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ARTICLE

Aggravation of Cancer, Heart Diseases and Diabetes Subsequent to COVID-19 Lockdown via Mathematical Modeling

Fatma Nese Efil[1], Sania Qureshi[1,2,3], Nezihal Gokbulut[1,4], Kamyar Hosseini[1,3], Evren Hincal[1,4,*] and Amanullah Soomro[2]

[1]Near East University, Department of Mathematics, Nicosia, 99010, North Cyprus

[2]Mehran University of Engineering and Technology, Department of Basic Sciences and Related Studies, Jamshoro, 76090, Pakistan

[3]Department of Computer Science and Mathematics, Lebanese American University, P.O. Box 13-5053, Beirut, Lebanon

[4]Near East University, Mathematics Research Center, Nicosia, 99010, North Cyprus

*Corresponding Author: Evren Hincal. Email: evren.hincal@neu.edu.tr

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ABSTRACT

The global population has been and will continue to be severely impacted by the COVID-19 epidemic. The primary objective of this research is to demonstrate the future impact of COVID-19 on those who suffer from other fatal conditions such as cancer, heart disease, and diabetes. Here, using ordinary differential equations (ODEs), two mathematical models are developed to explain the association between COVID-19 and cancer and between COVID-19 and diabetes and heart disease. After that, we highlight the stability assessments that can be applied to these models. Sensitivity analysis is used to examine how changes in certain factors impact different aspects of disease. The sensitivity analysis showed that many people are still nervous about seeing a doctor due to COVID-19, which could result in a dramatic increase in the diagnosis of various ailments in the years to come. The correlation between diabetes and cardiovascular illness is also illustrated graphically. The effects of smoking and obesity are also found to be significant in disease compartments. Model fitting is also provided for interpreting the relationship between real data and the results of this work. Diabetic people, in particular, need to monitor their health conditions closely and practice heart health maintenance. People with heart diseases should undergo regular checks so that they can protect themselves from diabetes and take some precautions including suitable diets. The main purpose of this study is to emphasize the importance of regular checks, to warn people about the effects of COVID-19 (including avoiding healthcare centers and doctors because of the spread of infectious diseases) and to indicate the importance of family history of cancer, heart diseases and diabetes. The provision of the recommendations requires an increase in public consciousness.

KEYWORDS

COVID-19; mathematical modeling; cancer; diabetes; heart diseases; sensitivity analysis

1 Introduction

Epidemiology is a field of study that analyzes the causes of illness and health by addressing the facts of a population [1]. Studies in this area have been mostly interested in infectious diseases until the

twentieth century. Recently, other than transmitted diseases by infection, diseases like cardiac heart diseases, diabetes, and stroke that can induce deaths worldwide have become a significant concern in the health sciences [1].

A new field derived from the interaction between epidemiology and genetics over many years has emerged, named genetic epidemiology. This new area concentrates on the connection between genetic and environmental parameters during disease in a human population. Genetic epidemiology provides benefits for comprehending the interaction between genetic roots and major chronic disorders like coronary heart disease, cancer, and diabetes [2].

Cardiovascular disorders (CVDs) belong to the category of disorders involving blood veins and the heart. There are a variety of cardiovascular disorders (CVDs), including coronary heart, cerebrovascular, peripheral arterial, rheumatic heart, congenital heart, pulmonary embolism and deep vein thrombosis [3].

Coronary heart disease (CHD) is a disorder of the blood veins providing for the heart muscle [4]. CHD is a worldwide major chronic disease, and tobacco use, high cholesterol, an unhealthy diet, alcohol use, and physical inactivity dramatically increase the risk of CHD. Additionally, one significant risk of CHD is having a family history, especially a male family member under the age of 55 or a female family member under the age of 65 with CHD. Approximately 17.9 million people passed away due to CVDs in 2019. CVD is one of the leading causes of deaths globally, making up 32% of deaths worldwide. Additionally, stroke and heart attacks cause 85% of deaths worldwide [5].

Cancer is another disorder that includes a wide group of diseases. It describes unpreventable abnormal or damaged cell growth almost anywhere in human parts or organs. Cancer does not differentiate between age, gender, family background, or other categories. However, cancer statistics enable us to recognize the similarities and differences between categories identified with sex, age, ethnic groups, etc. The mathematical model proposed in [6] provides a picture of cancer rates over time by collecting information statistically. Cancer is classified in the first place by its founding in the human body, like lung cancer, colon cancer, skin cancer, breast cancer, and prostate cancer. It can also be classified by cell types like soft tissues, such as muscles, nerves, blood vessels, or deep skin [7,8].

According to the basic cancer facts, there are plenty of factors that raise the risk of having cancer. High tobacco use, high alcohol use, and being overweight are some of these factors. These factors are alterable within the realm of possibility. On the other hand, other risk factors are not modifiable, like inherited genetic mutations [8]. Globally, roughly 10 million people passed away in 2020 from cancer [9]. In other words, one in six deaths in 2020 was caused by cancer. The most common cancers are breast cancer, with 2.26 million cases; lung cancer, with 2.21 million cases; and colon and rectum cancer, with 1.93 million cases. Prostate cancer and skin (non-melanoma) cancer are next in line [10]. In 2022, the estimated number of new cases and deaths was 1.9 million and 609,360 in the U.S. Moreover, cancer is the second-leading cause of death in USA [11].

Diabetes mellitus, simply called diabetes, is a disease caused by insufficient insulin production by the pancreas. It leads to uncontrolled amounts of glucose or sugar in the human body [12]. The most well-known categories are type 1 diabetes (5%) and type 2 diabetes (95%) in the obese community. There are other categories of diabetes, such as diabetes LADA, diabetes MODY, and gestational diabetes, which are rare and occur in the mutation of a single gene [13]. Statistically, around 442 million people have diabetes worldwide, while 1.5 million people's deaths are caused by diabetes every year [14].

Mathematical models allow us to foresee the future outcomes of an epidemic or health issues. Besides this, they might be used as interpretive tools for the clarification of basic principles of

transmission or extension [15,16]. Kermack and McKendrick increased the level of mathematical epidemiology by proposing a new model concerning the spread of contagious diseases in 1927 [1]. The first mathematical modeling of contagious diseases, by Daniel Bernoulli, was structured to determine the impact of smallpox inoculation on the population. Due to the description of complicated mutual interaction between human (or animal) hosts' environment and biology, modern contagious disease epidemiology mostly depends on mathematical models [17].

In recent years, the most well-known contagious disease has been the Coronavirus disease (COVID-19), caused by the SARS-CoV-2 virus. COVID-19 is transmitted by liquid particles from the mouth or nose of an infected person. It is categorized as a pandemic disease since it affects many countries within international boundaries [18,19]. At the beginning of the pandemic, there was a large concern about its contagiousness and fatality since the structure of the disease was unknown. However, with the vaccination and some restrictions, the fatality of the disease was taken under control. Hence, almost every restriction has been lifted.

In recent years, many articles have been published in mathematical modeling that analyze COVID-19. Article [20] studied COVID-19's epidemic development using a mathematical model in China. It proposes an SEIR (a varied Susceptible, Exposed, Infectious, Recovered) model [21]. Research by [22,23] and [24] studied the effect of vaccination on COVID-19 while [25] focused on both vaccination and mobility. Mathematical models that include fractional orders are widely applied to COVID-19 in different regions with many different approaches [26–30]. The work by [31] discussed the change in health behavior during the COVID-19 lockdown in the United Kingdom by applying descriptive statistics. The methods of another field, machine learning, are applied in the paper [32] to examine the transfusion of the best convalescent plasma for critical COVID-19 patients. The paper [33] deliberated on artificial intelligence techniques concerning the detection and classification of medical images of COVID-19. Also, in [34], artificial intelligence was applied to a fractional model dealing with COVID-19. In the papers [35–37], the authors proposed fractional models for transmitting COVID-19 and Zika viruses. More papers regarding COVID-19 and infectious diseases with mathematical models can be found in [38–41].

Mathematical modeling plays a remarkable role in infectious (epidemic/pandemic) diseases and chronic diseases. In the health sciences, mathematical models can be applied to identify the dynamics and aspects of diseases such as cancer, coronary heart disease (CHD), and diabetes. In [42], the proposed mathematical models provide approaches for a better understanding of the parameters of chronic disorders.

This paper aims to present the effect of COVID-19 on other significant diseases, specifically cancer, heart disease, and diabetes. This study aims to warn people and increase their awareness so that the necessity of doctor and hospital visits in the upcoming years can be reduced. The presented study has a significant role in health sciences by being one of the strong and rare models that discuss the effect of the COVID-19 pandemic from different and serious perspectives. On that note, two mathematical models are proposed: one for the relationship between cancer and COVID-19 and one for the relationship between heart disease, diabetes, and COVID-19. This study aims to demonstrate how doctor controls are important for the future of human beings and how COVID-19 will negatively affect these doctor visits. In this regard, two mathematical models are constructed. In Sections 2–4, models are given with the necessary existence theorems and proofs. Section 5 includes the sensitivity analysis and its results as numerical simulations. The results and discussion, conclusions, and future recommendations sections are explained in Sections 6–8, respectively.

2 Materials and Methods

In this study, compartmental mathematical models are constructed. For the analysis of models, invariance, basic reproduction numbers, and equilibrium point properties are obtained and proved. Furthermore, for the effectiveness of parameters, sensitivity analysis is applied. All the data used in this paper for both models are gathered from the references [4,43–46].

3 Construction and Analysis of the First Model

In this section, the first model of the paper is proposed, and the entity of the solution is demonstrated. The model is constructed with the help of ordinary differential equations (ODEs) to obtain the change in compartments at time t. Then, an analysis of the model is given.

