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Research Article

Sensitivity Analysis of a General Lung Diseases Progression Stochastic Model Considering Two Types of Diagnostic Tests

Suman* and Rajeev Kumar

Department of Mathematics, Maharshi Dayanand University, Rohtak, Haryana, India
***Corresponding author:** suman.uiet@mdurohtak.ac.in

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Abstract. Lung is a vital organ in the human body that is affected by many diseases each with different causes, symptoms and treatments. In the present paper, a general stochastic model for lung diseases has been developed considering various stages of progression of the disease. In the model, two types of diagnostic tests viz. normal and advance diagnostic tests have been taken into account. For the survival analysis purpose, mean sojourn times and mean survival time have been calculated for the model using concepts of Markov process and regenerative point techniques. Sensitivity and relative sensitivity analyses have also been performed to find out how the variation in parameters affect the mean survival time under certain specific conditions.

Keywords. Lung disease, Mean sojourn time, Mean survival time, Markov process, Regenerative point technique, Sensitivity analysis

Mathematics Subject Classification (2020). 60K15, 60J27

1. Introduction

Lung disease includes problems like asthma, *Chronic Obstructive Pulmonary Disease* (COPD), and lung cancer that affect breathing. Asthma, the most common chronic disease among children, affects both children and adults, with an estimated 262 million people affected in 2019 and causing 455,000 deaths. Inhaled medications can effectively control asthma symptoms, enabling individuals to maintain normal, active lives[1]. Lung diseases can be caused by smoking, infections, genetic conditions, and other factors. To find out what's wrong, doctors use various tests. Once diagnosed, the disease treatments might include medications, therapies, or lifestyle changes to help improve lung health.

A lot of work has been done in the recent past to study chronic lung diseases. Frey *et al*. [3] predicted the risk of asthma attacks from fluctuation analysis of airway function. Early identification of high-risk asthmatic patients helps doctors manage and intervene sooner. The study of Xiong *et al*. [14] showed that *Machine Learning* (ML) can accurately predict asthma exacerbations. Zoltan [15] developed a stochastic lung model to simulate how different inhaled particles deposit in the airways during a severe asthma attack. Computational models of lung deposition by Ganguly *et al*. [4] have traditionally been developed based on the anatomy and physiology of healthy lungs. The COPD progression model by Iheanacho *et al*. [6] serves as a valuable tool for providing the detailed insights into the future burden of COPD. Moderate-to-severe COPD is very expensive for healthcare systems, even with good treatments and guidelines. Verma *et al*. [12] reviewed the studies done in India from 2000 to 2020 about the prevalence of COPD and its risk factors in people over the age of 30. Gargano *et al*. [5] discussed about the survival analysis of COPD patients from the data collected over 13 years from Brazil. The study helps us understand the health and treatment of these patients better. Early smoked COPD patients, as given by Wu *et al*. [13], have serious health problems, including strong addiction to cigarettes, poor lung function, enlarged heart, and a higher risk of dying. Dong *et al*. [2] investigated how COPD affects the effectiveness and safety of combining immune checkpoint inhibitors with chemotherapy for treating resectable non-small cell lung cancer. Jeon *et al*. [7] used the information collected in 2015 from the 'Korean Association of Lung Cancer Registry' to understand five-year survival rates of lung cancer patients. Computer process modeling methods are being applied to streamline the lung cancer diagnosis-to-treatment process, improving efficiency, decision-making, and patient outcomes (Ju *et al*. [8]). Schöllnberger *et al*. [10] explained the risk of developing lung cancer due to smoking, using data from a large group of people in Europe. Using latest techniques in imaging and computer modelling, lung function can be studied and also understood the problems in way that can not be done with regular clinical tests (Burrowes *et al*. [1]). The advancement of deep learning has led to significant improvements in the detection and diagnosis of lung diseases (Kieu *et al*. [9]). People with asthma, COPD or asthma COPD overlap might have a higher risk of dying from COVID-19 compared to those without these lung diseases. Additionally, patients with COPD or asthma COPD overlap are more likely to need oxygen therapy and a mechanical ventilator (Shin *et al*. [11]).

According to *Global Initiative of Chronic Obstructive Lung Disease* (GOLD) system[2], there are four stages of COPD. Stage-I is mild, Stage-II is moderate, Stage-III is severe and Stage-IV is very severe. Asthma has also four stages, i.e., intermittent, mild persistent, moderate persistent

[1] *Asthma*, World Health Organisation (WHO), accessed: 22.10.2024, URL: https://www.who.int/news-room/fact-sheets/detail/asthma.

[2] *COPD Stages and the GOLD Criteria*, Global Initiative of Chronic Obstructive Lung Disease (WebMD.com), accessed: 19.10.2024, URL: https://www.webmd.com/lung/copd/gold-criteria-for-copd.

and severe persistent as given in [3]. Similarly, according to Cancer Research UK, lung cancer also classifies into four stages[4]. It means that the chronic lung diseases in general are of four stages. The aim of the present paper is to discuss sensitivity analysis of a general stochastic model for chronic lung disease that can be fitted to the chronic lung diseases like asthma, COPD and lung cancer etc. to study the effect of various parameters on survivability of lung disease patients.

