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A Binary Stability and Monte Carlo Simulation Analysis of the Simultaneous Impact of Smoking on the Dynamics of Lung Cancer

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Abstract
In this study, the mathematical model of the dynamics of Lung cancer defined by system of non-linear ordinary differential equations was investigated. The study considered a binary stability and Mente Carlos simulation analysis approach in the determination of the impact of cigarette smoking on Lung Cancer prevalence. The analysis of a total population size in a region N(t) at any time t which is subdivided into five compartments such as, S(t) (susceptible population that is the vulnerable subpopulation who are not infected with lung cancer, but at a high risk of infection as a result of smoking), population who are active smoker E_a(t) , population who are victim of smoking Ep (t), number of individual infected with lung cancer I(t) and number of population recovered from lung cancer R(t) was involved in the study. The positivity, uniqueness and boundedness of solutions were verified whereas the sensitivity and basic reproductive number was determined analytically. The study adopted numerical approach to achieve the objectives. On the binary stability states across parameter ranges, results obtained shows a critical value which marks the threshold for bifurcation, indicating a shift in system behaviour. The transitions are sharp in these simplified models, ideal for illustrative purposes. The sensitivity of five eigenvalues (λ1 through λ5) to changes in various parameters (r, m, g, d, h, e, f) was obtained. Generally, it is observed that on parameter dominance, the parameter m shows the highest sensitivity across all eigenvalues, with consistently positive and significant values. This suggests m is the most influential parameter in the system, Having a high positive sensitivity to parameter m (value 0.95 with negligible to no sensitivity to other parameters, except for a slight negative sensitivity to r (-0.05) and h (-0.01). this implies the behavior of λ1 is predominantly influenced by m, while the other parameters play a minimal role. Also, the results of a Monte Carlo simulation for seven parameters highlighting their mean values and 95% confidence intervals (CIs) with a growth rate (r) mean around 0.048 and mortality rate (m) has a noticeably higher mean, around 0.097. the study has provided provides a conceptual framework to model how behaviours like smoking lead to drastic changes in health outcomes. And understanding the thresholds can inform public health policies, emphasizing the importance of early cessation before reaching critical levels of exposure.

Keywords: Lung Cancer, Cigarette Smoking, Mathematical Model, sensitivity analysis, Binary Stability, Mente Carlos Simulation.

Introduction

One of the importance of health informatics modelling is the use of ordinary differential equations to study the infectious disease transmission and control dynamics. A lot of studies on infectious diseases has been carried out by experts in mathematical modelling and simulations, Biomathematics, and Epidemiology of Chronic Diseases (Nwagor, 2020; Ilmayasinta et al., 2021). Lung cancer is the leading cause of cancer deaths worldwide with approximately 2.09 million new diagnoses each year and around 1.76 million deaths (Biswas et al, 2014). In 2018 lung cancer is estimated to be the second top most prevalent cancers in the world according to the number of new incidences and be at the top of the list according to number of deaths. Bangladesh (one of the most populous countries of the world) are facing danger with cancer disease with 13 to 15 lakh cancer patients and about 2 lakh patients are newly diagnosed each year. Lung cancer can start anywhere in the lungs and affect any part of the respiratory system. Unlike normal cells, cancer cells grow without control and destroy the healthy lung tissue around them. This growth can spread, or metastasize, beyond the lung to the lymph nodes by the process of metastasis into nearby tissue or other parts of the body. Smoking tobacco is by far the leading cause of lung cancer and about 80% of lung cancer deaths are caused by smoking. Other diseases caused by smoking includes the following; Heart Disease, Chronic Obstructive Pulmonary Disease (COPD), Respiratory Problems, Cancer,

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Premature Birth: Gum Disease and Tooth Loss, Eye Problems, Weakened Bones, Memory Loss and Cognitive Decline.

It is important to remember that quitting smoking can greatly reduce the risk of developing these health problems, as well as improve overall health and well-being. If you or someone you know is a smoker, there are many resources available to help quit. You can start by talking to a doctor, reaching out to a support group, or using nicotine replacement therapy or prescription medications to aid in quitting. This research work involved a linear Ordinary differential equation of SEIR (susceptible, Exposed, Infected and Recovered) model describing smoking dynamics which has no Closed form solution. Analytical Solutions without an approximate result was adopted by most researchers. Hence, the technique of numerical Simulation was adopted to study the Interaction between the variables and parameters of the lung infections. Alternative approach of mathematical modelling in predicting the control of the cancer induced lung infection without considering a clinical approach was Involved in this research.

Modeling the dynamics of the impact of smoking on the lungs can be done through various mathematical and computational approaches, including: Ordinary Differential Equations (ODEs) for the descriptions of the rates of change of lung function and damage over time. Partial Differential Equations (PDEs) used in modelling the spatial and temporal dynamics of lung damage and inflammation. Agent-Based Models (ABMs), for simulation of the interactions between lung cells, inflammatory agents, and smoke particles. A Network Models which represents the interactions between different lung regions and the spread of damage. Also, Machine Learning (ML) and Artificial Intelligence (AI), used in the analysis of medical images and predict lung function decline. The aim this study is to define an appropriate mathematical model for the analysis of Simultaneous impact of Smoking on the Dynamics of Lung Cancer Disease.

SEIR-DRIVEN Approach

In the considerations of all the fatalities of lung cancer, model-based study on lung cancer was discussed by many mathematicians. A number of mathematical models have been proposed on smoking behavior and lung cancer. Acevedo-Estefania et al. (2000) constructed the model to describe the dynamics of lung cancer at the population level caused by smoking and second-hand smoke. The model determined that the best way to lower the number of smokers and individuals developing lung cancer is by increasing the number of well-educated individuals about the effect of smoking.

Andest (2013) also formulated a mathematical model that describes nicotine accumulation in lung of a smoker which is the main cause of lung cancer. Wardah et al. (2017) presented a mathematical model that discuss of lung cancer as the effect of smoking behavior on both active and passive smoker. Trisilowati (2019) analyze the stability as well as used optimal control strategy to Wardah et al. (2017) model and illustrate that the optimal control is effective to control the growth of passive, active smoker and lung cancer patient. There is an extensive body of work which develops models associating with the treatment of cancer using chemotherapy, radiotherapy, targeted agent treatment etc (Pang et al., 2015). Beljanski et al. (2012) mentioned that multi-drug resistance to this therapeutic treatment is the major cause of failure in clinical therapeutic treatment. Genetically modified oncolytic viruses (OVs) kill tumor cell via completely unique mechanisms compare to other therapeutic treatments. Thus Beljanski et al. (2012) claims that treatments with oncolytic viruses (OVs), which is under development will open the possibility to overcome drug resistance and module the immune response to fight against cancer.

Taking the above discussions into account, we propose a model to study the dynamics of lung cancer and its relation with smoking. Many theopretical as well as mathematical models of lung cancer have been proposed by researchers. But this is a newly proposed mathematical model of lung cancer on the basis of some basic assumptions. We observed from real phenomena that patients recovered from lung cancer are not out of danger at all. They can be affected with lung cancer again. It indicates that people recovered from lung cancer are becoming susceptible again and can develop this fatal disease for multiple time. So, the SEIR model will be more realistic and effective than other SIR or SEIR model discussed above. Our goal is to study the disease dynamics of lung cancer and the relation between smoking and lung cancer both analytically and numerically.