3.1 Mathematical Model Formulation

The whole population, N, is divided into 2 compartments: susceptible individuals (S) and cancer diagnosed individuals (C). That is, $N(t) = S(t) + C(t)$, at time t. Positive and negative signs in the equations of the below system (1) indicate the flow between compartments. In the model, π represents the recruitment rate; f_1 represents the transmission rate due to hereditary/family history; o represents the rate of obese individuals with cancer; b represents the rate of smokers with cancer; γ represents the recovery rate of cancer patients; μ represents the natural death rate and η represents the cancer-caused death rates. In the study, parameter c (the negative effect of COVID-19), defines the rate of cancer individuals who wave doctor checks aside because of lockdowns or COVID-19 scares. As a result, individuals cannot be diagnosed earlier with cancer. The flow between compartments of the model is illustrated in Fig. 1 as a flow diagram. The model is constructed by using a system of ODEs as follows:

$$\begin{aligned}\frac{dS}{dt} &= \pi - f_1 CS - (o+b)\,S - \mu S + \gamma C + cC,\\ \frac{dC}{dt} &= f_1 CS + (o+b)\,S - \mu C - \eta C - \gamma C - cC\end{aligned} \tag{1}$$

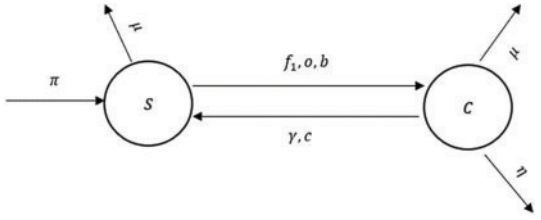

Figure 1: The flow diagram of the model (1)

In Tables 1 and 2, descriptions of variables and parameters are explained, respectively.

Table 1: Descriptions of variables

Variables	Descriptions
S	Susceptible individuals
C	Cancer patients

Table 2: Descriptions of parameters

Parameters	Descriptions
π	Recruitment rate
f_1	Transmission rate of hereditary
o	Rate of obese individuals with cancer
b	Rate of smokers with cancer
γ	Recovery rate
c	Negative effect of COVID-19
η	Disease-caused death rate
μ	Natural death rate

Theorem 1. *Let* (S, C) *be the solution of the constructed system with the initial conditions* $S \geq 0$ *and* $C \geq 0$*. Then, the following set*

$$\Lambda = \left\{(S, C) \in R_+^2 : S + C \leq \pi\right\}$$

is invariant and positive. Moreover, all of the solutions in R_+^2 *stay in* Λ *with respect to the constructed system.*

Proof of Theorem 1. By adding all of the terms that are on the right side of the proposed system,

$$\frac{dN}{dt} = \pi - \mu\,(S + C) - \eta C$$

is obtained. From the equality, it can be seen that $\frac{dN}{dt} \leq \pi$ always holds. Applying integration with respect to t to both sides yields

$$N\,(t)\,e^t \leq \pi e^t + k,$$

for some arbitrary constant k. After applying Rota and Birkhoff to the above differential inequality, as t tends to infinity, ∞, $0 \leq N \leq \pi$ hold. As a result, the solutions of the system enter the region Λ. Hence, the model is feasible in terms of biology, which is enough to consider the dynamics on the model in Λ.

3.2 Equilibrium Points

For the constructed model, two equilibrium points, disease-free and endemic equilibrium points, are evaluated. At the disease-free equilibrium point, denoted by $E_{0,1}$, the disease is expected to die out. In other words, for the presented model, $E_{0,1}$ is the point where cancer does not exist in the population. The endemic equilibrium point, $E_{*,1}$, is defined as the point where the disease is maintained with no need for external inputs [47].

$E_{0,1}$ of this model is unique and is obtained as

$$E_{0,1} = \left(S_{0,1}, C_{0,1}\right) = \left(\frac{\pi}{o + b + \mu}, 0\right).$$

It is obvious that $E_{0,1}$ attracts the region so that

$$E_{0,1} = \left\{\left(S_{0,1}, C_{0,1}\right) \in R_2^+ : C = 0\right\}.$$

The endemic equilibrium point, denoted by $E_{*,1}$, consists of $S_{*,1}$ and $C_{*,1}$. That is

$$E_{*,1} = \left(S_{*,1}, C_{*,1}\right),$$

where S_1 is the solution of

$$A\left(S_{*,1}\right)^2 + BS_{*,1} + F = 0,$$

for

$$A = f_1\left[(o+b)\left(1+\gamma+c\right) - (o+b+\mu)\right],$$

$$B = (\mu+\eta+\gamma+c)\left[(o+b)\left(1-\gamma-c\right)+\mu\right] - f_1\pi,$$

$$F = -(\mu+\eta+\gamma+c)\,\pi,$$

and

$$C_{*,1} = \frac{(o+b)\,S_{*,1}}{\mu+\eta+\gamma+c-f_1S_{*,1}}.$$

On the other hand, a real solution of the quadratic equation that depends on $S_{*,1}$ exists only if the coefficient A is positive. That is, if

$$(o+b)\left(1+\gamma+c\right) - (o+b+\mu) > 0,$$

$$(o+b)\left(1+\gamma+c\right) > (o+b+\mu),$$

$$\gamma + c > \frac{\mu}{o+b}.$$

This inequality always holds since the value of the natural death rate is very small.

Theorem 2. *Disease Free Equilibrium, $E_{0,1}$, is globally asymptotically stable whenever $\gamma + c > f_1$.*

Proof of Theorem 2. Consider the Lyapunov function

$$V(S, C) = S - S_{0,1} - S_{0,1}ln\left(\frac{S}{S_{0,1}}\right) + C.$$

The above function is always positive and at the point $E_{0,1}$, it is equal to 0. So, for the stability, it is enough to show that $\dot{V}$ is a definite negative [48,49].

$$\begin{aligned}\dot{V} &= \dot{S} - S_{0,1}\frac{\dot{S}}{S} + \dot{C}\\ &= \pi - (f_1C + o + b + \mu)\,S + (\gamma + c)\,C\\ &\quad - \frac{S_{0,1}}{S}\left[\pi - (f_1C + o + b + \mu)\,S + (\gamma + c)\,C\right] + (f_1C + o + b)\,S\\ &\quad - (\mu + \eta + \gamma + c)\,C.\end{aligned}$$

Since $\pi = S_{0,1}(o+b+\mu)$,

$$\pi - (f_1 C + o + b + \mu) S + (\gamma + c) C - \frac{S_{0,1}}{S} [\pi - (f_1 C + o + b + \mu) S + (\gamma + c) C] + (f_1 C + o + b) S$$
$$- (\mu + \eta + \gamma + c) C = \pi \left(2 - \frac{S_{0,1}}{S}\right) + (f_1 - \gamma - c) \frac{C}{S} S_{0,1}.$$

It is clear that $2 - \frac{S_{0,1}}{S} < 0$. Hence, for the condition $\dot{V} < 0, f_1 - \gamma - c < 0$ should hold. Therefore, $E_{0,1}$ is globally asymptotically stable if $\gamma + c > f_1$.

Theorem 3. *Endemic Equilibrium, $E_{*,1}$, is globally asymptotically stable.*

Proof of Theorem 3. For the proof of the above theorem, the following Lyapunov function is constructed:

$$W(S, C) = S_{*,1} g\left(\frac{S}{S_{*,1}}\right) + C_{*,1} g\left(\frac{C}{C_{*,1}}\right),$$

where $g(x) = x - 1 - ln\, x$. The function W is positive, and $W\left(S_{*,1}, C_{*,1}\right) = 0$. So, it is enough to show that $\dot{W} < 0$ [48,49].

$$\dot{W} = \dot{S} - S_{*,1} \frac{\dot{S}}{S} + \dot{C} - C_{*,1} \frac{\dot{C}}{C}$$
$$= \pi - f_1 CS - (o+b) S - \mu S + \gamma C + cC$$
$$- \frac{S_{*,1}}{S} [\pi - f_1 CS - (o+b) S - \mu S + \gamma C + cC] + f_1 CS + (o+b) S$$
$$- (\mu + \eta + \gamma + c) C - \frac{C_{*,1}}{C} [f_1 CS + (o+b) S - (\mu + \eta + \gamma + c) C]$$
$$= \pi \left(1 - \frac{S_{*,1}}{S}\right) - \mu S - (\mu + \eta) C < 0,$$

Thus, $E_{*,1}$ is globally asymptotically stable.

3.3 Parameter Fitting Using Real Clinical Data

In mathematical epidemiology, deterministic models of diseases rely significantly on data fitting to verify that their predictions are in line with observed data. The capacity to predict the spread of disease is enhanced since it simplifies the estimation of model parameters like transmission and recovery rates. By contrasting the model with the data, researchers can learn more about illness trends, treatment outcomes, and discrepancies and undertake what-if analyses. If policymakers had more faith in the model's projections, they could make more educated choices. Improving future model development is another benefit of expanding the scientific knowledge base.

The least squares method has been extensively used in a wide variety of fields, from epidemiology to finance, to estimate parameters in mathematical models. When developing a deterministic model for infectious diseases, we first start with a set of differential equations that describe the dynamics of the disease. These equations may contain imprecise values for parameters like the rate of transmission or the rate of recovery. Model predictions produced with arbitrary settings for these parameters will not match the observed data. Finding these parameters' values that yield predictions as close to the data

as possible is the goal. To strike this equilibrium, the least squares approach minimizes the squared differences (also known as "residuals") between the observed and expected values. Once the parameter values have been obtained, the squared deviations between the model's predictions and the data can be easily calculated. Finding parameter values that minimize this sum is desirable since it indicates that the model's predictions are close to the data. The model's parameters are considered to be "fit" to the data once this constraint minimization is complete. With these modified parameters, the model should more faithfully capture the dynamics of the infectious disease's transmission and impact as observed in the real world.