Further, the work pertaining to investigation of parameters related to survivability of patients having lung diseases progression considering two types of diagnostic tests has not been reported in the literature. Keeping the above facts in view, in the present paper, a general stochastic model is developed for lung diseases progression considering two types of diagnostic tests. Mean sojourn time and *Mean Survival Time* (MST) have been calculated using the concepts of Markov process and regenerative point technique. Graphical and sensitivity analyses have also been done to investigate the parameters that improve the survival time of lung disease patients.

In Section 2 below, the proposed model, description and its assumptions are described. The states of transitions and various notations used in the model are given in Section 3. In Section 4 and Section 5, the steady-state probabilities and mean sojourn time are obtained. Section 6 and Section 7, deal with the computations of unconditional mean times and *Mean Survival Time* (MST) for the model. Numerical computations and graphical analysis have been done in Section 8. Sensitivity and relative sensitivity analyses have been presented in Section 9. Finally, Section 10 gives conclusion.

2. Model Description and Assumptions

The present paper introduces a general lung diseases progression stochastic model considering two types of diagnostic tests. In the model, it is considered that any healthy person may have some infection and that infected patient may or may not have symptoms of disease. When patient approaches to the doctor, normal clinical tests are recommended to the patients to diagnose the disease and through these tests, lung infection may or may not be diagnosed. When lung infection is diagnosed, then doctor recommends some advanced/additional tests to diagnose the type and the stage of lung disease. When the lung infection is in initial stage, then the patients will be recovered by treatments. In case the patients have lung disease like asthma, COPD, lung cancer etc., then disease specific treatments will be given to the patients according to the stage of the lung disease. The lung diseases progression stages, as given in footnotes [2, 3, 4], are considered in the model. That is, Lung Disease Stage-I (LDS-I) is mild, Lung Disease Stage-II (LDS-II) is moderate, Lung Disease Stage-III (LDS-III) is severe and Lung Disease Stage-IV (LDS-IV) is very severe. The patient reaches the doctor in negligible time. Each testing is perfect and instantaneous.

[3] *Understanding The Four Different Stages of Asthma*, Asthma.net, accessed: 19.10.2024, URL: https://asthma.net/living/understanding-the-different-stages-of-asthma.

[4] *Stages of Lung Cancer*, Cancer Research UK, accessed: 19.10.2024, URL: https://www.cancerresearchuk.org/about-cancer/lung-cancer/stages-types.