SIRS Susceptible (S), Infected (I) recovery (R) and susceptible (S)] model is extension of the SIR (susceptible, Infected, Recovered) model where it is believed that individuals can become Coronavirus infections have been studied by many researchers and epidemiologists to curtail the disease and its further spread in the community. The researchers tried to develop the vaccine and vaccinated most of the individuals in order to better reduce the

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number of infected people and their future spread. Although, with the passage of time and the emergence of the new variants of COVID-19, the world still facing infections in many countries. Some mathematical models in integer and non-integer order to study the infectious diseases are discussed in this paper. For example, the early infection of COVID-19 in China through a very comprehensive mathematical model is discussed in Atangana (2020). The optimal control analysis for the elimination or control of the disease in Pakistan, by considering the real viral disease cases has been studied in Atangana, (2021). The viral infection is transferrable to other healthy humans very fast, so the best and most effective way is to reduce the infection, is the isolation and quarantine, which is discussed through a mathematical modelling approach by the authors in (Atangana et al., 2021). Lockdown and its impact on disease control was also considered using an SEIR modelling approach while adopting real data from Italy and France and presented the disease control scenario for the epidemic. Different reported cases and their modelling in Nigeria, with comparison, have been discussed in (Sun et al., 2020). A fractional study on infectious disease to address the isolation, quarantine, and environmental vital loads has been explored. A robust study on infectious disease in a fractional environment is considered in (Ali et al., 2021; Zang et al., 2020; Haidong, et al 2022).

Fractional calculus is gaining attention from researchers around the world due to its many properties and its applications to physical and engineering problems. The heredity properties, the memory, and the crossover behaviour can only be observed in a model with a fractional-order system (Jim et al., 2022). The fractional calculus with different fractional operators and their applications have been found, in integro-differential equations (Wang 2022), the development in the operators (Nazir et al., 2021), application to epidemiology (Nabi et al., 2021), application to wave dynamics equations, etc. The COVID-19 model with time delay and stochastic differential equation is explored. (Lu et al, 2020; Rihan et al, 2022)

Materials and Methods

A mathematical model of a system of nonlinear ordinary differential equations (ODEs) governed in this study. The basic reproduction number will be determined by next generation matrix. The condition for the existence of equilibrium points (smoke free and endemic equilibrium points) and their stability analysis will be investigated. The study considered a total population size in a region is N(t) at any time t which is subdivided into five compartments such as, S(t) (susceptible population that is the vulnerable subpopulation who are not infected with lung cancer, but at a high risk of infection as a result of smoking), population who are active smoker E_a(t) , population who are victim of smoking Ep (t), number of individual infected with lung cancer I(t) and number of population recovered from lung cancer R(t) . Considering the above compartments, the mathematical model of the dynamics of Lung cancer can be represented by the following system of non-linear ordinary differential equations

$$\frac{dS}{dt} = r - (a+b)E_aS - mS + hR \quad (1)$$

$$\frac{dE_a}{dt} = aE_aS + eE_p - gE_a - mE_a \quad (2)$$

$$\frac{dE_p}{dt} = bE_aS - eE_p - dE_p - mE_p \quad (3)$$

$$\frac{dI}{dt} = gE_a + dE_p - SI - (m+f)I \quad (4)$$

$$\frac{dR}{dt} = SI - (m+h)R \quad (5)$$

In the above model, r is the natural growth rate of population, m is the natural mortality rate, a and b is rate at which susceptible population become active and passive smoker respectively. We are not involving the interaction between passive and active smoker population and e is the rate of passive smoker transforming into active smoker. The constant g and d represent the rate at which active and passive smoker become infected with lung cancer.
The constant s represents the recovery rate from lung cancer by getting proper treatment and f represents the disease induced death rate. In real life, despite of getting treatment and recovered from lung cancer, people may become susceptible of lung cancer again and the rate is denoted by h.

The model (1-5) can be analyzed in order to describe the dynamics of lung cancer. The desire of this analysis is to show the effect of smoking in lung cancer and the object of this analysis is to control the adverse situation from locality. Since it is impossible to find the exact solution of the nonlinear autonomous system (1-5), the qualitative behaviour of the solutions in the neighbourhood of the equilibrium points is analysable. First, we find the boundedness and positivity of the solutions then find out the equilibrium points followed by analyzing the stability of the equilibrium points and basic reproduction number $R0$. The basic reproduction ratio is important because it

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tells us if a disease will persist or extinct. For the analysis of model (1-5), a closed set has been considered as

$$\Omega = \left\{\left(S(t), E_a(t), E_p(t), I(t), R(t)\right) \in i_+^s | 0 \leq N \leq \frac{r}{\mu}\right\}$$

$$with\ initial\ condition\ S(0) > 0, E_a(0) \geq 0, E_p(0) \geq 0, I(0) \geq 0, R(0) \geq 0$$

Table 1: Definitions and values of Parameters of the Model

Descriptions	Parameters	Values
growth rate of population	*r*	0.05 d-1
natural mortality rate	*m*	0.01 d-1
active smoker recruitment rate from susceptible population	*a*	0.25
rate of population become victim of smoking	*b*	0.75
rate of population migrate from victim group to smokers	*e*	0.35
smoker's lung cancer incidence rate	*g*	0.2
lung cancer incidence rate from victim group	*d*	0.05
lung cancer recovery rate	*s*	0.2
cancer incident mortality rate	*f*	0.6
migration rate from recovered to susceptible compartments	*h*	0.5

Model Analysis

Sensitivity Analysis

This is the study of how the sensitivity in the output of a mathematical model or system (numerical or otherwise) can be. It is a method to determine the robustness of an assessment by examining the extent to which results are affected by changes in methods, models, values of unmeasured variables, or assumptions to identify results that are most dependent on questionable or unsupported. It is an assessment of the sensitivity of a mathematical model to its modeling assumptions and is sometimes called "simulation analysis"

This equilibrium point represents a population with endemic lung cancer.

Monte Carlo simulation analysis

Monte Carlo simulation is a computational technique used to model and analyze systems that are influenced by uncertainty or randomness. It relies on repeated random sampling to obtain numerical results. Here's a breakdown of the concept:

The Core Idea

Monte Carlo simulation uses probability and random sampling to simulate real-world processes or systems. By performing a large number of simulations, it provides insight into the range of possible outcomes and their probabilities.

2. Key Steps in a Monte Carlo Simulation

1. Define the Problem or System: Identify the uncertain parameters or variables influencing the system.
2. Specify the Probability Distributions: Assign probability distributions (e.g., uniform, normal) to each uncertain variable based on available data or assumptions.
3. Generate Random Samples: Use random sampling to generate possible values for each variable according to its distribution.
4. Perform Calculations: Simulate the system or process using the sampled values, calculating the outcome for each iteration.
5. Repeat: Repeat the simulation many times (e.g., 10,000 iterations) to capture the full range of outcomes.
6. Analyze Results: Aggregate the outcomes to calculate summary statistics (mean, variance, percentiles) or visualize distributions.

Applications of Monte Carlo Simulation

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- Finance: Assessing risk, pricing options, or projecting portfolio performance.
- Engineering: Evaluating system reliability under varying conditions.
- Science: Modeling physical processes like particle physics or weather forecasting.
- Business: Estimating project completion times and costs.
- Medicine: Predicting the spread of diseases or treatment outcomes.

