Global Scientific JOURNALS

GSJ: Volume 12, Issue 1, January 2024, Online: ISSN 2320-9186
www.globalscientificjournal.com

MATHEMATICAL MODELLING AND ANALYSIS OF ALCOHOL-TRAMADOL CO-ABUSE IN INDIGENT SUBURBS OF NIGERIA

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KEYWORDS: Substance Co-Abuse, Reproduction Number, Sensitivity Analysis.

Abstract

It is not uncommon the menace substance abuse contributes to the wellness and developmental structure of a country. In this research work, a deterministic mathematical model of substance abuse consisting of multiple substance(s) viz Alcohol and Tramadol is constructed from compartmentalized model. The co-abuse of alcohol and tramadol have deteriorated the substance epidemic in Nigeria, with specialty to the indigent sub-regions. Building on the insights from epidemiology, our model entails for controlling the spread of co-abusers ideologies in the society. We introduce a simple compartmental model suitable to describe co-abusers group; The population $N(t)$ is divided into five compartments: $S(t)$, $A(t)$, $T(t)$, $C(t)$ and $R(t)$ denoting the Susceptible, Alcohol substance users, Tramadol substance users, Combined substance users group and Rehabilitated populations respectively. We establish that the equilibria of the submodels are locally and globally asymptotically stable when the sub-model threshold parameters are less than one(1). The basic reproduction number R_0 due to co-abuse was derived with the Next Generation Matrix method; Also sensitivity analysis shows that the most sensitive parameters in the co-abuse epidemic is the Alcohol and Tramadol recruitment rates β_1 and β_2 respectively, implying as more susceptible individuals imitate alcohol-tramadol intake, co-abuse will more likely increase and this would lead to the continuous co-abuse of substances by individuals of the populace. Excel sheets was employed for plot-visibility of each parameter behaviour indicating the need to design awareness campaigns of the precariousness instituted by alcohol use and thus co-abuse with tramadol; through counsellings, sanatoriums, the media and law-enforcement agencies.

1 Introduction

Abuse of substance(s) poses a significant threat to the health and socio-economic fabric of individuals and nations. The combined abuse of alcohol and the highly

addictive Tramadol has worsened the drug epidemic in Nigeria, especially in the indigent suburbs(UNODC, 2021)

Tramadol is (supposedly)a synthetic opiate drug that is useful in treating moderate to severe pain associated with surgery or numerous conditions. It goes by several different trade names, including Ultram, Rybix, and ConZip, and a combination of acetaminophen and tramadol also marketed as Ultracet. According to the American Addiction Centres (AAC, 2023); Drugs in this class are considered to have moderate potentials for abuse and may result in the development of physical dependence on the drug if it is used repeatedly. Its mechanism of action is similar to the mechanism of action of other narcotic/opioid drugs. It readily attaches to specific neurons in the brain that are specialized for a group of neurotransmitters that are commonly referred to collectively as the endogenous opioid neurotransmitters. These neurotransmitters include substances like enkephalins and endorphins, and they assist individuals in coping with stress, exertion, and pain. The drug may also increase the availability of norepinephrine and serotonin when it is used. Tramadol is classified as a central nervous system depressant drug, like other opiate drugs, meaning that its overall effects result in reduction of neuron firing in the central nervous system (the brain and spinal cord).

Alcohol on the other hand is the number one substance of abuse in the United States, and the majority of substance use disorders in the United States involve alcohol, according to the Substance Abuse and Mental Health Services Administration (SAMHSA). Alcohol is a central nervous system depressant like tramadol, but it operates on different neurotransmitters. It affects a number of neurotransmitters, including the inhibitory neurotransmitters gamma-aminobutyric acid (GABA) and glycline as well as the excitatory neurotransmitter N-methyl-d-aspartate (NMDA). According to sources like SAMHSA, the abuse of alcohol and other opiate drugs like tramadol is a concern across all age groups, but it is a particular concern for indigent regions where easy access medical facilities are limited and also to younger

individuals under the age of 25.

Concurrent alcohol- and tramadol- induced health problems are quite serious and can result in death. Individuals abusing high levels of alcohol or tramadol together should be immediately taken to hospital; a few of adverse effects are listed as Severely low blood pressure. Breathing problems. Anxiety. Hallucinations. Diarrhea. Seizures. Memory loss. Dangerous behavior that can put multiple individuals at risk. Abdominal problems. Vertigo. Loss of coordination. Memory loss. Lethargy. Irregular breathing. Seizures.

Taking both alcohol and tramadol increases the potential for a drug overdose, as the combination modifies the individual effects of the substances. Unfortunately, alcohol is commonly abused with tramadol, which enhances the sedative effects of each, leading to an increased risk for life-threatening depressant effects such as slowed or stopped breathing American Addiction Centres (AAC, 2023)

A study by Solayide *et al.* (2022) opined Psychoactive substance use as a social and public health issue that has become a global epidemic affecting various countries, including Nigeria. The work observed high occurrences of this menace have been recorded among students in different settings with limited reports on university students in Nigeria. Therefore investigated the magnitude of substance use among students in a Nigerian University and evaluated the strategies to address the problem; they employed a structured self - administered questionnaire to obtain information from randomly selected undergraduate students and obtained informations including socio - demographic characteristics, knowledge and perception of substance users and analyzed using Statistical Package for Social Sciences (version 20). The mean age of the respondents being 20 years and the proportions of female and male students also 58.9% and 41.1% respectively; Twenty percent (20%) of them had consumed alcohol while 16% had taken marijuana and /or opoids including tramadol and codeine, students who had used electronic vapor products were 27 (11.4%). Except for hashish, the use of substances was not statistically significant

for both genders across all substances included in their study. Most (46; 78.0%) of those who had used substances were introduced to the vice by friends, while 4(6.7%) were by their parent/family members. Students (70.4%) who had used substances did so at parties. Peer pressure (73.7%) and curiosity were the highest influencing factors for the use of substances among the students. About 37% agreed that offenders should be punished, 45(19.1%) said no to the idea, 54 (22.9%) were unsure and the remaining 49(20.8%) did not respond, eighty-one (34.3%) of the students sampled believed that guidance and counseling would be effective in dealing with drug abuse/substance use. Proposed intervention strategies include whistle blowing by the students and organisation of drug free club/association for students and also continued study within the university community will help in the monitoring of patterns and the implementation of effective control strategies.