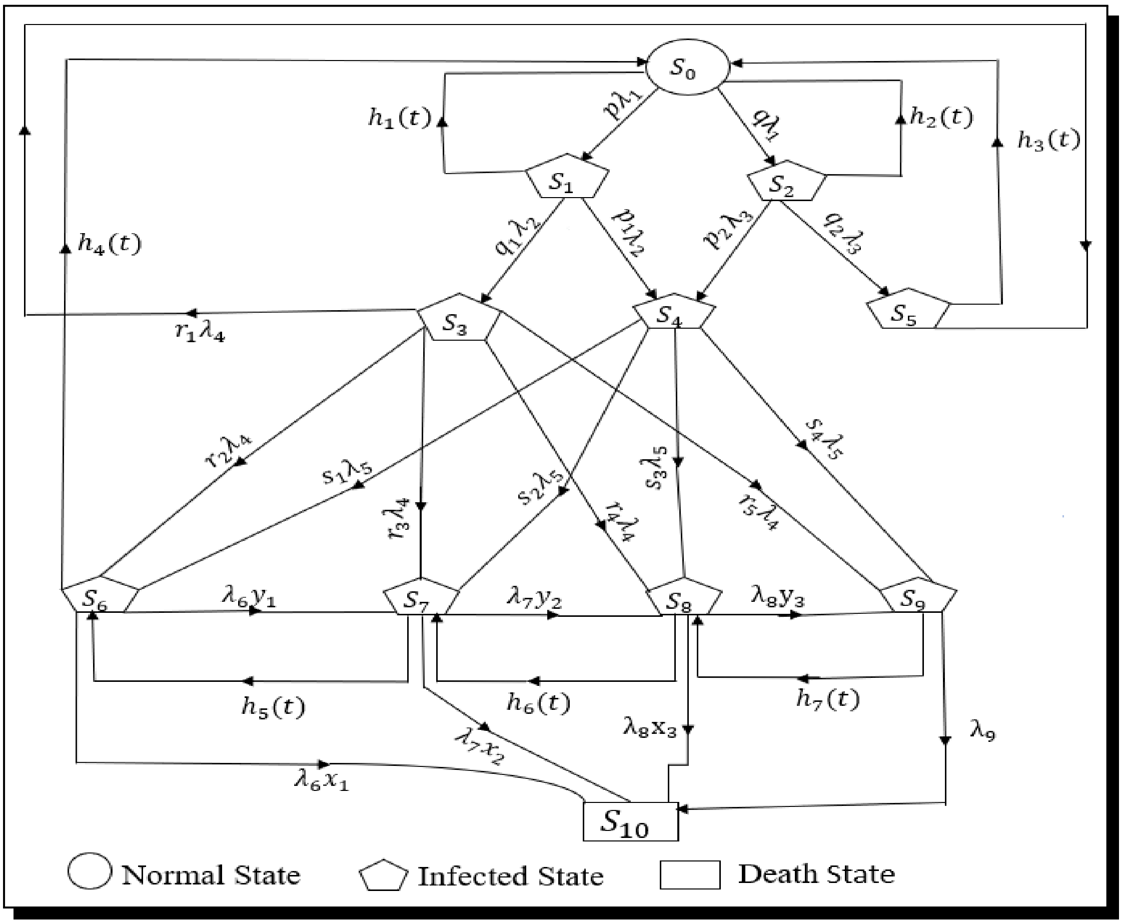

Figure 1. State transition diagram

Other assumptions of the model are as under:

- Times to inspection, damage and testing follow exponential distribution and other times follow general distributions.
- All the random variables are mutually independent.

3. States of Transition and Notations

Different states of transition of the model and various notations used are described as below:

States	*Description*
S_0	Healthy state
S_1	Symptomatic state
S_2	Non-symptomatic state
S_3	Non-diagnosed state
S_4	Diagnosed state
S_5	No lung infection state
S_6	LDS-I state

S_7	LDS-II state
S_8	LDS-III state
S_9	LDS-IV state
S_{10}	Death state

Notations	*Description*
λ_1	Infection rate
λ_2	Ordinary clinical testing rate of symptomatic patients
λ_3	Ordinary clinical testing rate of non-symptomatic patients
λ_4	Advanced testing rate of non-diagnosed patients
λ_5	Advanced testing rate of diagnosed patients
λ_6	Damage rate at LDS-I
λ_7	Damage rate at LDS-II
λ_8	Damage rate at LDS-III
λ_9	Damage rate at LDS-IV
p	Probability that healthy person has infection and symptoms; $q = 1-p$
p_1	Probability that lung infection is diagnosed in symptomatic patients; $q_1 = 1-p_1$
p_2	Probability that lung infection is diagnosed in non-symptomatic patients; $q_2 = 1-p_2$
r_1	Probability that non-diagnosed patients on advanced/additional tests revealed no lung infection
r_2	Probability that non-diagnosed patients on advanced/additional tests revealed LDS-I
r_3	Probability that non-diagnosed patients on advanced/additional tests revealed LDS-II
r_4	Probability that non-diagnosed patients on advanced/additional tests revealed LDS-III
r_5	Probability that non-diagnosed patients on advanced/additional tests revealed LDS-IV ($r_5 = 1-r_1-r_2-r_3-r_4$)
s_1	Probability that diagnosed patients on advanced/additional tests revealed LDS-I
s_2	Probability that diagnosed patients on advanced/additional tests revealed LDS-II
s_3	Probability that diagnosed patients on advanced/additional tests revealed LDS-III
s_4	Probability that diagnosed patients on advanced/additional tests revealed LDS-IV ($s_4 = 1-s_1-s_2-s_3$)
x_1	Probability of patient death at LDS-I; $y_1 = 1-x_1$
x_2	Probability of patient death at LDS-II; $y_2 = 1-x_2$
x_3	Probability of patient death at LDS-III; $y_3 = 1-x_3$
$h_1(t)/H_1(t)$	p.d.f./c.d.f. of time of recovery from infection symptomatic state
$h_2(t)/H_2(t)$	p.d.f./c.d.f. of time of recovery from infection non-symptomatic state
$h_3(t)/H_3(t)$	p.d.f./c.d.f. of time of recovery from non-lung infection state
$h_4(t)/H_4(t)$	p.d.f./c.d.f. of time of recovery from LDS-I

$h_5(t)/H_5(t)$ p.d.f./c.d.f. of time of recovery from LDS-II
$h_6(t)/H_6(t)$ p.d.f./c.d.f. of time of recovery from LDS-III
$h_7(t)/H_7(t)$ p.d.f./c.d.f. of time of recovery from LDS-IV

4. Transition Probabilities

The steady-state transition probabilities $p_{ij} = \lim_{t\to\infty} L(q_{ij}(t))$ are given by