In epidemiology, fitting parameters to models using the ODE system in (1) demonstrates an innovative strategy. Some of the complexity of pandemic spread may be better understood with the use of deterministic models, such as those that use ordinary derivatives. However, such models cannot make accurate predictions in the real world without trustworthy parameter-fitting methods and high-quality data. For this purpose, we aspire to select authentic cancer patient clinical data, such as COVID-19 daily confirmed cases from March 13 to April 01, 2023, as made available on the Worldometer website [50]. Some of the model's most crucial parameters are derived from the fitted data, while others are taken from the cited analysis in the available literature. Fig. 2 displays the results of a comparison between real clinical data and model (1) simulations, including residuals in Fig. 3 and the corresponding box-plot in Fig. 4. Fig. 2 shows that the curve of the simulated data agrees well with the actual clinical data, and the scatter in the associated residuals, as shown in Fig. 3. Lends credence to this conclusion. A similar claim is valid for the box-plot in Fig. 4. The following initial conditions are used during the simulations:

$S(0) = 88780, C(0) = 491.$

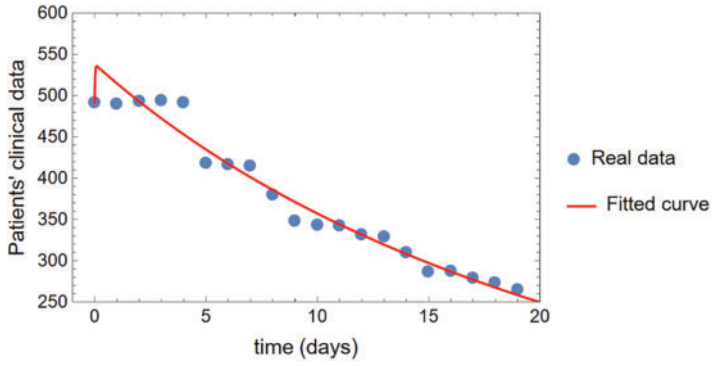

Figure 2: The comparison of simulations of model (1) with the real clinical data

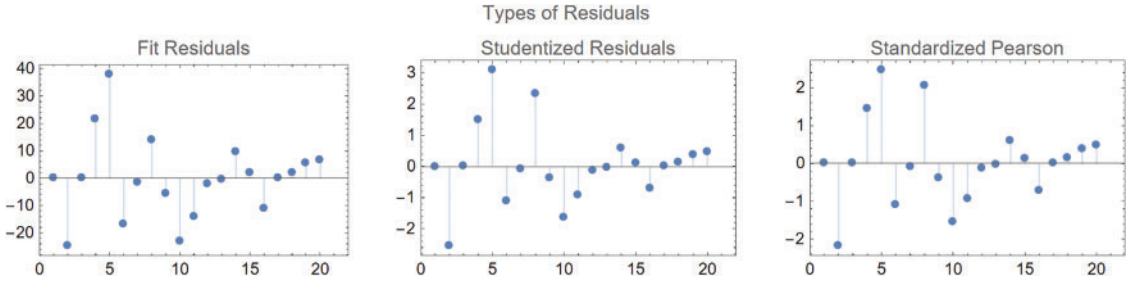

Figure 3: Different types of residuals for the curve fitting of the model (1)

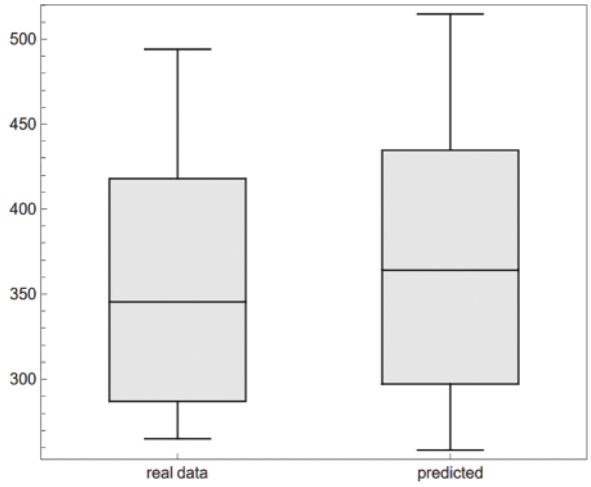

Figure 4: The comparison of the box-plots for the real clinical data and the observed (predicted) data from simulations of the model (1)

The fitted parameters are obtained as follows:

$$f\_1 = 1.7576e-04, b = 3.4756e-02, o = 2.6415e-01, c = 5.9183e+01, and\ \eta = 5.6503.$$

The rest of the parameters are taken to be fixed and given to be $\mu = \frac{1}{75.6 * 365}$, $\pi = 36.855 * \mu$, and $\gamma = 0.1$. It may be noted that the fitted R-squared value is 0.9987, showing a greater degree of confidence in the estimated fitted parameters. With the above parameters, the least-squares curve fitting of the model is shown below, and it has a high degree of agreement with the real clinical data.

It may further be seen that the statistical measures (minimum, first, second, and third quartile (Q1, Q2, Q3), arithmetic mean, maximum, and standard deviation) computed in Table 3 are also in very good agreement with each other. This enhances the validation and verification of the model (1) since the standard deviation of magnitude 82.1, obtained under the simulations of the model (1), is close enough to the standard deviation based on the real clinical data as shown in the last column of Table 3.

Table 3: Descriptive summary of statistical measures for the model (1)

Summary	Min.	Q1	Q2	Q3	Mean	Max	SD
Real	2.65 * 10^(2)	2.87 * 10^(2)	3.43 * 10^(2)	4.18 * 10^(2)	3.74 * 10^(2)	4.94 * 10^(2)	8.33 * 10^(1)
Observed	2.58 * 10^(2)	2.97 * 10^(2)	3.57 * 10^(2)	4.35 * 10^(2)	3.74 * 10^(2)	5.15 * 10^(2)	8.21 * 10^(1)

4 Construction and Analysis of the Second Model

In this section, the model is proposed with proof of the existence of the solution. Afterwards, analyses of equilibrium points are given.

4.1 Mathematical Model Formulation

The population, which is stated by N, is separated into three compartments: susceptible individuals (S), individuals who have heart disease (H), and diabetes-diagnosed individuals (D). That is, $N(t) = S(t) + H(t) + D(t)$, at time t. As in model (1), the positive and negative signs in the equations of the below system (2) indicate the flow between compartments. In the model, Λ represents the recruitment rate; f_1 and f_2 represent the transmission rate due to hereditary/family history; o represents the rate of obese individuals with cancer; b represents the rate of smokers with cancer; γ_1 and γ_2 represent the recovery rate of heart-diseases patients and diabetes patients, respectively; μ represents the natural death rate; η_1 and η_2 represent the heart diseases-caused and diabetes-caused death rates, respectively. a is the transmission rate from the compartment H to the compartment D and e is the transmission rate from the compartment D to the compartment H. In this study, parameters c_1 and c_2 (negative effect of COVID-19) define the rates of heart and diabetes patients, respectively, who did not attend doctor visits due to lockdown or fear of COVID-19. As a result, individuals cannot be diagnosed earlier. The flow between the compartments of the model is illustrated in Fig. 5 in a flow diagram. The model is built by using a system of ODEs as follows:

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - (b+o)\,S - f_1 HS - f_2 DS + (c_1+\gamma_1)\,H + (c_2+\gamma_2)\,D - \mu S,\\
\frac{dH}{dt} &= (b+k_1 o)\,S + f_1 HS - (c_1+\gamma_1+\mu+\eta_1+a)\,H + eD,\\
\frac{dD}{dt} &= (1-k_1)\,oS + f_2 DS - (c_2+\gamma_2+\mu+\eta_2+e)\,D + aH.
\end{aligned} \tag{2}$$

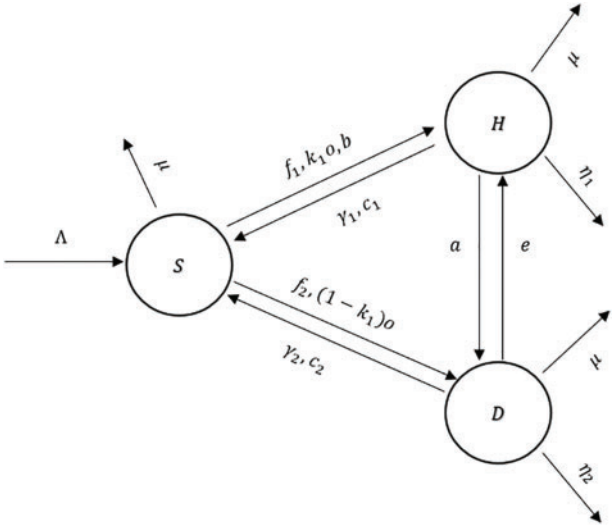

Figure 5: The flow diagram of the model (2)

An explanation of the variables and parameters is given in Tables 4 and 5.

Theorem 4. *Assume that* (S, H, D) *is the solution of the constructed system above with the initial conditions* $S \geq 0, H \geq 0,$ *and* $D \geq 0$. *Then, the following set*

$$\pi = \left\{(S, H, D) \in R_+^3 : S + H + D \leq \Lambda\right\}$$

is positive, invariant, and the solutions in R_+^3 *stay in* π *with respect to the constructed system.*

Table 4: Descriptions of variables

Variables	Descriptions
S	Susceptible individuals
H	Heart disease patients
D	Diabetes patients

Table 5: Descriptions of parameters

Parameters	Descriptions
Λ	Recruitment rate
b	Rate of smokers who are heart patients
$k_1 o$	Rate of obese individuals who are heart patients
$(1-k_1)\,o$	Rate of obese individuals who have diabetes
$f_i, i=1,2$	Transmission rate of hereditary
$c_i, i=1,2$	Negative effect of COVID-19
$\gamma_i, i=1,2$	Survival rate of diseases
μ	Natural death rate
η_1	Heart-disease-caused death rates
η_2	Diabetes-caused death rates
a	Transmission rate from H to D
e	Transmission rate from D to H

Proof of Theorem 4. The addition of all of the terms that are on the right side of the system gives

$$\frac{dN}{dt} = \Lambda - \mu\,(S+H+D) - \eta_1 H - \eta_2 D.$$

From the above equality, it is obvious that $\frac{dN}{dt} \leq \Lambda$. Integrating both sides with respect to t yields

$$N\,(t)\,e^t \leq \Lambda e^t + m,$$

for some constant m. Applying Rota and Birkhoff to the above differential inequality, it is obtained that as t tends to infinity, $0 \leq N \leq \Lambda$ holds. As a result, the solutions of the system enter the region π. Therefore, it is certain that the model is feasible by means of biology and it is enough to consider the dynamics of the model in π.