4. Advantages

- Flexibility: Can model complex systems with multiple sources of uncertainty.
- Insightful: Provides a full probability distribution of outcomes rather than a single estimate.
- Realistic: Accounts for randomness and variability in inputs.

Monte Carlo methods are powerful tools for decision-making in uncertain environments, offering probabilistic insights to complement deterministic models**.**

Numerical Results

We perform numerical simulations of our model proposed in (1-5) by the ODE45-solver using MATLAB programming. All the values of the parameters used in Table 1, are obtained from different organizations such as the CDC (Center for Disease Control), the American Lung Cancer Society, WCRF (world cancer research foundation), WHO (world health organization) Global cancer observatory (GLOBOCAN) and other non-profit and government agencies. The available data from this source and the approximate result have been taken, which will fit our model more appropriately.

Results

The theoretical analysis of the time delay model proposed in this study is fully established, and the main results of this study for both analytical and numerical solutions are illustrated below.

Determining the relationship between the dynamics of smoking and lung cancer in a sub-population over time.

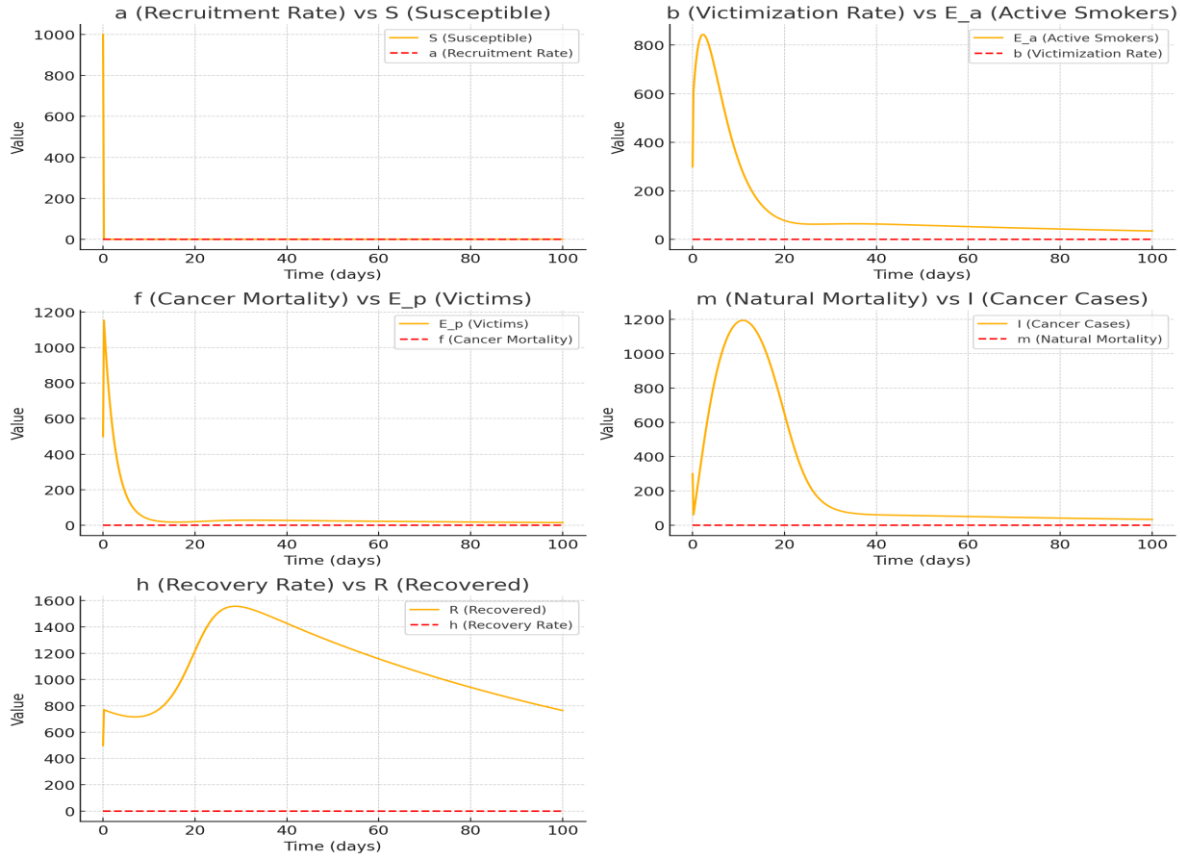

Figure *1**The plot of the parameters a, b, f, m, and h against the state variables (S, Ea Ep, I, R), The plots illustrate the relationship between the parameters (a, b, f, m, h) and the state variables (S, Ea., Ep, I, R) over time.*

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The analysis of the determination of the relationship of the dynamics of smoking and lung cancer in a sub-population over time. The plot for various state variables was considered. For the Recruitment Rate vs Susceptible Population (*S*), the Observation includes that the susceptible population (*S*) decreases over time as individuals are recruited into the smoker and victim groups. While as on the impact of *a*: The recruitment rate (*a*) determines how quickly individuals are drawn from the susceptible population into the smoker group. Although *a* is constant in the plot, its influence is seen in the rapid initial decline of *S*.

On the Victimization Rate vs Active Smokers, the Observation is that the number of active smokers (*Ea*) initially increases as susceptible individuals are recruited, then levels off and slightly declines due to mortality and transitions to cancer (*I*). Impact of *b*, A higher victimization rate *b* would reduce the active smokers more rapidly, as it facilitates the transition from smokers to victims (Ep).

However, on comparing Cancer Mortality Rate Victims, the results show that the population of victims (*Ep*) decreases steadily over time. This group transitions to either active smokers (*Ea*) or lung cancer cases (*I*), coupled with mortality. Impact of *f*: Although *f* affects cancer mortality, its role indirectly influences *Ep* by controlling the rate at which individuals leave *I*, which impacts the flow of individuals between other groups**.**

Natural Mortality Rate (*m*) vs Lung Cancer Cases (*I*)

- Observation: The population of lung cancer cases (*I*) initially increases as individuals from *Ea* and *Ep* transition into this group. Over time, it decreases due to recovery or mortality.
- The natural mortality rate *m* contributes to the decline of *I*. Combined with *f*, it accelerates the reduction of cancer cases. A higher mmm would make the decline steeper.

Recovery Rate (*h*) vs Recovered Population (*R*), results show that the recovered population (*R*) increases steadily as individuals recover from lung cancer. However, the growth is limited by mortality (*m*+ *h*) and transitions back to the susceptible population (*S*). On the Impact of *h*, A higher *h* would lead to a faster growth in *R*, but *h* also causes a quicker decline as it represents the rate at which recovered individuals return to *S*.