$$p_{01} = p; \quad p_{02} = q; \quad p_{10} = h_1^*(\lambda_2); \quad p_{13} = q_1 - q_1 h_1^*(\lambda_2);$$
$$p_{14} = p_1 - p_1 h_1^*(\lambda_2); \quad p_{20} = h_2^*(\lambda_3); \quad p_{24} = p_2 - p_2 h_2^*(\lambda_3); \quad p_{25} = q_2 - q_2 h_2^*(\lambda_3);$$
$$p_{35} = r_1; \quad p_{36} = r_2; \quad p_{37} = r_3; \quad p_{38} = r_4;$$
$$p_{39} = r_9; \quad p_{46} = s_1; \quad p_{47} = s_2; \quad p_{48} = s_3;$$
$$p_{49} = s_4; \quad p_{50} = 1; \quad p_{60} = h_4^*(\lambda_6); \quad p_{67} = y_1 - y_1 h_4^*(\lambda_6);$$
$$p_{6,10} = x_1 - x_1 h_4^*(\lambda_6); \quad p_{76} = h_5^*(\lambda_7); \quad p_{78} = y_2 - y_2 h_5^*(\lambda_7); \quad p_{7,10} = x_2 - x_2 h_5^*(\lambda_7);$$
$$p_{87} = h_6^*(\lambda_8); \quad p_{89} = y_3 - y_3 h_6^*(\lambda_8); \quad p_{8,10} = x_3 - x_3 h_6^*(\lambda_8); \quad p_{98} = h_7^*(\lambda_9);$$
$$p_{9,10} = 1 - h_7^*(\lambda_9).$$

Clearly,

$$p_{01} + p_{02} = 1; \quad p_{10} + p_{13} + p_{14} = 1; \quad p_{20} + p_{24} + p_{25} = 1;$$
$$p_{35} + p_{36} + p_{37} + p_{38} + p_{39} = 1; \quad p_{46} + p_{47} + p_{48} + p_{49} = 1; \quad p_{50} = 1;$$
$$p_{60} + p_{67} + p_{6,10} = 1; \quad p_{76} + p_{78} + p_{7,10} = 1; \quad p_{87} + p_{89} + p_{8,10} = 1;$$
$$p_{98} + p_{9,10} = 1.$$

5. Mean Sojourn Time

The mean sojourn time refers to the average time spent by the patient in a certain state before moving to another state. It is denoted by μ_i and is given by

$$\mu_i = \int_0^\infty P(T_i > t)dt.$$

Thus,

$$\mu_0 = \frac{1}{\lambda_1}; \quad \mu_1 = \frac{1 - h_1^*(\lambda_2)}{\lambda_2}; \quad \mu_2 = \frac{1 - h_2^*(\lambda_3)}{\lambda_3}; \quad \mu_3 = \frac{1}{\lambda_4}; \quad \mu_4 = \frac{1}{\lambda_5};$$
$$\mu_5 = -h_3^{*'}(0); \quad \mu_6 = \frac{1 - h_4^*(\lambda_6)}{\lambda_6}; \quad \mu_7 = \frac{1 - h_5^*(\lambda_7)}{\lambda_7}; \quad \mu_8 = \frac{1 - h_6^*(\lambda_8)}{\lambda_8}; \quad \mu_9 = \frac{1 - h_7^*(\lambda_9)}{\lambda_9}.$$

6. Unconditional Mean Time

Unconditional mean time m_{ij} is mathematically stated as

$$m_{ij} = \int_0^\infty t q_{ij}(t)dt = -q_{ij}^{*\prime}(0).$$

Then,

$$m_{01} = \frac{p}{\lambda_1}; \qquad m_{02} = \frac{q}{\lambda_1};$$
$$m_{10} = -h_1^{*\prime}(\lambda_2); \qquad m_{20} = -\,h_2^{*\prime}(\lambda_3);$$
$$m_{13} = \frac{q_1 - q_1 h_1(\lambda_2)}{\lambda_2} + q_1 h_1^{*\prime}(\lambda_2); \qquad m_{14} = \frac{p_1 - p_1 h_1(\lambda_2)}{\lambda_2} + p_1 h_1^{*\prime}(\lambda_2);$$
$$m_{24} = \frac{p_2 - p_2 h_2(\lambda_3)}{\lambda_3} + p_2 h_2^{*\prime}(\lambda_3); \qquad m_{25} = \frac{q_2 - q_2 h_2(\lambda_3)}{\lambda_3} + q_2 h_2^{*\prime}(\lambda_3);$$
$$m_{35} = \frac{r_1}{\lambda_4}; \qquad m_{36} = \frac{r_2}{\lambda_4};$$
$$m_{37} = \frac{r_3}{\lambda_4}; \qquad m_{38} = \frac{r_4}{\lambda_4};$$
$$m_{39} = \frac{r_5}{\lambda_4}; \qquad m_{46} = \frac{s_1}{\lambda_5};$$
$$m_{47} = \frac{s_2}{\lambda_5}; \qquad m_{48} = \frac{s_3}{\lambda_5};$$
$$m_{49} = \frac{s_4}{\lambda_5}; \qquad m_{50} = -h_3^{*\prime}(0);$$
$$m_{60} = -h_4^{*\prime}(\lambda_6); \qquad m_{76} = -h_5^{*\prime}(\lambda_7);$$
$$m_{67} = \frac{y_1 - y_1 h_4(\lambda_6)}{\lambda_6} + y_1 h_4^{*\prime}(\lambda_6); \qquad m_{6,10} = \frac{x_1 - x_1 h_4(\lambda_6)}{\lambda_6} + x_1 h_4^{*\prime}(\lambda_6);$$
$$m_{78} = \frac{y_2 - y_2 h_5(\lambda_7)}{\lambda_7} + y_2 h_5^{*\prime}(\lambda_7); \qquad m_{7,10} = \frac{x_2 - x_2 h_5(\lambda_7)}{\lambda_7} + x_2 h_5^{*\prime}(\lambda_7);$$
$$m_{87} = -h_6^{*\prime}(\lambda_8); \qquad m_{98} = -h_7^{*\prime}(\lambda_9);$$
$$m_{89} = \frac{y_3 - y_3 h_6(\lambda_8)}{\lambda_8} + y_3 h_6^{*\prime}(\lambda_8); \qquad m_{8,10} = \frac{x_3 - x_3 h_6(\lambda_8)}{\lambda_8} + x_3 h_6^{*\prime}(\lambda_8);$$
$$m_{9,10} = \frac{1 - h_7^{*\prime}(\lambda_9)}{\lambda_9} + h_7^{*\prime}(\lambda_9).$$

