose that condition (H6) holds. Without loss of generality, suppose that Eq. (30) has a finite number of positive roots denoted by $\omega_{11}, \omega_{12}, \ldots, \omega_{1n}$. For every ω_{1k} ($k = 1, 2, \ldots, n$) and using the equations in (36), we obtain the corresponding critical delays as follows:

$$\tau_{1k}^{(j)} = \frac{1}{\omega_{1k}}\cos^{-1}\left\{-\frac{\mu}{\alpha}\right\} + \frac{2j\pi}{\omega_{1k}}, \quad j = 0, 1, 2, \ldots.$$

Let $\tau_{10} = \min_{k\in\{1,2,\ldots,n\}} \{\tau_{1k}^{(0)}\}$ be the first critical value for which Eq. (35) has roots on the imaginary axis and $\lambda_5 = \pm i\omega_{10}$ are denoted as the corresponding roots. Then, the equilibrium point T^* is locally asymptotically stable for $\tau_1 \in [0, \tau_{10})$. To establish the occurrence of Hopf bifurcation at $\tau_1 = \tau_{10}$, we need to show that:

$$\text{sign}\left\{\Re\left[\frac{d\lambda_5}{d\tau_1}\right]\Big|_{\lambda_5(\tau_{10})=i\omega_{10}}\right\} > 0.$$

By differentiating Eq. (35) with respect to τ_1, we obtain:

$$\left[\frac{d\lambda_5}{d\tau_1}\right]^{-1} = \frac{2\lambda_5 + b_1 + \mu + \alpha e^{-\lambda_5\tau_1} - (\gamma\tau_2\lambda_5 - \gamma + \mu\gamma\tau_2)e^{-\lambda_5\tau_2} - \alpha\gamma\tau_2 e^{-\lambda_5(\tau_1+\tau_2)}}{(\alpha\lambda_5^2 + b_1\alpha\lambda_5)e^{-\lambda_5\tau_1} + \alpha\gamma\lambda_5 e^{-\lambda_5(\tau_1+\tau_2)}} - \frac{\tau_1}{\lambda_5}. \quad (37)$$

Evaluating Eq. (37) at $\lambda_5(\tau_{10}) = i\omega_{10}$ yields:

$$\left[\frac{d\lambda_5}{d\tau_1}\right]^{-1}\Big|_{\lambda_5(\tau_{10})=i\omega_{10}} = \frac{V_0 + iV_1}{V_2 + iV_3} - \frac{\tau_{10}}{i\omega_{10}}, \quad (38)$$

where V_0, V_1, V_2, and V_3 are as given in Eqs. (32). The real part of Eq. (38) is given by:

$$\Re\left[\frac{d\lambda_5}{d\tau_1}\right]^{-1}\Big|_{\lambda_5(\tau_{10})=i\omega_{10}} = \frac{V_0V_2 + V_1V_3}{V_2^2 + V_3^2}.$$

If condition (H7) is satisfied, then

$$\text{sign}\left\{\Re\left[\frac{d\lambda_5}{d\tau_1}\right]^{-1}\Big|_{\lambda_5(\tau_{10})=i\omega_{10}}\right\} = \text{sign}\left\{\Re\left[\frac{d\lambda_5}{d\tau_1}\right]\Big|_{\lambda_5(\tau_{10})=i\omega_{10}}\right\} > 0.$$

This completes the proof of Theorem 3(ii).

Remark 3 We discussed the criteria implying that there exists a periodic orbit for the delay model (1) for some parameter values. Such results are interesting because the equilibrium point T^* can become unstable and not approach T^*. In this case, T^* of the delay model (1) is not globally asymptotically stable, and the Lyapunov direct method would not work.

5 Sensitivity analysis

Model (1) has four model outputs (state variables) and sixteen model inputs (parameters and initial conditions). The model outputs are denoted as $\mathbf{x} = \{P, D, D_c, D_p\}$, while the model inputs are denoted as $\boldsymbol{\varsigma} = \{\Lambda, \alpha, \gamma, \kappa, \beta, \sigma, \mu, \mu_1, \mu_2, \mu_3, \tau_1, \tau_2, \phi_1(\theta), \phi_2(\theta), D_{c0}, D_{p0}\}$. Following [20, 21], the sensitivity index of an arbitrary model output x_i with respect to an arbitrary model input ς_j is as given by:

$$S_{\varsigma_j}^{x_i}(t) = \frac{\partial x_i(t)}{\partial \varsigma_j}, \quad i = 1, 2, 3, 4, \quad j = 1, \ldots, 16.$$

For simplifying the notations, the variable $S_{\varsigma_j}^{x_i}(t)$ is denoted as $S_{\varsigma_j}^{x_i}$, unless the argument is other than t. Following [21, 22], the system of differential equations for the sensitivity indices of the

outputs P, D, D_c, and D_p with respect to an arbitrary model input ς_j is given by:

$$\begin{aligned}
\begin{bmatrix} \frac{dS^P_{\varsigma_j}}{dt} \\ \frac{dS^D_{\varsigma_j}}{dt} \\ \frac{dS^{D_c}_{\varsigma_j}}{dt} \\ \frac{dS^{D_p}_{\varsigma_j}}{dt} \end{bmatrix} &= \begin{bmatrix} -\mu & 0 & 0 & 0 \\ 0 & -(\mu+\mu_1) & 0 & 0 \\ 0 & 0 & -\left(\frac{\kappa}{(1+\beta D_c)^2}+(\mu+\mu_2)\right) & \sigma \\ 0 & 0 & \frac{\kappa}{(1+\beta D_c)^2} & -(\sigma+\mu+\mu_3) \end{bmatrix} \begin{bmatrix} S^P_{\varsigma_j} \\ S^D_{\varsigma_j} \\ S^{D_c}_{\varsigma_j} \\ S^{D_p}_{\varsigma_j} \end{bmatrix} \\
&+ \begin{bmatrix} -\alpha & 0 & 0 & 0 \\ \alpha & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} S^P_{\varsigma_j}(t-\tau_1) \\ S^D_{\varsigma_j}(t-\tau_1) \\ S^{D_c}_{\varsigma_j}(t-\tau_1) \\ S^{D_p}_{\varsigma_j}(t-\tau_1) \end{bmatrix} + \begin{bmatrix} 0 & 0 & 0 & 0 \\ 0 & -\gamma & 0 & 0 \\ 0 & \gamma & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} S^P_{\varsigma_j}(t-\tau_2) \\ S^D_{\varsigma_j}(t-\tau_2) \\ S^{D_c}_{\varsigma_j}(t-\tau_2) \\ S^{D_p}_{\varsigma_j}(t-\tau_2) \end{bmatrix} \\
&+ \left[\frac{\partial}{\partial \varsigma_j}\left(\frac{dP}{dt}\right) \quad \frac{\partial}{\partial \varsigma_j}\left(\frac{dD}{dt}\right) \quad \frac{\partial}{\partial \varsigma_j}\left(\frac{dD_c}{dt}\right) \quad \frac{\partial}{\partial \varsigma_j}\left(\frac{dD_p}{dt}\right) \right]^\top,
\end{aligned} \tag{39}$$

with the initial conditions

$$\begin{bmatrix} S^P_{\varsigma_j}(\theta) \\ S^D_{\varsigma_j}(\theta) \\ S^{D_c}_{\varsigma_j}(0) \\ S^{D_p}_{\varsigma_j}(0) \end{bmatrix} = \left[\frac{\partial \phi_1(\theta)}{\partial \varsigma_j} \quad \frac{\partial \phi_2(\theta)}{\partial \varsigma_j} \quad \frac{\partial D_{c0}}{\partial \varsigma_j} \quad \frac{\partial D_{p0}}{\partial \varsigma_j} \right]^\top, \quad \theta \in [-\tau_{\max}, 0].$$

In particular, the system of differential equations for the sensitivity indices of the model outputs P, D, D_c, and D_p with respect to the recruitment rate of non-diabetics (Λ) is given by:

$$\frac{dS^P_\Lambda}{dt} = -\mu S^P_\Lambda - \alpha S^P_\Lambda(t-\tau_1) + 1, \tag{40a}$$

$$\frac{dS^D_\Lambda}{dt} = -(\mu+\mu_1) S^D_\Lambda + \alpha S^P_\Lambda(t-\tau_1) - \gamma S^D_\Lambda(t-\tau_2), \tag{40b}$$

$$\frac{dS^{D_c}_\Lambda}{dt} = -\frac{\kappa S^{D_c}_\Lambda}{(1+\beta D_c)^2} - (\mu+\mu_2) S^{D_c}_\Lambda + \sigma S^{D_p}_\Lambda + \gamma S^D_\Lambda(t-\tau_2), \tag{40c}$$

$$\frac{dS^{D_p}_\Lambda}{dt} = \frac{\kappa S^{D_c}_\Lambda}{(1+\beta D_c)^2} - (\sigma+\mu+\mu_3) S^{D_p}_\Lambda, \tag{40d}$$

with the initial conditions:

$$S^P_\Lambda(\theta) = 0,\ \theta \in [-\tau_{\max}, 0],\ S^D_\Lambda(\theta) = 0,\ S^{D_c}_\Lambda(0) = 0,\ S^{D_p}_\Lambda(0) = 0.$$

The equilibrium solutions of system (40) is given by:

$$S^{P^*}_\Lambda = \frac{1}{\alpha+\mu},$$

$$
\begin{aligned}
S_{\Lambda}^{D^*} &= \frac{\alpha S_{\Lambda}^{P^*}}{\gamma+\mu+\mu_1},\\
S_{\Lambda}^{D_c^*} &= \frac{\gamma S_{\Lambda}^{D^*}(\sigma+\mu+\mu_3)(1+\beta D_c^*)^2}{\kappa(\mu+\mu_3)+(\mu+\mu_2)(\sigma+\mu+\mu_3)(1+\beta D_c^*)^2},\\
S_{\Lambda}^{D_p^*} &= \frac{\kappa S_{\Lambda}^{D_c^*}}{(\sigma+\mu+\mu_3)(1+\beta D_c^*)^2}.
\end{aligned}
$$