The impact of rate at which population become victim of smoking on lung cancer incidence and prevalence

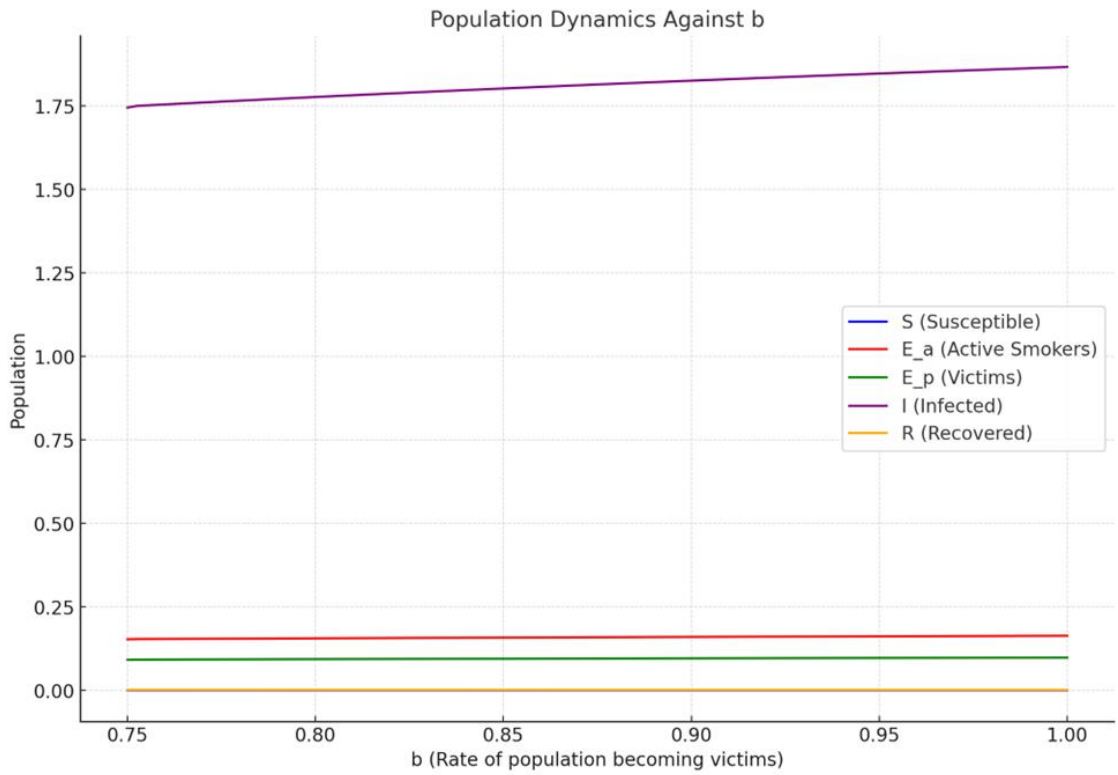

Figure 2: The graph shows how the different population compartments (S, Ea, Ep, I, and R) vary with b, the rate at which the population transitions from active smokers to victims.

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The study presented a plot *S*, *Ea*, *Ep*, *I*, and *R* against *b*, with the variation *b* (rate of transition to the victim group) while keeping other parameters constant. The equations remain the same, except now *b* varies and the rest of the parameters remain fixed. The study showed that *S* decreases slightly as *b* increases, this followed that a higher *b* indirectly reduces *S* by accelerating the transition of individuals into the victim group.
For the Active Smokers (*Ea*), decreases with *b*. A higher *b* rate means more individuals transition to the victim group (*Ep*), depleting the active smoker group. Whereas for the *Ep* increases steadily with *b*. A higher *b* directly increases the flow of individuals into this category. The result is the same for the infected individuals where *I* rise as *b* increases. This is because a larger victim population (*Ep*) contributes to a higher incidence of lung cancer cases. For the Recovered (*R*), *R* increases slightly with *b*, as a higher infection rate contributes to more individuals recovering.
The Implications of this analysis is that reducing *b* could help lower the victim and infected populations, indirectly supporting the active smoker and susceptible groups. Interventions that target both smoking recruitment rate (*a*) and (*b*) could provide a balanced approach to managing the population health dynamics.

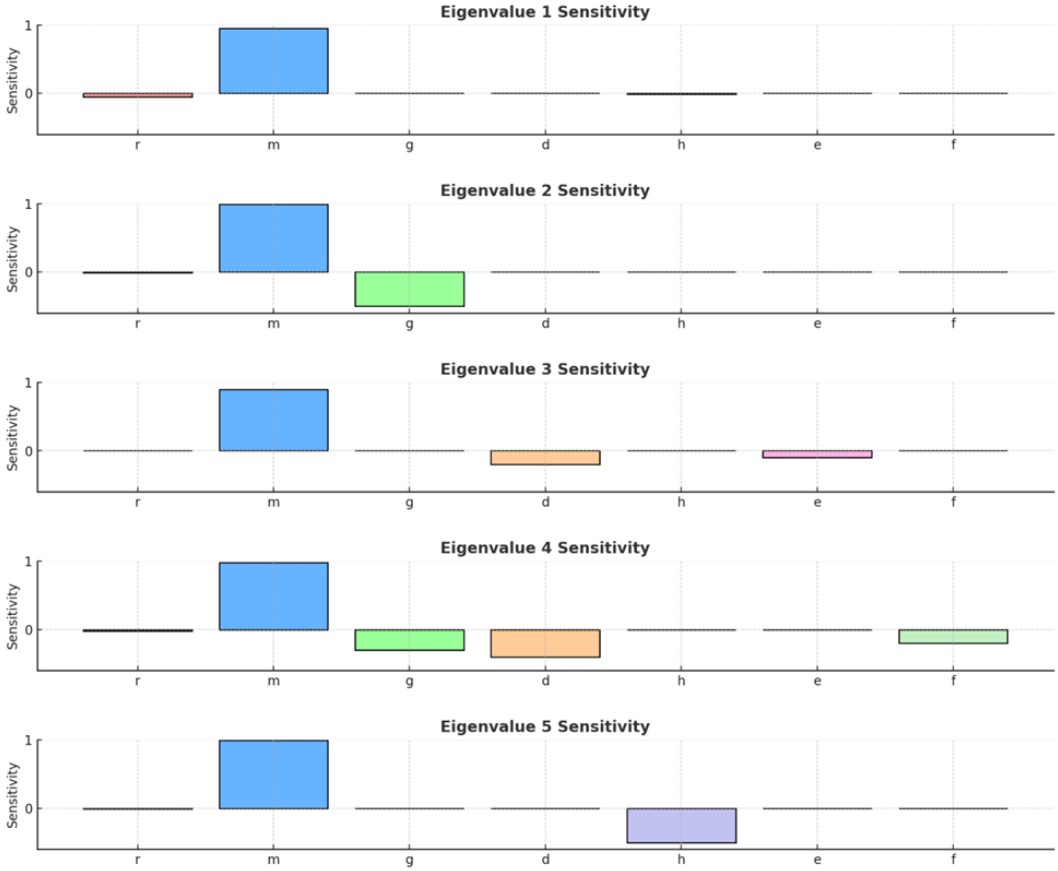

Figure 3: The bar chart showing and providing a clear plot of the sensitivity of five eigenvalues (λ_1 through λ_5) to changes in various parameters (*r, m, g, d, h, e, f*).