Clearly,

$$m_{01} + m_{02} = \mu_0; \qquad m_{10} + m_{13} + m_{14} = \mu_1; \qquad m_{20} + m_{24} + m_{25} = \mu_2;$$
$$m_{35} + m_{36} + m_{37} + m_{38} + m_{39} = \mu_3; \qquad m_{46} + m_{47} + m_{48} + m_{49} = \mu_4; \qquad m_{50} = \mu_5;$$
$$m_{60} + m_{67} + m_{6,10} = \mu_6; \qquad m_{76} + m_{78} + m_{7,10} = \mu_7; \qquad m_{87} + m_{89} + m_{8,10} = \mu_8;$$
$$m_{98} + m_{9,10} = \mu_9.$$

7. Mean Survival Time

On obtaining and solving the recursive relations for $\phi_i(t)$, the cumulative distribution function of first passage time for the state S_i to death state and using Laplace Stieltje's transform and solving for $\phi_0^{**}(s)$, we get

$$\phi_0^{**}(s) = \frac{N(s)}{D(s)}, \tag{7.1}$$

where $\phi_0^{**}(s)$ is Laplace Stieltje's transform of $\phi_0(t)$. Here $N(s)$ and $D(s)$ can be easily obtained.

The mean survival time (T_0) is given by

$$T_0 = \frac{1-\phi_0^{**}(s)}{s}.$$

Using L'Hospital's rule and putting the values of $\phi_0^{**}(s)$ from equation (7.1), we get

$$T_0 = \frac{N}{D},$$

where

$$\begin{aligned}
N = {} & [\mu_0 + \mu_1 p_{01} + \mu_2 p_{02} + \mu_3 p_{01} p_{13} + \mu_4(p_{01}p_{14} + p_{02}p_{24}) + \mu_5(p_{01}p_{13}p_{35} + p_{02}p_{25})] \\
& \times [1 - p_{67}p_{76} - p_{78}p_{87} - p_{89}p_{98} + p_{67}p_{76}p_{89}p_{98}] \\
& + \mu_6[p_{01}p_{13}(p_{36} - p_{36}p_{78}p_{87} - p_{36}p_{89}p_{98} + p_{37}p_{76} - p_{37}p_{76}p_{89}p_{98} + p_{39}p_{76}p_{87}p_{98}) \\
& + (p_{01}p_{14} + p_{02}p_{24})(p_{46} - p_{46}p_{78}p_{87} - p_{46}p_{89}p_{98} + p_{47}p_{76} - p_{47}p_{76}p_{89}p_{98} + p_{49}p_{76}p_{87}p_{98})] \\
& + \mu_7[p_{01}p_{13}(p_{37} + p_{36}p_{67} + p_{38}p_{87} - p_{37}p_{89}p_{98} + p_{39}p_{87}p_{98} - p_{36}p_{67}p_{89}p_{98}) \\
& + (p_{01}p_{14} + p_{02}p_{24})(p_{47} + p_{46}p_{67} + p_{48}p_{87} - p_{47}p_{89}p_{98} + p_{49}p_{87}p_{98} - p_{46}p_{67}p_{89}p_{98})] \\
& + \mu_8[p_{01}p_{13}(p_{38} + p_{37}p_{78} + p_{39}p_{98} + p_{36}p_{67}p_{78} - p_{38}p_{67}p_{76} - p_{39}p_{67}p_{76}p_{98}) \\
& + (p_{01}p_{14} + p_{02}p_{24})(p_{48} + p_{47}p_{78} + p_{49}p_{98} + p_{46}p_{67}p_{78} - p_{48}p_{67}p_{76} - p_{49}p_{67}p_{76}p_{98})] \\
& + \mu_9[p_{01}p_{13}(p_{39} + p_{38}p_{89} + p_{37}p_{78}p_{89} - p_{39}p_{67}p_{76} - p_{39}p_{78}p_{87} + p_{36}p_{67}p_{78}p_{89} \\
& - p_{38}p_{67}p_{76}p_{89}) + (p_{01}p_{14} + p_{02}p_{24})(p_{49} + p_{48}p_{89} + p_{47}p_{78}p_{89} - p_{49}p_{67}p_{76} \\
& - p_{49}p_{78}p_{87} + p_{46}p_{67}p_{78}p_{89} - p_{48}p_{67}p_{76}p_{89})]
\end{aligned}$$