Moreover, some of other co-abused substances are Opium, Amphetamine, Cocaine, Alcohol, Ayahausca, Central Nervous System Depressants, DMT, GHB, Hallucinogens, Heroin, Inhalants, Netamine, Khat, Kratim, LSD, MDMA (Ecstacy/Mocky), Mescaline (Peyote), Methanphetamine, Over - The - Counter Medicines (Dextromethorphan, Loperamide), PCP, Prescription Opioids, Prescription Stimulants, Psilocybin, Rohypnol (Fluintrazepam), Salvia, Steroids (Anabolic), Synthetic Cathinones (Bat salts), Tobacco; NIDA(2013).

2 Literature Review

A study conducted by World Bank collection of development indicators placed smoking prevalence among adult male in Nigeria at 17.4% and alcohol consumption study conducted by the World Health Organisation (WHO) placed 56% of Nigerians over the age of 15 consume alcohol. The study also reveals that 50% of Nigerians in urban area consume alcohol.

Orwa and Nyabadza (2019) formulated a mathematical model to examine the dy-

namics of alcohol and methamphetamine co-abuse. It was proven that the equilibria of the submodels are locally and globally asymptotically stable when the sub-model threshold parameters are less than unity; also the Sensitivity analysis revealed that the most sensitive parameters in the co-abuse epidemic are the alcohol and methamphetamine recruitment rates r1 and r2 respectively; and that the prevalence curve was indicative of a persistent drug problem in the region. Thus advised the need to promote social programs that raise awareness of the dangers posed by multiple substance abuse, through educational campaigns in learning institutions, social media and health institutions; also transmission control must focus on enhancing the quitting process while promoting support services to substance users during and after treatment to minimize cases of relapse.

Katelyn et al. (2021) examined young adults changes in cigarette, e-cigarette, marijuana, and alcohol use from pre- to during COVID-19(given the potential for increased substance use during COVID-19); and related risk/protective factors. They examined risk/protective factors (i.e. adverse childhood experiences [ACEs], depressive symptoms, resilience) in relation to changes in past 30-day substance use frequency. In their sample (N?=?1084, Mage=24.76, SD = 4.70; 51.8% female; 73.6% White; 12.5% Hispanic), W3/W4 past 30-day use prevalence was: 29.1% cigarettes (19.4% increased/26.4% decreased), 36.5% e-cigarettes (23.2% increased/28.6% decreased), 49.4% marijuana (27.2% increased/21.2% decreased), and 84.8% alcohol (32.9% increased/20.7% decreased). Multivariate regressions indicated that, greater increases were predicted by: for e-cigarettes, greater ACEs; and for alcohol, greater depression. Among those with low resilience, predictors included: for e-cigarettes, greater depression; and for marijuana, greater ACEs. Concluding that Interventions to reduce substance use during societal stressors should target both risk and protective factors, particularly resilience.

Research findings by Joana et al (2023) inferred that Tramadol and tapentadol, synthetic opioids commonly prescribed for moderate-to-severe pain, have a unique

pharmacology that optimizes their analgesia and safety. They were however not devoid of risks, presenting addictive, abuse, and dependence potential; as tramadol-reinforcing properties have been documented by various studies with human and animal models, including conditioned place preference (CPP) assays which are used to analyze drug-positive reinforcing effects

A study by Solayide *et al.* (2022) opined Psychoactive substance use as a social and public health issue that has become a global epidemic affecting various countries, including Nigeria. The work observed high occurrences of this menace have been recorded among students in different settings with limited reports on university students in Nigeria. Therefore investigated the magnitude of substance use among students in a Nigerian University and evaluated the strategies to address the problem; they employed a structured self - administered questionnaire to obtain information from randomly selected undergraduate students and obtained informations including socio - demographic characteristics, knowledge and perception of substance users and analyzed using Statistical Package for Social Sciences (version 20). The mean age of the respondents being 20 years and the proportions of female and male students also 58.9% and 41.1% respectively; Twenty percent (20%) of them had consumed alcohol while 16% had taken marijuana and /or opoids including tramadol and codeine, students who had used electronic vapor products were 27 (11.4%). Except for hashish, the use of substances was not statistically significant for both genders across all substances included in their study. Most (46; 78.0%) of those who had used substances were introduced to the vice by friends, while 4(6.7%) were by their parent/family members. Students (70.4%) who had used substances did so at parties. Peer pressure (73.7%) and curiosity were the highest influencing factors for the use of substances among the students. About 37% agreed that offenders should be punished, 45(19.1%) said no to the idea, 54 (22.9%) were unsure and the remaining 49(20.8%) did not respond, eighty-one (34.3%) of the students sampled believed that guidance and counseling would be effective in dealing with

drug abuse/substance use. Proposed intervention strategies include whistle blowing by the students and organisation of drug free club/association for students and also continued study within the university community will help in the monitoring of patterns and the implementation of effective control strategies.

Douglas et al. (2019) generalized that estimating equations models showed women who were heavy drinkers at baseline in the IMI condition reduced heavy drinking more than those in the SMI condition at 2-, 6-, and 12-month follow-up. Their analyses of disaggregated subgroups showed IMI was most effective for women with low psychiatric severity, more severe physical and impulse control consequences associated with drinking, and higher motivation. They also deduced however that formal 3-way interaction models (condition by moderator by time) showed significant effects primarily at 2?months; and concluded that improvements associated with IMI were limited to heavy drinking and varied among subgroups of women.

