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Analysis of Linear and Nonlinear Mathematical Models for Monitoring Diabetic Population with Minor and Major Complications

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Abstract A Mathematical analysis of linear and nonlinear models for monitoring diabetic populations with minor and major complications are considered in this work. The equilibrium point of the linear system is shown to be globally asymptotically stable (GAS) using direct Lyapunov method. For the nonlinear model, three positive equilibrium points were obtained and analyzed and only one of the equilibrium points is globally asymptotically stable (GAS), shown using the direct Lyapunov method. Some numerical simulations are carried out to demonstrate the analytical results. It is found that the prevalence/incidence of diabetes is on the rise. Our results are effective in monitoring diabetic populations with minor and major complications and the mathematical methods used in the analysis can be applied in different work. The models can be used to monitor global diabetic populations over time.

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1. Introduction

Diabetes is a disorder of metabolism caused by total (or relative) absence of insulin which manifests clinically as an elevated blood glucose. The disorder is usually due to a combination of hereditary and environmental causes [40], resulting in abnormally high blood sugar levels known as hyperglycemia. No one is certain as to what starts the processes that cause diabetes [32]. But scientists believed that genes and environmental factors interacts to cause diabetes in most cases [32].
The prevalence of the disease is steadily increasing everywhere, most markedly in the world's middle-income countries. Unfortunately, effective policies to create supportive environment for diabetic patients are not obtainable in most society. Pursuing such policies is important. This is because when diabetes is uncontrolled, it has a dire consequences for health and well-being of the society [13].
Initially, diabetes was considered as a disease with less harm to the society. But in the last few years there has been an alarming increase in the number of people diagnosed with the disease. Report released by World Health Organization (WHO) in 2003 [37] showed that 194 million people were diabetic globally. This represents a global prevalence exceeding three percent of the world's population. The recent report [38] put the estimated number of people with diabetes at 422 million (representing number of diabetic patients as of 2014). Comparing with 108 million and 194 million in 1980 and 2003 respectively, one can see that the prevalence of the disease has multiplied four times from 1980. Out of this number 1 person die every 6 seconds, totaling approximately 5.3 million deaths annually [41]. The ten countries estimated to have the highest number of diabetes in 2000 and 2030 are listed in Figure 1 below as presented in [39].

2000			2030	
Ranking	country	people with diabetes (in millions)	country	people with diabetes (in millions)
1	India	31.7	India	79.4
2	China	20.8	China	42.3
3	U.S	17.7	U.S	30.3
4	Indonesia	8.4	Indonesia	21.3
5	Japan	6.8	Pakistan	13.9
6	Pakistan	5.2	Brazil	11.3
7	Russian	4.6	Bangladesh	11.1
8	Brazil	4.6	Japan	8.9
9	Italy	4.3	Philippines	7.8
10	Bangladesh	3.2	Egypt	6.7

Figure 1. Top ten countries to have highest number of diabetes in 2000 and 2030 [39]

Generally, two forms of diabetes are considered: type 1 diabetes, also known as Insulin Dependence Diabetes Mellitus (IDDM), typically occurs in children and young adults and it represents (10-15) % of the diabetic population, and type 2 diabetes formally known as Non Insulin Dependence Diabetes Mellitus (NIDDM), represents the major part (85-90) % [19]. However, there is third type called gestational diabetes which affects pregnant women and it goes away the moment pregnancy is over.
Complications of diabetes are broadly classified into two; minor (acute) and major (chronic) complications [1]. Minor complications of the disease are very serious and have strong health implication. They are usually dangerous complications and are always medical emergency. They include; hyperglycemia hyperosmolar state, diabetic coma, respiratory infections and periodontal disease. On the other hand, major complications are those complications of disease that continues for a long time and are not easily cured.
From the above statements, it is clear that diabetes aid in developing different kind of diseases. Thus, monitoring the size of the diabetic population is important. Different strategies can be adopted provided they yield the desired results. Our interest is to show that investment in primary health care is necessary and to convince policy makers that bold decisions must be taken for a sustainable development which ensures better quality of life and well-being for the present and future generations of human [13].

2. Model Formulation

Suppose that $D = D(t)$,$C_1 = C_1(t)$ and $C_2 = C_2(t)$ $(t > 0)$ represents the numbers of diabetic patients without complications, with minor complications and with major complications respectively, and let $N = N(t)$=$D(t) + C_1(t) + C_2(t)$ denote the size of the population of diabetic patients at time t. Let I=$I(t)$ denote the incidence of diabetes.

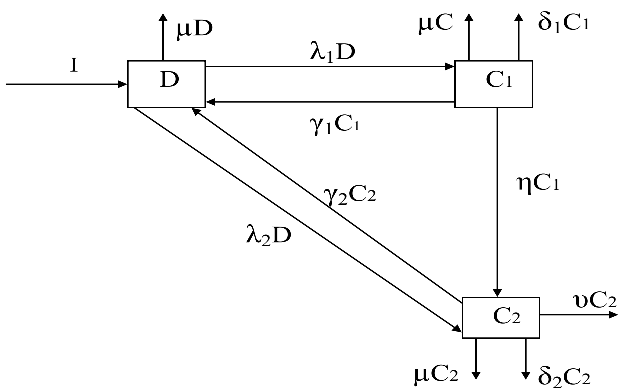


Figure 2. Schematic representation of the model

A person may develop the disease without complications and develop complications with time or die naturally. A diabetic patient with minor complications may die naturally, die as a result of minor complications, develop major complications or have his/her complications cured. A diabetic patient with major complications may die naturally, as a result of the complications, have his/her blood normalized through some control measures and become diabetic patient without complications. On the basis of this, we have the following dynamics; the diagram above shows $I{=}I(t)$ cases that are diagnosed in a time interval of length t and are assumed to have no complications upon diagnosis. In this same time interval, the number of diabetic patients without complications $D{=}D(t)$ is seen to increase by the amount $\gamma_1 C_1$ (those who recovered from minor complications) and $\gamma_2 C_2$ (patients who recovered from major complications), and to decrease by μD (patients without complications who die naturally),$\lambda_1 D$ (patients who develop minor complications) and $\lambda_2 D$ (patients who develop major complications). During this same time interval, the number of diabetic patients with minor complications, $C_1{=}C_1(t)$ is increased by $\lambda_1 D$ (patients who develop minor complications) and decrease by μC_1 (patients with minor complications who die naturally),$\delta_1 C_1$ (patients who die as a result of the minor complications) and ηC_1 (patients with minor complications who develop major complications). On the other hand, the number of diabetic patients with major complications increases by $\lambda_2 D$ (patients who develop major complications) and ηC_1 (patients with minor complications who develop major complications) and decreases by μC_2, $\delta_2 C_2$, νC_2, and $\gamma_2 C_2$; patients with major complications who die naturally, patients who die as a result of major complications, patients who are severely disabled and are removed and patients who achieve glucose regulation respectively.

These rates of change are formalized by the ordinary differential equations:

$$\begin{aligned}
\frac{dD}{dt} &= -(\lambda_1 + \lambda_2 + \mu)D + \gamma_1 C_1 + \gamma_2 C_2 + I,\\
\frac{dC_1}{dt} &= \lambda_1 D - (\delta_1 + \eta + \gamma_1 + \mu)C_1,\\
\frac{dC_2}{dt} &= \lambda_2 D + \eta C_1 - (\delta_2 + \gamma_2 + \mu + \nu)C_2.
\end{aligned}$$

And since $N{=}D + C_1 + C_2$, the initial value problems (IVP) in term of C_1, C_2 and N are

$$\begin{aligned}
\frac{dC_1}{dt} &= -(\xi + \lambda_1)C_1 - \lambda_1 C_2 + \lambda_1 N,\\
\frac{dC_2}{dt} &= (\eta + \lambda_1)C_1 - (\theta + \lambda_2)C_2 + \lambda_2 N,\\
\frac{dN}{dt} &= -\delta_1 C_1 - \Lambda C_2 - \mu N + I,
\end{aligned} \tag{2.1}$$

$C_1(0){=}C_{10}$, $C_2(0) = C_{20}$, $N(0) = N_0$, $\xi = \delta_1 + \gamma_1 + \eta + \mu$, $\theta{=}\delta_2 + \gamma_2 + \mu + \nu$, $\Lambda{=}\delta_2 + \nu$, and C_{10}, C_{20}, N_0 are the initial values of C_1, C_2 and N respectively. The models are extensions of the models of diabetes considered in [10, 13] by subdividing the compartment for diabetic population with complications into two based on the classification of diabetic complications mentioned in [1].

3. Basic qualitative properties of the model

Since the model (2.1) describes human population it is necessary to show that all the state variables C_1, C_2, N are nonnegative for all $t \geq 0$. Solution with positive initial

TABLE 1. Description of Variables for the Model (2.1)

Variable	**Description**
$D(t)$	: number of diabetic patients without complications,
$C_1(t)$	: number of diabetic patients with minor complications,
$C_2(t)$	: number of diabetic patients with major complications,
$N(t)$	: total population of diabetic patients,
t	: time as a continuous variable.