4.2 Equilibrium Points

In the proposed model, there are two equilibrium points: the disease-free equilibrium point, denoted by $\left(E_{0,2}\right)$, and the endemic equilibrium point, denoted by $\left(E_{*,2}\right)$. $E_{0,2}$ of this model is obtained as

$$E_{0,2} = \left(S_{0,2}, H_{0,2}, D_{0,2}\right) = \left(\frac{\Lambda}{o+b+\mu}, 0, 0\right).$$

Here, $E_{0,2}$ attracts the region so that

$$E_{0,2} = \left\{\left(S_{0,2}, H_{0,2}, D_{0,2}\right) \in R_3^+ : H = D = 0\right\}.$$

The endemic equilibrium point, denoted by $E_{*,2}$, consists of $S_{*,2}$ and $C_{*,2}$. That is,

$$E_{*,2} = \left(S_{*,2}, C_{*,2}, D_{*,2}\right),$$

where $S_{*,2}$ is the solution of

$$A\left(S_{*,2}\right)^4 + B\left(S_{*,2}\right)^3 + E\left(S_{*,2}\right)^2 + FS_{*,2} + G = 0,$$

for

$$A = (b + k_1 o) f_2^2 + f_1 f_2^2 (1 - k_1 o - b + o + \mu),$$

$$\begin{aligned} B = {} & f_1 f_2 [\Lambda f_2 + (c_2 + \gamma_2)(k_1 - 1) o + (o + \mu - k_1 o)(c_2 + \gamma_2 + \mu + \eta_2 + e)] \\ & + f_2 \{f_2 (b + k_1 o)(-a - c_1 - \gamma_1) + [(c_1 + \gamma_1 + \mu + \eta_1 + a) f_2 \\ & + (c_2 + \gamma_2 + \mu + \eta_2 + e) f_1] (b + \mu + k_1 o) - o\} (\mu + \eta + \gamma + c) \\ & \times [(o + b)(1 - \gamma - c) + \mu] - f_1 \pi, \end{aligned}$$

$$\begin{aligned} E = {} & \Lambda f_2 [-f_1 (c_1 + \gamma_1 + \mu + \eta_1 + a) f_2 + (c_2 + \gamma_2 + \mu + \eta_2 + e) f_1] \\ & + f_2 (c_1 + \gamma_1 - k_1 o - b - \mu) [(c_1 + \gamma_1 + \mu + \eta_1 + a)(c_2 + \gamma_2 + \mu + \eta_2 + e) - ea] \\ & + f_2 (b + k_1 o) [(c_1 + \gamma_1)(c_2 + \gamma_2 + \mu + \eta_2 + e) + a (c_2 + \gamma_2)] \\ & + [(c_2 + \gamma_2 + \mu + \eta_2 + e)(b + k_1 o) + eo (1 - k_1)] [(c_2 + \gamma_2 + \mu + \eta_2 + e) f_1 - af_2] \\ & + o (1 - k_1)(c_2 + \gamma_2) [(c_1 + \gamma_1 + \mu + \eta_1 + a) f_2 + (c_2 + \gamma_2 + \mu + \eta_2 + e) f_1], \end{aligned}$$

$$\begin{aligned} F = {} & [(c_1 + \gamma_1 + \mu + \eta_1 + a) f_2 \\ & + (c_2 + \gamma_2 + \mu + \eta_2 + e) f_1] [(c_1 + \gamma_1 + \mu + \eta_1 + a)(c_2 + \gamma_2 + \mu + \eta_2 + e) - ea] (b + o + \mu - c_1 - \gamma_1) \\ & + \Lambda \{(c_2 + \gamma_2 + \mu + \eta_2 + e) [(c_1 + \gamma_1 + \mu + \eta_1 + a) f_2 \\ & + (c_2 + \gamma_2 + \mu + \eta_2 + e) f_1] \\ & + f_2 [(c_1 + \gamma_1 + \mu + \eta_1 + a)(c_2 + \gamma_2 + \mu + \eta_2 + e) - ea]\} \\ & - (c_2 + \gamma_2) \{o (1 - k_1) [(c_1 + \gamma_1 + \mu + \eta_1 + a)(c_2 + \gamma_2 + \mu + \eta_2 + e) - ea] \\ & + a [(c_2 + \gamma_2 + \mu + \eta_2 + e)(b + k_1 o) + eo (1 - k_1)]\}, \end{aligned}$$

$$G = -\Lambda (c_2 + \gamma_2 + \mu + \eta_2 + e) [(c_1 + \gamma_1 + \mu + \eta_1 + a)(c_2 + \gamma_2 + \mu + \eta_2 + e) - ea]$$

and so

$$S_{*,2} = \Lambda (c_2 + \gamma_2 + \mu + \eta_2 + e)((c_1 + \gamma_1 + \mu + \eta_1 + a)(c_2 + \gamma_2 + \mu + \eta_2 + e) - ea),$$

$$H_{*,2} = \frac{\left[(b + k_1 o)\left(c_2 + \gamma_2 + \mu + \eta_2 + e - f_2 S_{*,2}\right) + (1 - k_1) eo\right] S_{*,2}}{\left(c_1 + \gamma_1 + \mu + \eta_1 + a - f_1 S_{*,2}\right)\left(c_2 + \gamma_2 + \mu + \eta_2 + e - f_2 S_{*,2}\right) - ea},$$

$$D_{*,2} = \frac{(1-k_1)\, oS_{*,2}}{c_2+\gamma_2+\mu+\eta_2+e-f_2S_{*,2}} + \frac{\left[(b+k_1o)\left(c_2+\gamma_2+\mu+\eta_2+e-f_2S_{*,2}\right)+(1-k_1)\, eo\right] aS_{*,2}}{\left(c_2+\gamma_2+\mu+\eta_2+e-f_2S_{*,2}\right)\left[\left(c_1+\gamma_1+\mu+\eta_1+a-f_1S_{*,2}\right)\left(c_2+\gamma_2+\mu+\eta_2+e-f_2S_{*,2}\right)-ea\right]}.$$

Theorem 5. *Disease Free Equilibrium, $E_{0,2}$, is globally asymptotically stable whenever $f_1 < c_1+\gamma_1$ and $f_2 < c_2+\gamma_2$.*

Proof of Theorem 5. Consider the below Lyapunov function

$$T(S,H,D) = S\left(\frac{S}{S_{0,2}} - 1 - ln\left(\frac{S}{S_{0,2}}\right)\right) + H + D.$$

Here, the constructed function T is always positive and equal to zero at $E_{0,2}$. So, it will be enough to show that $\dot{T} < 0$ holds [48,49].

$$\begin{aligned}\dot{T} &= S_{0,2}\left(\frac{\dot{S}}{S_{0,2}} - \frac{\dot{S}}{S_{0,2}}\frac{S_{0,2}}{S}\right) + \dot{H} + \dot{D}\\ &= \Lambda - \Lambda\frac{S_{0,2}}{S} + bS_{0,2} + oS_{0,2} + f_1HS_{0,2} + f_2DS_{0,2} - \frac{c_1HS_{0,2}}{S} - \frac{c_2DS_{0,2}}{S}\\ &\quad - \frac{\gamma_1HS_{0,2}}{S} - \frac{\gamma_2DS_{0,2}}{S} + \mu S_{0,2} - \mu(S+H+D) - \eta_1H - \eta_2D\\ &= \Lambda\left(1-\frac{S_{0,2}}{S}\right) + \left(f_1 - \frac{c_1}{S} - \frac{\gamma_1}{S}\right)HS_{0,2} + \left(f_2 - \frac{c_2}{S} - \frac{\gamma_2}{S}\right)DS_{0,2} - \mu(S+H+D)\\ &\quad - \eta_1H - \eta_2D,\end{aligned}$$

since $\Lambda = S_0(o+b+\mu)$. It is obvious that $2 - \frac{S_0}{S} < 0$. For the rest, if

$$f_1 - \frac{c_1}{S} - \frac{\gamma_1}{S} < 0,$$
$$f_1 < \frac{c_1}{S} + \frac{\gamma_1}{S} < c_1+\gamma_1.$$

Similarly, if

$$f_2 - \frac{c_2}{S} - \frac{\gamma_2}{S} < 0,$$
$$f_2 < \frac{c_2}{S} + \frac{\gamma_2}{S} < c_2+\gamma_2.$$

Hence, $E_{0,2}$ is globally asymptotically stable if $f_1 < c_1+\gamma_1$ and $f_2 < c_2+\gamma_2$.

Theorem 6. *Endemic Equilibrium Point, $E_{*,2}$, is globally asymptotically stable if* $\frac{D_{*,2}}{D} - \frac{H_{*,2}}{H} < 0$.

Proof of Theorem 6. Consider the below Lyapunov function

$$X(S,H,D) = S_{*,2}\left(\frac{S}{S_{*,2}} - 1 - ln\left(\frac{S}{S_{*,2}}\right)\right) + H_{*,2}\left(\frac{H}{H_{*,2}} - 1 - ln\left(\frac{H}{H_{*,2}}\right)\right) + D_{*,2}\left(\frac{D}{D_{*,2}} - 1 - ln\left(\frac{D}{D_{*,2}}\right)\right).$$

The constructed function X is positive for each value and equal to 0 at $E_{*,2}$. It is enough to show that $\dot{X} < 0$ is true [48,49].

