SEMARAK ILMU PUBLISHING

Journal of Advanced Research in Applied Sciences and Engineering Technology

Journal homepage:
https://semarakilmu.com.my/journals/index.php/applied_sciences_eng_tech/index
ISSN: 2462-1943

Sensitivity Analysis-Based Validation of the Modified NERA Model for Improved Performance

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ARTICLE INFO

Article history:
Received 20 May 2023
Received in revised form 5 September 2023
Accepted 12 September 2023
Available online 1 October 2023

Keywords:
Modified NERA Model; invariant region; reproduction number; sensitivity analysis; validation

ABSTRACT

Marijuana is an illicit narcotic with multiple negative health effects as it continues to pose a severe danger to the health of people in emerging regions. Marijuana is spread through interactions between users and non-users. This study utilizes first-order non-linear ordinary differential equations to modify the Non-user, Experimental, Recreational, and Addicted (NERA) users' model by adding a new class known as the hospitalized class of marijuana smokers. Moreover, this paper focuses on validating the NERA model using the sensitivity analysis concept. The NERA model presented in a previous study for marijuana usage among the target population consists of four distinct stages: the first stage is known as the non-user stage and is represented by the letter N; the second stage is known as the experimental stage of marijuana smoking and is represented by the letter E; the third stage is known as the recreational stage of marijuana smoking and is represented by the letter R; the fourth stage is represented by the letter A; and this last stage is known as the addicted stage of marijuana smoking. The suggested mathematical method achieved the reproduction number ($\Re_0$) for marijuana use. The results of the sensitivity tests indicate how crucial a variety of variables are to the spread of marijuana. The parameters that have a key impact on marijuana consumption were discovered based on sensitivity analysis. All these procedures, including the reproductive number and invariant region, using the sensitivity analysis concept were utilized to validate the updated model. In this study, the NERA model is modified by utilizing first-order non-linear ordinary differential equations. Furthermore, as demonstrated by the graphical and technique sections, the proposed modified models were successfully validated for improved performance.

1. Introduction

The aim of this paper is to modify the NERA model by incorporating a new component and validate the modified model for further performance. War and terrorism are two factors that hinder

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https://doi.org/10.37934/araset.32.3.111

a nation's development, but so can drug abuse among the population. The term "drug" describes a pharmaceutical ingredient used to expedite any chemical method occurring in the nervous system, including treating disease and enhancing mental function. There are many different forms of drugs, with marijuana serving as the primary focus of my research study. Marijuana use is frequently seen as a red flag for other illegal substances or as a "gateway" drug for more dangerous substances. Youths using gateway drugs or more likely to move on to other, more dangerous drugs. One of the most widely used illicit substances worldwide is marijuana, also known as Indian hemp, hay, pot, vape, tough, herb, flame, dried, reefer, grub, cannabis, etc. [1]. The idea that the heaviest drug users start with the least harmful drugs provides the gateway concept for drugs. It is similar to stairs leading from light to heavy narcotics, i.e., tobacco to ice, heroin, beer, etc. [2]. The usage of marijuana is a serious public health issue [3]. The most often used illegal substance in the US is marijuana. According to recent research, 18.7 million Americans acknowledged smoking marijuana, and 75% of cannabis smokers said they used it consistently [4].

In addition, 72 million Americans have smoked cannabis at least once. The outcomes of Ref. [5] showed a tendency towards a rise in the percentage of people who disclose using marijuana in emergency rooms, with some major cities reporting rises of up to 121% between 1999 and 2000. Besides that, marijuana hospitalizations at substance misuse center's increased by double from 1992 to 1997, accounting for 25% of all patients [4]. Eight states have legalized marijuana for recreational use, and 29 states and the District of Columbia have laws concerning medical marijuana (MMLs) [5]. The probability of marijuana use may rise if the drug is legalized at the state and local levels [6-8].