Sara et al. (2020) analysed that the response to treatment from co-abuse may have varied as a function of six empirically-based baseline moderators and predictors: biological sex, age, race/ethnicity, mental health problems, parent-adolescent communication, and peer deviance. They used data from the parent trial randomizing 102 parents to either the FCU (n?=?51) or PE (n?=?51) interventions were re-analyzed across four time points (baseline, 3-, 6-, and 12-months). Moderators and predictors were tested via a series of hierarchical linear models; giving result that Parent-adolescent communication and peer deviance emerged as significant predictors of adolescent treatment response. And specifying that low-levels of parent-adolescent communication or peer deviance were associated with worse treatment response

Emeka and Ogochukwu (2022) explored the awareness and understanding/interpretations of the alcohol industry-sponsored Responsible drinking message?(RDM) among Nigerian youth. Data were elicited through 53 semi-structured interviews and 3 focus groups (N=26), and also observed product labels and industry websites. Under-

graduate participants were aware of ?drink responsibly? (one of the RDMs), but some out-of-school participants with low-level education did not know it existed. This is likely because drink responsibly message is promoted in English language without any indigenous language alternatives. It is embedded in conventional advertisements that glamorize drinking without stand-alone public health messages encouraging low-risk drinking behaviours. Participants shared divergent but subjective interpretations of drink responsibly, but none associated it with abstinence. Some associated drink responsibly with the ability to hold one? drink, stating that it means: Drinks very well, but don't get drunk and drink to your satisfaction, but don't misbehave. Other interpretations included: know your limit and ?rink in moderation; Drink responsibly was also understood to mean drink in excess but respect yourself Inferring that Alcohol companies in Nigeria redirect consumers to Drinkaware? and DrinkIQ? websites in the UK but use inconspicuous fonts to inscribe ?drink responsibly on product labels. Alcohol companies frame RDMs to promote drinking and individual responsibility. Thus, it engenders subjective interpretations, including high-risk drinking behaviours. Policymakers should jettison self-regulation, implement alcohol policies, and introduce LRDG to encourage low-risk drinking. Stand-alone public health interventions that promote abstinence or low-risk drinking behaviours should be developed, while Drinkaware? and DrinkIQ? websites should be avoided. To be effective, all RDMs should include the indigenous language versions.

Abubakar et al. (2021) conducted a systematic search of the literature on PubMed to identify information on drug abuse and drug laws in Nigeria from the inception of the database to March 2020. Using Additional information from Google Scholar, a manual search of included articles, discussion with experts on the subject matter, and gray literature. Their Study selection was performed using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statements. Information from gray literature was assessed for quality and accuracy using the

AACODS checklist (authority, accuracy, coverage, objectively, date, significance). A prevalence of 20 to40% and 20.9% of drug abuse was reported among students and youths, respectively. Commonly abused drugs include cannabis, cocaine, amphetamine, heroin, diazepam, codeine, cough syrup and **tramadol**. Sources where abusers obtained drugs, were pharmacies/patent medicine shops, open drug markets, drug hawkers, fellow drug abusers, friends, and drug pushers. Drug abuse was common among undergraduates and secondary school students, youths, commercial bus drivers, farmers, and sex workers. Reason for use included to increase physical performance, stress and to derive pleasure. Poor socioeconomic factors and low educational background were the common risk factors associated with drug abuse. They identified several drug laws and policies that were established under government agencies such as the National Drug Law Enforcement Agency (NDLEA), National Agency for Foods and Drugs Administration and Control (NAFDAC), Pharmacists Council of Nigeria (PCN) and a Presidential Advisory Committee. They concluded that the burden of drug abuse is still high despite the existing drug laws, policies, and strategies for prevention. Measures to reduce the burden should involve the community, government, and religious bodies. Preventive measures should target the youths, the students, identified sources of the drugs, reasons and risk factors associated with drug abuse in Nigeria.

The work by Ashok *et al.* (2019) observed that mixing of alcohol with other drugs of abuse (such as opioids, cocaine, methamphetamine, nicotine, cannabis, and ?-hydroxybutyric acid) and medications has become an emerging trend, exacerbating the public health concerns and that the phenomenon may additively or synergistically augment the seriousness of the adverse effects such as the withdrawal symptoms, cardiovascular disorders, liver damage, reproductive abnormalities, and behavioral abnormalities. Despite the seriousness of the situation, possible mechanisms underlying the interactions is not yet understood; which has been one of the key hindrances in developing effective treatments. Therefore reviewed the conse-

quences of alcohols interaction with other drugs and decipher the underlying mechanisms

Research findings by Guijin *et al.* (2023) opine that Alcohol can have serious side effects alone and can enhance the side effects of prescription Opioids(like Tramadol) in unpredictable and dangerous ways; they thus suggested that further efforts are needed to minimize the increasing polysubstance-involved overdose mortality among young adults.

This work serves as a modification and an extension to the existing work by the inclusion of a Tramadol compartment; A different mathematical concept is also employed (see Fig. 2).

In the next section, the model of substance co-abuse as a disease will be developed and analyzed.

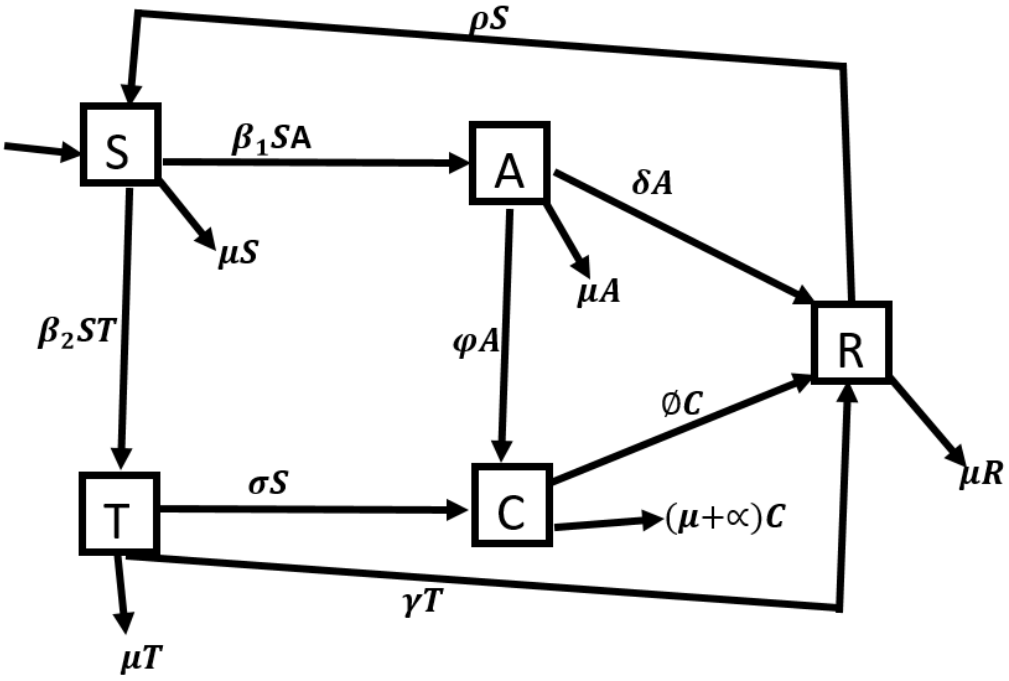
3 Methodology

This work will divide the societal populace into five compartments depending on their substance use status, determine the supposed assumption behind them, formulation of the mathematical model of substance co-abuse with control strategies, establish the existence and positivity, use the Differential Transform Method to solve the model.