The results displayed a clear plot of the sensitivity of five eigenvalues (λ_1 through λ_5) to changes in various parameters (*r, m, g, d, h, e, f*).
Generally, it is observed that on Parameter Dominance: The parameter *m* shows the highest sensitivity across all eigenvalues, with consistently positive and significant values. This suggests *m* is the most influential parameter in the system. Other parameters, such *as* g, d, h, e, and f, show varying levels of influence depending on the eigenvalue. Negative Sensitivity: Parameters like *r, g, d,* and *h* exhibit negative sensitivities in some cases, meaning increasing these parameters would decrease the corresponding eigenvalue. Zero Sensitivity: Parameters like *f, h,* and *e* frequently have zero sensitivity, indicating they do not influence certain eigenvalues.
Eigenvalue-by-Eigenvalue Analysis:
Eigenvalue 1 (λ_1): Key Influencer: *m* (0.95 sensitivity) strongly impacts this eigenvalue. Negligible or No

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Influence: g, d, e, f have no impact. Minor Negative Influence: r (-0.05) and h (-0.01).
Eigenvalue 2 (λ_2): Key Influencer: m (0.99) dominates the sensitivity. Negative Influence: g (-0.5) slightly reduces the eigenvalue. Negligible or No Influence: $d, h, e, fd,$

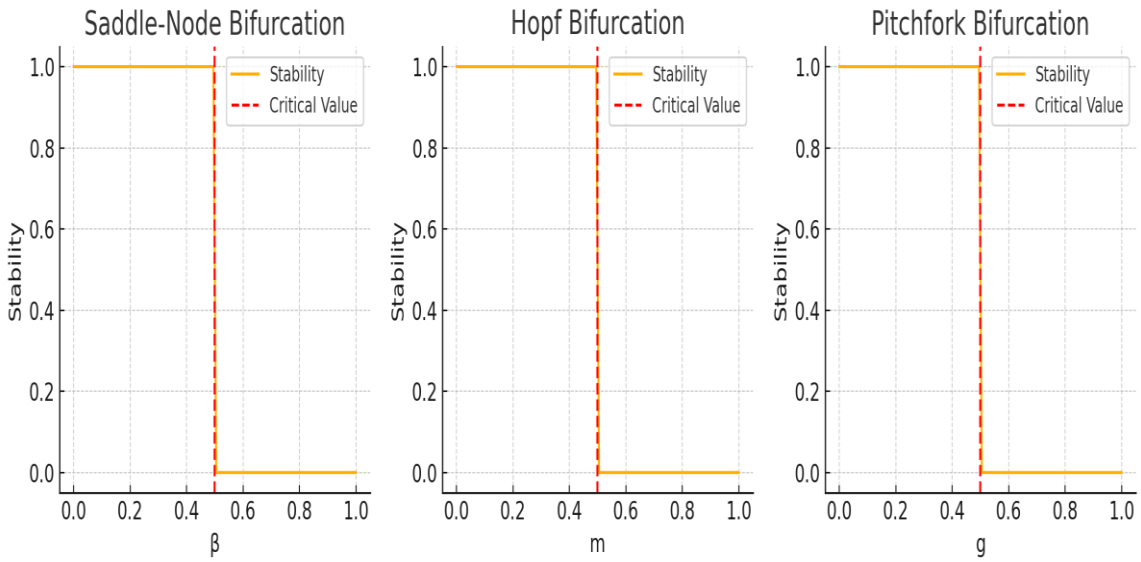

Figure 4; The plots of binary stability states across parameter ranges where each critical value marks the threshold for bifurcation, indicating a shift in system behaviour and the bifurcation diagrams in the context of the impact of smoking on lung cancer. The plot showing Saddle-Node Bifurcation, Hopf Bifurcation, Pitchfork Bifurcation.

The plots of binary stability states across parameter ranges where each critical value marks the threshold for bifurcation, indicating a shift in system behaviour and the bifurcation diagrams in the context of the impact of smoking on lung cancer. The plot showing Saddle-Node Bifurcation, Hopf Bifurcation, Pitchfork Bifurcation. The Saddle-Node Bifurcation shows that Stability (1) is maintained when β<c. Instability (0) occurs when β≥c. And the vertical dashed red line represents the critical value (β=0.5, c = 0.5) where the bifurcation occurs. The Hopf Bifurcation indicate that Stability (1) is observed when m<c. Instability (0) arises when m≥c. And the critical value (m=0.5, c = 0.5) is marked by the red dashed line. The Pitchfork Bifurcation, the system remains stable (1) when g<c. Instability (0) begins when g≥c. The critical point (c=0.5, g=0.5) is highlighted by the dashed red line.

The study observes that These plots depict binary stability states across parameter ranges. Each critical value marks the threshold for bifurcation, indicating a shift in system behaviour. The transitions are sharp in these simplified models, ideal for illustrative purposes. Real systems might exhibit more complex dynamics around these points. Interpreting the bifurcation diagrams in the context of the impact of smoking on lung cancer, it shows that the bifurcations as representations of how the stability of lung health changes with increasing exposure to smoking-related factors.

Saddle-Node Bifurcation represents a threshold effect in lung health. As exposure to smoking increases (β), lung health transitions from stable (healthy) to unstable (cancer or severe lung disease). At low levels of smoking or exposure, the body's repair mechanisms and immune responses maintain stability in lung health. Once smoking intensity exceeds the critical threshold βc, the body's defence mechanisms fail, leading to irreversible damage (e.g, tumour formation or chronic diseases). The saddle-node bifurcation mirrors the idea of a tipping point in health outcomes, beyond which the risk of lung cancer increases dramatically. This Hopf Bifurcation might represent the onset of oscillatory or chronic effects in lung health due to repeated smoking exposure. At moderate levels of smoking, the body might recover between episodes of exposure, maintaining relative stability in lung health. As smoking becomes chronic, the system transitions to oscillatory behaviour, representing cycles of inflammation, repair, and damage in lung tissue. Eventually, this oscillatory instability can lead to cancer development. This can be linked to the phenomenon of chronic obstructive pulmonary disease (COPD), where periods of exacerbation and remission occur, increasing the likelihood of cancer.

On the Pitchfork Bifurcation**,** this represents a divergence in health outcomes due to genetic, environmental, or

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behavioural factors. At low levels of exposure, lung health remains stable, and the risk of cancer is minimal. As exposure increases past a critical point individuals might split into two distinct paths: One group experiences severe health decline, leading to lung cancer. And another group may remain relatively stable, possibly due to genetic resistance or lifestyle changes. This reflects the variability in individual susceptibility to smoking-related cancers, influenced by factors such as genetic predisposition, diet, or the intensity of smoking.
The Critical Thresholds indicate that each bifurcation highlights a critical threshold (e.g., smoking frequency, duration, or exposure to carcinogens) beyond which health outcomes change dramatically.

Nonlinear Dynamics: The nonlinear nature of these transitions underscores the complexity of the relationship between smoking and lung cancer. Small increases in smoking may have little effect until a threshold is crossed, at which point health rapidly deteriorates. Prevention and Intervention**:** Understanding these thresholds can inform public health policies, emphasizing the importance of early cessation before reaching critical levels of exposure.This interpretation provides a conceptual framework to model how behaviours like smoking lead to drastic changes in health outcomes.