and

$$\begin{aligned}
D = {} & (p_{01}p_{03} - p_{01}p_{03}p_{35} + p_{01}p_{14} + p_{02}p_{24})(1 - p_{67}p_{76} - p_{78}p_{87} - p_{89}p_{98} + p_{67}p_{76}p_{89}p_{98}) \\
& - (p_{01}p_{13}p_{36} + p_{01}p_{14}p_{46} + p_{02}p_{24}p_{46})p_{60}(1 - p_{78}p_{87} - p_{89}p_{98}) \\
& - (p_{01}p_{13}p_{37} + p_{01}p_{14}p_{47} + p_{02}p_{24}p_{47})p_{76}p_{60}(1 - p_{89}p_{98})) \\
& - (p_{01}p_{13}p_{38} + p_{01}p_{14}p_{48} + p_{02}p_{24}p_{48})p_{87}p_{76}p_{60} \\
& - (p_{01}p_{13}p_{39} + p_{01}p_{14}p_{49} + p_{02}p_{24}p_{49})p_{98}p_{87}p_{76}p_{60}.
\end{aligned}$$

8. Numerical Computation and Graphical Analysis

The expression for mean survival time involves several parameters and hence is complex and tedious to handle. Therefore, the following specific case is considered for the purpose of analysis:

$$h_i(t) = \beta_i e^{-\beta_i(t)}, \quad \text{where } i = 1,2,\dots,7.$$

The specific case mentioned above is utilized for numerical computation and graphical analysis. Whenever a parameter is varied then the values of remaining parameters are taken as under:

$\lambda_1 = 0.75$, $\lambda_2 = 0.25$, $\lambda_3 = 0.86$, $\lambda_4 = 0.14$, $\lambda_5 = 0.65$, $\lambda_6 = 0.35$, $\lambda_7 = 0.7$, $\lambda_8 = 0.4$, $\lambda_9 = 0.1$, $p = 0.6$, $q = 0.4$, $p_1 = 0.85$, $q_1 = 0.15$, $p_2 = 0.12$, $q_2 = 0.88$, $\beta_1 = 0.9$, $\beta_2 = 0.7$, $\beta_3 = 0.9$, $\beta_4 = 0.8$, $\beta_5 = 0.6$, $\beta_6 = 0.4$, $\beta_7 = 0.3$, $r_1 = 0.35$, $r_2 = 0.30$, $r_3 = 0.15$, $r_4 = 0.15$, $r_5 = 0.05$, $s_1 = 0.30$, $s_2 = 0.28$, $s_3 = 0.25$, $s_4 = 0.17$, $x_1 = 0.15$, $x_2 = 0.30$, $x_3 = 0.60$, $y_1 = 0.85$, $y_2 = 0.70$, $y_3 = 0.40$.

Several graphs have been plotted for mean survival time with different values of the parameters involved in its expression. A few of them are presented here. Figure 2 to Figure 11 show how mean survival time changes with rates $\lambda_1, \lambda_2, \lambda_3, \lambda_5, \lambda_7, \lambda_8$ and λ_9 for different recovery rates $\beta_1, \beta_5, \beta_6, \beta_7$ and probabilities $p, p_1, p_2, r_5, s_4, y_3$. In Figure 2 to Figure 11, as infection rate λ_1, clinical testing rates (λ_2, λ_3), advance testing rate λ_5, damage rate $(\lambda_7, \lambda_8, \lambda_9)$ increase, MST(T_0) decreases whereas MST(T_0) gives higher value with larger values of recovery rates $(\beta_1, \beta_5, \beta_6, \beta_7)$ and probabilities $(p, p_1, p_2, r_5, s_4, y_3)$.

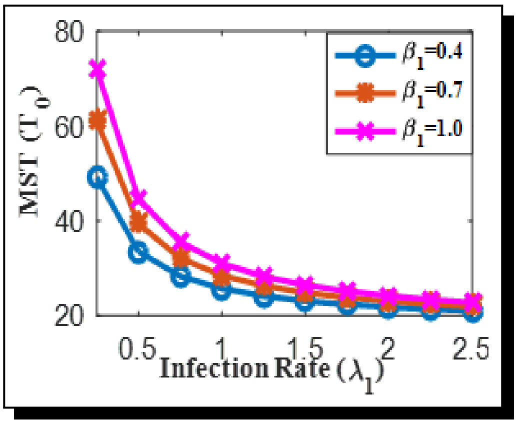

Figure 2. MST(T_0) versus infection rate (λ_1) for varying recovery rate (β_1)