The sum total of the entire population, $N(t)$, takes form;

$$N(t) = S(t) + A(t) + T(t) + C(t) + R(t)$$

Figure 3.1: Model Diagram



$S \Rightarrow$ Susceptible Class

$A \Rightarrow$ Alcohol Users

$T \Rightarrow$ Tramadol Users

$C \Rightarrow$ Combined Class

$R \Rightarrow$ Rehab Compartment

$$\frac{dS(t)}{dt} = \Lambda + \rho R - (\beta_1 A + \beta_2 T + \mu)S$$
$$\frac{dA(t)}{dt} = \beta_1 SA - (\psi + \delta + \mu)A$$
$$\frac{dT(t)}{dt} = \beta_2 ST - (\sigma + \gamma + \mu)T$$
$$\frac{dC(t)}{dt} = \sigma T + \psi A - (\phi + \alpha + \mu)C$$
$$\frac{dR(t)}{dt} = \gamma T + \delta A + \phi C - (\rho + \mu)R$$

Assumptions

1. The natural mortality rate is uniform for all compartments.
2. A vulnerable(susceptible) individual can not co-abuse without previously abusing each substance independently
3. Only considered substances are co-abused in this work, such that $\alpha + \beta = 1$
4. Recovered population don't experience relapse, but rather back to the susceptible population
5. We have also assumed that mortality does not occur as a result of either Alcohol or Tramadol use; but its Co-abuse
6. In the absence of substance, all variable(s) except S parameters trade goes to zero

3.1 The Substance Invariant Region

The population size N can be determined by

$$N(t) = S(t) + A(t) + T(t) + C(t) + R(t),$$

The solution of the system remains positive at any point in time if the initial values of all the variables are positive.

Theorem 1

Consider $\Omega = \{S(t), A(t), T(t), C(t), R(t) \in \mathbb{R}^5, S(0) > 0, A(0) > 0, T(0) > 0, C(0) > 0, R(0) > 0\}$, then, the solution of $\{S(t), A(t), T(t), C(t), R(t)\}$ are positive for $t \geq 0$.

Proof :

Boundedness refers to the region in which solutions of the model or system is uniformly bounded in the proper subset $\Omega \subset \mathbb{R}^5_+$.

Looking at the total population at any time (t):

$$N(t) = S(t) + A(t) + T(t) + C(t) + R(t) + C(t),$$

$$\frac{dN(t)}{dt} = \Lambda - \mu S,$$

$$\frac{dN}{dt} = \Lambda + \rho R - (\beta_1 A + \beta_2 T + \mu)S + \beta_1 SA - (\psi + \delta + \mu)A + \beta_2 ST - (\sigma + \gamma + \mu)T + \sigma T + \psi A$$

$$\frac{dN}{dt} = \Lambda + \rho R - \beta_1 SA + \beta_1 SA - \beta_2 ST + \beta_2 ST - \mu S - (\psi + \delta + \mu - \psi - \delta)A - (\sigma + \gamma +$$

$$\Longrightarrow \frac{dI}{}$$

There exists no A, T, C and R in the absence of substance. Thus $A = 0$, $T = 0$, $C = 0$, $R = 0$.

The equation thus becomes

$$\frac{dN}{dt} = \Lambda - \mu S.$$

If the total population N is equal to the number of susceptible S, it implies that $N = S$, such that,

$$\frac{dN}{dt} = \Lambda - \mu N.$$

On integrating both sides of the equation

$\int \frac{dN}{\Lambda - \mu N} \leq \int dt$

$-\frac{In(\Lambda - \mu N)}{\mu} \leq t + C$

$In(\Lambda - \mu N) \leq t + C$

$In(\Lambda - \mu N) \geq -\mu(t + C)$

$(\Lambda - \mu N) \geq e^{-\mu(t+C)}$

$(\Lambda - \mu N) \geq e^{-\mu t} + e^{-\mu C}$

where $e^{-\mu C} = K$. Then $\Lambda - \mu N \geq Ke^{-\mu t}$. Utilizing the condition at $N(0) = S(0)$, $\Lambda - \mu N(0) = K$.

Therefore, $\Lambda - \mu N = (\Lambda - \mu N(0))e^{-\mu(t)}$. Further simplification yields

$N \leq \frac{\Lambda}{\mu} - (\frac{\Lambda - \mu N(0)}{\mu})e^{-\mu(t)}$.

As time tends to infinite, i.e. $t \to \infty$, then the side of population $N \to \frac{\Lambda}{\mu}$.

Deductively, $0 \leq N \leq \frac{\Lambda}{\mu}$ and $N(t) \leq \frac{\Lambda}{\mu}$. Hence,

$\Omega = \{(S, A, T, C, R) \in \mathbb{R}^5_+ : S + A + T + C + R \leq \frac{\Lambda}{\mu}\}$.

3.2 Existence and Positivity of solution

The below results guaranteed by the substance co-abuse model governed in equation (1) is well posed in a feasible region Ω

Lemma 1.2 Suppose the initial conditions be

$$\{S(0) > 0,\ A(0) > 0,\ T(0) > 0,\ C(0) > 0,\ R(0) > 0\} \in \Omega$$

Then the solution set $\{S, A, T, C, R\}(t)$ of the model system is positive $\forall t > 0$

Proof: Employing similar methods in (Gao and Hethcote, 2006), the first equation of the model (1) gives

$$\frac{dS}{dt} = \Lambda + \rho R - (\beta_1 A + \beta_2 T + \mu)S \geq -(\beta_1 A + \beta_2 T + \mu)S$$

$$\implies \frac{dS}{dt} \geq -(\beta_1 A + \beta_2 T + \mu)S$$

Applying the variable separable approach

$$\frac{dS}{S} \geq -(\beta_1 A + \beta_2 T + \mu)dt$$

Applying integrals to both sides

$$\int \frac{dS}{S} \geq -\int -(\beta_1 A + \beta_2 T + \mu)dt$$

$$\ln S(t) \geq -(\beta_1 A + \beta_2 T + \mu)t + C$$

$$\implies S(t) \geq K \exp(-[\beta_1 A + \beta_2 T + \mu]t)$$

At time $t = 0$ and applying the initial conditions yield

$$S(0) \geq 0$$

In a likewise manner

$$A(t), \quad T(t), \quad C(t) \quad \text{and} \quad R(t) > 0 \quad \forall t \geq 0$$