The system of differential equations for the sensitivity indices of the model outputs P, D, D_c, and D_p with respect to the time delay parameter (τ_1) is given by:

$$\frac{dS_{\tau_1}^{P}}{dt} = -\mu S_{\tau_1}^{P} - \alpha S_{\tau_1}^{P}(t-\tau_1) + \alpha\frac{dP(t-\tau_1)}{dt}, \tag{41a}$$

$$\frac{dS_{\tau_1}^{D}}{dt} = -(\mu+\mu_1)S_{\tau_1}^{D} + \alpha S_{\tau_1}^{P}(t-\tau_1) - \gamma S_{\tau_1}^{D}(t-\tau_2) - \alpha\frac{dP(t-\tau_1)}{dt}, \tag{41b}$$

$$\frac{dS_{\tau_1}^{D_c}}{dt} = -\frac{\kappa S_{\tau_1}^{D_c}}{(1+\beta D_c)^2} - (\mu+\mu_2)S_{\tau_1}^{D_c} + \sigma S_{\tau_1}^{D_p} + \gamma S_{\tau_1}^{D}(t-\tau_2), \tag{41c}$$

$$\frac{dS_{\tau_1}^{D_p}}{dt} = \frac{\kappa S_{\tau_1}^{D_c}}{(1+\beta D_c)^2} - (\sigma+\mu+\mu_3)S_{\tau_1}^{D_p}, \tag{41d}$$

with the initial conditions:

$$S_{\tau_1}^{P}(\theta) = 0,\ \theta\in[-\tau_{\max},0],\ S_{\tau_1}^{D}(\theta) = 0,\ S_{\tau_1}^{D_c}(0) = 0,\ S_{\tau_1}^{D_p}(0) = 0. \tag{42}$$

The equilibrium solution of system (41) is given by

$$S_{\tau_1}^{P^*} = 0, \quad S_{\tau_1}^{D^*} = 0, \quad S_{\tau_1}^{D_c^*} = 0, \quad S_{\tau_1}^{D_p^*} = 0.$$

Similarly, we can derive the sensitivity indices with respect to the other model inputs using system (39). Then, we compute the normalized forward sensitivity indices by using:

$$\Upsilon_{\varsigma_j}^{x_i} = S_{\varsigma_j}^{x_i}\frac{\varsigma_j}{x_i}, \quad i=1,2,3,4, \quad j=1,\ldots,16.$$

Sensitivity index of equilibrium point T^*

In this section, we compute the normalized forward sensitivity indices of T^* with respect to each model input using the values in Table 2.

The normalized forward sensitivity indices of the equilibrium point $T^* = (P^*, D^*, D_c^*, D_p^*)$ with respect to every model input are presented in Table 3.

From Table 3, changes in the model inputs $\phi_1(\theta)$, $\phi_2(\theta)$, D_{c0}, D_{p0}, τ_1, and τ_2 have no effects on the equilibrium point T^*. Furthermore, we can decrease the total number of diabetics by increasing the death-related model inputs (μ, μ_1, μ_2, and μ_3). However, these actions are impractical and unethical. A similar argument applies to the recruitment rate of non-diabetics (Λ). It is unreasonable to restrict the growth of non-diabetics in order to reduce the equilibrium solution of all diabetic subpopulations. Apart from these model inputs $(\phi_1(\theta), \phi_2(\theta), D_{c0}, D_{p0}, \mu, \mu_1, \mu_2, \mu_3, \Lambda, \tau_1$, and $\tau_2)$, we rank the normalized forward sensitivity indices of D^*, D_c^*, and D_p^* with respect to the other model inputs from the most sensitive to least (see Table 4). The signs and magnitudes of

Table 2. List of values for the model inputs of model (1)

Model input	Value	Dimension	Source
$\phi_1(\theta)$	17375603	individuals	Assumed after [2]
$\phi_2(\theta)$	2558998	individuals	[16]
D_{c0}	666483	individuals	[16]
D_{p0}	666483	individuals	[16]
Λ	274314.75	individuals year^{-1}	Estimated after [2]
α	5.2108×10^{-3}	year^{-1}	Estimated after [2]
γ	0.1	year^{-1}	[16]
σ	0.15	year^{-1}	[16]
μ	0.008678	year^{-1}	[16]
μ_1	5.84×10^{-4}	year^{-1}	[16]
μ_2	0.002336	year^{-1}	[16]
μ_3	0.001752	year^{-1}	[16]
κ	0.988986	year^{-1}	[16]
β	5×10^{-6}	individuals^{-1}	[16]
τ_1	10	years	[10]
τ_2	5	years	[16]

Table 3. Normalized forward sensitivity indices of the equilibrium point T^* of model (1) using the model inputs in Table 2

ς_j	$\Upsilon_{\varsigma_j}^{P^*}$	$\Upsilon_{\varsigma_j}^{D^*}$	$\Upsilon_{\varsigma_j}^{D_c^*}$	$\Upsilon_{\varsigma_j}^{D_p^*}$
Λ	1	1	1.1487	0.0302
α	−0.3752	0.6248	0.7177	0.0188
γ	0	−0.9152	0.0974	0.0026
κ	0	0	−0.1527	0.9960
β	0	0	0.1487	−0.9698
σ	0	0	0.1428	−0.9312
μ	−0.6248	−0.7043	−1.7125	−0.0991
μ_1	0	−0.0053	−0.0061	-1.613×10^{-4}
μ_2	0	0	−0.2112	−0.0055
μ_3	0	0	−0.0240	−0.0116
τ_1	0	0	0	0
τ_2	0	0	0	0
$\phi_1(\theta)$	0	0	0	0
$\phi_2(\theta)$	0	0	0	0
D_{c0}	0	0	0	0
D_{p0}	0	0	0	0

$\Upsilon_{\varsigma}^{P^*}$ are not given because we are only concerned with the diabetic subpopulations.

Reducing the overall diabetes prevalence is the primary concern. Based on the status of individuals with diabetes, we should give extra precautions to reduce diabetics with complications (D_c) as they can affect the availability of the treatment of the complications. From Table 4(B), the diabetes incidence rate (α) is at the highest rank but in the positive direction. Thus, decreasing α will affect the most in reducing the equilibrium solution of diabetics with complications (D_c^*). In addition, the decrease in α will also decrease the equilibrium solution of diabetics who never had any complications (D^*) and diabetics with recovered complications (D_p^*), making α the most

Table 4. Magnitude and sign of the normalized forward sensitivity indices of D^*, D_c^*, and D_p^* with respect to the model inputs α, γ, κ, β, and σ

(A) indices of D^*		
ς	$\lvert\Upsilon_\varsigma^{D^*}\rvert$	sign
γ	0.9152	$-$
α	0.6248	$+$
κ	0	
β		
σ		

(B) indices of D_c^*		
ς	$\lvert\Upsilon_\varsigma^{D_c^*}\rvert$	sign
α	0.7177	$+$
κ	0.1527	$-$
β	0.1487	$+$
σ	0.1428	
γ	0.0974	

(C) indices of D_p^*		
ς	$\lvert\Upsilon_\varsigma^{D_p^*}\rvert$	sign
κ	0.9960	$+$
β	0.9698	$-$
σ	0.9312	
α	0.0188	$+$
γ	0.0026	

important model input to curb the overall diabetes cases.

A 1% increase in the recurrence rate of complications (σ) increases the equilibrium solution of diabetics with complications (D_c^*) by approximately 0.1428%, while a 1% increase in the rate of the first incidence of complication (γ) increases the equilibrium solution of diabetics with complications (D_c^*) by approximately 0.0974%. Thus, decreasing γ and σ are beneficial to lower D_c^*.

From Table 4(C), the recovery rate of complications (κ) is the most sensitive model input in changing the equilibrium solution of diabetics with recovered complications (D_p^*), where a 1% increase in κ increases D_p^* by approximately 0.9960%. However, the value of κ is at maximum because if the inhibition effect $\beta = 0$ individuals^{-1}, $\kappa + \mu + \mu_2 = 1$ year^{-1} (the total rates of individuals leaving the compartment of diabetics with complications (D_c)). The value of κ gets smaller due to the inhibition effect of limited medical resources measured by the term $\dfrac{1}{1+\beta D_c}$. In reality, $\dfrac{1}{1+\beta D_c}$ can be described as the reverse effect of diabetics with complications being postponed for treatment [14]. From Table 4(B, C), a 1% increase in the inhibition effect β results in an approximately 0.1487% increase in the equilibrium solution of diabetics with complications (D_c^*) and an approximately 0.9698% decrease in the equilibrium solution of diabetics with recovered complications (D_p^*). Thus, decreasing β is crucial to decrease D_c^*.

6 Numerical simulation

Stability of equilibrium point T^*

In this section, we give some numerical simulations for several cases of model (1) to validate and illustrate our theoretical results. Five examples are presented, and Table 5 shows the differences between them.