$$\begin{aligned}
\dot{X} &= \dot{S} - \frac{S_{*,2}}{S}\dot{S} + \dot{H} - \frac{H_{*,2}}{H}\dot{H} + \dot{D} - \frac{D_{*,2}}{D}\dot{D} \\
&= \Lambda - \mu S - \frac{\Lambda S_{*,2}}{S} + (b+o)S_{*,2} + f_1 H S_{*,2} + f_2 D S_{*,2} - (c_1+\gamma_1)\frac{H S_{*,2}}{S} \\
&\quad - (c_2+\gamma_2)\frac{D S_{*,2}}{S} + \mu S_{*,2} - (\mu+\eta_1)H - \frac{bS}{H}H_{*,2} - \frac{k_1 oS}{H}H_{*,2} - f_1 H_{*,2} S \\
&\quad + (c_1+\gamma_1)H_{*,2} + (\mu+\eta_1)H_{*,2} + aH_{*,2} - \frac{eD}{H}H_{*,2} - (\mu+\eta_2)D - \frac{oS}{D}D_{*,2} \\
&\quad + \frac{k_1 oS}{D}D_{*,2} - f_2 S D_{*,2} + (c_2+\gamma_2)D_{*,2} + (\mu+\eta_2)D_{*,2} - \frac{aH}{D}D_{*,2} + eD_{*,2} \\
&= \Lambda\left(1 - \frac{S_{*,2}}{S}\right) + bS_{*,2}\left(2 - \frac{S}{S_{*,2}}\frac{H_{*,2}}{H}\right) + oS_{*,2}\left(2 - \frac{S}{S_{*,2}}\frac{D_{*,2}}{D}\right) \\
&\quad + k_1 o\left(2 - \frac{H_{*,2}}{H} - \frac{D_{*,2}}{D}\right) + f_1 S_{*,2}H_{*,2}\left(1 - \frac{H}{H_{*,2}} - \frac{S}{S_{*,2}}\right) \\
&\quad + f_2 S_{*,2}D_{*,2}\left(1 - \frac{D}{D_{*,2}} - \frac{S}{S_{*,2}}\right) + (eD+aH)\left(\frac{D_{*,2}}{D} - \frac{H_{*,2}}{H}\right) \\
&\quad < (eD+aH)\left(\frac{D_{*,2}}{D} - \frac{H_{*,2}}{H}\right).
\end{aligned}$$

So, $\dot{X}$ is negative only if

$$\left(\frac{D_{*,2}}{D} - \frac{H_{*,2}}{H}\right) < 0.$$

According to the statistics proposed in [47] and [51], there are more diabetic patients than heart patients in the world. Hence, for the stability of the endemic equilibrium point, this situation should be reversed and $\frac{D_{*,2}}{D} < \frac{H_{*,2}}{H}$.

5 Sensitivity Analysis and Numerical Simulations

Sensitivity analysis is a method that can be applied to the parameters of any mathematical model to identify the effect of the parameters on the compartments. This analysis aims to demonstrate how a small change in parameters can affect whether a disease exists or dies out [43]. In this section, sensitivity

analysis of the parameters is given separately for both models. Data for the parameters are taken from the references [43–46,52]. All the computations have been accomplished by MatLab.

5.1 Sensitivity Analysis of the First Model

In this part, a sensitivity analysis is implemented to the parameters of the first model.

Figs. 6 and 7 show the expected pattern for cancer patients when the b and o values are increased, respectively. In both cases, increases in the parameters will cause an increase in the C compartment. Hence, an increase in the cancer patients is expected in the case of an increase in obesity (o) and smoking (b).

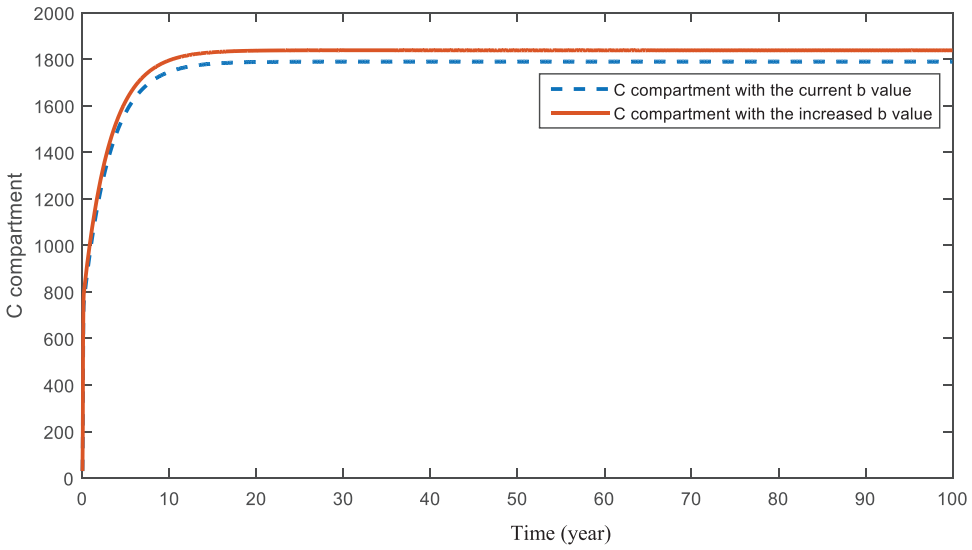

Figure 6: Sensitivity analysis of parameter b in compartment C

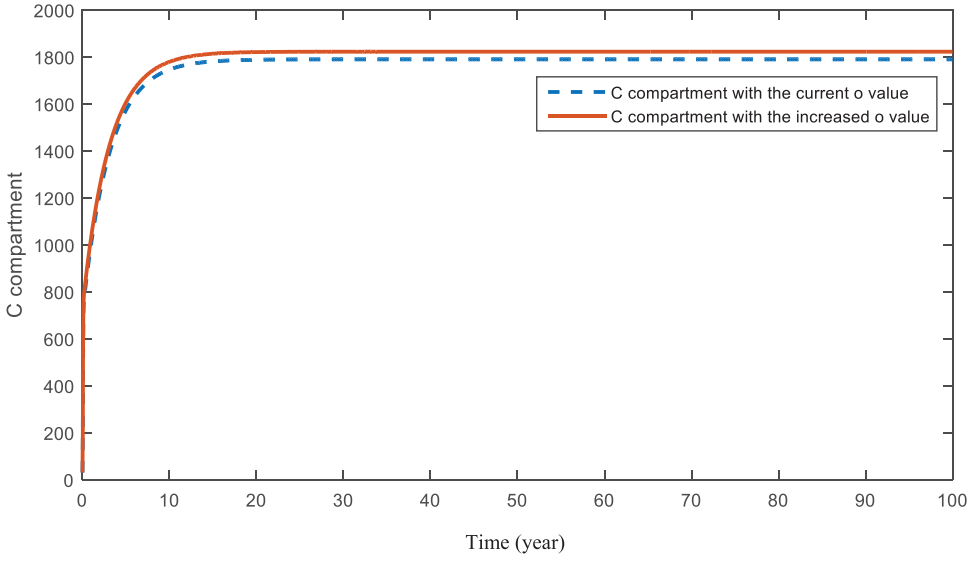

Figure 7: Sensitivity analysis of parameter o in compartment C

Figs. 8 and 9 present the effect of parameter c when it is increased and decreased, respectively. Both of the figures emphasize the negative effect of COVID-19 pandemic on the diagnosis of cancer.

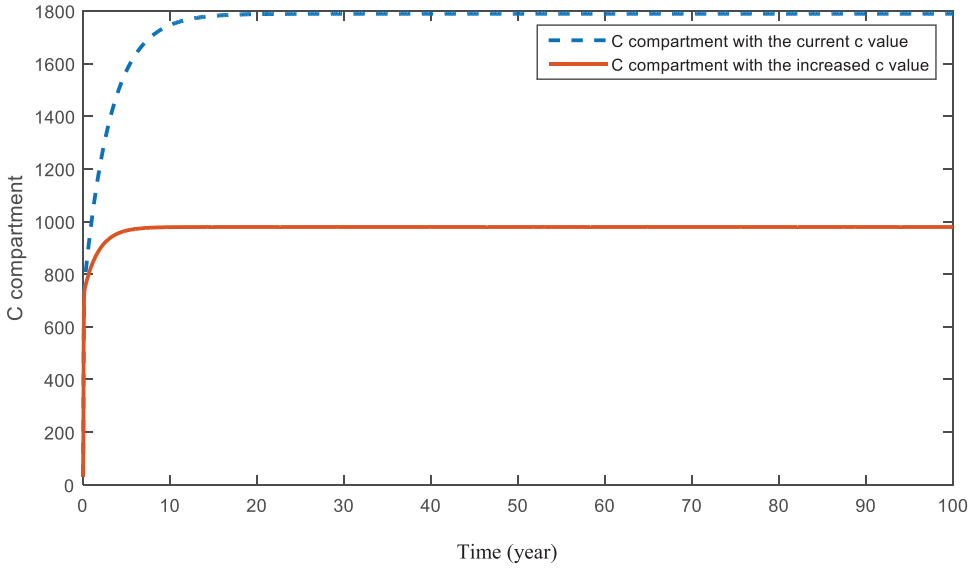

Figure 8: Sensitivity analysis of parameter c in compartment C when it is increased

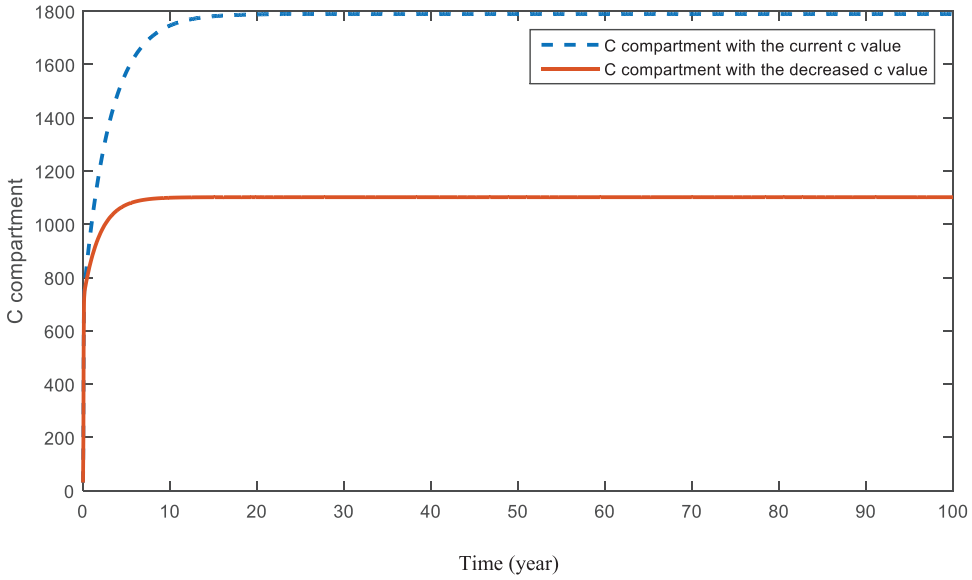

Figure 9: Sensitivity analysis of parameter c in compartment C when it is decreased

5.2 Sensitivity Analysis of the Second Model

In this part, a sensitivity analysis is implemented to the parameters of the second model.