3.3 Stability Analysis of the Model

3.4 Basic Reproduction Number of Substance Abuse R_0

This is the average number of secondary cases per infectious case in a population made up of both susceptible and non-susceptible hosts. Here, we term it expected number of new substance abusers that arose by initial abuser in a susceptible population. Thus, R_0 is seen as a Threshold term to determine the condition for abusers outbreak

3.5 Substance Abuse Basic Reproduction Number

Here, we will use the concepts of Next Generation Matrix (Shaibu etal, 2018) to establish the linear stability of the substance-free equilibrium. The basic reproduction number is the number of secondary infections produced by one infected person in a completely susceptible population.

The reproduction number combines the biology of infections with the social and behavioral factors causing contact rates (Van den Driessche P., 2017).

The basic reproduction number R_0 is defined as the spectral radius of the next generation matrix.

Definition: The spectral radius of a matrix X is defined as the maximum of the absolute values of the matrix

$$\text{i.e. } \rho(X) = \sup\{|\lambda| : \lambda \in \rho(X)\}$$

with $\rho(X)$ representing the set of eigenvalues of the matrix X.

3.6 Substance Co-Abuse Basic Reproduction Number by Next Generation Matrix

Theorem 1.2 Li (2002) stated that suppose F a non zero non negative matrix and V a non-singular M-matrix such that $F - V$ is irreducible.

Then

$$R_0 = \rho(FV^{-1})$$

and R_0 is the reciprocal of the smallest positive root x of the polynomial equation

Proof: From the assumptions,

$$FV^{-1}$$

is a non-zero non-negative matrix, and by Li etal.(2002) and Perron-Frobenius theory the principal submatrix corresponding to the non-zero rows of F is irreducible.

Thus

$$\lambda = \rho(FV^{-1}) > 0$$

is the largest positive root of the polynomial equation

$$\det(\lambda I - FV^{-1}) = 0$$

Since V is non-singular and $\lambda > 0$, the polynomial equation is equivalent to

$$\det(F\lambda^{-1} - V) = 0$$

(where $V - F\lambda^{-1}$ is a singular M-matrix) and λ^{-1} is the smallest positive root. The proof suffices from the definition of

$$R_0 = \rho(FV^{-1})$$

Next Generation matrix: This is the method used to derive the basic reproduction number, for a compartmental model of the spread of substance abuse.

Deriving R_0 with the next generation matrix (Van den Driessche, 2017) is sometimes difficult whenever the dimension of the model is increasing. An option of solution to

this problem is employing the graph-theoretic method (de-Camino-Beck etal, 2009) to derive the reproduction number R_0 in a simpler form.

Computing R_0, we first assume $f_i(x)$ the rate of appearance of new abusers in compartment i, and $v_i(x)$ the net reducing rate of substance abusers in compartment i due to substance abusers flow inside system of abusers compartments.

Supposing

$$F = (f_1, \cdots, f_{2n}) \text{ and}$$

$$V = (v_1, \cdots, v_{2n}),$$

Let partition the derivative

$$TF(E_0)$$

and $TV(E_0)$ as

$$TF(E_0) = \begin{pmatrix} F & 0 \\ 0 & 0 \end{pmatrix}, \; TV(E_0) = \begin{pmatrix} V & 0 \\ J_3 & J_4 \end{pmatrix}$$

with

$$F = \begin{pmatrix} \frac{\partial F_1}{\partial A} & \frac{\partial F_1}{\partial T} & \frac{\partial F_1}{\partial C} \\ \frac{\partial F_2}{\partial A} & \frac{\partial F_2}{\partial T} & \frac{\partial F_2}{\partial C} \\ \frac{\partial F_3}{\partial A} & \frac{\partial F_3}{\partial T} & \frac{\partial F_3}{\partial C} \end{pmatrix} (x_0)$$

$$V = \begin{pmatrix} \frac{\partial V_1}{\partial A} & \frac{\partial V_1}{\partial T} & \frac{\partial V_1}{\partial C} \\ \frac{\partial V_2}{\partial A} & \frac{\partial V_2}{\partial T} & \frac{\partial V_2}{\partial C} \\ \frac{\partial V_3}{\partial A} & \frac{\partial V_3}{\partial T} & \frac{\partial V_3}{\partial C} \end{pmatrix} (x_0)$$

Suppose $X = (S,\ A,\ T,\ C,\ R,)^T$, thus F and V can be derived from the model equation; also with its Jacobian matrices at substance-free equilibrium.

Thus $R_0 = \Gamma(FV^{-1})$

with Γ, the spectral radius

Using the Next Generation Matrix, we can derive the threshold value for substance co-abuse.

We recall that set of D.Es for Model 1 is;

$$\begin{aligned}
\frac{dS(t)}{dt} &= \Lambda + \rho R - (\beta_1 A + \beta_2 T + \mu)S \\
\frac{dA(t)}{dt} &= \beta_1 SA - (\psi + \delta + \mu)A \\
\frac{dT(t)}{dt} &= \beta_2 ST - (\sigma + \gamma + \mu)T \\
\frac{dC(t)}{dt} &= \sigma T + \psi A - (\phi + \alpha + \mu)C \\
\frac{dR(t)}{dt} &= \gamma T + \delta A + \phi C - (\rho + \mu)R
\end{aligned}$$

Setting the Jacobian matrix of the system of differential equations, we have Thus