Table 5. Numerical example with respect to model (1)

Example	Theorem					
	1	2		3		
		(H3)	(H4)	(H5)	(H6)	(H7)
1	•					
2		•		•		
3		•			•	•
4			•	•		
5			•		•	•

Example 1 *Consider the model inputs:* $\Lambda = 35$, $\alpha = 0.005$, $\gamma = 0.05$, $\kappa = 0.5$, $\beta = 0.0005$, $\sigma = 0.4$, $\mu = 0.01$, $\mu_1 = 0.075$, $\mu_2 = 0.25$, $\mu_3 = 0.1$, $\tau_1 = 0$, $\tau_2 = 0$, $P_0 = 3000$, $D_0 = 200$, $D_{c0} = 15$, *and* $D_{p0} = 80$, *which give the following particular non-delay case of model* (1)*:*

$$\frac{dP}{dt} = 35 - 0.005P - 0.01P, \tag{43a}$$

$$\frac{dD}{dt} = 0.005P - 0.05D - 0.085D, \tag{43b}$$

$$\frac{dD_c}{dt} = 0.05D - \frac{0.5D_c}{1 + 0.0005D_c} + 0.4D_p - 0.26D_c, \tag{43c}$$

$$\frac{dD_p}{dt} = \frac{0.5D_c}{1 + 0.0005D_c} - 0.51D_p, \tag{43d}$$

with the initial conditions:

$$P(0) = 3000,\ D(0) = 200,\ D_c(0) = 15,\ D_p(0) = 80.$$

We obtain the equilibrium point $T^* = (2333.3333, 86.4198, 11.7670, 11.4688)$. *According to Theorem 1, T^* of system* (43) *is locally asymptotically stable (see Figure 3).*

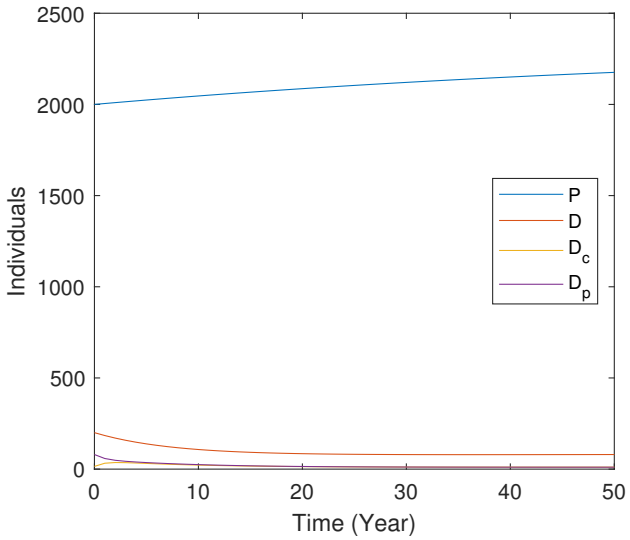

Figure 3. The dynamics of system (43)

Example 2 *Consider the model inputs:* $\Lambda = 35$, $\alpha = 0.005$, $\gamma = 0.05$, $\kappa = 0.5$, $\beta = 0.0005$, $\sigma = 0.4$, $\mu = 0.01$, $\mu_1 = 0.075$, $\mu_2 = 0.25$, $\mu_3 = 0.1$, $\phi_1(\theta) = 3000$, $\phi_2(\theta) = 200$, $D_{c0} = 15$, *and* $D_{p0} = 80$, *which give the following particular case of model* (1)*:*

$$\frac{dP}{dt} = 35 - 0.005P(t - \tau_1) - 0.01P, \tag{44a}$$

$$\frac{dD}{dt} = 0.005P(t - \tau_1) - 0.05D(t - \tau_2) - 0.085D, \tag{44b}$$

$$\frac{dD_c}{dt} = 0.05D(t - \tau_2) - \frac{0.5D_c}{1 + 0.0005D_c} + 0.4D_p - 0.26D_c, \tag{44c}$$

$$\frac{dD_p}{dt} = \frac{0.5D_c}{1 + 0.0005D_c} - 0.51D_p, \tag{44d}$$

with the initial conditions:

$$P(\theta) = 3000,\ \theta \in [-\tau_{\max}, 0],\ D(\theta) = 200,\ D_c(0) = 15,\ D_p(0) = 80.$$

We obtain the equilibrium point $T^* = (2333.3333, 86.4198, 11.7670, 11.4688)$.

We first check the existence of critical value τ_{20} *when* $\tau_1 = 0$. *From Theorem 2, condition (H3) is satisfied because* $b_1 - \gamma = 0.035 \geq 0$. *According to Theorem 2(i), the equilibrium point* T^* *of system (44) with* $\tau_1 = 0$ *is locally asymptotically stable for* $\tau_2 \geq 0$.

Furthermore, for condition (H3) holds, we check the existence of critical value τ_{10} *provided* τ_2 *can be any non-negative value. From Theorem 3 and choosing* $\tau_2 = 13$, *Eq. (30) becomes*

$$\begin{aligned}&\omega_1^4 + 0.0098\omega_1^2 + (7.2938 \times 10^{-7}) + 0.0085(\omega_1^2 + 7.5 \times 10^{-5})\cos 13\omega_1 \\ &- 0.1\omega_1(\omega_1^2 + 7.5 \times 10^{-5})\sin 13\omega_1 = 0.\end{aligned} \tag{45}$$

Eq. (45) has no root, and condition (H5) is satisfied. Thus, from Theorem 3(i), T^* *of system (44) with* τ_2 *can be any non-negative value (in this case,* $\tau_2 = 13$*) is locally asymptotically stable for* $\tau_1 \geq 0$. *Figure 4 shows the dynamics of system (44) with two sets of* τ_1 *and* τ_2*: (i)* $\tau_1 = 15$ *and* $\tau_2 = 13$, *and (ii)* $\tau_1 = 150$ *and* $\tau_2 = 13$.

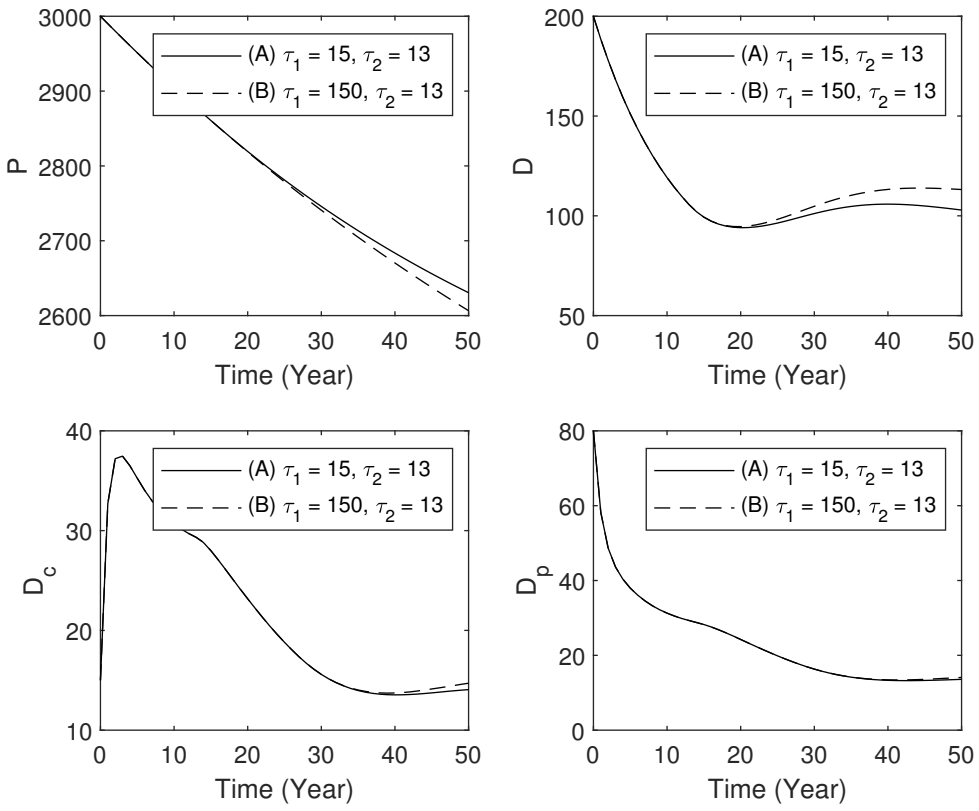

Figure 4. Dynamics of system (44) with: (A) $\tau_1 = 15$ and $\tau_2 = 13$. (B) $\tau_1 = 150$ and $\tau_2 = 13$

When conditions (H3) and (H5) are satisfied, the solution (P, D, D_c, D_p) *converges to* T^* *regardless of the value of* τ_1 *and* τ_2.

Example 3 *Consider the model inputs:* $\Lambda = 35$, $\alpha = 0.125$, $\gamma = 0.05$, $\kappa = 0.5$, $\beta = 0.0005$, $\sigma = 0.4$, $\mu = 0.05$, $\mu_1 = 0.075$, $\mu_2 = 0.25$, $\mu_3 = 0.1$, $\phi_1(\theta) = 300$, $\phi_2(\theta) = 100$, $D_{c0} = 30$, *and* $D_{p0} = 40$, *which give the following particular case of model (1):*

$$\frac{dP}{dt} = 35 - 0.125P(t-\tau_1) - 0.05P, \tag{46a}$$

$$\frac{dD}{dt} = 0.125P(t-\tau_1) - 0.05D(t-\tau_2) - 0.125D, \tag{46b}$$

$$\frac{dD_c}{dt} = 0.05D(t-\tau_2) - \frac{0.5D_c}{1+0.0005D_c} + 0.4D_p - 0.3D_c, \tag{46c}$$

$$\frac{dD_p}{dt} = \frac{0.5D_c}{1+0.0005D_c} - 0.55D_p, \tag{46d}$$

with the initial conditions:

$$P(\theta) = 300,\ \theta \in [-\tau_{\max}, 0],\ D(\theta) = 100,\ D_c(0) = 30,\ D_p(0) = 40.$$

We obtain the equilibrium point $T^* = (200, 142.8571, 16.4108, 14.7975)$.
We first check the existence of critical value τ_{20} *when* $\tau_1 = 0$. *From Theorem 2, condition (H3) is satisfied because* $b_1 - \gamma = 0.075 \geq 0$. *According to Theorem 2(i),* T^* *of system (46) with* $\tau_1 = 0$ *is locally asymptotically stable for* $\tau_2 \geq 0$.
Furthermore, for the condition (H3) holds, we check the existence of critical value τ_{10} *provided* τ_2 *can be any non-negative value. From Theorem 3 and choosing* $\tau_2 = 100$, *Eq. (30) becomes*

$$\begin{aligned}&\omega_1^4 + 0.005\omega_1^2 - (2.3789 \times 10^{-4}) + 0.0125(\omega_1^2 - 0.0131)\cos 100\omega_1 \\ &- 0.1\omega_1(\omega_1^2 - 0.0131)\sin 100\omega_1 = 0.\end{aligned} \tag{47}$$