The risk of consuming other drugs, such as cigarettes, is raised when marijuana is used [9,10]. These studies investigate the eight-fold higher risk of starting to smoke cigarettes that marijuana use is connected to Ref. [11] cigarettes and marijuana use carries a potential risk [12].

Both medicinal and pleasure-seeking uses have seen an increase in legalization in recent decades at the national level. Eleven states, as well as the District of Columbia, presently allow the use of marijuana for recreational purposes, and additional states are considering adopting similar laws. As of July 2019, medicinal cannabis was accepted in 33 states. Several reports have indicated increased cannabinoid-related negative health consequences due to rising marijuana usage patterns and intensity [13]. However, most of these correlations are determined by case studies, published cases, or direct observations [14].

According to this research, 2.3% of the 89.6 million people in the US who acknowledged using cannabis in 2015–2016 had heart disease. These results were, however, exposed to response bias because of the significant non-response bias. Using administrative classification, an examination of the National Inpatient Sample (NIS) from 2010 to 2014 revealed 465,959 hospitalizations of individuals with a record of cannabis use (approximately 2.3 million adjusted hospitalizations in the US population). Mellitus, sudden infarction, and vague chest pain were the most typical primary indication for non-psychiatric discharges. It is significant to note that individuals with peripheral arterial diseases and myocardial atherosclerosis individually posed the highest chances of in-hospital death [15]. According to the results of the National Survey on Health and Drug Use, conducted annually among the general, quasi-American population, more than 39 million people have reported using cannabis in the previous year in both 2016 and 2017. Men consume cannabis more frequently than women; this gender imbalance grew from 2007 to 2014.

Those with medical illnesses were substantially more inclined to report heavy cannabis use, according to a new analysis of the behavioral risk factors surveillance system [16].

Cannabis sativa, a kind of hemp, is the hemp plant whose leaves, flowers, stems, and seeds are dried and shredded into marijuana. It is typically smoked in tubes or palm cigars. Nonetheless, some users brew it as tea or blend it with food. It is crucial to remember that when marijuana is smoked, the effects begin to take effect practically immediately and last for one to three hours. On the other side, eating cannabis in food prolongs the endurance of the impact. Delta-9-tetrahydrocannabinol (THC) is the primary psychoactive component in cannabis. THC interacts with the endocannabinoid system, which is on neurons throughout the brain. Mainly, cannabinoid receptors are present in the brain regions involved in enjoyment, learning, thought, attention, subjective experience, and regulated activity. Smoking marijuana raises the likelihood of lung infections and cardiac arrest by more than four times within the first hour of consumption. Even worse, a sizable retrospective study revealed that individuals who start using cannabis as adolescents have a considerable drop in their IQ and that their lost mental skills were never recovered when this population finally stopped using cannabis in adulthood [17]. Commercial hemp milk and other cannabinoid-free hemp solutions are readily accessible. Many nations, including Spain, China, Korea, Japan, France, and Ireland, allow the legal cultivation of hemp. The hemp plant also yields marijuana, primarily found in "buds." Smoking tobacco has the same leukemias elements as tobacco smoke [18]. The dried leaves, flowers, stems, and seeds of the *Cannabis sativa* or *Cannabis indica* plant are also combined to make marijuana. More than 100 molecules chemically related to THC, the main psychotropic component in marijuana, are also present in the marijuana Indica plant, along with 400 other substances [19]. As more states legalize these items for therapeutic and social reasons, cannabis usage and its variations are rising. [7,20]. The American Heart Association has issued remarks regarding the legalization of vaporizers and the increased use of new nicotine products, including e-cigarettes and shisha [21,22].