In Figs. 10 and 11, the effects of the parameters b and o on compartment H are given, respectively. Increases in both smoking and obesity will lead to an increase in compartment H, as can be seen from the figures.

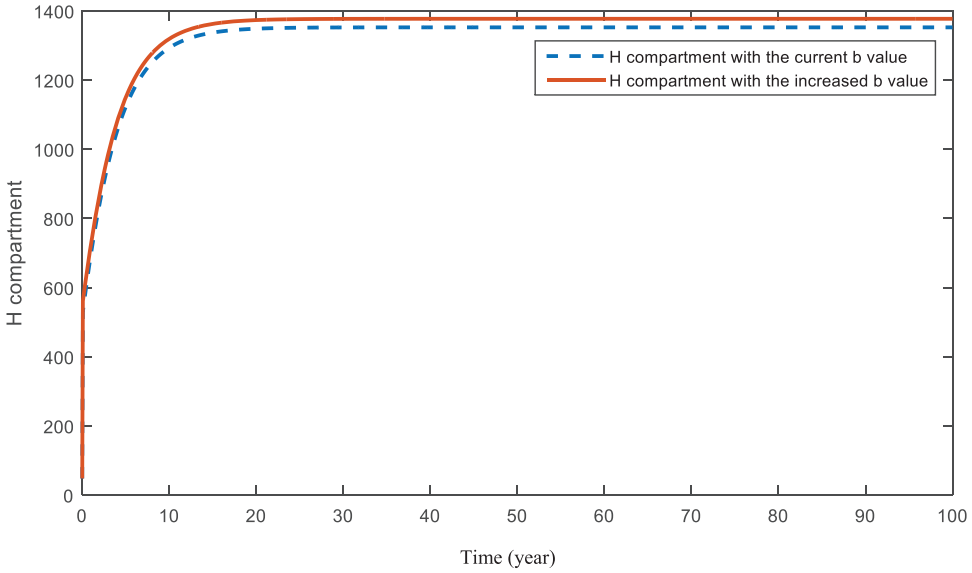

Figure 10: Sensitivity analysis of parameter b in compartment H

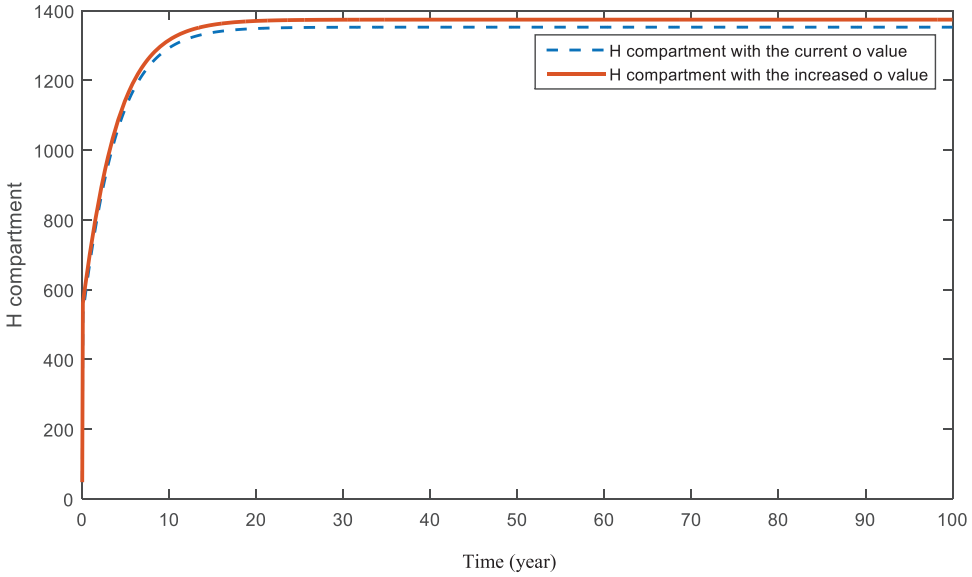

Figure 11: Sensitivity analysis of parameter o in compartment H

Fig. 12 represents what is expected to happen in compartment H when the percentage of hereditary/family history, f_1, increases. Figs. 13 and 14 show the compartment capacity in the case of increases and decreases in parameter c_1. Both of the figures emphasize the negative effect of COVID-19 pandemic on the diagnosis of heart-diseases.

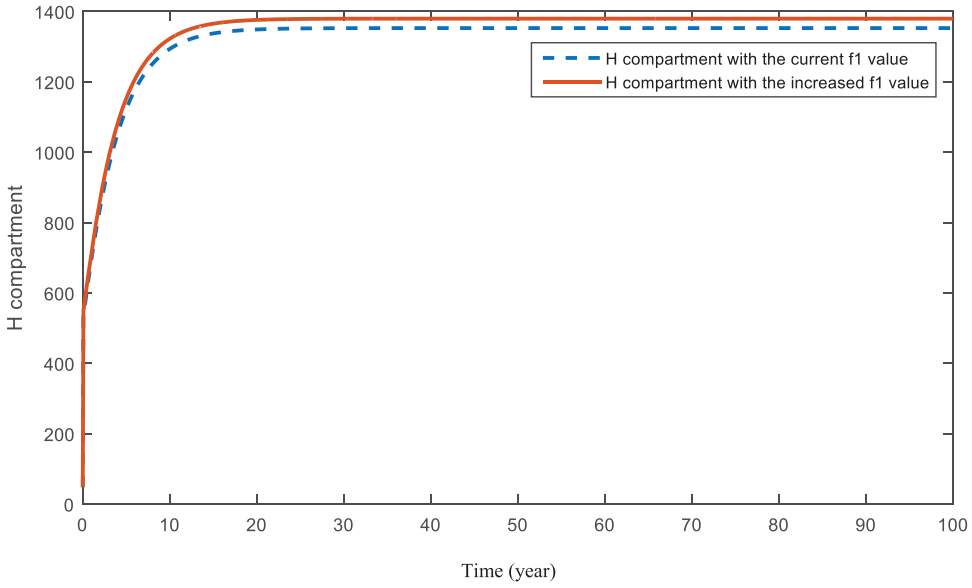

Figure 12: Sensitivity analysis of parameter f_1 in compartment H

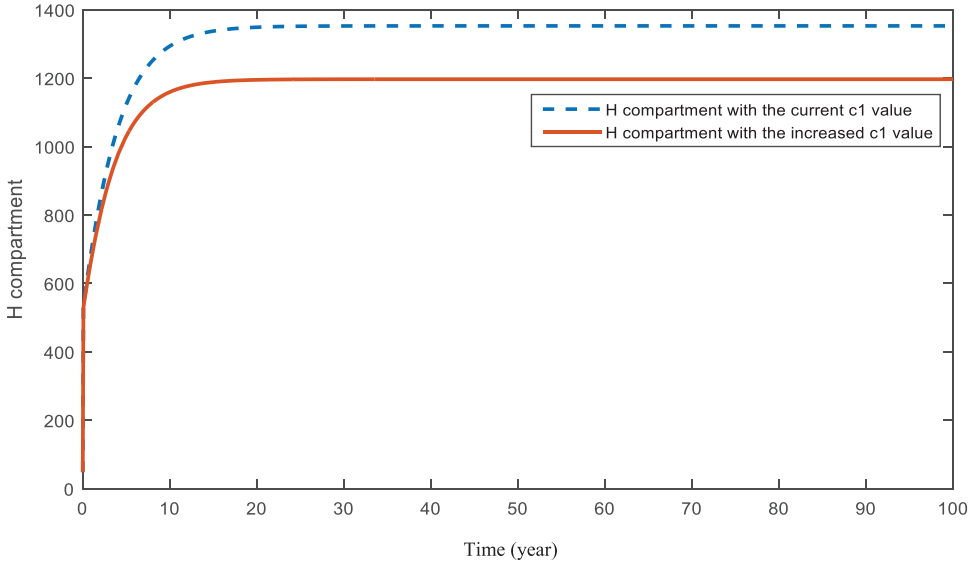

Figure 13: Sensitivity analysis of parameter c_1 in compartment H when it is increased

Fig. 15 demonstrates the pattern of heart-diseased individuals in the case of an increase in diabetes. This is the effect of diabetes on heart-diseases.

The effect of the obesity parameter, o, on compartment D is presented in Fig. 16, while Fig. 17 shows the effect of the hereditary/family history parameter, f_2, on the same compartment.

Figs. 18 and 19 are revealed in order to show the significance of the COVID-19 parameter, c_2, on compartment D. Both of the figures emphasize the negative effect of COVID-19 pandemic on the diagnosis of diabetes.