We obtain one positive root of Eq. (47), which is $\omega_{11} = 0.1146$, *and the condition (H6) is satisfied. Then, we obtain* $\tau_{10} = 17.3030$. *We also satisfy condition (H7), which is* $V_0V_2 + V_1V_3 = 6.1780 \times 10^{-4} > 0$. *From Theorem 3(ii),* T^* *of system (46) with* τ_2 *can be any non-negative value (in this case,* $\tau_2 = 100$*) is locally asymptotically stable when* $\tau_1 \in [0, 17.3030)$, *where the solution* (P, D, D_c, D_p) *converges to* T^* *as time t increases (see Figure 5(A)).*
The equilibrium point T^* *becomes unstable when* $\tau_1 > 17.3030$, *where the solution* (P, D, D_c, D_p) *gets larger and away from* T^* *as time t increases (see Figure 5(B)). System (46) with* τ_2 *can be any non-negative value (in this case,* $\tau_2 = 100$*) undergoes a Hopf bifurcation at* T^* *when* $\tau_1 = 17.3030$, *and a periodic orbit arises from* T^* *(see Figure 5(C)).*

Example 4 *Consider the model inputs:* $\Lambda = 35$, $\alpha = 0.005$, $\gamma = 0.175$, $\kappa = 0.5$, $\beta = 0.0005$, $\sigma = 0.4$, $\mu = 0.05$, $\mu_1 = 0.075$, $\mu_2 = 0.25$, $\mu_3 = 0.1$, $\phi_1(\theta) = 550$, $\phi_2(\theta) = 10$, $D_{c0} = 35$, *and* $D_{p0} = 20$, *which give the following particular case of model (1):*

$$\frac{dP}{dt} = 35 - 0.005P(t-\tau_1) - 0.05P, \tag{48a}$$

$$\frac{dD}{dt} = 0.005P(t-\tau_1) - 0.175D(t-\tau_2) - 0.125D, \tag{48b}$$

$$\frac{dD_c}{dt} = 0.175D(t-\tau_2) - \frac{0.5D_c}{1+0.0005D_c} + 0.4D_p - 0.3D_c, \tag{48c}$$

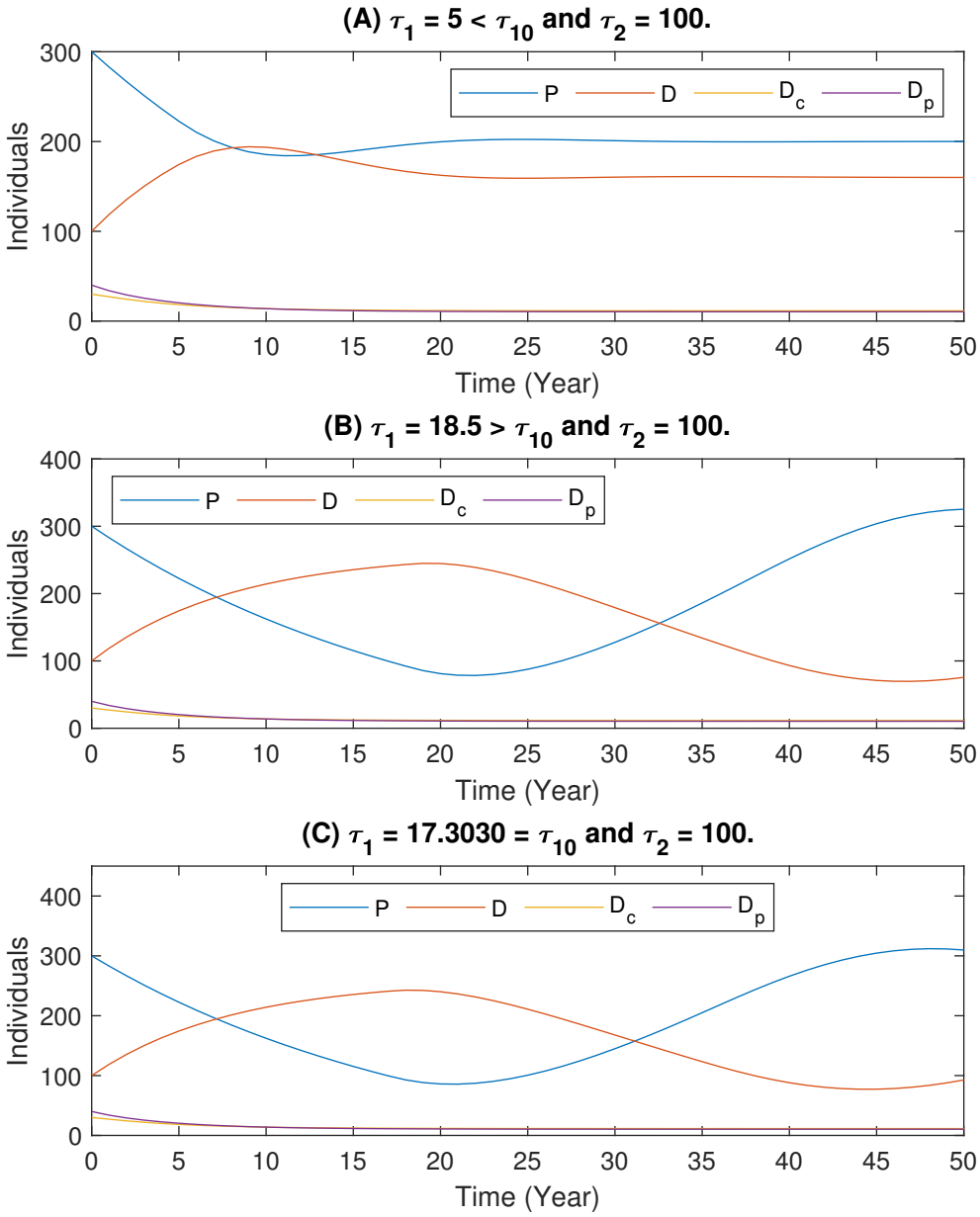

Figure 5. When τ_2 can be any non-negative value (in this case, $\tau_2 = 100$): (A) The equilibrium point T^* of system (46) is locally asymptotically stable for $\tau_1 = 5 < \tau_{10}$. (B) T^* is unstable for $\tau_1 = 18.5 > \tau_{10}$. (C) System (46) undergoes a Hopf bifurcation at $\tau_1 = 17.3030 = \tau_{10}$

$$\frac{dD_p}{dt} = \frac{0.5D_c}{1 + 0.0005D_c} - 0.55D_p, \tag{48d}$$

with the initial conditions:

$$P(\theta) = 550,\ \theta \in [-\tau_{\max}, 0],\ D(\theta) = 10,\ D_c(0) = 35,\ D_p(0) = 20.$$

We obtain the equilibrium point $T^* = (636.3636, 10.6061, 4.2563, 3.8611)$.

We first check the existence of critical value τ_{20} when $\tau_1 = 0$. From Theorem 2, condition (H4) is satisfied because $b_1 - \gamma = -0.05 < 0$. Then, we obtain $\tau_{20} = 19.3216$. By Theorem 2(ii), the equilibrium point T^* of system (48) with $\tau_1 = 0$ is locally asymptotically stable when $\tau_2 \in [0, 19.3216)$, where the solution converges to T^* as time t increases (see Figure 6(A)).

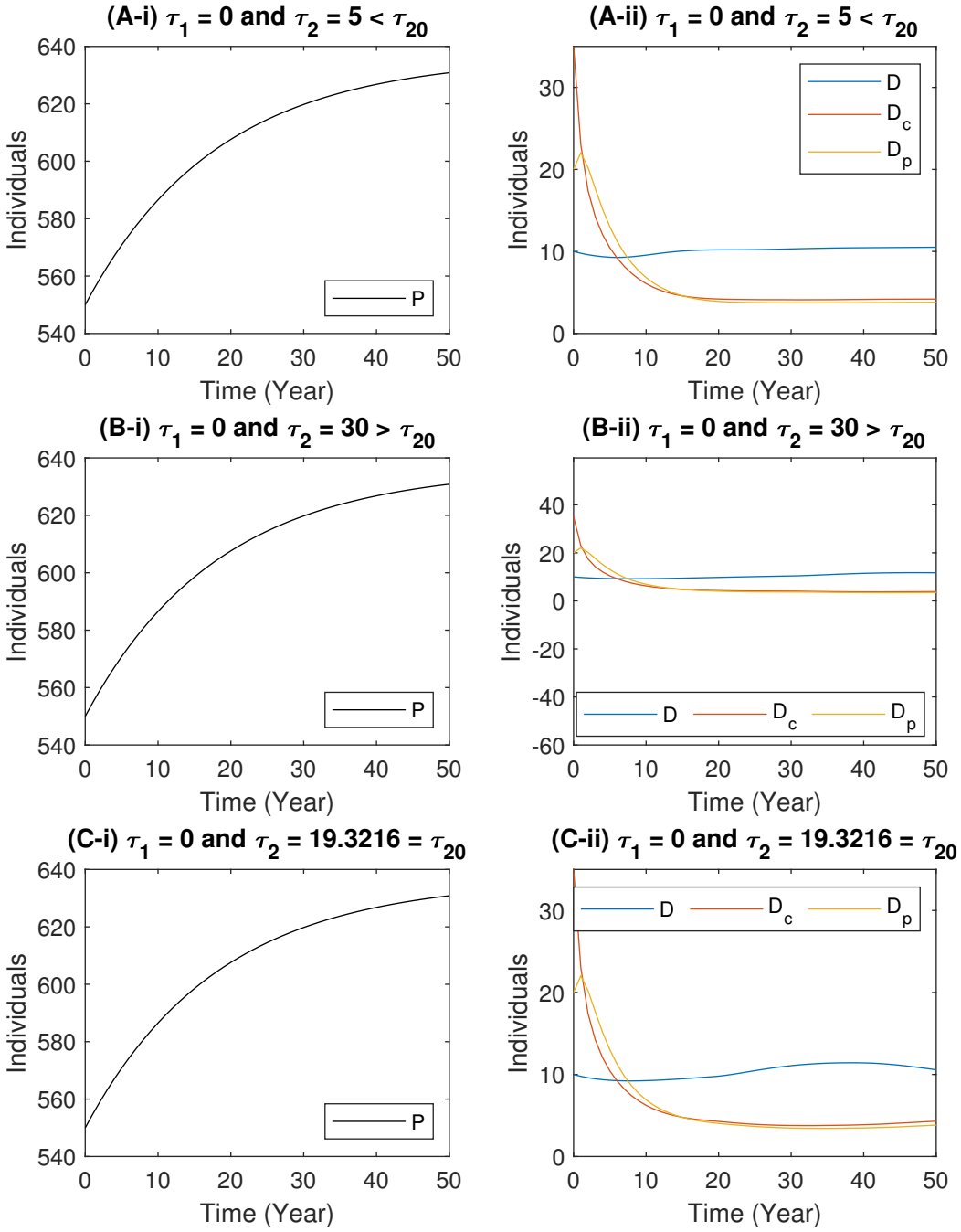

Figure 6. For system (48) with $\tau_1 = 0$: (A) The equilibrium point T^* is locally asymptotically stable for $\tau_2 = 5 < \tau_{20}$. (B) T^* is unstable for $\tau_2 = 30 > \tau_{20}$. (C) System (48) undergoes a Hopf bifurcation when $\tau_2 = 19.3216 = \tau_{20}$

T^* becomes unstable when $\tau_2 > 19.3216$, where the solutions D, D_c, and D_p move away from the equilibrium solutions D^*, D_c^*, and D_p^*, respectively, as time t increases (see Figure 6(B)). System (48) with $\tau_1 = 0$ undergoes a Hopf bifurcation when $\tau_2 = 19.3216$, where the solutions D, D_c, and D_p show periodic behaviors (see Figure 6(C)).
Notice that the solution P for Figure 6(B–C) does not oscillate like the other variables. The differential equation of P (Eq. (1a)) is unaffected by D, D_c, and D_p. Hence, the oscillation of other variables does not affect P since if $\tau_1 = 0$, P is locally asymptotically stable (see Remark 4). On the contrary, if the solution P has an oscillating behavior, the other variables will also oscillate.