In the United States, alcohol and marijuana are two of the most popular drugs among young adults. 42% of young individuals aged 19 to 30 and 82% overall reported using marijuana and alcohol in the previous year.1 Both of these medications have a variety of potential short- and long-term dangers and negative effects [23,24]. Recent research has focused on developments in simultaneously use, including how modifications in consumption of marijuana are related to transforms in consumption of alcohol and if use of the two drugs is based on replacement (i.e., one substitutes use of the other) effects. It might be challenging to summarize the literature specifically on simultaneous alcohol and marijuana (SAM) use because operationalizations of SAM use vary and the same phrases are frequently applied to SAM use and simultaneous use [25-28].

The author of this article provided a summary of the peer-reviewed research on marijuana use in people aged 50 and older, including marijuana use patterns, marijuana use relationships, and marijuana use prevalence. Based on observations of the population, marijuana use has increased most among adults 50 and older. Compared to recreational use, a higher percentage of adults in the older adult group used marijuana for medical purposes; older marijuana users utilized medical marijuana in a variety of ways depending on the state. Male gender, single status, multiple chronic conditions, and psychological stress were all associated with marijuana use among older adults. The way these characteristics were addressed in the publications we analyzed differed depending on race and educational attainment [29].

The probabilistic model for the regulation of marijuana spread was developed by Yusuf *et al.,* [30]. As control methods, a campaign for awareness, rehabilitation, and education were implemented. To determine the best arrangement of preventive actions that would reduce the cost and spread of marijuana use in a community, various treatments are put under optimal control. The characteristics of illegal marijuana consumption in a certain population were mathematically formulated by Dauhoo *et al.,* [1]. The population at large both used and did not use substances. Three additional categories-recreational (R), experimental (E), and addicted (A), are used to categorize marijuana users further. The aim of this paper to modify and validate the NERA model. The model, which integrates population structure and cannabis usage, is known as the NERA model [1] (refer to Figure 1) and is the following set of differential equations

$$
\begin{aligned}
{}^{dN}/_{dt} &= \beta - r_1EN - r_1RN + r_5R + r_6A + r_3E - \beta N, \\
{}^{dE}/_{dt} &= -r_2RE - r_3E + r_1NR + r_1NE - \beta E, \\
{}^{dR}/_{dt} &= -r_4R + r_2ER - r_5R - \beta R, \\
{}^{dA}/_{dt} &= r_4R - r_6A - \beta A. \qquad (1)
\end{aligned}
$$