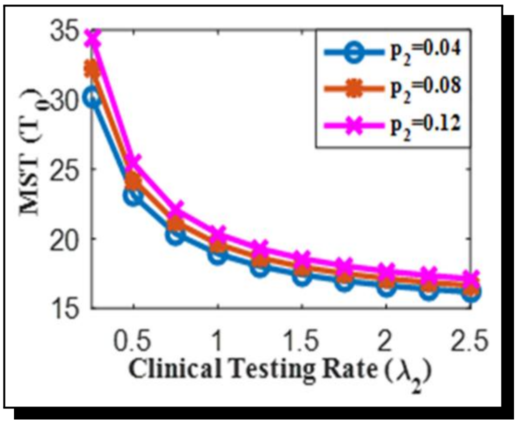

Figure 3. MST(T_0) versus clinical testing rate (λ_2) for varying probability (p_2)

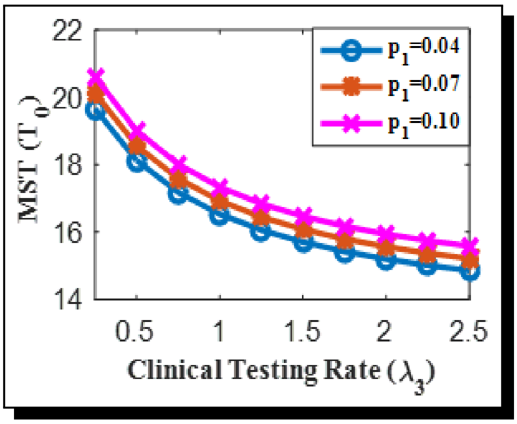

Figure 4. MST(T_0) versus clinical testing rate (λ_3) for varying probability (p_1)

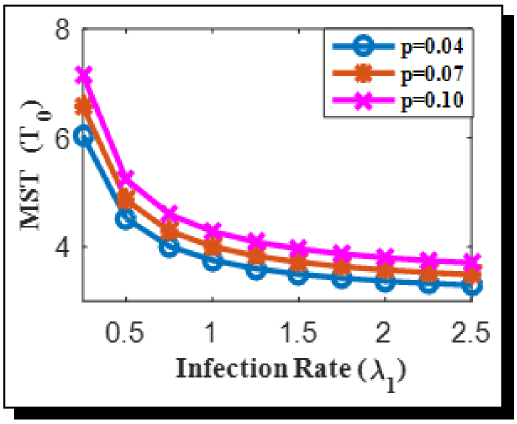

Figure 5. MST(T_0) versus infection rate (λ_1) for varying probability (p)

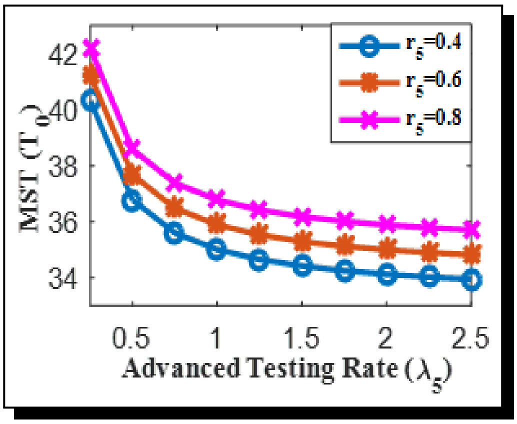

Figure 6. MST(T_0) versus advance testing rate (λ_5) for varying probability (r_5)

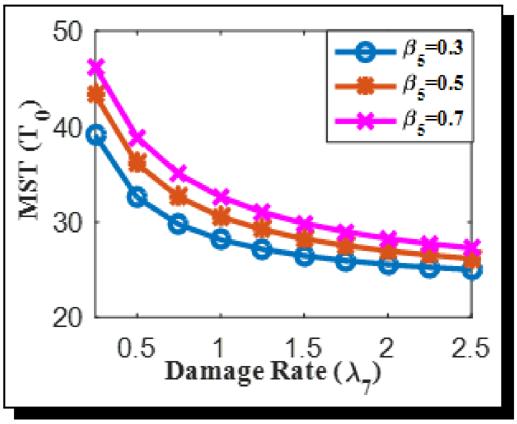

Figure 7. MST(T_0) versus damage rate (λ_7) for varying recovery rate (β_5)

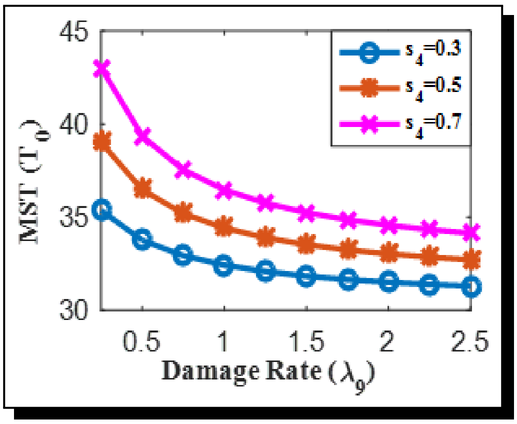

Figure 8. MST(T_0) versus damage rate (λ_9) for varying probability (s_4)