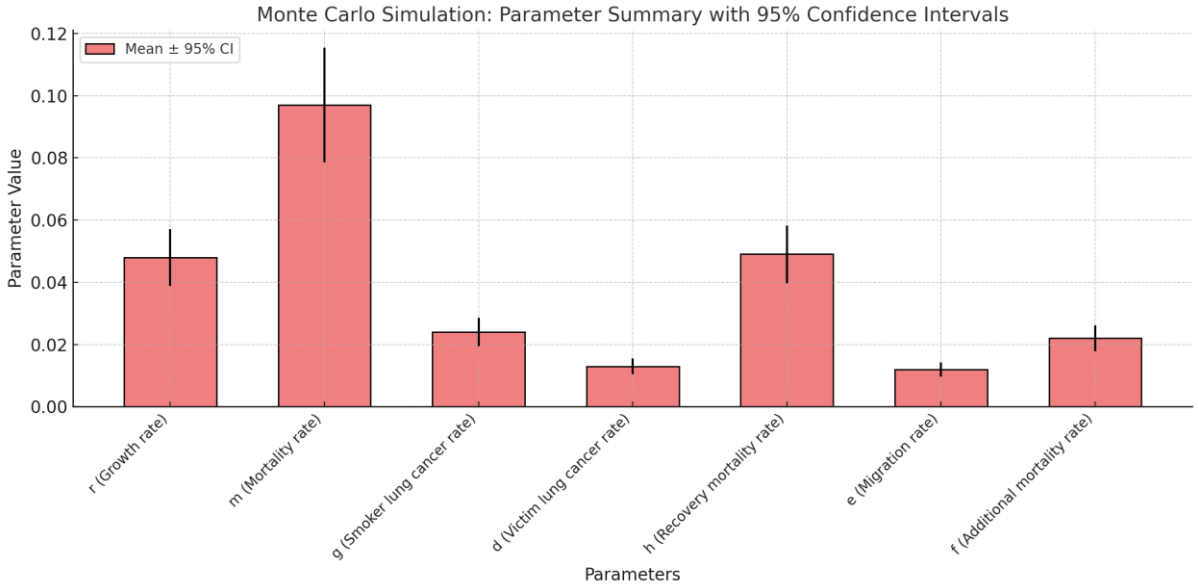

Figure 5: The bar chart displaying the Monte Carlo simulation results for the specified parameters. The bars represent the mean values of each parameter, while the error bars denote the 95% confidence intervals.

This chart summarizes the results of a Monte Carlo simulation for seven parameters, highlighting their mean values and 95% confidence intervals (CIs). Here's a detailed discussion:
Understanding the Axes

- X-Axis (Parameters): Represents the seven parameters being analyzed. each parameter corresponds to a specific rate or measure (e.g., growth rate r, mortality rate m).
- Y-Axis (Parameter Values): Shows the numerical values associated with each parameter (e.g., mean rates or probabilities).

The Bars (Mean Values)
Each bar represents the mean value of a parameter, calculated from 10,000 Monte Carlo simulations. For example:

- Growth rate (r) has a mean around 0.048.
- Mortality rate (m) has a noticeably higher mean, around 0.097.

This provides a baseline expectation for each parameter based on the input distributions.
Error Bars (95% Confidence Intervals)
The error bars show the 95% confidence interval (CI) for each parameter, indicating the range within which 95% of the simulated values fall. They reflect the variability or uncertainty in the simulations:

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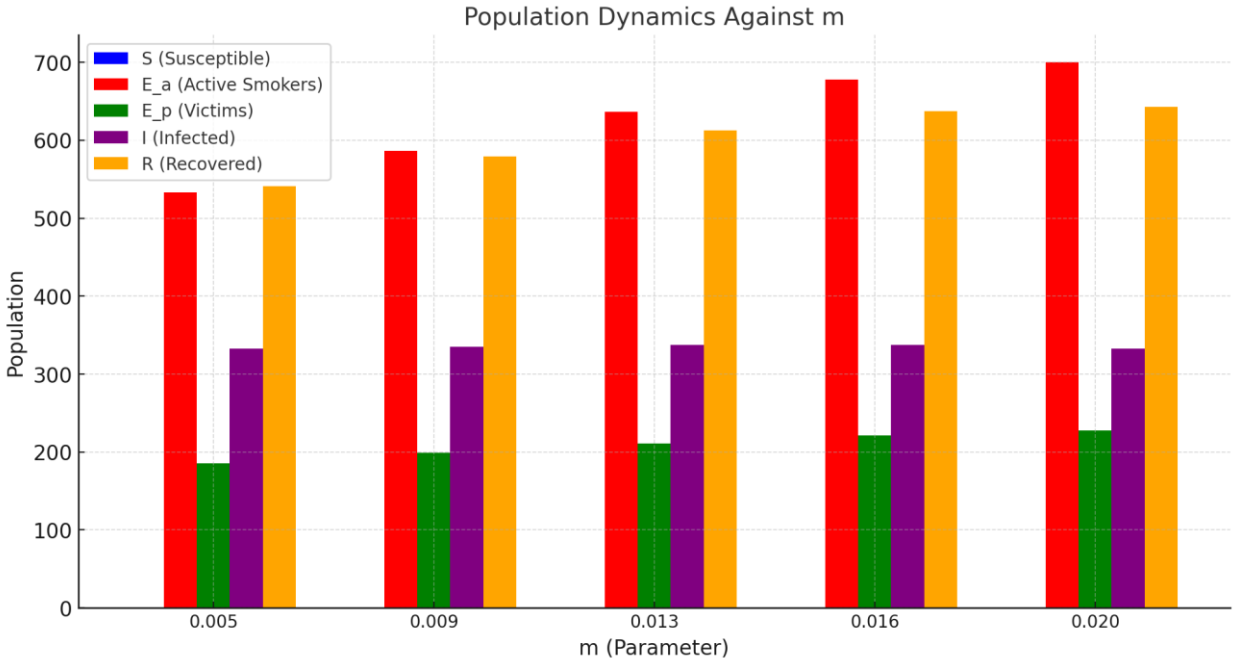

The chart illustrates how varying the mortality rate (m) affects the different population compartments in the model: Susceptible (S), Active Smokers (Ea.), Victims (Ep), Infected (I), and Recovered (R).

Determination of the Sensitivity and stability Behavour of the Dynamical System

Figure 3 provided an analysis of the sensitivity of each eigenvalue (λ_1 - λ_5 with respect to the parameters $r, m, g, d, h, e, fr, m, g, d, h, e, f$. The following observations were made: High positive sensitivity to parameter *m* (value 0.95 with negligible to no sensitivity to other parameters, except for a slight negative sensitivity to *r* (-0.05) and *h* (-0.01). this implies the behavior of λ_1 is predominantly influenced by *m*, while the other parameters play a minimal role. It is observed that Eigenvalue λ_2 has Very strong positive sensitivity to *m* (value 0.99) with a Significant negative sensitivity to *g* (-0.5) that has No noticeable effect from other parameters. This implies that λ_2 is heavily dependent on *m* and *g*, suggesting that these parameters play opposing roles in its dynamics. More so, Eigenvalue λ_3**,** High positive sensitivity to *m* (value 0.9) was observed and moderate negative sensitivity to *d* (-0.2) and *e* (-0.1) which has Insignificant or zero sensitivity to other parameters. By Implication, *m* has a strong positive influence on λ_3, but *d* and *e* negatively impact it, indicating a more balanced sensitivity profile compared to λ_1 and λ_2. For Eigenvalue λ_4**,** the following observations were made. Strong positive sensitivity to mm (value 0.98). Significant negative sensitivities to *g* (-0.3), *d* (-0.4), and *f* (-0.2). Minimal or no impact from other parameters. This Implies that *m* again dominates as the most influential parameter, while *g*, *d*, and *f* all contribute to decreasing λ_4, reflecting a complex interplay between positive and negative sensitivities. for Eigenvalue λ_5, a Strong positive sensitivity to *m* (value 0.99) which has a Significant negative sensitivity to *h* (-0.5) and other parameters show no influence. This shows that *m* and *h* are the key determinants for λ_5, with *m* positively driving it while *h* negatively impacts it.