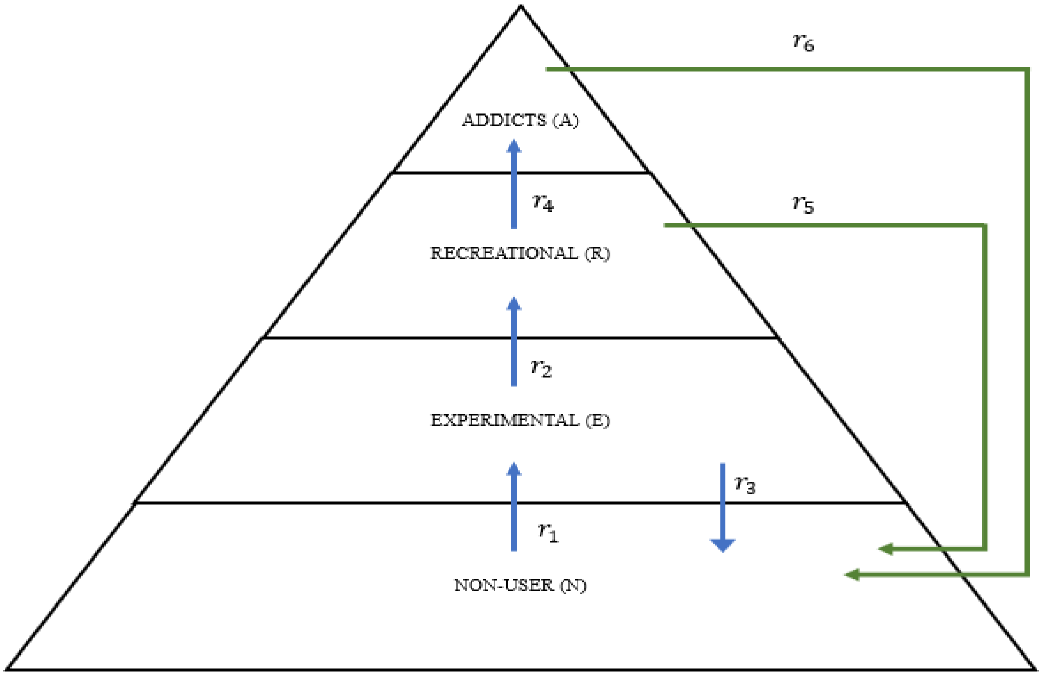

Fig. 1. A geometric illustration of the existing model

2. Model Formulation

In this portion, a new variant of the NERA model (refer to Figure 2) will be developed, from the perspective of a global outbreak. The overall population is divided into two main stages, marijuana users and non-users. Four categories of users are distinguished, each illustrating a different stage on the pathway to addiction. These classes include susceptible persons (S), experimental subjects (E), casual smokers (C), addicts (A), and hospitalized subjects (H). Eq. (2) shows the total population T(t) at time 't'

$$T(t) = N_S(t) + E_S(t) + R_S(t) + A_S(t) + H_S(t). \qquad (2)$$

The following set of first-order non-linear ordinary differential equations represents marijuana smokers' general behaviors

$$
\begin{aligned}
{}^{dN_S}/_{dt} &= £ - (cR_S - c_3A_S + \mu)N_S + c_2E_S + c_4R_S + c_7H_S, \\
{}^{dE_S}/_{dt} &= cR_SN_S - (c_1 + c_2 + \mu)E_S, \\
{}^{dR_S}/_{dt} &= c_3A_SN_S + c_1E_S - (c_4 + c_5 + \mu)R_S, \\
{}^{dA_S}/_{dt} &= c_5R_S - (c_6 + \mu)A_S, \\
{}^{dH_S}/_{dt} &= c_6A_S - (c_7 + \mu)H_S. \qquad (3)
\end{aligned}
$$

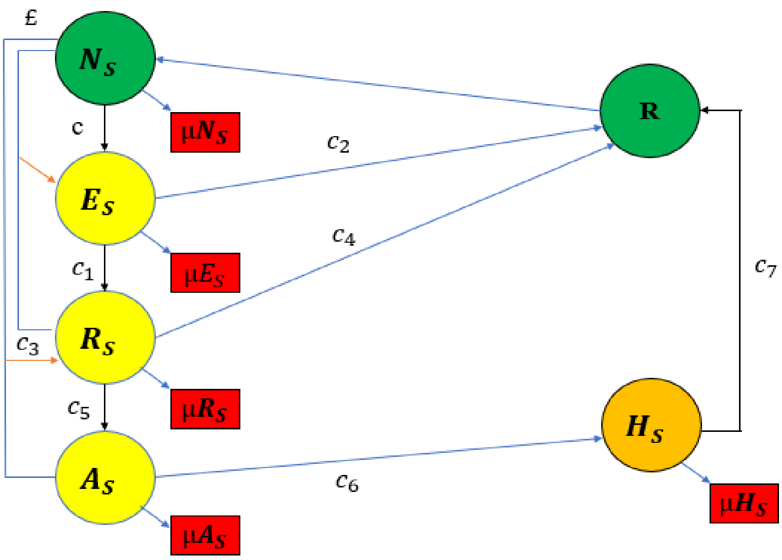

Fig. 2. A geometric illustration of the modified model

The parameter explanations are listed in the table 1 below.