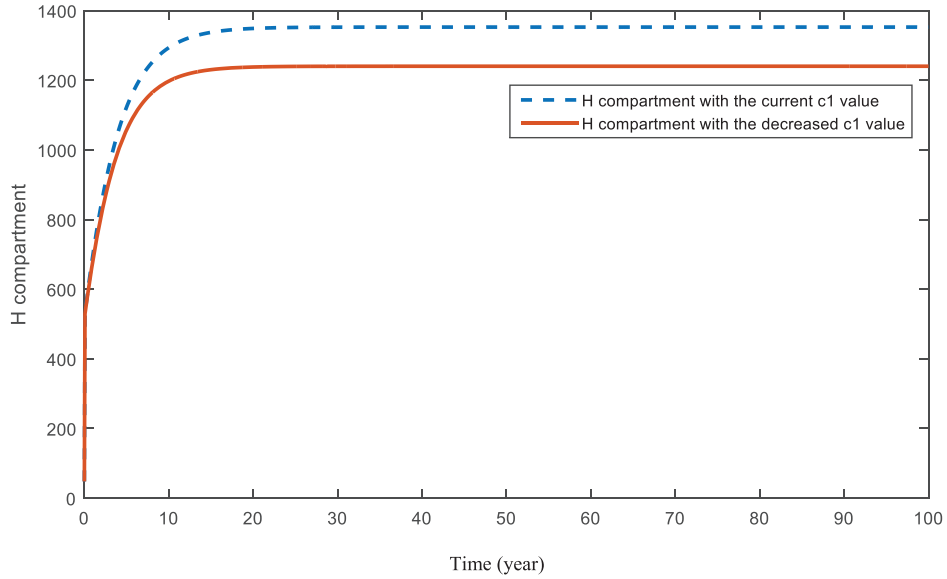

Figure 14: Sensitivity analysis of parameter c_1 in compartment H when it is decreased

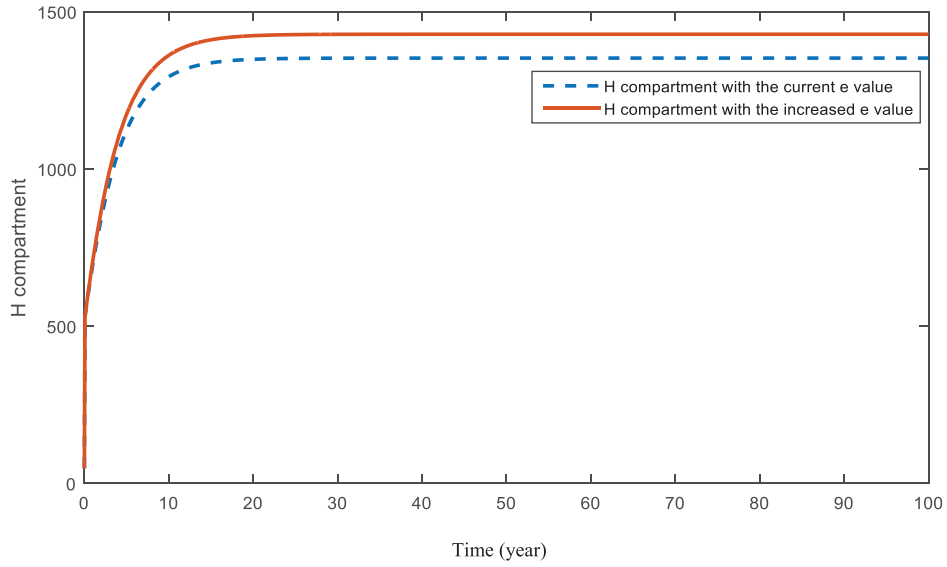

Figure 15: Sensitivity analysis of parameter e in compartment H

Fig. 20 demonstrates the pattern of diabetes patients in the case of an increase in patients with heart-diseases. This is the effect of heart-diseases on diabetes.

6 Results and Discussion

The main purpose of this study was to demonstrate how COVID-19 will affect the future of chronic diseases such as cancer, heart disease, and diabetes. In this regard, two mathematical models were proposed and proved with the required theorems. The first model consists of cancer-diagnosed and susceptible individuals, while in the second model, heart disease patients, diabetic patients,

and susceptible individuals are included. The reason for the two separate models is the unrelated connection of cancer with heart disease and diabetes.

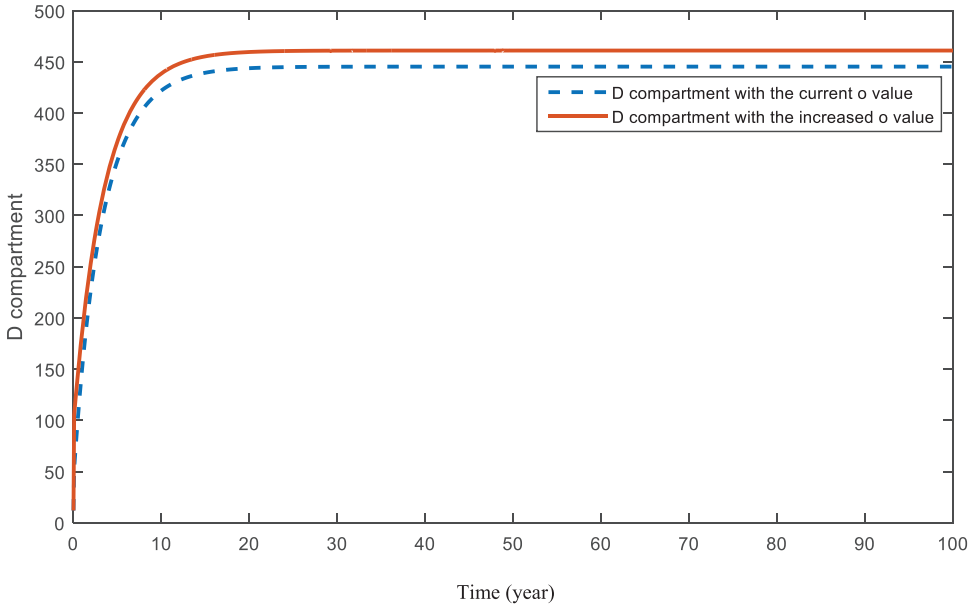

Figure 16: Sensitivity analysis of parameter o in compartment D

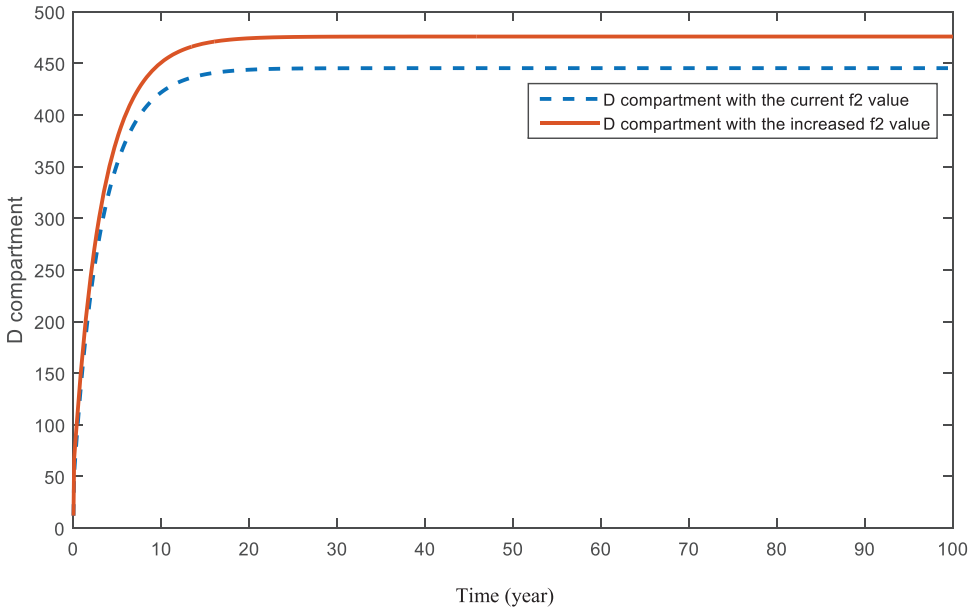

Figure 17: Sensitivity analysis of parameter f_2 in compartment D

In the analysis of the first model, disease-free equilibrium, $E_{0,1}$, and endemic equilibrium, $E_{*,1}$, points are found with their existence proofs. Moreover, the globally asymptotically stability property of both points is proved under some conditions. This suggests that there can be a population without cancer disease at point $E_{0,1}$ and an endemic situation at point $E_{*,1}$.

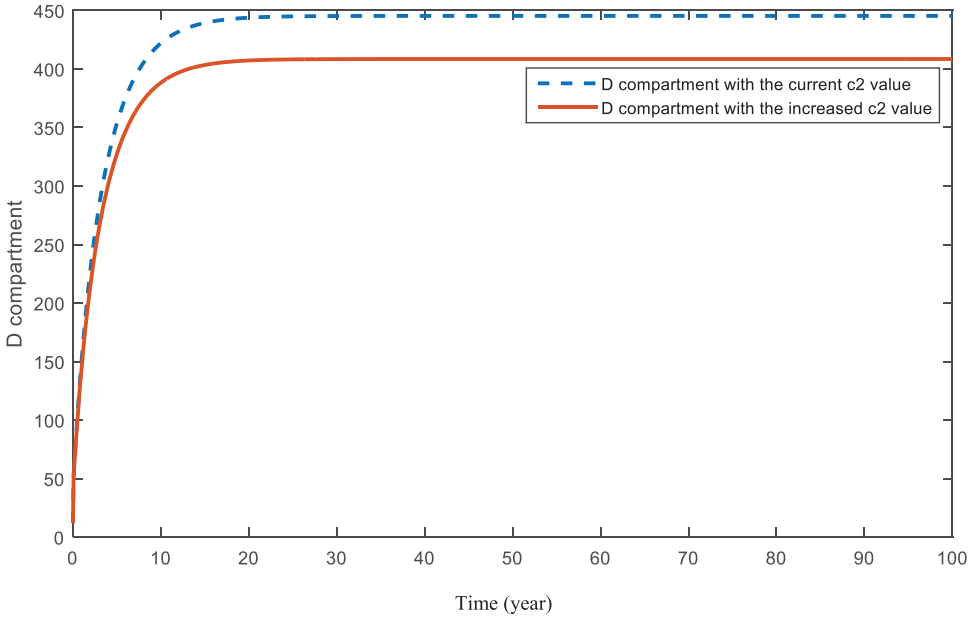

Figure 18: Sensitivity analysis of parameter c_2 in compartment D when it is increased