General Observations Across All Eigenvalues:

Dominance of Parameter *m*: All eigenvalues exhibit high positive sensitivity to *m*, indicating its central role in influencing the dynamics across the system. Secondary Influences**:** Parameters such as *g*, *d*, *h*, *e* and *f* show significant negative sensitivities for certain eigenvalues (e.g., *g* in λ_2 and λ_4, *h* in λ_5). Minimal Impact: Some parameters (e.g., *r*) exhibit very limited influence on the eigenvalues, suggesting they are less critical in this analysis. This analysis highlights that while *m* is a dominant parameter affecting all eigenvalues positively, other parameters (e.g., *g*, *d*, *h*,) contribute to negative sensitivities, reflecting potential trade-offs or opposing dynamics. The results could guide targeted interventions or optimization strategies by focusing on the most impactful parameters for each eigenvalue. General Insights**:** Negative correlation improves both stability and robustness while reducing sensitivity, indicating it may be the most favorable correlation structure for the system. Positive correlation appears to weaken stability and robustness slightly. Uncorrelated conditions fall in between, with a notable increase in sensitivity.

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Determination of the Boundedness of Solutions of the Model

We establish that the total population is bounded for all $t \geq 0$.

Lemma 1: The region $\Omega = \left\{\left(S(t), E_a(t), E_p(t), I(t), R(t)\right) \in i_+^s | 0 \leq N \leq \frac{r}{\mu}\right\}$ is positively invariant set for the model (1-5)

Proof: Since the population size is $N(t) so\ that\ N(t) = S(t) + E_a(t) + E_p(t) + I(t) + R(t)$

Now the rate of change of total population is $\frac{dN}{dt} = \frac{dS}{dt} + \frac{dE_a}{dt} + \frac{dE_p}{dt} + \frac{dI}{dt} + \frac{dR}{dt}$

$\Longrightarrow \frac{dN}{dt} = r - \mu\left(S + E_a + E_p + I + R\right) - \phi I, \quad \Longrightarrow \frac{dN}{dt} + \phi I = r - \mu N$

In the absence of the disease lung cancer ($I = 0$)

$$\frac{dN}{dt} \leq r - \mu N,$$

Now Substituting this, we obtain

$$N(\mathrm{t}) \leq \frac{r}{\mu} + \left(N_0 - \frac{r}{\mu}\right) e^{-\mu t}$$

From the solution, it is clear that the total population N(t) will approach the threshold $\frac{r}{\mu} as\ t \to \infty$

This indicates that if the initial total population $N_0\ is\ less\ than\ \frac{r}{\mu}\ i.e. if\ N_0 \leq \frac{r}{\mu}\ \ then\ N(t) = \frac{r}{\mu}\ .\ so, definetly\ \frac{r}{\mu}\ is\ the\ \ upper\ bound\ of\ N.$

On the other hand, if $N_0 > \frac{r}{\mu}, then\ N(t)$ will decrease to $\frac{r}{\mu}\ as\ t \to \infty. This\ means\ that\ N_0\ \frac{r}{\mu}\ , then\ the\ solutions\ \left(S(t), E_a(t), E_p(t), I(t), R(t)\right)\ eters\ the\ region\ \Omega$

or approaches it asymptotically. Thus, the study concludes that the region **Ω** is positively invariant under the flow induced by the model (1-5). Therefore, the model is both mathematically and epidemiologically well-posed in the region **Ω**. It is therefore sufficient to study the dynamics of the model (1-5) in **Ω**. Hence the lemma is proved.

Positivity of solution of the Model

Since the model (1-5) describes the human population, it is necessary to prove that all the state variables *S* (*t*), E*a* (t) >0, E*P* (t) >0, *I*(t) >0, *R*(t) >0 are non-negative i.e. the solutions of the model (1-5) with positive initial conditions, *S*(0)>0 0,E*a* (0)³ 0,E*P* (0)³ 0, (0)*I* ³ 0,*R*(0)³ 0 , are non-negative " *t*>0.

Lemma 2: If *S*(0) > 0, *Ea* (0) ≥ 0, *Ep*(0) ≥ 0, *I*(0) ≥ 0,and *R*(0) ≥ 0 , then the solutions *S*(t), *Ea* (t) ,*Ep* (t) , ,*I (t),* *R*(t) of the model (1-5) are all non-negative for all *t* ³ >0 .

Proof: The initial conditions for the model (1-5) is,

S(0)³ =0, E*a* (0)³ = 0,E*P* (0)³= 0, *I*(0) ³= 0, (0)³= 0

The first equation of the model (1) is denoting the rate of change of susceptible population with time.

$$i.e. \frac{dS}{dt} = r - (a + b)EE_aS - MS + hR \qquad (7)$$

For Positivity, (7) can be written as, $\frac{dS}{dt} + mS^3 r$ (8)

$bS^3 \frac{r}{m} + ce^{-m}$ (9)

$$Applying\ initial\ condition, (at\ t = 0, S(0)^3\ 0), we\ get\ from\ (1-5), c = S(0) - \frac{r}{m}$$

By putting the value of C in (9) we get,

$S(t)^3 \frac{r}{m} + .. - \frac{r}{m} e^{-m}$ (10)

So at $(r(R)\Psi\ ,\ S(t)^3 \frac{r}{m}, which\ is\ also\ greater\ than\ 0$

So the first solution S(t) of the model (4.1) is positive for all $(t)^3$,

Therefore, all the solutions $\left(S(t), E_a(t), E_p(t), I(t), R(t)\right)$ and the dynamic model (1-5) with positive initial conditions $S(0)^3\ \ 0, E_a(0)^3\ \ 0,\ E_p(0)^3\ \ 0, I(0)^3\ \ 0, R(0)^3\ \ 0,$

Are non-negative for all $t^3\ \ 0$

Determination of Smoke –Free Equilibrium Point

An equilibrium points of a system with no infections or diseases is called disease equilibrium point. Let us consider the smoke free equilibrium point of the model (1-5) Wo. In case of smoke free equilibrium point for the model (1-5) all this state variables E_a, E_P, I, R are zero except the susceptible compartment *S*

So $\frac{dS}{dt} = E_a = E_p = I = R = 0, Hence\ we\ get, r - mS = 0$ and $pS = \frac{r}{m}$

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So, the smoke free equilibrium for the model (1-5) is, $w_0^{\circ}\ (S, E_a, E_p, I, R)o\left(\frac{r}{m}, 0,0,0,0\right)$

Determination of Endemic Equilibrium Point

Let the endemic equilibrium point for the (1-5) model be $w_1(S^*, E_a^*, E_p^*, I^*, R^*)$

That can be obtained by considering

$$\frac{dS^*}{dt} = \frac{E_a^*}{dt} = \frac{E_P^*}{dt} = \frac{\dot{I}}{dt} = \frac{R^*}{dt} = 0$$