Table 1
Explanations of the parameters

Notations	Parameters	Values	References
£	Individuals birth rate	$0.0015875 day^{-1}$	[31]
c	Impact of users (in an experiment) relative to non-users (susceptible)	$0.446 day^{-1}$	[1]
c_1	The percentage of users who are experimentally compared to those that are casual	$0.5 day^{-1}$	[1]
c_2	Percentage of test drug users who gave up smoking upon receiving guidance	$0.17 day^{-1}$	[1]
c_3	Addicts' amount of influence over non-addicts (susceptible)	$0.001201 day^{-1}$	Assumed
c_4	Probability of occasional cannabis smokers quitting because of the surroundings	$0.0002 day^{-1}$	Assumed
c_5	How often do average users develop addictions when the transition phase is over?	$0.025 day^{-1}$	[1]
c_6	Probability of drug addiction resulting in hospital admissions because of widespread marijuana use	$0.22 day^{-1}$	Assumed
c_7	Addicts' probability of rehabilitation after medication	$0.2010 day^{-1}$	Assumed
μ	Individuals' death ratio	$0.006 day^{-1}$	[31]

2.1 Invariant Region

Since the suggested model's system parameters and characteristics (state variables) are all relevant to the real-life human community, we assumed they are all non-negative at time t = 0. This includes the behavior of the whole population of humans, where the non-linear system below illustrates the overall population

$$\text{Ꝁ} = N_S + E_S + R_S + A_S + H_S. \tag{4}$$

Eq. (4) is solved to obtain

$$\dot{\text{Ꝁ}} = \text{£} - \mu \text{Ꝁ}, \tag{5}$$

Eq. (5) gives us

$$\dot{\text{Ꝁ}} = \text{£} \leq \mu \text{Ꝁ}, \tag{6}$$

By solving Eq. (6), we get

$$\text{Ꝁ} \leq \text{Ꝁ}(0)e^{-\mu t} + \frac{\text{£}}{\mu}(1 - e^{\mu t}) \Rightarrow \text{Ꝁ} \leq \frac{\text{£}}{\mu} \text{ when t} \dashrightarrow \infty \tag{7}$$

In accordance with the previous analysis, we propose the following claim:

2.2 Proposition

The area of the proposed model is given by

$$\aleph = \left[(N_S, E_S, R_S, A_S, H_S) \epsilon\ \mathbb{R}_+^5, \text{Ꝁ} \leq \frac{\text{£}}{\mu}\right]. \tag{8}$$

It is a positively invariant domain, the model is well-formulated from an epidemiological and mathematical perspective [31], and all the pathway borders are in the forward direction. It means that the population is bound. It is the first step to prove the validation of the formulated model.

3. Reproduction Number ($\mathfrak{R}_0$)

The basic $\mathfrak{R}_0$, which is read "R nought," is meant to measure the rates of addiction/infection or transmissibility of pathogenic and parasitic organisms. $\mathfrak{R}_0$ is frequently used in the literature on epidemiology and public health as well as in the media [32,33]. There is a discussion of the population's initial marijuana prevention rate. Reproductive frequency is the initial propagation rate, represented by ($\mathfrak{R}_0$): A well-known technique called the "Next Generation Matrix Technique" is used to establish the starting network throughput (reproduction number).
As

$$\mathfrak{R}_0 = \rho(\mathcal{F}\mathrm{V}^{-1}) \text{ [31,34]}. \tag{9}$$

where provides the spectral range. Moreover, the Jacobian of $'\text{ꜰ}'$ is $\mathcal{F} = \mathcal{J}_{\text{ꜰ}}$

$$\text{ꜰ} = \begin{pmatrix} \text{ꜰ}_1 \\ \text{ꜰ}_2 \\ \text{ꜰ}_3 \end{pmatrix} = \begin{pmatrix} cR_S N_S \\ c_3 A_S N_S \\ 0 \end{pmatrix}. \tag{10}$$