TABLE 2. Parameters for the Model (2.1)

Parameter	**Description**
μ	: natural death,
λ_1	: probability of developing minor complications,
λ_2	: probability of developing major complications,
η	: rate of developing major complications from minor complications,
γ_1	: rate of recovery from minor complications,
γ_2	: rate of recovery from major complications,
δ_1	: death induced by minor complications,
δ_2	: death induced by major complications,
ν	: rate of which diabetic patient with major complications become severely disabled,
I	: incidence of diabetes.

data remains positive for all $t \geq 0$ and are bounded. Based on biological consideration therefore, the model (2.1) will be studied in the region

$$\Omega = \left\{ (C_1, C_2, N) \in \Re^3_+ : C_1 \geq 0, C_2 \geq 0, N \leq \frac{I}{\mu} \right\}.$$

3.1. Positivity and boundedness of solutions

Lemma 3.1. *The region Ω is positively-invariant for the model* (2.1) *with non-negative initial conditions in $\mathbb{R}^3_+$.*

Proof. The system (2.1) is Lipschitz continuous in Ω, from the standard Theorem in [24], there exists a unique solution to (2.1). We use the method of contradiction as in [6, 26] to show that Ω is positively-invariant.
Under the initial conditions, assume that there exists a first time t_1 such that
$C_1(t_1) = 0,\ \frac{dC_1(t_1)}{dt} < 0,\ C_2(t_1) > 0,\ N(t_1) > 0$ for $0 < t < t_1$,
or there exists a t_2 such that

$C_2(t_2) = 0,\ \frac{dC_2(t_2)}{dt} < 0,\ C_1(t_2) > 0,\ N(t_2) > 0$ for $0 < t < t_2$.

$$\text{In the first case } (t_1)\text{: } \frac{dC_1(t_1)}{dt} = -\lambda_1 C_1 + \lambda_1 N, \\ = \lambda_1(N - C_1), \\ > 0,$$

which is a contradiction. Meaning $C_1(t) > 0$.

$$\text{In the second case } (t_2)\text{: } \frac{dC_2(t_2)}{dt} = (\eta - \lambda_2)C_1 + \lambda_2 N, \\ = \lambda_2 N + \eta C_1 - \lambda_2 C_1, \\ > 0,$$

which is a contradiction. Meaning $C_2(t) > 0$.
Thus, in any case C_1, C_2 remain positive. Also, since $N(t) \geq C_1(t) + C_2(t)$ and

$$\frac{dN}{dt} = -\delta_1 C_1 - \eta C_2 - \mu N + I, \\ \leq I - \mu N,$$

$$\Rightarrow \frac{dN}{dt} + \mu N \leq I. \tag{3.1}$$

That is to say $\frac{dN}{dt} \leq 0$ if $N \geq \frac{I}{\mu}$. Thus, $N \leq \frac{I}{\mu}(1 - e^{-\mu t}) + N(0)e^{-\mu t}$. In particular, $N \leq \frac{I}{\mu}$. Thus, the region Ω is positively-invariant. Further, if $N(0) > \frac{I}{\mu}$ then either the solution enters Ω in finite time, or $N \to \frac{I}{\mu}$ asymptotically. Hence the region Ω attracts all solutions in $\mathbb{R}^3_+$. ■

4. Analysis of the models

The model is considered in two cases: linear and nonlinear.

4.1. Analysis of the linear model

In the linear model (2.1), the probabilities of developing minor and major complications, λ_1 and λ_2 will respectively be estimated to have constant values [13]:

$$\lambda_1 = \frac{C_{10}}{N_0},\ \lambda_2 = \frac{C_{20}}{N_0}. \tag{4.1}$$

4.2. Local stability analysis of the equilibrium point of the linear model

The linear model (2.1) has unique equilibrium point given by:

$$E_l = \left(\frac{\lambda_1 \theta I^*}{\lambda_1 A_1 + \lambda_2 A_2 + A_3}, \frac{(\lambda_1 \eta + \lambda_2 \xi)I^*}{\lambda_1 A_1 + \lambda_2 A_2 + A_3}, \frac{[\lambda_1(\eta + \theta) + (\lambda_2 + \theta)\xi]I^*}{\lambda_1 A_1 + \lambda_2 A_2 + A_3} \right), \tag{4.2}$$

$A_1 = \eta(\mu + \Lambda) + \theta(\delta_1 + \mu),\ A_2 = \xi(\mu + \Lambda),\ A_3 = \mu\theta\xi$

Lemma 4.1. *The unique equilibrium point E_l of the model (2.1) is locally asymptotically stable (LAS).*

Proof. The proof of Lemma 4.1 is given in Appendix A.1. ■

4.3. Global Stability analysis of the equilibrium point in the linear model

Having established that the equilibrium point in the linear case is locally asymptotically stable, we prove the global stability of this equilibrium point. to do this we employ the use of Lyapunov functional approach as in [7]. Let us introduce new variables $u_1 = C_1 - C_1^*$, $u_2 = C_2 - C_2^*$, $u_3 = N - N^*$ and $\phi_1 = I - I^*$, $u_i = u_i(t)$, $i = 1, 2, 3$ $\phi_1 = \phi_1(t)$.
Note that

$$\begin{aligned} -(\xi + \lambda_1)C_1^* - \lambda_1 C_2^* + \lambda_1 N^* &= 0, \\ (\eta - \lambda_2)C_1^* - (\theta + \lambda_2)C_2^* + \lambda_2 N^* &= 0, \\ -\delta_1 C_1^* - \Lambda C_2^* - \mu N^* + I^* &= 0. \end{aligned}$$

With this change of variables, system (2.1) becomes

$$\begin{aligned} \frac{du_1}{dt} &= -(\xi + \lambda_1)u_1 - \lambda_1 u_2 + \lambda u_3, \\ \frac{du_2}{dt} &= (\eta - \lambda_2)u_1 - (\theta + \lambda_2)u_2 + \lambda_2 u_3, \\ \frac{du_3}{dt} &= -\delta_1 u_1 - \Lambda u_2 - \mu u_3 + \phi_1, \end{aligned} \tag{4.3}$$

Theorem 4.2. *Suppose that (C_1^*, C_2^*, N^*) is below or above (C_1, C_2, N) along the solution curves, the unique equilibrium point E_l is globally asymptotically stable in the region Ω if the following inequalities hold: $\eta < \lambda_2$ and $\Lambda > (1 + \lambda_2)$.*

Proof. The proof of Theorem 4.2 is based on the proof given in [7] and is given in Appendix A.2. ∎

4.4. Analysis of the nonlinear model

In this case, we assumed that the probability of developing minor and major complications, λ_1 and λ_2 respectively to be [13]:

$$\lambda_1 = \alpha\frac{C_1}{N},\ \lambda_2 = \alpha\frac{C_2}{N},\ \alpha \in (0, 1]\ .$$

Thus,by substituting $\lambda_1 = \alpha\frac{C_1}{N}$ and $\lambda_2 = \alpha\frac{C_2}{N}$ in the linear system (2.1), it becomes nonlinear and is written thus:

$$\begin{aligned} \frac{dC_1}{dt} &= (\alpha - \xi)C_1 - \alpha\frac{C_1 C_2}{N} - \alpha\frac{C_1^2}{N}, \\ \frac{dC_2}{dt} &= \eta C_1 + (\alpha - \theta)C_2 - \alpha\frac{C_1 C_2}{N} - \alpha\frac{C_2^2}{N}, \\ \frac{dN}{dt} &= -\delta C_1 - \Lambda C_2 - \mu N + I. \end{aligned} \tag{4.4}$$

It should be noted that the feasibility region is the same as the one in the linear model, that is Ω.

4.5. Local stability analysis of the equilibrium points in the nonlinear case

The nonlinear model (4.4) has three positive equilibrium points as follow:

$$\begin{aligned} EP1 &= (C_1^*, C_2^*, N^*),\\ &= (0,\ 0,\ \frac{I^*}{\mu}),\\ EP2 &= (C_1^{**}, C_2^{**}, N^{**}),\\ &= \left(0,\ \frac{w_1 I^*}{\alpha\mu + w_1\Lambda},\ \frac{\alpha I^*}{\alpha\mu + w_1\Lambda}\right), \end{aligned}$$

$$EP3 = (C_1^{***}, C_2^{***}, N^{***}),\ = \left(\frac{w_2 w_3 I^*}{\Phi},\ \frac{\eta w_2 I^*}{\Phi},\ \frac{\alpha(\eta + w_3)I^*}{\Phi}\right),$$

$w_1 = \alpha - \theta,\ w_2 = \alpha - \xi,\ w_3 = \theta - \xi,\ \Phi = w_2(\delta_1 w_3 + \Lambda\eta) + \alpha\mu(\eta + w_3).$

To analyze the stability of the fixed points, we linearize the nonlinear system by taking a small perturbation about the equilibrium points.