$R_0 = \frac{\beta_1 S}{\beta_1 S - \phi - \delta - \mu}$

At equilibrium

$$\begin{aligned}
\frac{dT}{dt} &= \beta_2 ST - (\sigma + \gamma + \mu)T = 0 \\
\beta_2 ST &= (\sigma + \gamma + \mu)T \\
S &= \frac{\sigma + \gamma + \mu}{\beta_2}
\end{aligned}$$

$$F = \begin{pmatrix} -\beta_1 S & -\beta_2 S & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}, \quad V = \begin{pmatrix} (\phi + \delta + \mu) - \beta_1 S & -0 & 0 \\ 0 & (\sigma + \delta + \mu) - \beta_2 S & 0 \\ -\phi & -\sigma & (\phi + \delta + \mu) \end{pmatrix}$$

$$V^{-1} = \begin{pmatrix} \frac{1}{\beta_1 S - \phi - \delta - \mu} & 0 & 0 \\ 0 & \frac{1}{-\beta_2 S + \gamma + \mu + \sigma} & 0 \\ \frac{\phi}{(\beta_1 S - \phi - \delta - \mu)(\phi + \alpha + \mu)} & \frac{\sigma}{(-\beta_2 S + \gamma + \mu + \sigma)(\phi + \alpha + \mu)} & \frac{1}{\phi + \delta + \mu} \end{pmatrix}$$

$$FV^{-1} = \begin{pmatrix} \frac{\beta_1 S}{\beta_1 S - \phi - \delta - \mu} & \frac{\beta_1 S}{-\beta_2 S + \gamma + \mu + \sigma} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

Thus $R_0 = \frac{\beta_1 S}{\beta_1 S - \phi - \delta - \mu}$

suppose $Z = \frac{1}{V}$ i.e V^{-1}, thus

$$F \cdot V^{-1} = \begin{bmatrix} \frac{\beta_1 S}{\beta_1 S - \delta - \mu - \psi} & \frac{\beta_2 S}{\beta_2 S - \gamma - \mu - \sigma} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

$$R_0 = \Gamma(F \cdot V^{-1})$$

$$R_0 = \frac{\beta_1 S}{\beta_1 S - \delta - \mu - \psi} \tag{3.1}$$

Thus;

$$R_0 = \Gamma(F \cdot V^{-1}) = \frac{\beta_1 S}{\beta_1 S - \delta - \mu - \psi}$$

At equilibrium;

$$\frac{dT(t)}{dt} = \beta_2 ST - (\sigma + \gamma + \mu)T = 0$$

Which implies $\beta_2 ST = (\sigma + \gamma + \mu)T$

Thus $S = \frac{\sigma + \gamma + \mu}{\beta_2}$

Inputting this value of S in R_0, we have;

$$R_0 = \frac{\beta_1(\sigma + \gamma + \mu)}{\beta_1(\sigma + \gamma + \mu) - \beta_2(\delta + \mu + \psi)}$$

We deduce that; the substance-free equilibrium $E_0\left(\frac{\triangle}{\mu},\ 0,\ 0,\ 0,\ 0\right)$ associated with the mode set of D.Es is locally asymptotically stable iff $R_0 < 1$ i.e. substance co-abusers gets rehabilitation.

E_0 becomes unstable iff $R_0 > 1$ i.e. the act of co-abuse of substance is prevalent.

Table 1: Parameter Values

Parameter	Value	Unit	Source
$\wedge$	1500	$\frac{\text{people}}{\text{year}}$	Assumed
β_1	0.25	$\frac{1}{\text{year}}$	Bhunu & Mushayabasa (2012), Vol 2
β_2	0.20	$\frac{1}{\text{year}}$	Farai et al (2010)
ψ	0.40	$\frac{1}{\text{year}}$	UNODC (2021), Vol 3
δ	0.20	$\frac{1}{\text{year}}$	(Assumed)
μ	0.02	$\frac{1}{\text{year}}$	Li & Ma (2018)
σ	0.35	$\frac{1}{\text{year}}$	(Assumed), Vol 3
γ	0.30	$\frac{1}{\text{year}}$	Farai et al. (2010), Vol 3

Parameter	Description
$\wedge$	rate of recruitment into susceptible class
β_1	rate at which individuals imitate colleagues who takes alcohol
β_2	rate at which individuals imitates colleagues who takes tramadol
μ	natural death rate
ψ	rate at which alcohol users co-abuse with tramadol
σ	rate at which tramadol users co-abuse with alcohol
α	mortality rate arising from co-abuse
δ	alcohol users recovery rate
γ	tramadol users recovey rate
ϕ	recovery rate of co-abusers
ρ	susceptible return rate of recovered population

Table 2: Initial Conditions for each point for variables and source

Variables	Value	Source
$S(t)$	500	UNODC (2021)
$A(t)$	250	,,
$T(t)$	150	,,
$C(t)$	100	,,
$R(t)$	120	,,

4 Sensitivity Analysis of Substance Co-Abuse

Sensitivity analysis is the study of how the uncertainty in the output of a mathematical model or system can be divided and allocated to different sources of uncertainty in its inputs.

Parameter contribution analysis are usually meant to determine the effectiveness of the reproduction number. Usually, parameter values and model assumptions can be influenced as a result of changes and errors in the process of formulation and computing the reproduction number. Therefore sensitivity analysis are conducted to determine those changes and sources of error and their impact to the model (Renske et al, 2010). It is a technique that is mostly used by modelers whose objectives are to assist and support decision makers by providing with them informed decisions base on analysis of dynamic of the model. However, authors in (Renske et al, 2010), presented similar analogue that explains that models and parameters usually are uncertain. This analysis are usually required to determine on how sensitive they are to parameter values and determine which is the most sensitive parameter of the reproduction number. Hence, the uncertainty effects of the parameter is solely the cause sensitivity analysis.

The sensitivity analysis of a model parameter is normally evaluated by relating each parameter to the reproduction number, R_0. The sensitivity of a variable β_1 is

given by the below;

$$R_0 = \frac{\beta_1 \left(\frac{\sigma+\gamma+\mu}{\beta_2}\right)}{\beta_1 \left(\frac{\sigma+\gamma+\mu}{\beta_2}\right) - \phi - \delta - \mu}$$

$$= \frac{\beta_1(\sigma+\gamma+\mu)}{\beta_2} - \frac{\beta_1(\sigma+\gamma+\mu) - \beta_2(\delta+\mu+\phi)}{\beta_2}$$

$$R_0 = \frac{\beta_1(\sigma+\gamma+\mu)}{\beta_1(\sigma+\gamma+\mu) - \beta_2(\delta+\mu+\phi)}$$

$$S_{\beta_1}^{R_0} = \frac{\partial R_0}{\partial \beta_1}.\frac{\beta_1}{R_0}$$