The column in Eq. (10) represents the people who develop an addiction

$$\mathcal{F} = \begin{pmatrix} \frac{\partial(f_1)}{\partial(E_S)} & \frac{\partial(f_1)}{\partial(R_S)} & \frac{\partial(f_1)}{\partial(A_S)} \\ \frac{\partial(f_2)}{\partial(E_S)} & \frac{\partial(f_2)}{\partial(R_S)} & \frac{\partial(f_2)}{\partial(A_S)} \\ \frac{\partial(f_3)}{\partial(E_S)} & \frac{\partial(f_3)}{\partial(R_S)} & \frac{\partial(f_3)}{\partial(A_S)} \end{pmatrix} = \begin{pmatrix} 0 & cN_S & 0 \\ 0 & 0 & c_3N_S \\ 0 & 0 & 0 \end{pmatrix}. \tag{11}$$

For simplicity, we write Eq. (11) as

$$\mathcal{F} = \begin{pmatrix} 0 & \eta_1 & 0 \\ 0 & 0 & \eta_2 \\ 0 & 0 & 0 \end{pmatrix}_{(MFE)}. \tag{12}$$

In a similar way, the Jacobian of "v" is: $V = \mathcal{J}_{v}$, where

$$V = \begin{pmatrix} v_1 \\ v_2 \\ v_3 \end{pmatrix} = \begin{pmatrix} -(c_1 + c_2 + \mu)E_S \\ c_1E_S - (c_5 + c_4 + \mu)R_S \\ c_5R_S - (c_6 + \mu)A_S \end{pmatrix}. \tag{13}$$

The people who enter or quit the affected class, except those who come from the susceptible class, are shown in the column of the matrix $'V'$ (Eq. (13))

$$V = \begin{pmatrix} \frac{\partial(v_1)}{\partial(E_S)} & \frac{\partial(v_1)}{\partial(R_S)} & \frac{\partial(v_1)}{\partial(A_S)} \\ \frac{\partial(v_2)}{\partial(E_S)} & \frac{\partial(v_2)}{\partial(R_S)} & \frac{\partial(v_2)}{\partial(A_S)} \\ \frac{\partial(v_3)}{\partial(E_S)} & \frac{\partial(v_3)}{\partial(R_S)} & \frac{\partial(v_3)}{\partial(A_S)} \end{pmatrix}, \tag{14}$$

$$V = \begin{pmatrix} -(c_1 + c_2 + \mu) & 0 & 0 \\ c_1 & -(c_5 + c_4 + \mu) & 0 \\ 0 & c_5 & -(c_6 + \mu) \end{pmatrix}_{(MFE)}. \tag{15}$$

For simplicity, we write Eq. (15) as

$$V = \begin{pmatrix} -\flat_1 & 0 & 0 \\ c_1 & -\flat_2 & 0 \\ 0 & 0 & -\flat_3 \end{pmatrix}_{(MFE)}. \tag{16}$$

The dominant Eigenvalue of $(\mathcal{F}V^{-1})$ and hence $\mathfrak{R}_0$ is

$$\mathfrak{R}_0 = \sqrt{\left(\frac{c*N*c_1}{\flat_1*\flat_2}\right)}, \tag{17}$$

$$\mathfrak{R}_0 = \sqrt{\frac{cc_1£}{(c_1+c_2+\mu)(c_5+c_4+\mu)\mu}}. \tag{18}$$

4. Sensitivity Analysis of ($\mathfrak{R}_0$)

The ratio of the corresponding difference in the variable to the relative change in the parameter is known as the normalized forward sensitivity index of a variable to a parameter. Objective functions define the sensitivity index if the variable is a differentiable parameter function [35]. For example, the following is the definition of the normalized forward sensitivity index of a variable ß whose differentiability depends on a parameter Ŋ

$$\mathbb{Y}_{Ŋ}^{ß} = \frac{\partial ß}{\partial Ŋ} \times \frac{Ŋ}{ß}. \tag{19}$$

The multiple correspondence indices are provided in Table 2.