Remark 4 Recall Eq. (1a),

$$\frac{dP}{dt} = \Lambda - \alpha P(t-\tau_1) - \mu P. \tag{49}$$

The characteristic equation that associated with the equilibrium solution P^* of Eq. (49) is given by:

$$\lambda_6 + \mu + e^{-\lambda_6 \tau_1}\alpha = 0, \tag{50}$$

where λ_6 represents the eigenvalues. For the case of $\tau_1 = 0$, Eq. (50) has a negative root given by $-(\mu+\alpha)$. Hence, P^* of Eq. (49) with $\tau_1 = 0$ is locally asymptotically stable. This is the reason the solution P in Figure 6(B, C) does not oscillate even though τ_2 is not within its stable region. Apart from this, we discuss the case of $\tau_1 > 0$. Assume that $\lambda_6 = i\hat{\omega}$ ($i = \sqrt{-1}$ and $\hat{\omega} > 0$) is one of the roots of Eq. (50). By substituting $\lambda_6 = i\hat{\omega}$ into Eq. (50) and after some algebraic manipulations, we obtain $\hat{\omega} = \sqrt{(\alpha+\mu)(\alpha-\mu)}$. If $\alpha \leq \mu$, a contradiction occurs because we initially assumed $\hat{\omega} > 0$ and P^* is locally asymptotically stable for $\tau_1 \geq 0$. However, P^* loses its stability for some values of $\tau_1 > 0$ if $\alpha > \mu$.

Next, for the condition (H4) holds, we check the existence of critical value τ_{10} provided τ_2 is within $[0, 19.3216)$. From Theorem 3 and choosing $\tau_2 = 5 \in [0, 19.3216)$, Eq. (30) becomes

$$\begin{aligned}&\omega_1^4 + 0.0487\omega_1^2 + (1.1447 \times 10^{-4}) + 0.0438(\omega_1^2 + 0.0025)\cos 5\omega_1 \\ &- 0.35\omega_1(\omega_1^2 - 0.0025)\sin 5\omega_1 = 0.\end{aligned} \tag{51}$$

Eq. (51) has no root, and condition (H5) is satisfied. From Theorem 3(i), the equilibrium point T^* of system (48) with τ_2 within its stable region (in this case, $\tau_2 = 5 \in [0, 19.3216)$) is locally asymptotically stable for $\tau_1 \geq 0$. Figure 7 shows two simulations of two different values of τ_1 ($\tau_1 = 7$ and $\tau_1 = 87$) with $\tau_2 = 5 \in [0, 19.3216)$. In both figures, the solution (P, D, D_c, D_p) converges to T^* regardless of the value of τ_1.

Example 5 *Consider the model inputs: $\Lambda = 35$, $\alpha = 0.125$, $\gamma = 0.175$, $\kappa = 0.5$, $\beta = 0.0005$, $\sigma = 0.4$, $\mu = 0.05$, $\mu_1 = 0.075$, $\mu_2 = 0.25$, $\mu_3 = 0.1$, $\phi_1(\theta) = 60$, $\phi_2(\theta) = 10$, $D_{c0} = 40$, and $D_{p0} = 20$, which give the following particular case of model (1):*

$$\frac{dP}{dt} = 35 - 0.125P(t-\tau_1) - 0.05P, \tag{52a}$$

$$\frac{dD}{dt} = 0.125P(t-\tau_1) - 0.175D(t-\tau_2) - 0.125D, \tag{52b}$$

$$\frac{dD_c}{dt} = 0.175D(t-\tau_2) - \frac{0.5D_c}{1+0.0005D_c} + 0.4D_p - 0.3D_c, \tag{52c}$$

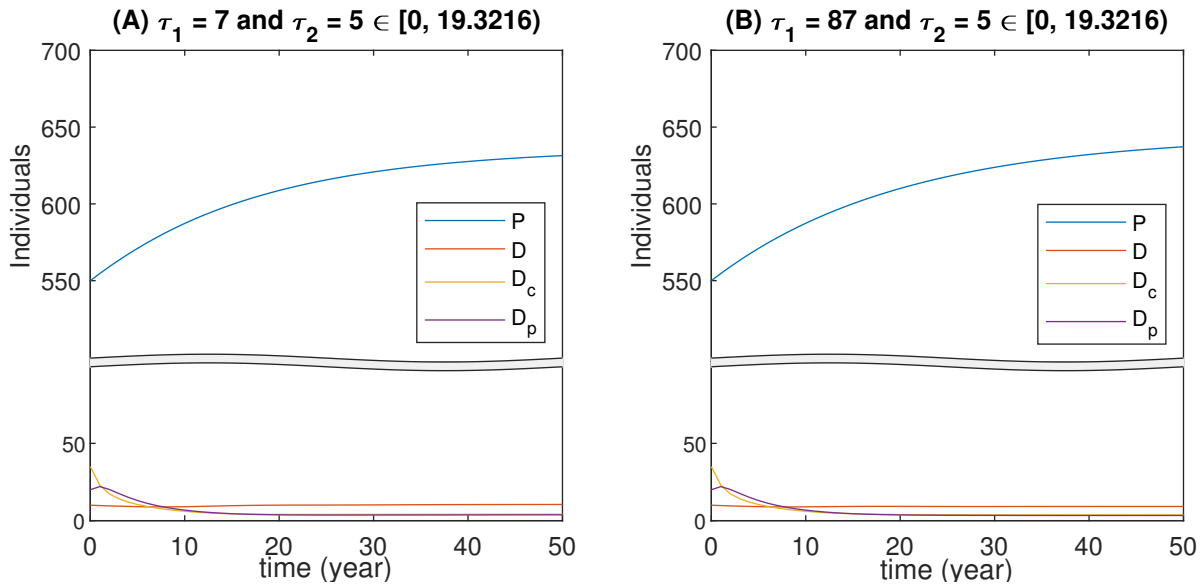

Figure 7. Dynamics of system (48) when τ_2 is within its stable region (in this case, $\tau_2 = 5 \in [0, 19.3216)$): (A) $\tau_1 = 7$. (B) $\tau_1 = 87$

$$\frac{dD_p}{dt} = \frac{0.5D_c}{1 + 0.0005D_c} - 0.55D_p, \tag{52d}$$

with the initial conditions:

$$P(\theta) = 60,\ \theta \in [-\tau_{\max}, 0],\ D(\theta) = 10,\ D_c(0) = 40,\ D_p(0) = 20.$$

We obtain the equilibrium point $T^* = (200, 83.3333, 33.5936, 30.0351)$.
We first check the existence of critical value τ_{20} *when* $\tau_1 = 0$. *From Theorem 2, condition (H4) is satisfied because* $b_1 - \gamma = -0.05 < 0$. *We obtain* $\tau_{20} = 19.3216$. *By Theorem 2(ii), the equilibrium point* T^* *of system (52) with* $\tau_1 = 0$ *is locally asymptotically stable when* $\tau_2 \in [0, 19.3216)$ *and becomes unstable when* $\tau_2 > 19.3216$. *System (52) with* $\tau_1 = 0$ *undergoes a Hopf bifurcation when* $\tau_2 = 19.3216$. *The corresponding plots and trajectories have similar characteristics as in Figure 6.*
Furthermore, for the condition (H4) holds, we check the existence of critical value τ_{10} *provided* τ_2 *is within* $[0, 19.3216)$. *From Theorem 3 and choosing* $\tau_2 = 4 \in [0, 19.3216)$, *Eq. (30) becomes*

$$\begin{aligned}&\omega_1^4 + 0.0331\omega_1^2 - (6.0703 \times 10^{-4}) + 0.0438(\omega_1^2 - 0.0131)\cos 4\omega_1 \\ &- 0.35\omega_1(\omega_1^2 - 0.0131)\sin 4\omega_1 = 0.\end{aligned} \tag{53}$$

The positive root of Eq. (53) is $\omega_{11} = 0.1146$ *and the condition (H6) is satisfied. Then, we obtain* $\tau_{10} = 17.3030$. *We also satisfy the condition (H7), which is* $V_0V_2 + V_1V_3 = 0.0011 > 0$. *From Theorem 3(ii), the equilibrium point* T^* *of system (52) with* τ_2 *within its stable region (in this case,* $\tau_2 = 4 \in [0, 19.3216)$*) is locally asymptotically stable when* $\tau_1 \in [0, 17.3030)$, *where the solution* (P, D, D_c, D_p) *converges to* T^* *as time* t *increases (see Figure 8(A)).* T^* *becomes unstable when* $\tau_1 > 17.3030$, *where the solution* (P, D, D_c, D_p) *gets larger and moves away from* T^* *as time* t *increases (see Figure 8(B)). System (52) with* τ_2 *within its stable region (in this case,* $\tau_2 = 4 \in [0, 19.3216)$*) undergoes a Hopf bifurcation when* $\tau_1 = 17.3030$, *that is, a periodic orbit arises from* T^* *(see Figure 8(C)).*