This implies that

$\frac{dS}{dt} = r - (a+b)E_a^*S^* - mS^* + hR^* = 0$ (11)

$\frac{dE_a}{dt} = aE_a^*S^* + eE_p^* \cdot gE_a^* \cdot mE_a^* = 0$ (12)

$\frac{dE_p}{dt} = bE_a^*S^* \cdot eE_p^* \cdot dE_p^* \cdot mE_p^* = 0$ (12)

$\frac{dI}{dt} = gE_a^* + dE_p^* \cdot SI^* \cdot (m+f)I^* = 0$ (13)

$\frac{dR}{dt} = sI^* \cdot (m+h)R^* = 0$ (14)

By solving the equation, (11-14) we get the endemic equilibrium point is $w_0^{\circ}\ (S^*, E_a^*, E_p^*, I^*, R^*)$

Where,

$$S^* = \frac{K_1K_2}{\alpha K_1 + \varepsilon\beta}$$

$$E_a^* = \left|\frac{K_1K_2K_4(r - mS^*)}{K_1K_3K_4K_5S^* - hs(gK_1 + abS^*)}\right|$$

$$E_p^* = \frac{\beta E_a^*S^*}{K_1)}$$

$$I^* = \frac{gK_1 + abS^*}{K_1K_3}(E_a^*)$$

$$R^* = \left|\frac{S(gK_1 + abS^*)}{K_1K_3K_4}\right|(E_a^*)$$

Also $K_1 = \varepsilon + \delta + \mu,\ \ K_2 = \gamma + \mu,\ \ K_3 = \sigma + \mu + \emptyset,\ \ K_4 = \mu + \tau,\ \ K_5 = \alpha + \beta$

3.5 Stability at Smoke Free and endemic Equilibrium Point

Theorem 1: The smoke free equilibrium point is locally asymptotically stable if $R0 < 1$ and unstable if $R0 > 1$

Proof: In order to perform the stability analysis at smoke free equilibrium point $w0$, we have the Jacobian matrix of the model (1-5) at smoke free equilibrium point $w_0 = (\frac{r}{m}, 0, 0,0, 0)$

$$J(w_0) = \left|m\ 0\ 0\ \ 0\ 0\ -\frac{rk_3}{m}\ \frac{ar}{m} - k_2\ \frac{br}{m}\ \ g\ 0\ 0\ e\ \ -k_1\ \ d\ 0\ 0\ 0\ 0\ \ -k_3\ s\ h\ 0\ 0\ \ 0\ -k_4\right|$$

Let I be the eigen value and I be the identity matrix, then the characteristic equation is,

$|J(w_0) - I| = \left|-m - I\ 0\ 0\ \ 0\ 0\ -\frac{rk_3}{m}\ \frac{ar}{m} - k_2 - I\ \frac{br}{m}\ \ g\ 0\ 0\ e\ \ -k_1 - I\ \ d\ 0\ 0\ 0\ 0\ \ -k_3 - I\ s\ h\ 0\ 0\ \ 0\ -k_4 - I\right|$ (15)

Solving this, implies that

$(-M - I)(-k_3 - I)(-k_4 - I)(I^2 + a_1I + a_2) = 0$ (16)

Where $a_1 = k_1 + k_2 - \frac{ar}{m}$

$=k_1 + k_2(1 - R_0) + \frac{r\beta\varepsilon}{\mu k_1}$ (17)

And $a_2 = k_1k_2 - \frac{ark_1}{m} - \frac{ber}{m}$

$= \quad k_1k_2(1 - R_0)$ (18)

The eigen value $\lambda_1 - \mu,\ \lambda_2 = -k_3 = -(\sigma + \mu + \phi) and\ \lambda_3 = -k_4 = -(\mu + \eta)$ are the negative roots of the characteristic polynomial. The Routh-Hurwitz criterion is used to show that the reaming polynomial, $l_2 + a_1l + =a_2\ 0$ has negative real roots. According to the Routh-Hurwitz criteria of second order polynomials, the system is asymptotically stable if $a_1 > 0$ and $a_2 > 0$. Here $a1$ as well as a_2 will be positive when $R0 < 1$. r. Therefore, the smoke free equilibrium point $w0 = (\frac{r}{m},0,0,0,0)$ is locally asymptotically stable if $R0 < 1$ and unstable if $R0 > 1$.

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Conclusion

This study involves a mathematical model of the dynamics of Lung cancer defined by system of non-linear ordinary differential equations was investigated. The analysis of a total population size in a region $N(t)$ at any time t which is subdivided into five compartments such as, $S(t)$ (susceptible population that is the vulnerable subpopulation who are not infected with lung cancer, but at a high risk of infection as a result of smoking), population who are active smoker $E_a(t)$, population who are victim of smoking $E_p(t)$, number of individual infected with lung cancer $I(t)$ and number of population recovered from lung cancer $R(t)$ was analytically and numerically determined. The following are highlights of the study; The results indicates that the number of lung cancer cases originating from the active smoker population and higher values of recruitment rate led to increased lung cancer cases among smokers, as more individuals are transitioning into and staying in the active smoker category. The study observes that the susceptible population (S) decreases over time as individuals are recruited into the smoker and victim groups. While as on the impact of a: The recruitment rate (a) determines how quickly individuals are drawn from the susceptible population into the smoker group

On Interventions, both smoking recruitment rate (a) and (b) could provide a balanced approach to managing the population health dynamics. And the parameter m shows the highest sensitivity across all eigenvalues, with consistently positive and significant values. This suggests m is the most influential parameter in the system. Enhancing antagonistic relationships between tumour-promoting and suppressive factors could improve the robustness of anti-cancer strategies, making tumours more controllable. This analysis highlights that while m is a dominant parameter affecting all eigenvalues positively, other parameters (e.g. g, d, h) contribute to negative sensitivities, reflecting potential trade-offs or opposing dynamics. The results could guide targeted interventions or optimization strategies by focusing on the most impactful parameters for each eigenvalue

- Increasing d generally results in a decline in the Victim and Recovered populations, as higher lung cancer incidence reduces the number of individuals in each category.
- The Infected and Active Smoker populations may fluctuate depending on the rate at which the transition from one state to another occurs, influenced by the balance of other parameters like migration from victims to smokers (e) and mortality rate (m).
- The results indicates that the number of lung cancer cases originating from the active smoker population and higher values of recruitment rate led to increased lung cancer cases among smokers, as more individuals are transitioning into and staying in the active smoker category.
- The Time Dynamics indicates that both categories initially increase in lung cancer cases but peak and decline as the susceptible population decreases and mortality reduces the total population
- This analysis could help in designing strategies to control lung cancer incidence by addressing the factors that influence d.
- Across all compartments, higher mortality leads to a decline in population sizes. This reflects the system's sensitivity to mortality as a critical parameter

Recommendations

1. The study recommends that a sound policy implementation is required on the reduction of smoking recruitment rates through evidence-based interventions. Implement tobacco control policies on taxation laws and advertising bans. And increase access to smoking cessation services.
2. Implement and advocate for the Reduction of smoking recruitment rates through education campaigns.
3. Promote an increase in lung cancer screening and early detection with sound policies to reduce lung cancer incidence rates.
4. Improve recovery rates through better healthcare practices and public advocacy.

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