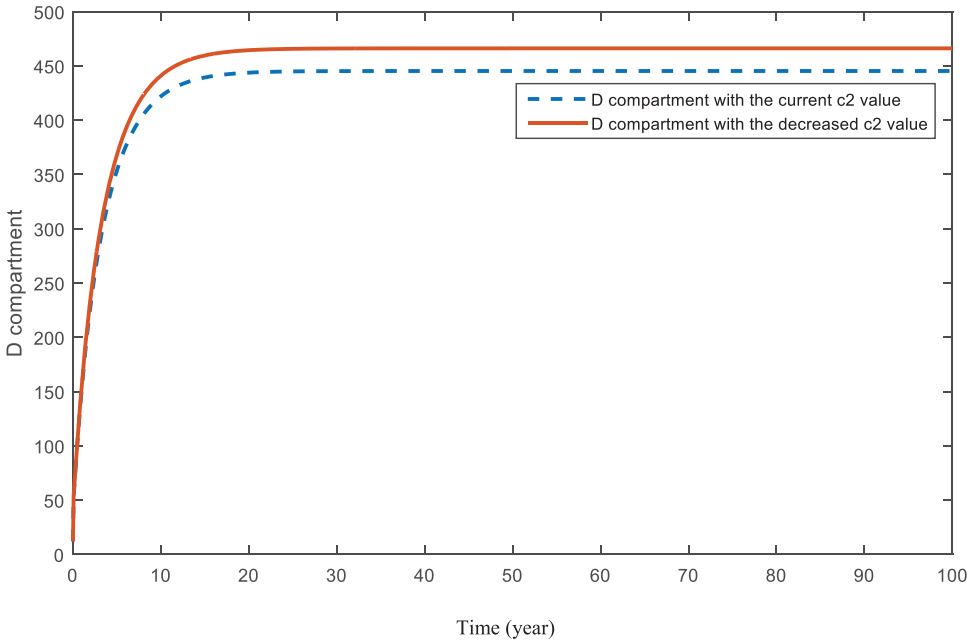

Figure 19: Sensitivity analysis of parameter c_2 in compartment D when it is decreased

In the same manner, the analysis of the second model demonstrated two existing equilibrium points for this model: the disease-free equilibrium point, $E_{0,2}$, and the endemic equilibrium point, $E_{*,2}$. Both points are globally asymptotically stable with necessary conditions, which means that it is possible for the diseases to occur in both environments.

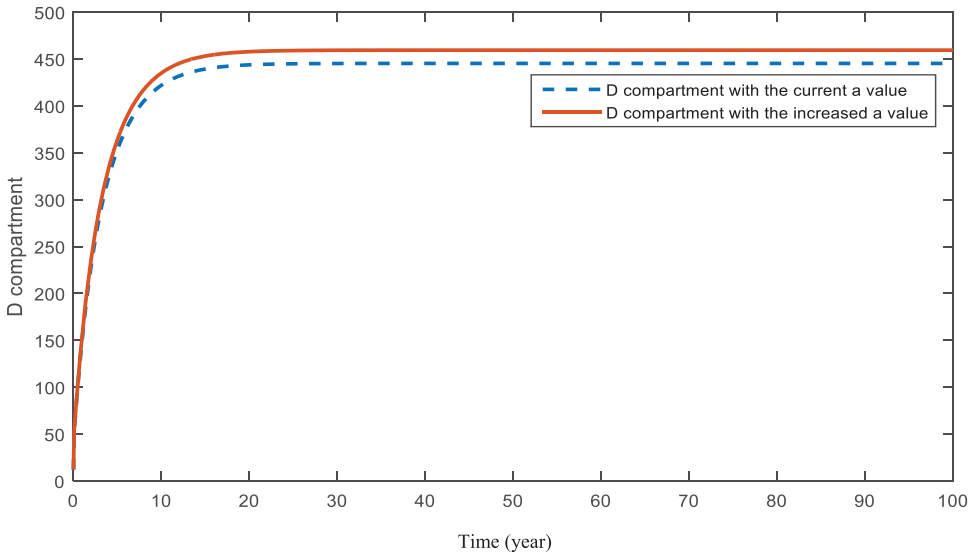

Figure 20: Sensitivity analysis of parameter a in compartment D when it is decreased

In Section 5, a sensitivity analysis was applied to the parameters of both models. This analysis aimed to specify the effects of the parameters on compartments C, H, and D. Figs. 6 and 7 demonstrate the result of an increase in smoking and obesity, respectively. Increases in both parameters will lead to an increase in the cancer compartment. However, even with a slight difference, the effect of smoking is bigger than the effect of obesity in compartment C. Similar results were also found and emphasized in papers [53–56]. In this model, the figure that shows the effect of hereditary transmission, f_1, is not given since the model did not present a meaningful result in this case. This result may be due to the population studied in this paper. Since compartment C includes many cancer patients (not a specific cancer type), the effect could not be seen. Many studies in the literature specify the relationship between specific cancer types and hereditary/family history [57,58].

Fig. 8 shows the expectation when the effect of parameter c is increased. As expected, increases in people's fear of seeing doctors will lead to a huge decrease in the diagnosis of cancer. Fig. 9 presents the situation of the cancer compartment a with a decreased c value. In this case, an increase is assumed again. However, this increase is much smaller than the increase in Fig. 8. Both Figs. 8 and 9 are a warning to the world about the COVID-19 pandemic. This problem can be solved by increasing people's awareness and encouraging them not to postpone their doctor visits.

Figs. 10 and 11 display the effects of smoking and obesity on heart disease patients. According to the figures, an increase in both parameters will cause a rise in the H compartment. In papers [59] and [60], it is also emphasized that smoking and obesity have a negative effect on heart diseases. Hereditary factors play an important role in heart diseases, which is proposed in Fig. 12. The impact of family history/hereditary factors on heart diseases is analyzed in papers [61] and [62]. Nevertheless, the most significant parameter for heart disease is COVID-19, c_1. It is obvious that c_1 is a very efficient parameter for the future patterns of heart disease. Both increases and decreases in this parameter cause a fall in the compartment H, which emphasizes the importance of awareness about doctor visits and COVID-19.

In [63], the authors dealt with the transmission of COVID-19 and the importance of preventive measures and lockdowns. On the other hand, reference [64] focused on discussing the complications

of COVID-19 disease in diabetes-diagnosed individuals. This study mostly focuses on the effect of the COVID-19 lockdown on cancer, heart-related diseases, and diabetes-diagnosed individuals to determine what is expected to happen for these diseases in the future because of this lockdown.

Figs. 16 and 17 demonstrate the pattern of diabetes patients when obesity and hereditary rates are increased, respectively. In a recent study [65], the impact of both obesity and smoking were analyzed. Authors of [65] also emphasized the importance of obesity and smoking in diabetes patients. Although the increase in the parameters causes a rise in the pattern of the D compartment, the effect of hereditary, f_2, is greater. The effect of COVID-19 is meaningful in the D compartment as well. In Fig. 18, an increase in parameter c_2 causes a fall in compartment D because of undiagnosed patients. However, for compartment D, even with a slight fall in parameter c_2, diagnosis for those with diabetes will be higher (Fig. 19). Figs. 15 and 20 are a warning that accentuates the relationship between diabetes and heart diseases.

7 Conclusions

As a result of the figures from the models, it is concluded that obesity is an effective parameter for the studied diseases and an increase in it will affect patients negatively. Smoking affects cancer and heart disease patients badly in the case of utilization. Heredity is a significant parameter for patients with diabetes and heart disease. Hence, people with a family history of these diseases should ensure that they attend their doctor visits. In addition, there is a strong relationship that cannot be ignored between diabetes and heart disease patients. As maintained in Figs. 15 and 20, people who are diagnosed with diabetes should be more careful and conscious about heart diseases.

On the other hand, both of the models indicated that the most dangerous parameter for the disease is c, (a negative effect of COVID-19), which is a result of the COVID-19 pandemic. In conclusion, the results showed that being aware of COVID-19 and its results may lead to a substantial decrease in deaths due to cancer, heart disease, and diabetes. That, combined with frequent doctor visits, could lead to the earlier diagnosis and treatment of these diseases.

This paper is prepared to emphasize the impact of COVID-19 on other serious diseases. The main purpose is to show that more epidemics and even pandemics may occur in the future in the case of insufficient control strategies. The study revealed that one of the reasons for this is to avoid doctor visits and regular checks because of the infectiousness of COVID-19. The presented study has a significant role in health sciences by being one of the strong models that discuss the effect of COVID-19 pandemic with different and serious perspectives.

8 Future Recommendations

The results of the sensitivity analysis should be utilized by healthcare systems and policymakers to develop control strategies to achieve better public health. Because obesity is linked to numerous health problems, tackling the issue is of the utmost significance. Public campaigns highlighting the dangers of obesity for one's health should be launched immediately. In addition, funding smoking cessation programs is essential because of the harm that smoking causes to people with cancer and cardiovascular diseases. These campaigns may include anything from a public information campaign to the distribution of free or low-cost cessation aid and community resources. Genetic counselling can be extremely helpful for people who have a history of diabetes or cardiovascular disease in their families. Individuals can learn more about the hazards they face and receive direction on how to mitigate those dangers during these sessions. Furthermore, given the well-documented link

between diabetes and cardiovascular disease, timely health checks are crucial. Patient results can be vastly improved by combining these checks with a holistic healthcare approach incorporating multidisciplinary teams. Cancer, heart disease, and diabetes are only some of the diseases whose rates and consequences have been significantly affected by the COVID-19 pandemic and its aftermath. Therefore, efforts to inform the public about the long-term consequences of the virus's spread are crucial. The transmission of the virus and the ensuing health consequences can be reduced by ensuring universal vaccination and the use of preventative measures. At the same time, there is a critical need for more in-depth studies to understand the entire extent of the virus's potential health effects. This knowledge is essential for the development of future public health treatments with greater precision. Individuals can be better prepared for disease treatment and prevention with the use of an integrated patient education framework that includes information on disease risks, symptom awareness, and the benefits of early diagnosis. Disease transmission that relies on memory qualities may also be better described by mathematical modeling with fractional derivatives [66–69], which is expected to increase degrees of freedom in the choice of order of the derivative. Finally, in order to effectively address the highlighted health risks and issues, it is essential to promote collaborations across health organizations, government bodies (Nongovernmental organizations), N.G.O.s, and other stakeholders.

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Author Contributions: Study conception and design: F.N.E., N.G., E.H.; data collection: S.Q., K.H., A.S.; analysis and interpretation of results: S.Q., N.G., K.H., E.H.; draft manuscript preparation: F.N.E., S.Q., N.G., K.H., A.S. All authors reviewed the results and approved the final version of the manuscript.

Availability of Data and Materials: All data generated or analyzed during this study are included in this article.

Conflicts of Interest: The authors declare that they have no conflicts of interest to report regarding the present study.

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