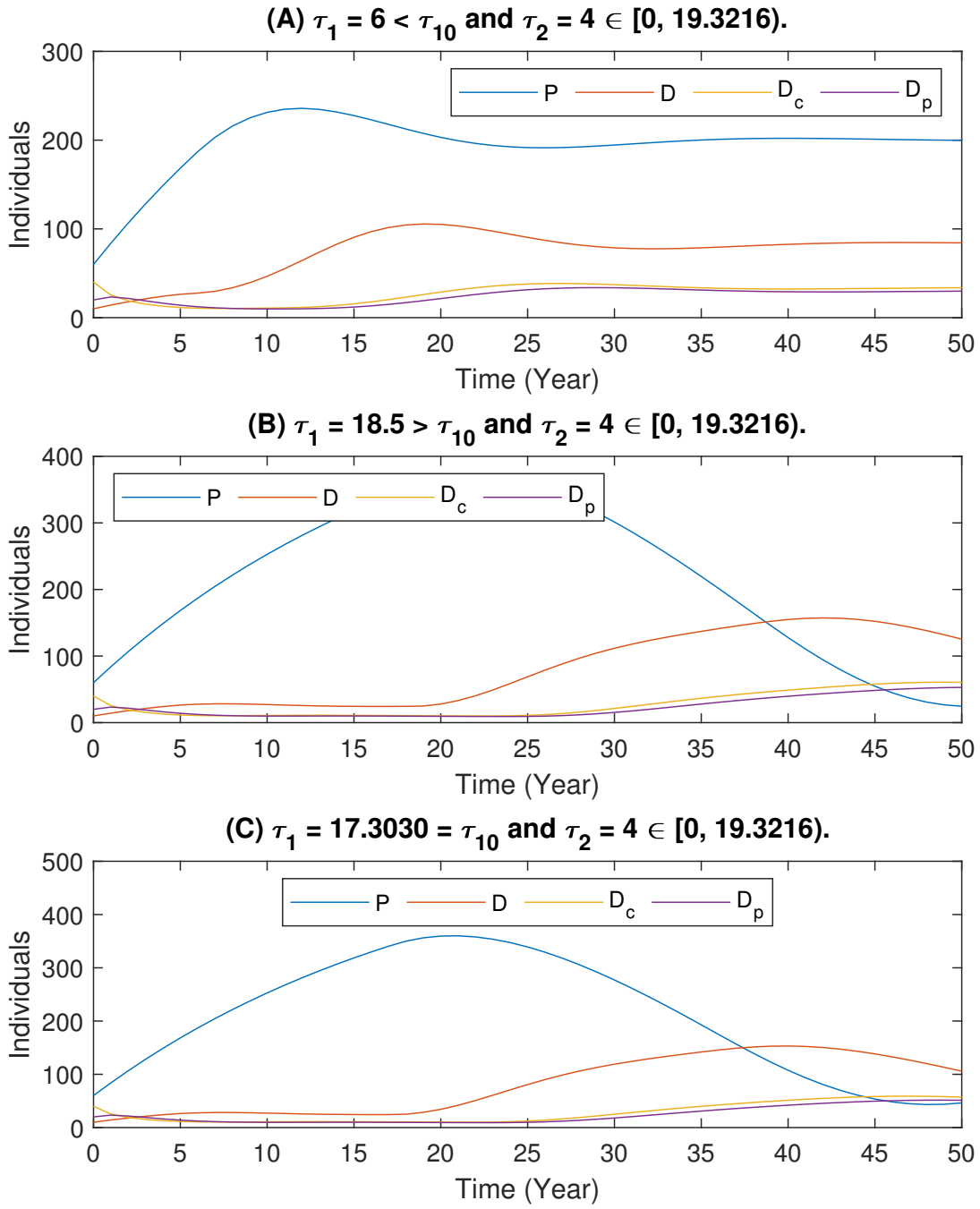

Figure 8. Dynamics of system (52) with τ_2 within its stable region (in this case, $\tau_2 = 4 \in [0, 19.3216)$): (A) The equilibrium point T^* is locally asymptotically stable for $\tau_1 = 6 < \tau_{10}$. (B) T^* is unstable for $\tau_1 = 18.5 > \tau_{10}$. (C) System (52) undergoes a Hopf bifurcation when $\tau_1 = 17.3030 = \tau_{10}$

Simulation with respect to the model inputs in Table 2

Stability of T^*

Based on the values in Table 2, the corresponding equilibrium point of model (1) is $T^* = (1.9751 \times 10^7, 9.4193 \times 10^5, 7.4153 \times 10^6, 1.2005 \times 10^6)$. Accordingly, from the discussion in Section 4, we

first set $\tau_1 = 0$ and look at the range of τ_2 for which T^* remains locally asymptotically stable. Condition (H4) of Theorem 2 is satisfied. We obtain the critical value $\tau_{20} = 16.7073$, where the switching stability occurs at $\tau_2 = \tau_{20}$. Note that from Table 2, we have $\tau_2 = 5$, which is within the stable region. We proceed with finding the critical value for the delay τ_1. Then, we obtain that condition (H5) of Theorem 3 is satisfied. From Theorem 3(i), T^* is locally asymptotically stable (see Figure 9).

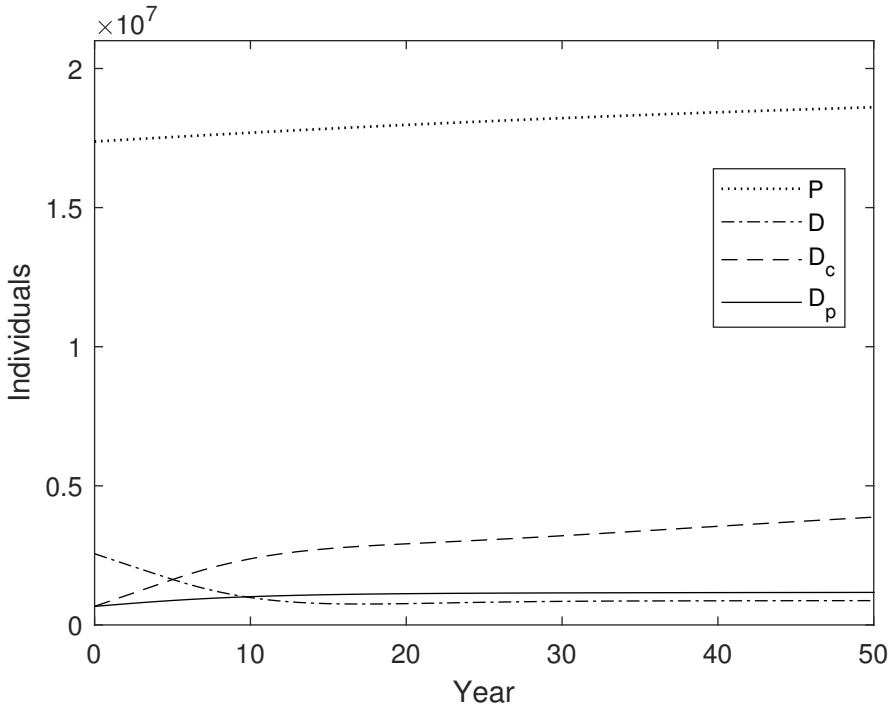

Figure 9. Dynamics of model (1) with the values in Table 2

From Figure 9, we may observe that the solution (P, D, D_c, D_p) approaches T^* as time t gets larger. If this tendency is left untreated, the number of diabetics with complications (D_c) would grow and approach D_c^* at the long-term simulation. This situation should be avoided because a large number of diabetics with complications (D_c) will slow down the recovery rate of complications as many are waiting for their turn to get appropriate treatment. This situation should be avoided because the medical team will be stressed and face some difficulties in handling this overcrowded situation.

Simulation with various α, γ, σ, and β

From the sensitivity analysis results (Section 5), we suggest lowering the diabetes incidence rate (α) to curb the overall diabetes cases. Figure 10 shows that by decreasing α, the number of non-diabetics increases significantly while all the diabetic subpopulations decrease.

The intervention is by increasing the awareness among non-diabetics about the severity of diabetes. Consequently, it may decrease the rate of developing diabetes (α).

Second, we suggest decreasing the rate of the first incidence of complication (γ) and the recurrence rate of complications (σ) in order to decrease the number of diabetics with complications. Figure 11 shows the simulations of decreasing values of γ and σ where the number of diabetics with complications (D_c) decreases to a much lower level.