The linearized version of the nonlinear system at the generic equilibrium point $x = x_f$ therefore may consequently be written in the form: $V' = JV,\ V(0) = V_0,\ V = V(t),\ V = (V_1, V_2, V_3)^T,\ J = (\alpha_{ij})_{3\times 3},\ \alpha_{ij} = \frac{\partial u_i}{\partial x_j}\Big|_{x=x_f}$

$x = (x_1, x_2, x_3)^T,\ x_1 = C_1,\ x_2 = C_2,\ x_3 = N,\ x_f = (x_{1f}, x_{2f}, x_{3f})^T,$

$x_{1f} = C_{1f},\ x_{2f} = C_{2f},\ x_{3f} = N_f,\ i, j = 1, 2, 3, ' = \frac{d}{dt}.$

Thus, the Jacobian matrix at $(C_1, C_2, N) = (C_{1f}, C_{2f}, N_f)$ is given by

$$J = \begin{pmatrix} w_2 - 2\alpha\frac{C_{1f}}{N_f} - \alpha\frac{C_{2f}}{N_f} & -\alpha\frac{C_{1f}}{N_f} & \alpha\frac{C_{1f}^2}{N_f^2} + \alpha\frac{C_{1f}C_{2f}}{N_f^2} \\ \eta - \alpha\frac{C_{2f}}{N_f} & w_1 - 2\alpha\frac{C_{2f}}{N_f} - \alpha\frac{C_{1f}}{N_f} & \alpha\frac{C_{2f}^2}{N_f^2} + \alpha\frac{C_{1f}C_{2f}}{N_f^2} \\ -\delta_1 & -\Lambda & -\mu \end{pmatrix} \tag{4.5}$$

4.6. Local stability analysis of the equilibrium point $EP1$

By the way of the Jacobian matrix (4.5), the Jacobian matrix associated to the equilibrium point $EP1$ of the system (4.4) is given as follows (J^*):

$$J^* = \begin{pmatrix} w_2 & 0 & 0 \\ \eta & w_1 & 0 \\ -\delta_1 & -\Lambda & -\mu \end{pmatrix}.$$

The characteristic polynomial associated to the Jacobian matrix at (4.5)$EP1$:

$$p_1(\chi) = \chi^3 - (w_1 + w_2 - \mu)\chi^2 + [w_1 w_2 - \mu(w_1 + w_2)]\chi + \mu w_1 w_2,$$

χ denote the eigenvalues of the Jacobian matrix J^*. Thus, the zeros of the polynomial are:

$$\chi_1 = w_1,\ \chi_2 = w_2,\ \chi_3 = -\mu,$$

and since for a equilibrium point to be locally asymptotically stable all the roots of the characteristic polynomial must have negative real parts, the equilibrium point $EP1$

is unstable since $w_1, w_2 > 0$. However, the equilibrium point $EP1$ is stable whenever $\alpha < \theta,\ \xi$.

4.7. Local stability analysis of the equilibrium point $EP2$

Here also, by the way of the Jacobian matrix (4.5) associated to the system (4.4), we obtain the Jacobian matrix at the equilibrium point $EP2$ as follows (J^{**}):

$$J^{**} = \begin{pmatrix} w_3 & 0 & 0 \\ \eta - w_1 & -w_1 & w_1^2 \\ -\delta_1 & -\Lambda & -\mu \end{pmatrix}.$$

The characteristic polynomial associated to $EP2$:

$$p_2(\chi) = \chi^3 - (w_3 - w_1 - \mu)\chi^2 + [w_1(w_1\Lambda + \mu) - w_3(\mu + w_1)]\chi - w_1 w_3(w_1\Lambda + \mu),$$

and the roots of this polynomial are:

$$\chi_1 = w_3,\ \chi_2 = \frac{-(\mu + w_1) + \sqrt{\Delta}}{2},\ \chi_3 = \frac{-(\mu + w_1) - \sqrt{\Delta}}{2},$$

$\Delta = (\mu - w_1)^2 - 4\Lambda w_1^2$, and since w_1 is positive, the fixed point $EP2$ is unstable.

4.8. Local stability analysis of the fixed point $EP3$

Lemma 4.3. *The equilibrium point $EP3$ of the nonlinear case (4.4) is locally asymptotically stable (LAS)*

Proof. The proof of Lemma 4.3 is given in Appendix A.3. ∎

4.9. Global stability analysis of the equilibrium points $EP3$

The goal of this section is to establish sufficient condition on the global asymptotic stability of the equilibrium point $EP3$ to the nonlinear system. We employ the use of Lyapunov functional.

Theorem 4.4. *Suppose that $\alpha = 1$, the fixed point $EP3$ of the nonlinear system (4.4) is globally asymptotically stable if the following inequalities are satisfied: $\delta_1 > \eta$,*
$\tau_1 - \tau_2 > 0,\ \varphi_3 - \varphi_4 > 0$.

Proof. The proof of this Theorem 4.4 is given in Appendix A.4 by considering a quadratic Lyapunov function. ∎

5. Numerical Simulation

This section gives a demonstration of the analytical results in the previous sections. The parameter values are given in table 3. These parameter values were obtained from the source(s) indicated in each case. The global incidence of diabetes used in the simulations is $I = 17000000$. This incidence, is the average of incidences for three years(2012-2014)[38] [16]. It should also be noted that the death as a result of minor complications of diabetes is slightly higher than that of major complications [38]. Parameter values that we were not able to obtain in the diabetes literature were assumed in the simulations.

$C_1(0) = 500000,\ C_2(0) = 600000,\ N(0) = 1500000$ were used as initial conditions. The probabilities of developing minor and major complications were estimated to be $\lambda_1 = 0.33,\ \lambda_2 = 0.40$, (in the linear case) using their definitions given in 4.1, while $\theta,\ \xi$

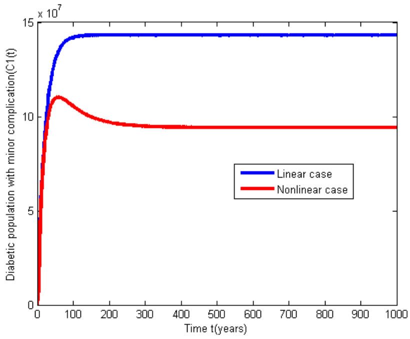
and Λ were obtained to be 0.10729142, 0.09379427 and 0.05500572 respectively.

With these values of the parameters, the equilibrium points are obtained as follow:
Linear Case: (143270000, 191880000, 375880000)
Nonlinear Case:
$EP1 = (0, 0, 1190000000)$,
$EP2 = (0, 239410000, 268180000)$,
$EP3 = (94140000, 209250000, 334800000)$ The profiles for $C_1(t)$, $C_2(t)$ and $N(t)$ in both

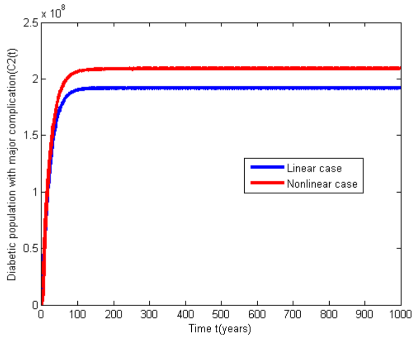
TABLE 3. Parameter values used in the numerical simulations

Parameter	**Value**	**Source**
δ_1	0.007508574	Estimated from [29]
δ_2	0.005005716	Estimated from [29]
η	0.03	Assumed
γ_1	0.042	Adopted from [13]
γ_2	0.038	Adopted from [13]
μ	0.0142857	[26]
ν	0.05	Adopted from[13]

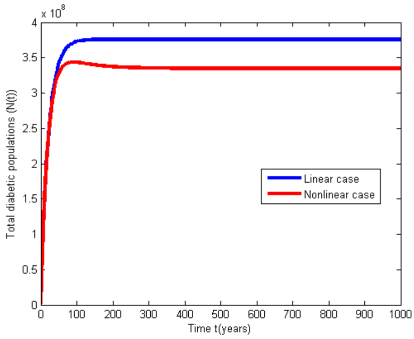
cases are shown in Figures 2(A) - 2(C) respectively. It can be seen from the figures that the fixed point in both cases was reached by time $t = 100$years. It also shows that there is an agreement between the analytical results and the numerical results.
A situation where there is no recovery from the complications of the disease (that is $\gamma_1 = 0,\ \gamma_2 = 0$) is also experimented (see Figures 3(A) - 3(C)). The equilibrium point in this case are:
Linear case: (145530000, 194820000, 363230000)
Nonlinear case:
$EP2 = (0, 241630000, 259620000)$, $EP3 = (119120000, 204230000, 340970000)$.
Note the equilibrium point $EP1$ was not included because it does not contain the recovery rates, so there will be no changes in that regard.