$$= \frac{(\sigma+\gamma+\mu)\beta_2(\delta+\mu+\phi)}{(\beta_1(\sigma+\gamma+\mu) - \beta_2(\delta+\mu+\phi))^2} \times \frac{\beta_1[\beta_1(\sigma+\gamma+\mu) - \beta_2(\delta+\mu+\phi)]}{(\sigma+\gamma+\mu)\beta_2}$$

$$= \frac{\beta_2(\delta+\mu+\phi)}{(\beta_1(\sigma+\gamma+\mu) - \beta_2(\delta+\mu+\phi))^2} \times \frac{\beta_1[\beta_1(\sigma+\gamma+\mu) - \beta_2(\delta+\mu+\phi)]}{(\sigma+\gamma+\mu)\beta_1}$$

$$= \frac{\beta_2(\delta+\mu+\phi)}{(\beta_1(\sigma+\gamma+\mu) - \beta_2(\delta+\mu+\phi))}$$

$$S_{\beta_2}^{R_0} = \frac{\partial R_0}{\partial \beta_2}.\frac{\beta_2}{R_0}$$

$$= \frac{-(\sigma+\gamma+\mu)\beta_1(-\delta-\mu-\phi)}{(\beta_1(\sigma+\gamma+\mu) - \beta_2(\delta+\mu+\phi))^2} \times \frac{\beta_2[\beta_1(\sigma+\gamma+\mu) - \beta_2(\delta+\mu+\phi)]}{(\sigma+\gamma+\mu)\beta_1}$$

$$= \frac{-\beta_2(-\delta-\mu-\phi)}{(\beta_1(\sigma+\gamma+\mu) - \beta_2(\delta+\mu+\phi))} = \frac{\beta_2(\delta+\mu+\phi)}{(\beta_1(\sigma+\gamma+\mu) - \beta_2(\delta+\mu+\phi))}$$

$$S_{\sigma}^{R_0} = \frac{-\beta_1\beta_2(\delta+\mu+\phi)}{(\beta_1(\sigma+\gamma+\mu) - \beta_2(\delta+\mu+\phi))^2} \times \frac{\sigma[\beta_1(\sigma+\gamma+\mu) - \beta_2(\delta+\mu+\phi)]}{\beta_1(\sigma+\gamma+\mu)}$$

$$= \frac{-\beta_2\sigma(\delta+\mu+\phi)}{(\sigma+\gamma+\mu)[\beta_1(\sigma+\gamma+\mu) - \beta_2(\delta+\mu+\phi)]}$$

$$S_{\gamma}^{R_0} = \frac{-\beta_1\beta_2(\delta+\mu+\phi)}{(\beta_1(\sigma+\gamma+\mu) - \beta_2(\delta+\mu+\phi))^2} \times \frac{\gamma[\beta_1(\sigma+\gamma+\mu) - \beta_2(\delta+\mu+\phi)]}{\beta_1(\sigma+\gamma+\mu)}$$

$$= \frac{-\beta_2\gamma(\delta+\mu+\phi)}{(\sigma+\gamma+\mu)[\beta_1(\sigma+\gamma+\mu) - \beta_2(\delta+\mu+\phi)]}$$

$$S_{\delta}^{R_0} = \frac{-\beta_1\beta_2(\delta+\mu+\phi)}{(\beta_1(\sigma+\gamma+\mu)-\beta_2(\delta+\mu+\phi))^2} \times \frac{\delta[\beta_1(\sigma+\gamma+\mu)-\beta_2(\delta+\mu+\phi)]}{\beta_1(\sigma+\gamma+\mu)}$$

$$= \frac{-\beta_2\delta}{(\sigma+\gamma+\mu)[\beta_1(\sigma+\gamma+\mu)-\beta_2(\delta+\mu+\phi)]}$$

$$S_{\phi}^{R_0} = \frac{-\beta_1\beta_2(\delta+\mu+\phi)}{(\beta_1(\sigma+\gamma+\mu)-\beta_2(\delta+\mu+\phi))^2} \times \frac{\phi[\beta_1(\sigma+\gamma+\mu)-\beta_2(\delta+\mu+\phi)]}{\beta_1(\sigma+\gamma+\mu)}$$

$$= \frac{-\beta_2\phi}{(\sigma+\gamma+\mu)[\beta_1(\sigma+\gamma+\mu)-\beta_2(\delta+\mu+\phi)]}$$

$$S_{\mu}^{R_0} = \frac{-\beta_1\beta_2(\sigma+\gamma-\delta-\phi)}{(\beta_1(\sigma+\gamma+\mu)-\beta_2(\delta+\mu+\phi))^2} \times \frac{\mu[\beta_1(\sigma+\gamma+\mu)-\beta_2(\delta+\mu+\phi)]}{\beta_1(\sigma+\gamma+\mu)}$$

$$= \frac{-\beta_2\mu(\sigma+\gamma-\delta-\phi)}{(\sigma+\gamma+\mu)[\beta_1(\sigma+\gamma+\mu)-\beta_2(\delta+\mu+\phi)]}$$

$$S_{\beta_1}^{R_0} = \frac{0.2(0.2+0.02+0.4)}{0.25(0.35+0.3+0.02)-0.2(0.2+0.02+0.4)} = \frac{0.2(0.62)}{0.25(0.67)-0.2(0.62)} = 2.8506$$

$$S_{\beta_2}^{R_0} = \frac{0.2(0.2+0.02+0.4)}{0.25(0.35+0.3+0.02)-0.2(0.2+0.02+0.4)} = 2.8506$$

$$S_{\gamma}^{R_0} = \frac{-0.3\dot{0}.2(0.2+0.02+0.4)}{(0.35+0.3+0.02)(0.435)} = -0.1276$$

$$S_{\sigma}^{R_0} = \frac{-0.35\dot{0}.2(0.2+0.02+0.4)}{(0.35+0.3+0.02)(0.435)} = -0.1489$$

$$S_{\delta}^{R_0} = \frac{-0.2\dot{0}.2}{0.435} = \frac{-0.04}{0.435} = -0.9195$$

$$S_{\phi}^{R_0} == \frac{-0.4\dot{0}.2}{0.435} = \frac{-0.08}{0.0435} = -1.8391$$

$$S_{\mu}^{R_0} = \frac{-0.02\dot{0}.2(0.35+0.3-0.2-0.4)}{(0.35+0.3+0.02)(0.0435)} = \frac{-0.004(0.05)}{0.0435} = 0.0046$$