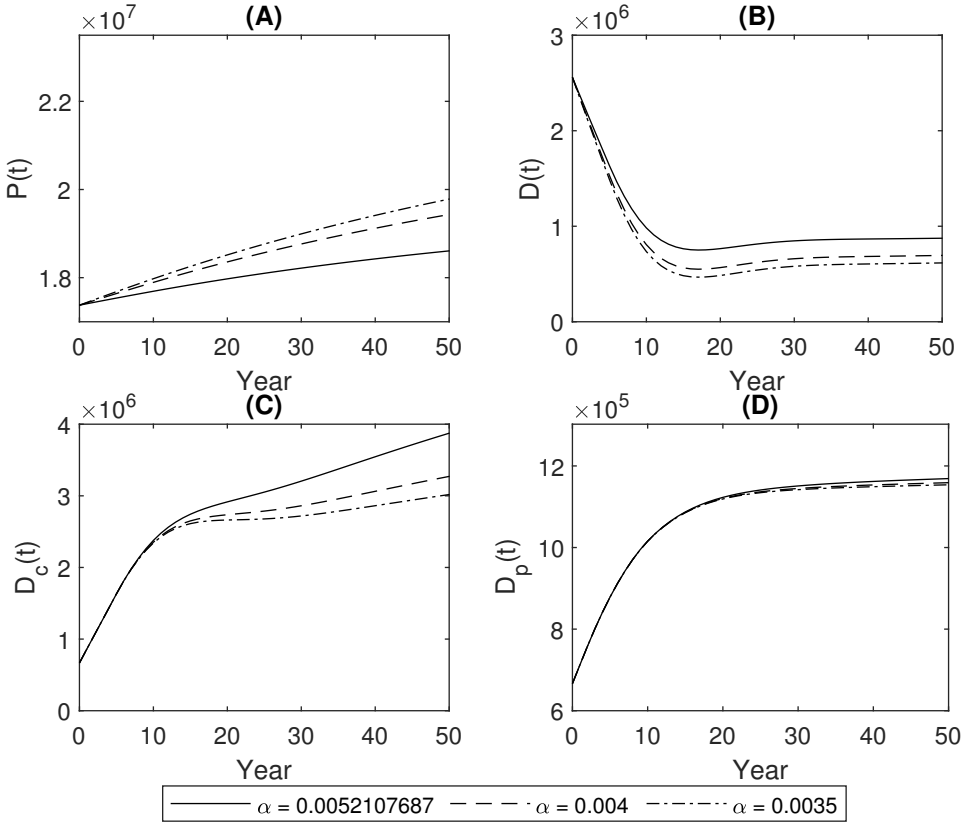

Figure 10. Simulation of model (1) with different rates of developing diabetes (α) ($\alpha = 0.0052108$, $\alpha = 0.004$, and $\alpha = 0.0035$) with the other model inputs in Table 2

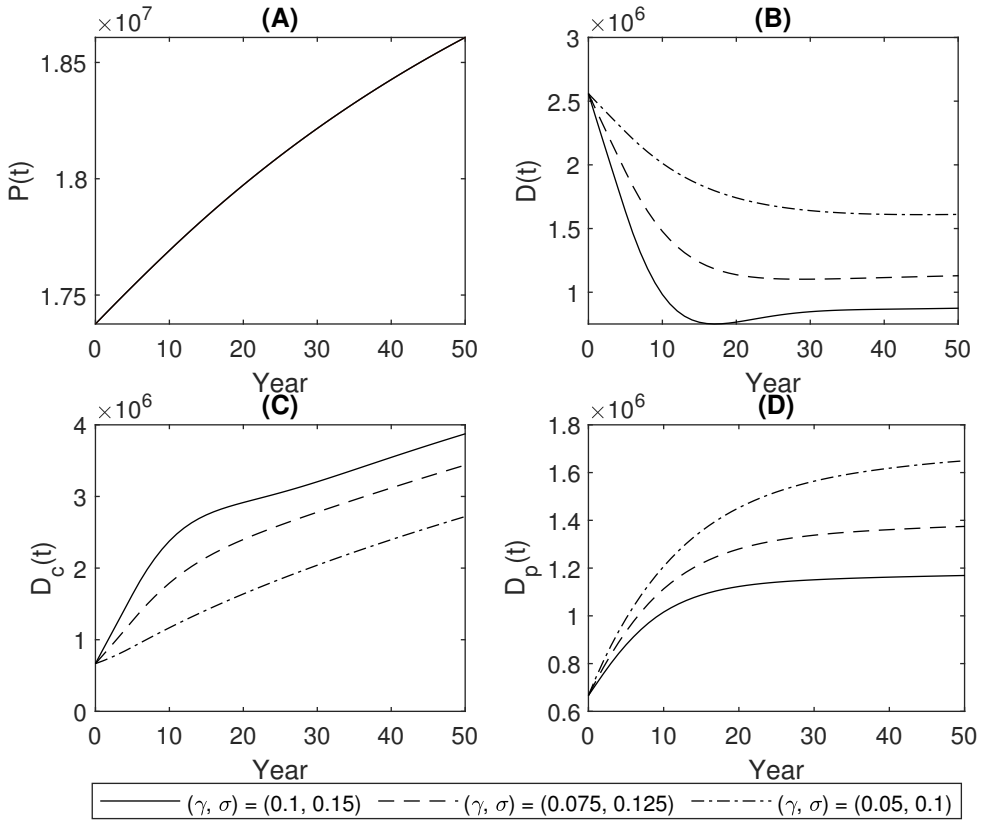

Figure 11. Simulation of model (1) with different values of the first and recurrence incidence of complications (γ,σ) ($(\gamma,\sigma) = (0.1, 0.15)$, $(\gamma,\sigma) = (0.075, 0.125)$, and $(\gamma,\sigma) = (0.05, 0.1)$) with the other model inputs in Table 2

Note that no changes can be observed in Figure 11(A) because the dynamics of non-diabetics (P) are unaffected by γ and σ. The interventions to decrease the rate of developing complications may include early detection of diabetes, education about the complications of diabetes, better self-management of diabetes, lifestyle modifications, and support from family members.

Lastly, we suggest decreasing the effect due to limited medical resources (β). Figure 12 shows the simulation of decreasing value of β.

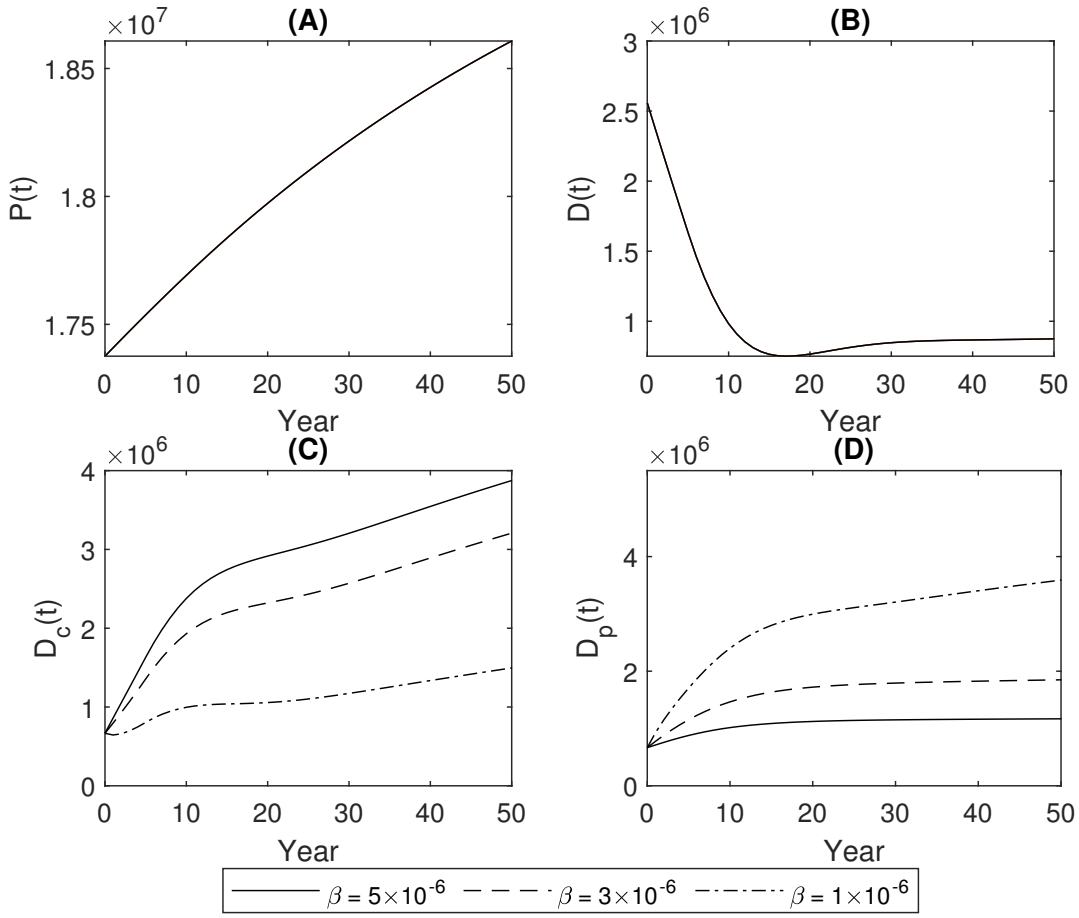

Figure 12. Simulation of model (1) using different values of the inhibition effect (β) ($\beta = 5 \times 10^{-6}$, $\beta = 3 \times 10^{-6}$, and $\beta = 1 \times 10^{-6}$) with the other model inputs in Table 2

Note that no changes can be observed in Figure 12(A–B) because the dynamics of P and D are unaffected by β. As the effect due to limited medical resources (β) decreases, the number of diabetics with complications (D_c) decreases and persists at a much lower level, while the number of diabetics with recovered complications (D_p) increases and persists at a much higher level. To decrease the effect of limited medical resources (β), we recommend providing adequate resources for the treatment of diabetes complications.

Influence of incidence rate of diabetes (α) on Hopf bifurcation corresponds to the time delay τ_1

From Remark 4, the indicator for the equilibrium point T^* of the delay model (1) to lose its stability for some $\tau_1 > 0$ is $\alpha > \mu$. Hence, we investigate the variation of the critical value of time delay τ_{10} (Eq. (31)) with respect to the various rates of incidence of diabetes (α). For the model inputs given in Table 2 and choosing $\alpha \in [0.01, 0.99]$, we plot the stable and unstable regions in Figure 13.