(A) Profile of $C_1(t)$

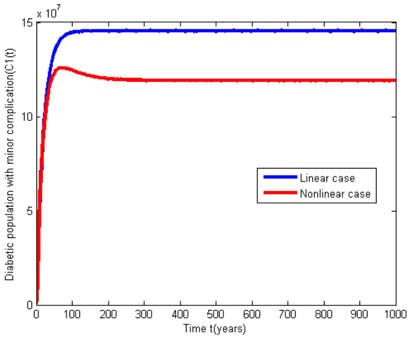


(B) Profile of $C_2(t)$

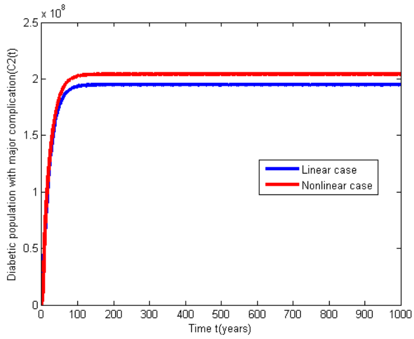


(C) Profile of $N(t)$

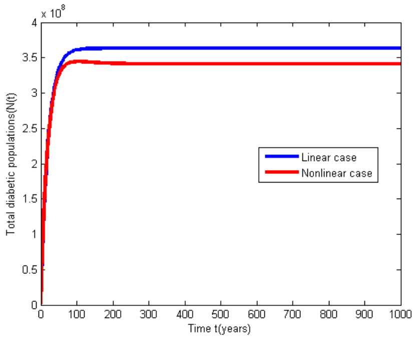
FIGURE 3. Profiles of $C_1(t),\ C_2(t),\ N(t)$ for both linear and the nonlinear cases



(A) Profile of $C_1(t)$ when $\gamma_1 = \gamma_2 = 0$



(B) Profile of $C_2(t)$ when $\gamma_1 = \gamma_2 = 0$



(C) Profile of $N(t)$ when $\gamma_1 = \gamma_2 = 0$

FIGURE 4. Profiles of $C_1(t),\ C_2(t),\ N(t)$ for both linear and the nonlinear cases
when $\gamma_1 = \gamma_2 = 0$

6. Conclusions

This modified models (linear and the nonlinear) is an extension of Boutayeb *et al* model considered in [13] and [10]. This extension was done by subdividing the compartment of diabetic population with complications into those with minor complications and those with major complications. The extended model shows no any sign of divergence as time increases.

In the linear model, a unique equilibrium point was obtained and is found to be globally asymptotically stable unconditionally by the use of direct Lyapunov function. The nonlinear has has three positive equilibrium points: $EP1, EP2$ and $EP3$. $EP1$ and $EP2$ were found to be unstable. $EP3$ is found to be globally asymptotically stable, which is equivalent to the endemic equilibrium point in infectious diseases.

It is seen clearly that the absence of the complications of the disease in the population is not guaranteed. However, the central work of the dissertation is to stress the importance of controlling the incidence of the disease and its various complications. It is hitherto important that a better strategy must be put in place to curtail the menace of the disease. The overall results obtained is that the models can monitor diabetic population globally without any condition as to the choice of time of monitoring.

In conclusion, we see that our models have given us insight into the various complications of diabetes. This gives a clear signal that health decision makers must invest heavily in health sector so that social and economic costs of uncontrolled diabetes in our societies will be minimal and productivity will be high. it has also given us the opportunity to show different mathematical methods to deal with difficult system.

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Further study

Bifurcation analysis of the nonlinear model can be investigated for more insight into the features or profiles of the model. Also, the effect of treatment of the complications of the disease can be investigated.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

A. Appendix

A.1. Proof of Lemma 4.1

The characteristic polynomial associated to the system (2.1) is given by

$$\therefore\ p(\chi) = \chi^3 + (\lambda_1 + \lambda_2 + B_1)\chi^2 + (\lambda_1 B_2 + \lambda_2 B_3 + B_4)\chi + \lambda_1 A_1 + \lambda_2 A_2 + A_3, \tag{A.1}$$

$B_1 = \mu + \xi + \theta,\ B_2 = \delta_1 + \mu + \eta + \theta,\ B_3 = \mu + \Lambda + \xi,\ B_4 = \xi(\mu + \theta) + \mu\theta,$
For the system's fixed point (4.2) to be stable, all the zeros of the characteristic equation (eigenvalues) (A.1) must be negative. We apply Routh stability criterion to achieve that. For convenience, we restate the criterion.

According to the Routh stability criterion, the necessary and sufficient conditions of asymptotic stability are that all the sign of the first column of the Routh table (as below) have the same sign. That is given the characteristic equation:

$$\sum_{i=0}^{n} b_i \chi^i = 0,$$

where $b_i,\ i = 0, 1, 2, ..., n$ ($b_i = 0$, when $n < i$) are the coefficients of the characteristic equation and forming the Routh table as follows:

χ^n	b_n	b_{n-2}	b_{n-4}	$\dots$
χ^{n-1}	b_{n-1}	b_{n-3}	b_{n-5}	$\dots$
.	c_1	c_2	c_3	$\dots$
.	d_1	d_2	d_3	$\dots$
.	$\dots$	$\dots$	$\dots$	$\dots$

$c_1 = \frac{b_{n-1}b_{n-2} - b_n b_{n-3}}{b_{n-1}},\ c_2 = \frac{b_{n-1}b_{n-4} - b_n b_{n-5}}{b_{n-1}}, ...,$
$d_1 = \frac{c_1 b_{n-3} - b_{n-1}c_2}{c_1},\ d_2 = \frac{c_1 b_{n-5} - b_{n-1}c_3}{c_1}, ...,$
if $b_n,\ b_{n-1},\ c_1,\ d_1$ have the same sign, then the fixed point to the system is stable.

Thus, the Routh table for the system is as follows:

χ^3	1	$\lambda_1 B_2 + \lambda_2 B_3 + B_4$	0
χ^2	$\lambda_1 + \lambda_2 + B_1$	$\lambda_1 A_1 + \lambda_2 A_2 + A_3$	0
χ^1	c_1	0	0
χ^0	b_0	0	0

$A_1 = \eta(\mu + \Lambda) + \theta(\delta_1 + \mu),\ A_2 = \xi(\mu + \Lambda),\ A_3 = \mu\theta\xi$
Since all the sign of the entries in the first column of the table are positive, then all the roots (eigenvalues) of the characteristic equation (A.1) are negative.
Hence, the fixed point(4.2) of the system (2.1) is asymptotically stable.

A.2. Proof of Theorem 4.2

Consider the Lyapunov function

$$V(u) = \frac{1}{2}k(u_1 + u_2)^2 + \frac{1}{2}(u_2^2 + u_3^2), u = (u_1, u_2, u_3), \tag{A.2}$$

where k is a positive constant to be determined later in the course of calculations, with Lyapunov derivative along the solution curves:

$$\begin{aligned}
V' &= k(u_1+u_2)(u_1'+u_2')+u_2u_2'+u_3u_3',\ {}'=\frac{d}{dt}\\
&= k(u_1+u_2)[-(\xi+\lambda_1)u_1-\lambda_1u_2+\lambda u_3+(\eta-\lambda_2)u_1-(\theta+\lambda_2)u_2+\lambda_2u_3]\\
&+ u_2[(\eta-\lambda_2)u_1-(\theta+\lambda_2)u_2+\lambda_2u_3]+u_3[-\delta_1u_1-\Lambda u_2-\mu u_3+\phi_1],\\
&= k(u_1+u_2)[(\eta-\xi-\lambda_1-\lambda_2)u_1-(\theta+\lambda_1+\lambda_2)u_2+(\lambda_1+\lambda_2)u_3]\\
&+ (\eta-\lambda_2)u_1u_2-(\theta+\lambda_2)u_2^2+\lambda_2u_2u_3-\delta_1u_1u_3-\Lambda u_2u_3-\mu u_3^2+\phi_1u_3,\\
&= k(\eta-\xi-\lambda_1-\lambda_2)u_1^2-[k(\theta+\lambda_1+\lambda_2)+\theta+\lambda_2]u_2^2-\mu u_3^2+[k(\eta-\xi-\theta-2\lambda_1\\
&- 2\lambda_2)+\eta-\lambda_2]u_1u_2+[k(\lambda_1+\lambda_2)-\delta_1]u_1u_3+[k(\lambda_1+\lambda_2)+\lambda_2-\Lambda]u_2u_3+\phi_1u_3,\\
&= g_1u_1^2-g_2u_2^2-\mu u_3^2+g_3u_1u_2+g_4u_1u_3+g_5u_2u_3+\phi_1u_3,
\end{aligned}$$