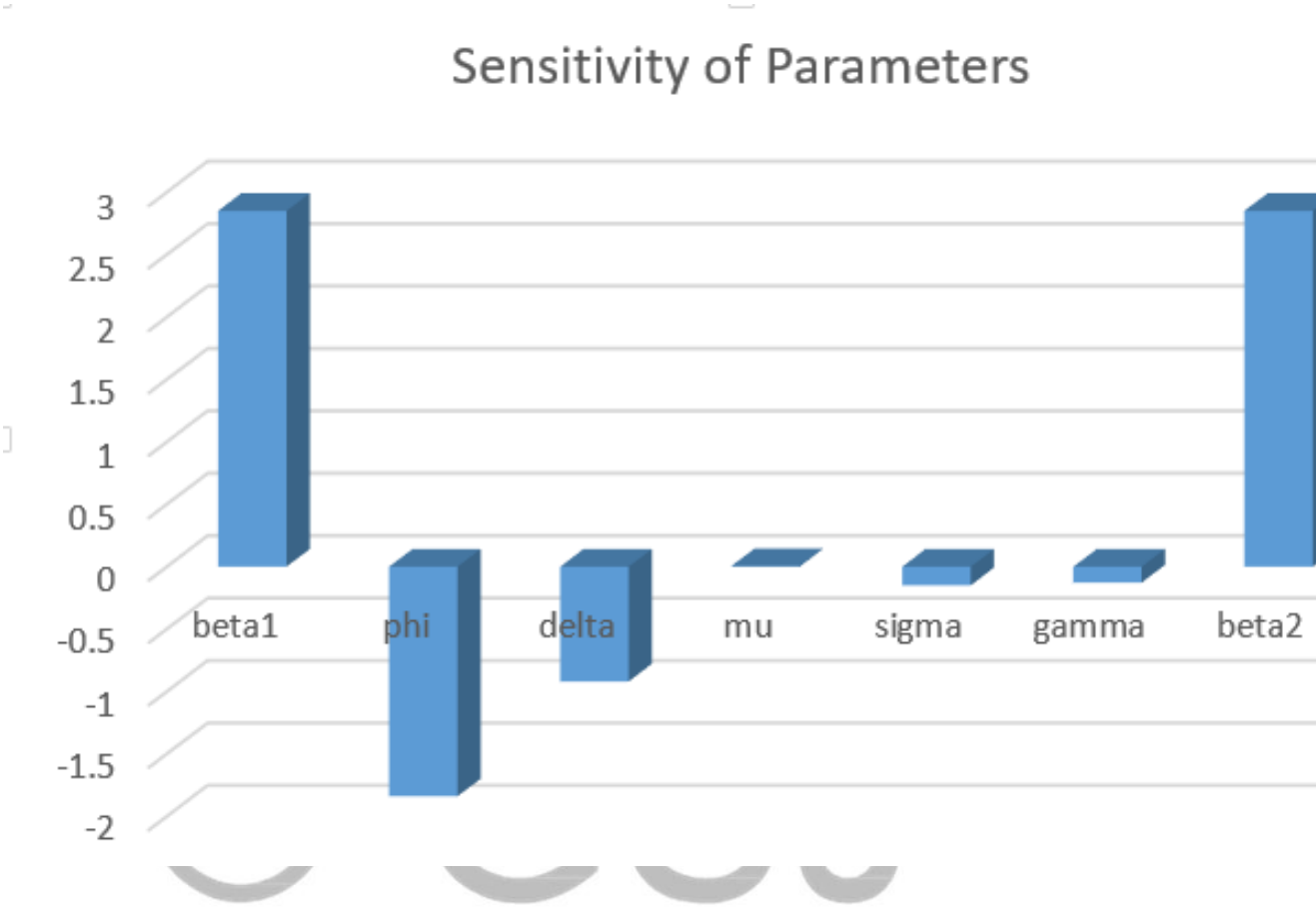


Figure 4.1: Model Diagram

The sign of the sensitivity index in table 1 indicates the contribution of each parameter to the drug abuse number. The essence of this work is to help reduce the co-abuse of drugs with specifics to alcohol and tramadol. Therefore, the contribution of each parameter is an important factor in determining which parameter contributes to the spread of substance among population.

Analysis have however shown a significant contribution of the alcohol and tramadol imitation rates of individuals β_1 and β_2 respectively to the susceptible compartment. The implication is that, as more susceptible individuals imitate to the intake of both alcohol and tramadol independently, the co-abuse will more likely increase and this would lead to the continuous co-abuse of substances by individuals in the population. However, the magnitude of the values of the recovery rate of

individuals who abuse alcohol is an indications that, it best helps in the reduction of the value of the substance co-abuse number; which would inturn assist in curbing the co-abuse of substances of alcohol and tramadol usage.

5 Results and Discussion

This research centres on derivation of our sensitive parameters through sensitivity analysis. We began by approach of deriving the basic reproduction number R_0, known as the Next Generation Matrix method for modelling substance(s) co-abuse; this approach is equivalent to Gaussian elimination & digraph reduction method, and since the rules of digraph reduction method does not take the path of direct calculation of matrix inverse or determinants, this approach can be practical for larger systems.

6 Conclusion

In this research, the next generation matrix method was employed to compute the threshold number for the co-abuse of substance, R_0. The co-abuse of alcohol and tramadol would continue to spread among the populace if the reproduction number is greater than one and the co-abuse of substances would die out of the system if R_0 is less than one (1).

Sensitivity Analysis showed a significant contribution of the alcohol and tramadol imitation rate of individuals to the susceptible compartment; implying that as more susceptible individuals imitate the intake of both alcohol and tramadol independently, the co-abuse will more likely increase and this would lead to the continuous co-abuse of substances by individuals in the populace. Thus we need to promote social programs that raise awareness of the dangers posed by Alcohol and Tramadol co-abuse, through educational campaigns in learning institutions, social

media, counsellings and sanatoriums; also transmission control must focus on enhancing the quitting process while promoting support services to substance users during and after treatment to minimize cases of retrogression

In a more developing studies, an optimal control approach to the spread of substance co-abusers population is examined using apprehension, prosecution and/or jailing facilities as a strategy for control.

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