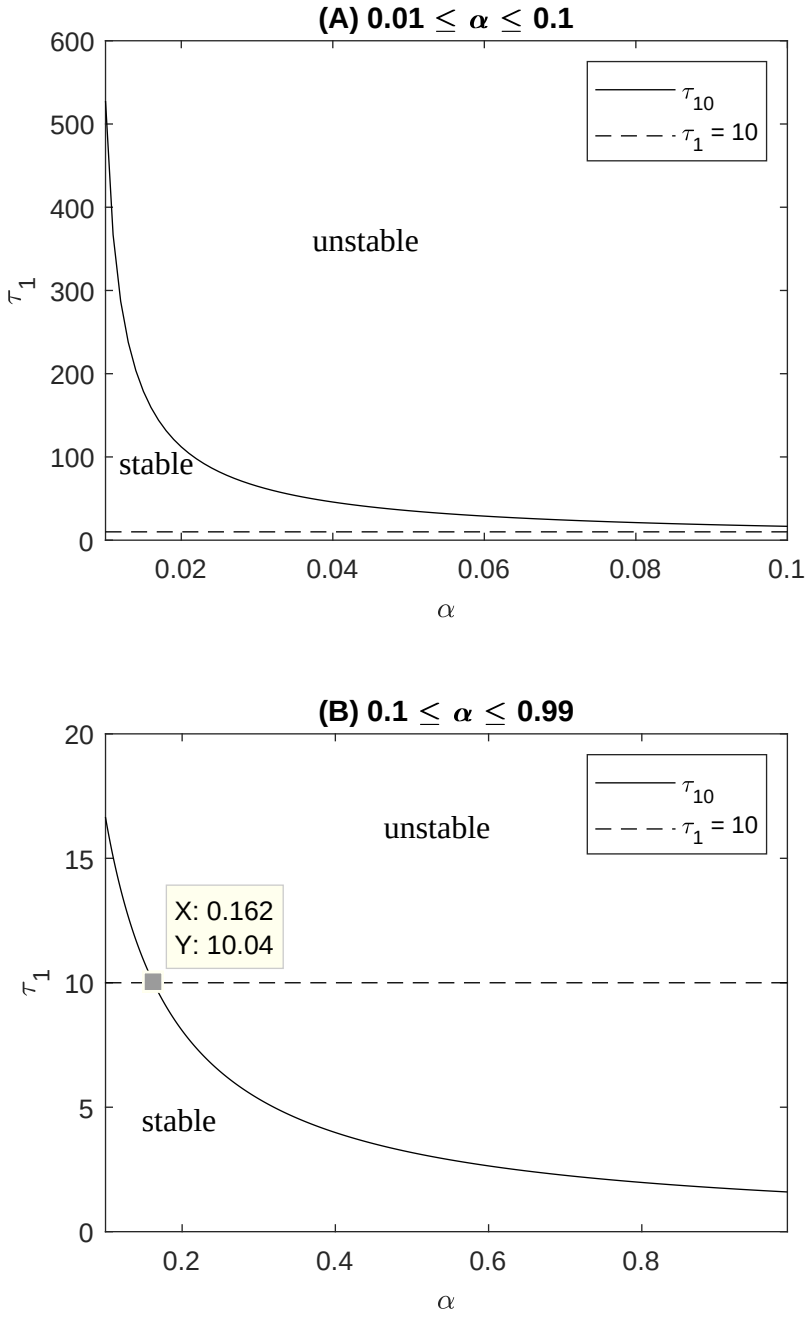

Figure 13. Graph of τ_1 versus α showing the stable and unstable regions of model (1) with the other model inputs in Table 2 (the dashed line represents the line $\tau_1 = 10$)

This figure shows the minimum value of α so that the equilibrium point T^* of model (1) remains locally asymptotically stable. This variation shows that the higher incidence rate of diabetes (α) results in a lower critical value τ_{10}. If the rate $\alpha > 0.162$ year^{-1}, then the solution (P, D, D_c, D_p) of model (1) will show unstable behaviors because $\tau_1 = 10 > \tau_{10}$ (see Figure 13(B)). Sometimes the number of diabetics is high and sometimes low. In this case, it may be difficult to predict the size of every subpopulation. Consequently, implementing control measures to lower diabetes cases will be difficult. If we wish to predict the number of diabetics, the incidence rate of diabetes (α) should be no more than 0.162 year^{-1} for the other model inputs in Table 2.

7 Conclusion

In this paper, we studied a four-state model of a type-2 diabetic population with a saturating recovery rate of diabetes complications. We first investigated the non-negativity and boundedness of the solution for delay and non-delay cases. However, the non-negativity of the solutions P, D, D_c, and D_p of the delay model (1) can only be guaranteed if the model inputs satisfy the conditions stated in Proposition 2.
In the absence of time delay, we discussed the local and global stability analysis. Numerical simulation to indicate the global stability of the non-delay model was given. In the presence of two delay parameters, we discussed the characteristic equation of delay model (1) under the case of $\tau_1 = 0$ to obtain the stable region of τ_2. After that, we derived the critical value corresponding to the delay parameter τ_1. Overall, we have five conditions (H3)-(H7) to characterize the stability properties of T^* (either locally asymptotically stable or unstable) and the manifestation of Hopf bifurcation. The delay values affect the stability of the equilibrium point T^*. A locally asymptotically stable equilibrium point T^* can become unstable under certain conditions. We have shown examples of a periodic orbit that arises from T^* as the model switches its stability.
From the sensitivity analysis, we give three conclusions as follows:

1. We may significantly reduce the overall diabetes cases by decreasing the rate of developing diabetes (α). This includes education on diabetes and the implementation of awareness programs.

2. Diabetes screening should continue so that the status of diabetes can be known earlier. Consequently, medications assist individuals with diabetes in controlling their glucose levels, and the rate of the first incidence of complication (γ) may decrease.

3. We may increase the availability of the treatment of complications for the diabetics with complications, as our sensitivity indices suggested that the diabetics with complications will decrease if the parameter (β) measuring the limited medical resources gets smaller. This concerns diabetics with complications receiving better treatment of the complications such as the improvement or shortening of waiting time for elective cases such as renal or heart transplant.

Declarations

Use of AI tools

The authors declare that they have not used Artificial Intelligence (AI) tools in the creation of this article.

Data availability statement

No Data associated with the manuscript.

Ethical approval (optional)

The authors state that this research complies with ethical standards. This research does not involve either human participants or animals.

Consent for publication

Not applicable

Conflicts of interest

The authors declare that they have no conflict of interest.

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Author's contributions

H.N.: Conceptualization, Methodology, Software, Formal Analysis, Investigation, Writing - Original Draft, Writing - Review & Editing, Visualization. A.A.M.D.: Conceptualization, Methodology, Formal Analysis, Investigation, Resources, Writing - Original Draft, Writing - Review & Editing, Supervision, Project Administration, Funding Acquisition. All authors have read and agreed to the published version of the manuscript.

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Not applicable

References

[1] IDF Diabetes Atlas, IDF Diabetes Atlas 2021, (2021). https://diabetesatlas.org/atlas/tenth-edition/

[2] National Health and Morbidity Survey 2019, NCDs–Non-Communicable Diseases: Risk Factors and other Health Problems, (2011). https://iku.gov.my/images/IKU/Document/REPORT/NHMS2019/Report_NHMS2019-NCD_v2.pdf

[3] IDF Diabetes Atlas, Malaysia Diabetes Report 2000-2045, (2021). https://www.diabetesatlas.org/data/en/country/120/my.html

[4] Mat Daud, A.A., Toh, C.Q. and Saidun, S. Development and analysis of a mathematical model for the population dynamics of Diabetes Mellitus during pregnancy. *Mathematical Models and Computer Simulations*, 12, 620-630, (2020). [CrossRef]

[5] Nasir, H. and Mat Daud, A.A. Population models of diabetes mellitus by ordinary differential equations: a review. *Mathematical Population Studies*, 29(3), 95-127, (2022). [CrossRef]

[6] Mat Daud, A.A., Toh, C.Q. and Saidun, S. A mathematical model to study the population dynamics of hypertensive disorders during pregnancy. *Journal of Interdisciplinary Mathematics*, 22(4), 433-450, (2019). [CrossRef]

[7] Mat Daud, A.A. Mathematical modeling and stability analysis of population dynamics. In Proceedings, *Dynamical Systems, Bifurcation Analysis and Applications (DySBA 2018)*, pp. 3-13, Penang, Malaysia, (2018, August). [CrossRef]

[8] Mat Daud, A.A., Toh, C.Q. and Saidun, S. Mathematical modeling and analysis of anemia during pregnancy and postpartum. *Theory in Biosciences*, 140, 87-95, (2021). [CrossRef]

[9] Nasir, H. Hopf bifurcation analysis for a diabetic population model with two delays and saturated treatment. *Physica Scripta*, 96, 125013, (2021). [CrossRef]

[10] Khetan, A.K. and Rajagopalan, S. Prediabetes. *Canadian Journal of Cardiology*, 34(5), 615-623, (2018). [CrossRef]

[11] IDF Diabetes Atlas, Diabetes around the world in 2021, (2021). https://www.diabetesatlas.org/en/

[12] Gómez-Peralta, F., Abreu, C., Cos, X. and Gómez-Huelgas, R. When does diabetes start? Early detection and intervention in type 2 diabetes mellitus. *Revista Clínica Española (English Edition)*, 220(5), 305-314, (2020). [CrossRef]

[13] National Diabetes Registry, National Diabetes Registry Report 2013-2019, (2020). https://www.moh.gov.my/moh/resources/Penerbitan/Rujukan/NCD/Diabetes/National_Diabetes_Registry_Report_2013-2019_26082021.pdf

[14] Zhang, X. and Liu, X. Backward bifurcation of an epidemic model with saturated treatment function. *Journal of Mathematical Analysis and Applications*, 348(1), 433-443, (2008). [CrossRef]

[15] Krebs, C.J. Some historical thoughts on the functional responses of predators to prey density. *Frontiers in Ecology and Evolution*, 10, 1052289, (2022). [CrossRef]

[16] Nasir, H. and Mat Daud, A.A. Dynamics of a three-state diabetic population model with a time delay and limited medical resources. *Submitted*.

[17] Allen, L.J.S. *An Introduction to Mathematical Biology*. Pearson/Prentice Hall: Italy, (2007).

[18] Tan, K.P. and Mat Daud, A.A. Modelling and qualitative analysis of an illicit drugs model with saturated incidence rate and relapse. *Journal of Mathematics and Computer Science*, 28(4), 373-392, (2023). [CrossRef]

[19] Smith, H. *An Introduction to Delay Differential Equations with Applications to the Life Sciences* (Vol. 57). Springer: New York, (2011).

[20] Zi, Z. Sensitivity analysis approaches applied to systems biology models. *IET Systems Biology*, 5(6), 336-346, (2011). [CrossRef]

[21] Nasir, H. and Mat Daud, A.A. Sensitivity analysis based on the direct differential method for dynamical systems with discrete delays. *AIP Conference Proceedings*, 2905(1), 030016, (2024). [CrossRef]

[22] Rihan, F.A. Sensitivity analysis for dynamic systems with time-lags. *Journal of Computational and Applied Mathematics*, 151(2), 445-462, (2003). [CrossRef]

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