$g_1=k(\eta-\xi-\lambda_1-\lambda_2),\ g_2=k(\theta+\lambda_1+\lambda_2)+\theta+\lambda_2,$
$g_3=k(\eta-\xi-\theta-2\lambda_1-2\lambda_2)+\eta-\lambda_2,\ g_4=[k(\lambda_1+\lambda_2)-\delta_1],$
$g_5=k(\lambda_1+\lambda_2)+\lambda_2-\Lambda$
Now,

$$\begin{aligned}
V' &= g_1u_1^2-g_2u_2^2-\mu u_3^2+g_3u_1u_2+g_4u_1u_3+g_5u_2u_3+\phi_1u_3,\\
&\le g_1u_1^2-g_2u_2^2-\mu u_3^2+g_3u_1u_2+g_4u_1u_3+g_5u_2u_3+u_2u_3,\\
&= g_1u_1^2-g_2u_2^2-\mu u_3^2+g_3u_1u_2+[g_4u_1+(g_5+1)u_2]u_3.
\end{aligned}$$

Clearly $g_4<g_5+1$.
Let $g_5+1=0$, this implies that

$$\begin{aligned}
k(\lambda_1+\lambda_2)+\lambda_2-\Lambda+1 &= 0,\\
k(\lambda_1+\lambda_2) &= \Lambda-(1+\lambda_2),\\
\Rightarrow k &= \frac{\Lambda-(1+\lambda_2)}{(\lambda_1+\lambda_2)},\ \text{provided } \Lambda>1+\lambda_2.
\end{aligned}$$

Substituting for k in $g_1,\ g_2,\ g_3,\ g_4$, we have

$$\begin{aligned}
g_1 &= \frac{\Lambda-(1+\lambda_2)}{(\lambda_1+\lambda_2)}(\eta-\xi-\lambda_1-\lambda_2),\\
&< 0,\\
g_2 &= \frac{[\Lambda-(1+\lambda_2)](\theta+\lambda_1+\lambda_2)}{(\lambda_1+\lambda_2)}+\theta+\lambda_2,\\
&> 0,\\
g_3 &= \frac{\Lambda-(1+\lambda_2)(\eta-\xi-\theta-2\lambda_1-2\lambda_2)}{(\lambda_1+\lambda_2)}+\eta-\lambda_2),\\
&< 0,\ \text{provided } \eta<\lambda_2,\\
g_4 &< 0, \text{since } g_5+1=0.
\end{aligned}$$

Thus, we have

$$\begin{aligned}
V' &\le g_1u_1^2-g_2u_2^2-\mu u_3^2+g_3u_1u_2+[g_4u_1+(g_5+1)u_2]u_3,\\
&= g_1u_1^2-g_2u_2^2-\mu u_3^2+g_3u_1u_2+g_4u_1u_3.
\end{aligned}$$

Since, at any time, t the equilibrium point (C_1^*, C_2^*, N^*) is either below or above (C_1, C_2, N) along the solution curves, then: either $C_1 - C_1^* > 0,\ C_2 - C_2^* > 0,\ N - N^* > 0$ at a time or $C_1 - C_1^* < 0,\ C_2 - C_2^* < 0,\ N - N^* < 0$. Whichever the case may be, u_1u_2 and u_1u_3 remain positive. And since $g_1 < 0,\ g_2 > 0,\ \mu > 0,\ g_3 < 0,\ g_4 < 0$, therefore $V' < 0$.

Thus, $V' = 0$, if and only if $u_1 = u_2 = u_3 = 0$.This indicates that the largest invariant set in $\{(u_1, u_2, u_3) \in \Omega : V' = 0\}$ is the origin. Therefore, by LaSalle's invariance principle[28], E_l is globally asymptotically stable.

A.3. Proof of Lemma 4.3

The equilibrium point $EP3$:

$$(C_1^{***}, C_2^{***}, N^{***})^T = \left(\frac{w_2w_3I^*}{\Phi}, \frac{\eta w_2 I^*}{\Phi}, \frac{\alpha(\eta + w_3)I^*}{\Phi}\right)^T$$

$\Phi = w_2(\delta_1 w_3 + \Lambda\eta) + \alpha\mu(\eta + w_3)$.

The Jacobian matrix associated to the equilibrium point $EP3$ is:

$$J^{***} = \begin{pmatrix} -\frac{w_2w_3}{\eta+w_3} & -\frac{w_2w_3}{\eta+w_3} & \frac{w_2^2w_3}{\alpha(\eta+w_3)} \\ \frac{\eta(\eta-w_1)}{\eta+w_3} & \frac{-w_3^2-\eta(w_2+w_3)}{\eta+w_3} & \frac{\eta w_2^2}{\alpha(\eta+w_3)} \\ -\delta_1 & -\Lambda & -\mu \end{pmatrix}.$$

The characteristic polynomial associated to this equilibrium point is given by:

$$\begin{aligned} \therefore\ P_3(\chi) &= \chi^3 + (\mu + w_2 + w_3)\chi^2 + \left[\mu(w_2 + w_3) + w_2w_3 + \frac{w_2^2(\delta_1 w_3 + \eta\Lambda)}{\alpha(\eta + w_3)}\right]\chi \\ &+ \left[\mu w_2 w_3 + \frac{w_2^2 w_3(\delta_1 w_3 + \eta\Lambda)}{\alpha(\eta + w_3)}\right], \end{aligned}$$

Applying Routh stability criterion as in the previous appendix, again the Routh table when $n = 3$ is as follows:

here, $b_3 = 1,\ b_2 = \mu + w_2 + w_3,\ b_1 = \mu(w_2 + w_3) + w_2w_3 + \dfrac{w_2^2(\delta_1 w_3 + \eta\Lambda)}{\alpha(\eta + w_3)}$,

$b_0 = \mu w_2 w_3 + \dfrac{w_2^2 w_3(\delta_1 w_3 + \eta\Lambda)}{\alpha(\eta + w_3)}$

$$\begin{aligned} c_1 &= \frac{b_2b_1 - b_3b_0}{b_2} \\ &= \frac{(\mu + w_2 + w_3)\left[\mu(w_2 + w_3) + w_2w_3 + \frac{w_2^2(\delta_1 w_3+\eta\Lambda)}{\alpha(\eta+w_3)}\right] - (1)\left[\mu w_2 w_3 + \frac{w_2^2 w_3(\delta_1 w_3+\eta\Lambda)}{\alpha(\eta+w_3)}\right]}{\mu + w_2 + w_3}, \\ &= \frac{\mu(\mu + w_2 + w_3)(w_2 + w_3) + w_2^2w_3 + w_2w_3^2 + \frac{w_2^2(\mu+w_2)(\delta_1 w_3+\eta\Lambda)}{\alpha(\eta+w_3)}}{\mu + w_2 + w_3}, \\ &> 0, \end{aligned}$$

$c_2 = 0,\ d_1 = b_0,\ d_2 = 0.$

Therefore the Routh table for the system at this equilibrium point is as follows

χ^n	1	$\mu(w_2 + w_3) + w_2w_3 + \frac{w_2^2(\delta_1 w_3+\eta\Lambda)}{\alpha(\eta+w_3)}$	0
χ^{n-1}	$\mu + w_2 + w_3$	$\mu w_2 w_3 + \frac{w_2^2 w_3(\delta_1 w_3+\eta\Lambda)}{\alpha(\eta+w_3)}$	0
.	c_1	0	0
.	b_0	0	0

It can be seen that all the elements in the first column of the Routh table are positive. Hence, the equilibrium point $EP3$ is locally asymptotically stable.

This result shows that the disease establishes itself in a community within certain period of time, but can be controlled at certain level if proper measures are put in place.

A.4. Proof of Theorem 4.4

Consider the Lyapunov function:

$$V = \frac{1}{2}(C_1 - C_1^{***} + N - N^{***})^2 + \frac{k_1}{2}(C_2 - C_2^{***} + N - N^{***})^2 + \frac{k_2}{2}(N - N^{***})^2, \quad (A.3)$$

$V = V(C_1, C_2, N)$, k_1, k_2 are positive constants to be determined later.
The derivative of V along the solution curves is:

$$\begin{aligned}
V' &= (C_1 - C_1^{***} + N - N^{***})(C_1' + N') + k_1(C_2 - C_2^{***} + N - N^{***})(C_2' + N') \\
&+ k_2(N - N^{***})N', \\
&= (C_1 - C_1^{***})(C_1' + N') + k_1(C_2 - C_2^{***})(C_2' + N') + (N - N^{***})[C_1' + N' \\
&+ k_1(C_2' + N') + k_2 N'], \\
&= (C_1' + N')C_1 - (C_1' + N')C_1^{***} + k_1(C_2' + N')C_2 - k_1(C_2' + N')C_2^{*} + [C_1' + N' \\
&+ k_1(C_2' + N') + k_2 N']N - [C_1' + N' + k_1(C_2' + N') + k_2 N']N^{***}, \\
&= -\theta_1 C_1^{***} - \theta_2 C_2^{***} - \theta_3 N^{***} + \theta_1 C_1 + \theta_2 C_2 + \theta_3 N,
\end{aligned}$$