Table 2
Parameters Sensitivity Indexes

Parameters	Parameters values	Sensitivity indexes
£	0.0015875	+0.5000
µ	0.066	-0.6372
c_5	0.25	-0.4006
c_4	0.002	-0.0032
c_2	0.17	-0.1164
c_1	0.5	+0.1575
c	0.446	+0.5000

5. Results and Discussion

The following resultant figures predict the results of the indicated methods. We have assumed $N_S(0) = 1000$, $E_S(0) = 20$, $A_S(0) = 20$, $R_S(0) = 20$, and $H_S(0) = 10$. We employ the RK-4 Method to produce the graphical findings using MATLAB programming language.

From the two figures, it is seen that in Figure 3, there are approximately 230 people who will be under control in 130 days. Whereas Figure 4 shows us that 290 persons will typically recover in 130 days. As a result, Figure 4, the outcome of the updated model for the addicted class, is more accurate than Figure 3, the outcome of the existing model for the addicted class.

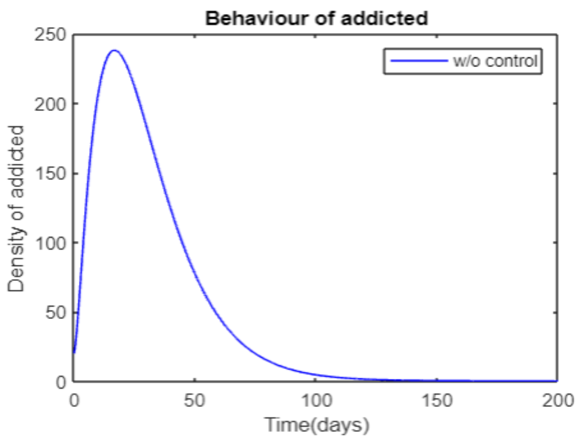

Fig. 3. displays the results of the addicted class (the existing model)

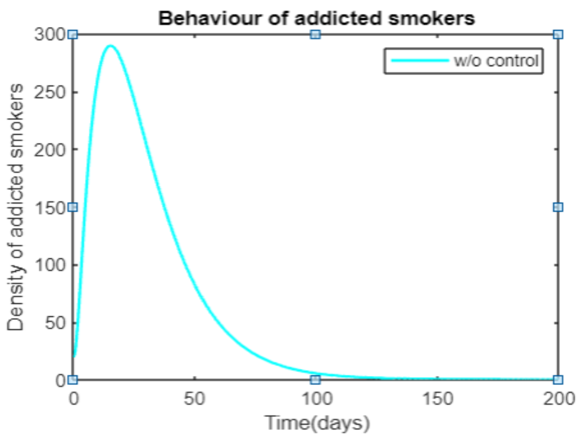

Fig. 4. displays the results of the addicted class (the updated model)

6. Conclusion

This study's conclusion included an improved mathematical model of marijuana users and non-users. Where the focus was on getting rid of the addicted class and comparing the result of this class from both the existing and improved model for the validation of the model. This comparison showed that the result indicated which model was more accurate for controlling marijuana smoking in the population. Also, it was clear from the first stage (the invariant zone) that the population is bound because the human population is positively invariant. The initial marijuana transmission rate ($\mathfrak{R}_0$) and its sociological analysis was shown to be significant. The proposed model was numerically simulated using the RK-4 technique. In this study, the NERA model is modified by utilising first-order non-linear ordinary differential equations. Furthermore, as demonstrated by the graphical and technique sections, the proposed modified models were successfully validated for improved performance. We therefore conclude that the updated model is demonstrated from the outcome of all these processes used for its validation to be well accurate and valid to use going forward for the prevention of marijuana smoking in the human population.

Acknowledgment
The first and third authors are thankful to Universiti Teknologi PETRONAS for providing postgraduate assistantships. Kamal Shah and Abdeljawad would like to thank Prince Sultan University for their support through the TAS research lab.

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