$\theta_1 = (C_1' + N')$, $\theta_2 = k_1(C_2' + N')$, $\theta_3 = C_1' + N' + k_1(C_2' + N') + k_2 N'$,
This implies,

$$V' = -\theta_1 C_1^{***} - \theta_2 C_2^{***} - \theta_3 N^{***} + \theta_1 C_1 + \theta_2 C_2 + \theta_3 N,$$

$$\begin{aligned}
&= -(\alpha - \delta_1 - \xi)C_1^{***}C_1 + \Lambda C_1^{***}C_2 + \mu C_1^{***}N + \alpha\frac{(C_1 + C_2)C_1^{***}C_1}{N} - C_1^{***}I \\
&- k_1(\eta - \delta_1)C_2^{***}C_1 - k_1(\alpha - \theta - \Lambda)C_2^{***}C_2 + k_1\mu C_2^{***}N + k_1\alpha\frac{(C_1 + C_2)C_2^{***}C_2}{N} \\
&- k_1 C_2^{*} I - [k_1(\eta - \delta) + (\alpha - \delta_1 - \xi) - k_2\delta_2]N^{***}C_1 - [k_1(\alpha - \Lambda - \theta) - k_2\Lambda - \Lambda]N^{***}C_2 \\
&+ \mu(k_1 + k_2 + 1)N^{***}N - (k_1 + K_2 + 1)N^{***}I + k_1\alpha\frac{(C_1 + C_2)N^{***}C_2}{N} \\
&+ \alpha\frac{(C_1 + C_2)N^{***}C_1}{N} + (\alpha - \delta_1 - \xi)C_1^2 - \Lambda C_1 C_2 - \mu C_1 N - \alpha\frac{(C_1 + C_2)C_1^2}{N} + IC_1 \\
&+ k_1(\eta - \delta_1)C_1 C_2 + k_1(\alpha - \theta - \Lambda)C_2^2 - k_1\mu C_2 N - k_1\alpha\frac{(C_1 + C_2)C_2^2}{N} + k_1 I C_2 \\
&+ [k_1(\eta - \delta) + (\alpha - \delta_1 - \xi) - k_2\delta_2]C_1 N + [k_1(\alpha - \Lambda - \theta) - k_2\Lambda - \Lambda]C_2 N \\
&- \mu(k_1 + k_2 + 1)N^2 + (k_1 + k_2 + 1)IN - k_1\alpha(C_1 + C_2)C_2 \\
&- \alpha(C_1 + C_2)C_1,
\end{aligned}$$

This implies,

$$\begin{aligned}
V' = {} & [-(\alpha-\delta_1-\xi)C_1^{***} - k_1(\eta-\delta_1)C_2^{***} - k_1(\eta-\delta_1)N^{***} - (\alpha-\delta_1-\xi)N^{***} \\
& + k_2\Lambda N^{***}]C_1 + [\Lambda C_1^{***} - k_1(\alpha-\Lambda-\theta)C_2^{***} - k_1(\alpha-\Lambda-\theta)N^{***} + \Lambda N^{***} \\
& + k_2\Lambda N^{***}]C_2 + \mu[C_1^{***} + C_2^{***} + (k_1+k_2+1)N^{***}]N - [C_1^{***} + C_2^{***} \\
& + (k_1+k_2+1)N^{***}]I + [k_1(\eta-\delta_1) - \Lambda]C_1C_2 + [k_1(\eta-\delta_1) \\
& + (\alpha-\delta_1-\xi-\mu-k_2\delta_1]C_1N + [k_1(\alpha-\Lambda-\theta) - k_1\mu - k_2\Lambda - \Lambda]C_2N \\
& + ((\alpha-\delta_1-\xi)C_1^2 + k_1(\alpha-\Lambda-\theta)C_2^2 - \mu(k_1+k_2+1)N^2 + (k_1+k_2+1)IN - Q_1 + Q_2 \\
& - k_1\alpha(C_1+C_2)C_2 - \alpha(C_1+C_2)C_1 + (C_1+k_1C_2)I,
\end{aligned} \tag{A.4}$$

$Q_1 = \alpha\frac{(C_1+C_2)C_1^2}{N} + k_1\alpha\frac{(C_1+C_2)C_2^2}{N}$
$Q_2 = k_1\alpha\frac{(C_1+C_2)C_1^{***}C_2}{N} + k_1\alpha\frac{(C_1+C_2)N^{***}C_2}{N} + \alpha\frac{(C_1+C_2)C_1^{***}C_1}{N} + \alpha\frac{(C_1+C_2)N^{***}C_1}{N}$,
Using the fact that if

$$a, b > 0 : a = \frac{p}{q},\ p < q,\ b, p, q \in \mathbf{N},\ \text{then } ab < b. \tag{A.5}$$

We have:

$$\begin{aligned}
Q_2 &= k_1\alpha\frac{(C_1+C_2)C_1^{***}C_2}{N} + k_1\alpha\frac{(C_1+C_2)N^{***}C_2}{N} + \alpha\frac{(C_1+C_2)C_1^{***}C_1}{N} \\
&+ \alpha\frac{(C_1+C_2)N^{***}C_1}{N}, \\
&\leq k_1\alpha C_2^{***}C_2 + k_1\alpha N^{***}C_2 + \alpha C_1^{***}C_1 + \alpha N^{***}C_1,
\end{aligned}$$

$$\therefore\ Q_2 \leq k_1\alpha C_2^{***}C_2 + k_1\alpha N^{***}C_2 + \alpha C_1^{***}C_1 + \alpha N^{***}C_1 \tag{A.6}$$

Also, the last three terms $-k_1\alpha(C_1+C_2)C_2 - \alpha(C_1+C_2)C_1 + (C_1+k_1C_2)I$,in (A.4) can be simplified thus;

$$-k_1\alpha(C_1+C_2)C_2 - \alpha(C_1+C_2)C_1 + (C_1+k_1C_2)I = (k_1C_1+C_2)[I - \alpha(C_1+C_2)], \tag{A.7}$$

Again, using the fact in (A.5), the term before $-Q_1$ simplifies thus;

$$\begin{aligned}
(k_1+k_2+1)IN &= k_1IN + k_2IN + IN, \\
&\leq (k_1+k_2+1)C_1N,
\end{aligned}$$

$$\therefore\ (k_1+k_2+1)IN \leq (k_1+k_2+1)C_1N,\ \text{since } I < C_1, \tag{A.8}$$

Using (A.6),(A.7) and (A.8) in (A.4) we have

$$\begin{aligned}
V' &= [-(\alpha-\delta_1-\xi)C_1^{***} - k_1(\eta-\delta_1)C_2^{***} - k_1(\eta-\delta_1)N^{***} - (\alpha-\delta_1-\xi)N^{***} \\
&+ k_2\Lambda N^{***}]C_1 + [\Lambda C_1^{***} - k_1(\alpha-\Lambda-\theta)C_2^{***} - k_1(\alpha-\Lambda-\theta)N^{***} + \Lambda N^{***} \\
&+ k_2\Lambda N^{***}]C_2 + \mu[C_1^{***} + C_2^{***} + (k_1+k_2+1)N^{***}]N - [C_1^{***} + C_2^{***} \\
&+ (k_1+k_2+1)N^{***}]I + [k_1(\eta-\delta_1) - \Lambda]C_1C_2 + [k_1(\eta-\delta_1) \\
&+ (\alpha-\delta_1-\xi-\mu-k_2\delta_1]C_1N + [k_1(\alpha-\Lambda-\theta) - k_1\mu - k_2\Lambda - \Lambda]C_2N \\
&+ ((\alpha-\delta_1-\xi)C_1^2 + k_1(\alpha-\Lambda-\theta)C_2^2 - \mu(k_1+k_2+1)N^2 + (k_1+k_2+1)IN \\
&- Q_1 + Q_2 - k_1\alpha(C_1+C_2)C_2 - \alpha(C_1+C_2)C_1 + (C_1+k_1C_2)I,
\end{aligned}$$

$$\begin{aligned}
&\leq [-(\alpha-\delta_1-\xi)C_1^{***}-k_1(\eta-\delta_1)C_2^{***}-k_1(\eta-\delta_1)N^{***}-(\alpha-\delta_1-\xi)N^{***}\\
&+ k_2\Lambda N^{***}]C_1+[\Lambda C_1^{***}-k_1(\alpha-\Lambda-\theta)C_2^{***}-k_1(\alpha-\Lambda-\theta)N^{***}+\Lambda N^{***}+k_2\Lambda N^{***}]C_2\\
&+ \mu[C_1^{***}+C_2^{***}+(k_1+k_2+1)N^{***}]N-[C_1^{***}+C_2^{***}+(k_1+k_2+1)N^{***}]I\\
&+ [k_1(\eta-\delta_1)-\Lambda]C_1C_2+[k_1(\eta-\delta_1)+(\alpha-\delta_1-\xi-\mu-k_2\delta_1]C_1N\\
&+ [k_1(\alpha-\Lambda-\theta)-k_1\mu-k_2\Lambda-\Lambda]C_2N+((\alpha-\delta_1-\xi)C_1^2\\
&+ k_1(\alpha-\Lambda-\theta)C_2^2-\mu(k_1+k_2+1)N^2+(k_1+k_2+1)C_1N-Q_1+k_1\alpha C_2^{***}C_2\\
&+ k_1\alpha N^{***}C_2+\alpha C_1^{***}C_1+\alpha N^{***}C_1+(k_1C_1+C_2)[I-\alpha(C_1+C_2)],
\end{aligned}$$

Simplifying and collecting terms, we have
V'

$$\begin{aligned}
&\leq [(\delta_1+\xi)C_1^{***}-k_1(\eta-\delta_1)C_2^{***}-k_1(\eta-\delta_1)N^{***}+(\delta_1+\xi)N^{***}+k_2\Lambda N^{***}]C_1\\
&+ [\Lambda C_1^{***}+k_1(\Lambda+\theta)C_2^{***}+k_1(\Lambda+\theta)N^{***}+\Lambda N^{***}+k_2\Lambda N^{***}]C_2\\
&+ \mu[C_1^{***}+C_2^{***}+(k_1+k_2+1)N^{***}]N-[C_1^{***}+C_2^{***}+(k_1+k_2+1)N^{***}]I\\
&+ [k_1(\eta-\delta_1)-\Lambda]C_1C_2+[k_1(\eta-\delta_1)+(\alpha-\delta_1-\xi-\mu-k_2\delta_1]C_1N\\
&+ [k_1(\alpha-\Lambda-\theta)-k_1\mu-k_2\Lambda-\Lambda]C_2N+((\alpha-\delta_1-\xi)C_1^2\\
&+ k_1(\alpha-\Lambda-\theta)C_2^2-\mu(k_1+k_2+1)N^2+(k_1+k_2+1)C_1N-Q_1\\
&+ (k_1C_1+C_2)[I-\alpha(C_1+C_2)],
\end{aligned}$$

$$\begin{aligned}
&= [k_1(\delta_1-\eta)(C_2^{***}+N^{***})+(\delta_1+\xi)(C_1^{***}+N^{***})+k_2\Lambda N^{***}]C_1\\
&+ [k_1(\Lambda+\theta)(C_2^{***}+N^{***})+\Lambda(C_1^{***}+N^{***})+k_2\Lambda N^{***}]C_2\\
&+ [C_1^{***}+C_2^{***}+(k_1+k_2+1)N^{***}](\mu N-I)+[k_1(\eta-\delta_1)-\Lambda]C_1C_2\\
&+ [k_1+k_2+1+k_1(\eta-\delta_1)+\alpha-\delta_1-\xi-\mu-k_2\delta_1]C_1N\\
&+ [k_1(\alpha-\Lambda-\mu-\theta)-k_2\Lambda-\Lambda]C_2N+((\alpha-\delta_1-\xi)C_1^2+k_1(\alpha-\Lambda-\theta)C_2^2\\
&- \mu(k_1+k_2+1)N^2-Q_1+(k_1C_1+C_2)[I-\alpha(C_1+C_2)].
\end{aligned}$$

This implies,

$$\begin{aligned}
V' &\leq \alpha_1C_1+\alpha_2C_2+[C_1^{***}+C_2^{***}+(k_1+k_2+1)N^{***}](\mu N-I)+\alpha_3C_1C_2+\alpha_4C_1N\\
&\quad+\alpha_5C_2N+\alpha_6C_1^2+\alpha_7C_2^2-\mu(k_1+k_2+1)N^2-Q_1+(k_1C_1+C_2)[I-\alpha(C_1+C_2)],
\end{aligned} \tag{A.9}$$

$\alpha_1=k_1(\delta_1-\eta)(C_2^{***}+N^{***})+(\delta_1+\xi)(C_1^{***}+N^{***})+k_2\Lambda N^{***}>0,$
$\alpha_2=k_1(\Lambda+\theta)(C_2^{***}+N^{***})+\Lambda(C_1^{***}+N^{***})+k_2\Lambda N^{***}>0,$
$\alpha_3=k_1(\eta-\delta_1)-\Lambda,$
$\alpha_4=k_1+k_2+1+k_1(\eta-\delta_1)+\alpha-\delta_1-\xi-\mu-k_2\delta_1,$
$\alpha_5=k_1(\alpha-\Lambda-\mu-\theta)-k_2\Lambda-\Lambda,$
$\alpha_6=\alpha-\delta_1-\xi,$
$\alpha_7=\alpha-\Lambda-\theta,$
using the same fact (A.5), we have

$$\alpha_1C_1\leq\alpha_1C_1N,\ \ \alpha_2C_2\leq\alpha C_2N, \tag{A.10}$$

Thus, V'

$$
\begin{aligned}
&\leq \alpha_1 C_1 + \alpha_2 C_2 + [C_1^{***} + C_2^{***} + (k_1 + k_2 + 1)N^{***}](\mu N - I) + \alpha_3 C_1 C_2 + \alpha_4 C_1 N \\
&+ \alpha_5 C_2 N + \alpha_6 C_1^2 + \alpha_7 C_2^2 - \mu(k_1 + k_2 + 1)N^2 - Q_1 + (k_1 C_1 + C_2)[I - \alpha(C_1 + C_2)], \\
&\leq \alpha_1 C_1 N + \alpha_2 C_2 N + [C_1^{***} + C_2^{***} + (k_1 + k_2 + 1)N^{***}](\mu N - I) + \alpha_3 C_1 C_2 + \alpha_4 C_1 N \\
&+ \alpha_5 C_2 N + \alpha_6 C_1^2 + \alpha_7 C_2^2 - \mu(k_1 + k_2 + 1)N^2 - Q_1 + (k_1 C_1 + C_2)[I - \alpha(C_1 + C_2)], \\
&= (\alpha_1 + \alpha_4)C_1 N + (\alpha_2 + \alpha_5)C_2 N + [C_1^* + C_2^* + (k_1 + k_2 + 1)N^*](\mu N - I) + \alpha_3 C_1 C_2 \\
&+ \alpha_6 C_1^2 + \alpha_7 C_2^2 - \mu(k_1 + k_2 + 1)N^2 - Q_1 + (k_1 C_1 + C_2)[I - \alpha(C_1 + C_2)].
\end{aligned}
\tag{A.11}
$$

It is easy to see that,
$\alpha_1 + \alpha_4 > \alpha_3,\ \alpha_6,\ \alpha_7,$
$\alpha_2 + \alpha_5 > \alpha_3,\ \alpha_6,\ \alpha_7$
Let $\alpha_1 + \alpha_4 = 0,\ \alpha_2 + \alpha_5 = 0.$
And since $\alpha_1 + \alpha_4 = 0,\ \alpha_2 + \alpha_5 = 0$, then $\alpha_3 < 0,\ \alpha_6 < 0,\ \alpha_7 < 0$
This implies

$$
\begin{aligned}
\alpha_1 + \alpha_4 &= k_1(\delta_1 - \eta)(C_2^{***} + N^{***}) + (\delta_1 + \xi)(C_1^{***} + N^{***}) + k_2 \Lambda N^{***} \\
&+ k_1 + k_2 + 1 + k_1(\eta - \delta_1) + \alpha - \delta_1 - \xi - \mu - k_2\delta_1, \\
&= k_1[(\delta_1 - \eta)(C_2^{***} + N^{***}) + 1 + \eta - \delta_1] + k_2(\Lambda N^{***} + 1 - \delta_1) \\
&+ (\delta_1 + \xi)(C_1^{***} + N^{***}) + \alpha + 1 \\
&= 0,
\end{aligned}
$$

This implies;

$$
k_1[(\delta_1 - \eta)(C_2^{***} + N^{***}) + 1 + \eta - \delta_1] + k_2(\Lambda N^{***} - \delta_1) + (\delta_1 + \xi)(C_1^{***} + N^{***}) + \alpha + 1 = 0 \tag{A.12}
$$

Also,

$$
\begin{aligned}
\alpha_2 + \alpha_5 &= k_1(\Lambda + \theta)(C_2^{***} + N^{***}) + \Lambda(C_1^{***} + N^{***}) + k_2 \Lambda N^{***} \\
&+ k_1(\alpha - \Lambda - \mu - \theta) - k_2\Lambda - \Lambda, \\
&= k_1[(\Lambda + \theta)(C_2^{***} + N^{***}) + \alpha - \Lambda - \mu - \theta] + k_2(\Lambda N^{***} - \Lambda) + \Lambda(C_1^{***} \\
&+ N^{***} - 1), \\
&= 0,
\end{aligned}
$$

$$
k_1[(\Lambda + \theta)(C_2^{***} + N^{***}) + \alpha - \Lambda - \mu - \theta] + k_2(\Lambda N^{***} - \Lambda) + \Lambda(C_1^{***} + N^{***} - 1) = 0 \tag{A.13}
$$

we solve the above two equations (A.12) and (A.13) for k_1 and k_2.
This implies,

$$
\begin{aligned}
(\sigma_1 - \sigma_2)k_1 + (\Lambda N^{***} - \delta_1)k_2 + \sigma_3 - \sigma_4 &= 0, \\
(\pi_1 - \pi_2)k_1 + \Lambda(N^{***} - 1) + \pi_3 - \Lambda &= 0, \\
\Longrightarrow (\sigma_1 - \sigma_2)k_1 + (\Lambda N^{*} - \delta_1)k_2 &= \sigma_4 - \sigma_3, \\
(\pi_1 - \pi_2)k_1 + \Lambda(N^{***} - 1)k_2 &= \Lambda - \pi_3,
\end{aligned}
$$

$\sigma_1 = \delta_1(C_2^{***} + N^{***}) + 1 + \eta,$
$\sigma_2 = \eta(C_2^{***} + N^{***}) + \delta_1$
$\sigma_3 = (\delta_1 + \xi)(C_1^{***} + N^{***}) + \alpha + 1$
$\sigma_4 = \delta_1 + \mu + \xi$
$\pi_1 = (\Lambda + \theta)(C_2^{***} + N^{***}) + \alpha,$

$\pi_2 = \Lambda + \mu + \theta,$
$\pi_3 = \Lambda(C_1^{***} + N^{***})$
Using the row echelon method, we form the augmented matrix as follows:

$$\left(\begin{array}{cc|c} \sigma_1 - \sigma_2 & \Lambda N^{***} - \delta_1 & \sigma_4 - \sigma_3 \\ \pi_1 - \pi_2 & \Lambda(N^{***} - 1) & \Lambda - \pi_3 \end{array}\right),$$

$$r_1 \to \left[\frac{1}{(\sigma_1 - \sigma_2)}\right] r_1,\ r_2 \to r_2,$$

$$\Longrightarrow \left(\begin{array}{cc|c} 1 & \frac{\Lambda N^{***} - \delta_1}{\sigma_1 - \sigma_2} & \frac{\sigma_4 - \sigma_3}{\sigma_1 - \sigma_2} \\ \pi_1 - \pi_2 & \Lambda(N^{***} - 1) & \Lambda - \pi_3 \end{array}\right),$$

$$r_1 \to r_1,\ r_2 \to -(\pi_1 + \pi_2) r_1 + r_2,$$

$$\Longrightarrow \left(\begin{array}{cc|c} 1 & \frac{\Lambda N^{***} - \delta_1}{\sigma_1 - \sigma_2} & \frac{\sigma_4 - \sigma_3}{\sigma_1 - \sigma_2} \\ 0 & \frac{\varphi_1 - \varphi_2}{\sigma_1 - \sigma_2} & \frac{\varphi_3 - \varphi_4}{\sigma_1 - \sigma_2} \end{array}\right),$$

$\varphi_1 = \Lambda N^{***}(\sigma_1 + \sigma_2) + \delta_1 \pi_1 + \sigma_2$
$\varphi_2 = \Lambda N^{***}(\sigma_2 + \pi_1) + \delta_1 \pi_2 + \sigma_1$
$\varphi_3 = \Lambda \sigma_1 + \sigma_2 \pi_3 + \sigma_3 \pi_1 + \sigma_4 \pi_2$
$\varphi_4 = \Lambda \sigma_2 + \sigma_1 \pi_3 + \sigma_4 \pi_1 + \sigma_3 \pi_2$

$$r_1 \to r_1,\ r_2 \to \left(\frac{\sigma_1 - \sigma_2}{\varphi_1 - \varphi_2}\right) r_2,\ \sigma_1 - \sigma_2 \neq 0,\ \varphi_1 - \varphi_2 \neq 0,$$

$$\left(\begin{array}{cc|c} 1 & \frac{\Lambda N^{***} - \delta_1}{\sigma_1 - \sigma_2} & \frac{\sigma_4 - \sigma_3}{\sigma_1 - \sigma_2} \\ 0 & 1 & \frac{\varphi_3 - \varphi_4}{\varphi_1 - \varphi_2} \end{array}\right)_{ref!},$$

$$\Longrightarrow k_1 + \left(\frac{\Lambda N^{***} - \delta_1}{\sigma_1 - \sigma_2}\right) k_2 = \frac{\sigma_4 - \sigma_3}{\sigma_1 - \sigma_2}, \tag{A.14}$$

$$k_2 = \frac{\varphi_3 - \varphi_4}{\varphi_1 - \varphi_2}, \tag{A.15}$$

List of basic variables: $k_1,\ k_2$
List of nonbasics: ϕ
Verdict: There is unique solution since there is no degenerate equation in (A.14) and (A.15).
Making the basic variables subject in their equations

$$\Longrightarrow k_1 = \frac{\sigma_4 - \sigma_3}{\sigma_1 - \sigma_2} - \left(\frac{\Lambda N^{***} - \delta_1}{\sigma_1 - \sigma_2}\right) k_2, \tag{A.16}$$

$$k_2 = \frac{\varphi_3 - \varphi_4}{\varphi_1 - \varphi_2}, \tag{A.17}$$

Applying backward substitution on (A.16) and (A.17),

$$\therefore k_2 = \frac{\varphi_3 - \varphi_4}{\varphi_1 - \varphi_2},$$

$$k_1 = \frac{\sigma_4 - \sigma_3}{\sigma_1 - \sigma_2} \left(\frac{\Lambda N^{***} - \delta_1}{\sigma_1 - \sigma_2}\right) \frac{\varphi_3 - \varphi_4}{\varphi_1 - \varphi_2},$$

$$= \frac{(\sigma_4 - \sigma_3)(\varphi_1 - \varphi_2) - (\Lambda N^{***} - \delta_1)(\varphi_3 - \varphi_4)}{(\sigma_1 - \sigma_2)(\varphi_2 - \varphi_2)},$$

$$\therefore k_1 = \frac{\tau_1 - \tau_2}{\tau_3 - \tau_4},$$

$$\frac{\varphi_1 \sigma_4 + \varphi_2 \sigma_3 + \Lambda N^{***} \varphi_1 + \delta_1 \varphi_3 - (\varphi_2 \sigma_4 + \varphi_1 \sigma_3 + \Lambda N^{***} \varphi_3 + \delta_1 \varphi_4)}{\varphi_1 \sigma_1 + \varphi_2 \sigma_2 - (\varphi_1 \sigma_2 + \varphi_2 \sigma_1)},$$

$\tau_1 = \varphi_1 \sigma_4 + \varphi_2 \sigma_3 + \varphi_4 \Lambda N^{***} + \delta_1 \varphi_3,$
$\tau_2 = \varphi_2 \sigma_4 + \varphi_1 \sigma_3 + \varphi_3 \Lambda N^{***} + \delta_1 \varphi_4,$

$\tau_3 = \varphi_1\sigma_1 + \varphi_2\sigma_2,$
$\tau_4 = \varphi_1\sigma_2 + \varphi_2\sigma_1,$

$$\therefore\ k_1 = \frac{\tau_1 - \tau_2}{\tau_3 - \tau_4},\ k_2 = \frac{\varphi_3 - \varphi_4}{\varphi_1 - \varphi_2},$$

We have seen that $\tau_3 - \tau_4 > 0,\ \varphi_1 - \varphi_2 > 0$ (whenever $\delta_1 > \eta$)
Therefore, $k_1 > 0,\ k_2 > 0$ provided $\tau_1 - \tau_2 > 0$ and $\varphi_3 - \varphi_4 > 0$. This implies,

$$\begin{aligned}
V' &\leq (\alpha_1 + \alpha_4)C_1N + (\alpha_2 + \alpha_5)C_2N + [C_1^{***} + C_2^{***} + (k_1 + k_2 + 1)N^{***}](\mu N - I)\\
&+ \alpha_3C_1C_2 + \alpha_6C_1^2 + \alpha_7C_2^2 - \mu(k_1 + k_2 + 1)N^2 - Q_1 + (k_1C_1 + C_2)[I - \alpha(C_1 + C_2)],\\
&= [C_1^{***} + C_2^{***} + (k_1 + k_2 + 1)N^{***}](\mu N - I) + \alpha_3C_1C_2 + \alpha_6C_1^2 + \alpha_7C_2^2\\
&- \mu(k_1 + k_2 + 1)N^2 - Q_1 + (k_1C_1 + C_2)[I - \alpha(C_1 + C_2)],
\end{aligned}$$

Since $\alpha_1 + \alpha_4,\ \alpha_2 + \alpha_5 > \alpha_3,\ \alpha_6,\ \alpha_7$ and $\alpha_1 + \alpha_4 = 0, \alpha_2 + \alpha_5 = 0$, implies that $\alpha_3 < 0,\ \alpha_6 < 0,\ \alpha_7 < 0$. Also, $I < \alpha(C_1 + C_2),\ (\alpha = 1)$ and $\mu N \leq I$.
$\therefore\ V' < 0.$

Thus, $V' = 0$ only if $C_1 = C_1^{***}, C_2 = C_2^{***}$ and $N = N^{***}$. This indicates that the largest invariant set in $\{(C_1, C_2, N) \in \Omega : V^{'} = 0\}$ is the singleton $FP3$. Therefore by LaSalle's invariance principle [28], $FP3$ is globally asymptotically stable in Ω.

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