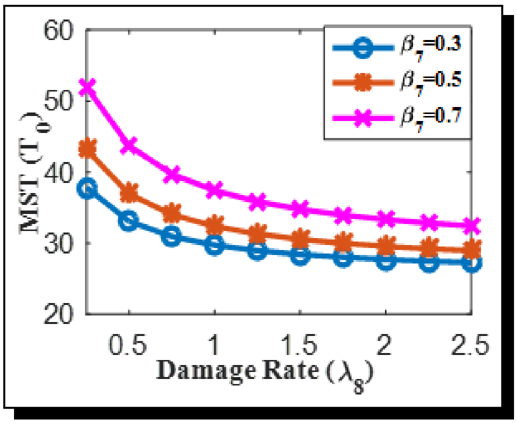

Figure 9. MST(T_0) versus damage rate (λ_8) for varying recovery rate (β_7)

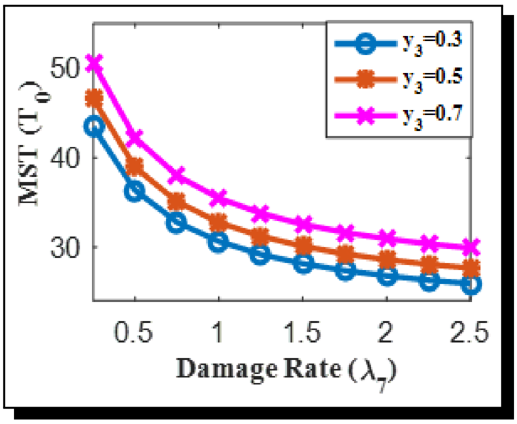

Figure 10. MST(T_0) versus damage rate (λ_7) for varying probability (y_3)

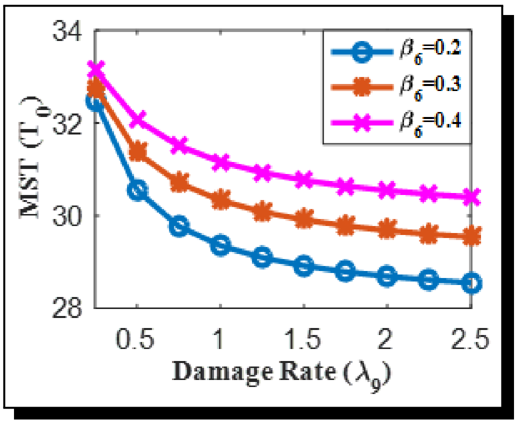

Figure 11. MST(T_0) versus damage rate (λ_9) for varying recovery rate (β_6)

9. Sensitivity and Relativity Sensitivity Analysis

Sensitivity analysis is conducted to understand how changes in the parameters affect the mean survival time (T_0) under specific conditions. The sensitivity and relative sensitivity functions for mean survival time (T_0) are formulated as follows:

$$\pi_k = \frac{\partial(T_0)}{\partial k} \quad \text{and} \quad \delta_k = \pi_k\left(\frac{k}{T_0}\right),$$

where $k = \lambda_1, \lambda_2, \lambda_5, \lambda_7, \lambda_8, \lambda_9, \beta_1, \beta_5, \beta_7, p_1, p_2, r_5, s_4, y_3$. While computations of values of sensitivity and relative sensitivity, each of the parameters have been considered and then values of the remaining parameters are taken as given in Section 8.

The sensitivity and relative sensitivity of mean survival time are evaluated with respect to the parameters ($\lambda_1, \lambda_2, \lambda_5, \lambda_7, \lambda_8, \lambda_9, \beta_1, \beta_5, \beta_7, p_1, p_2, r_5, s_4$) have been presented in Table 1 to Table 13. Table 1 to Table 6 show that signs of sensitivity of mean survival time with parameters $\lambda_1, \lambda_2, \lambda_5, \lambda_7, \lambda_8$ and λ_9 are negative which implies that increase in these parameters decline the value of MST. Tables 7 to Table 13 show that signs of the sensitivity values of mean survival time with parameters $\beta_1, \beta_5, \beta_7, p_1, p_2, r_5$ and s_4 are positive which lead to the conclusion that increase in these parameters improve the value of mean survival time. As infection rate, clinical testing rates, advanced testing rates and damage rates increase, sensitivity function decreases whereas recovery rates, probability of clinical testing and probability of advanced testing increase, sensitivity function increases. It has been observed from the absolute values of sensitivity and relative sensitivity function that mean survival time is more sensitive towards the rates $\lambda_1, \lambda_2, \lambda_7, \beta_5$ and p_2.

Table 1. Sensitivity and relative sensitivity values of MST(T_0) with transition rate (λ_1)

λ_1	$\pi_{\lambda_1} = \frac{\partial(T_0)}{\partial\lambda_1}$	$\delta_{\lambda_1} = \pi_{\lambda_1}\left(\frac{\lambda_1}{T_0}\right)$	$\left\lvert\pi_{\lambda_1} = \frac{\partial(T_0)}{\partial\lambda_1}\right\rvert$	$\left\lvert\delta_{\lambda_1} = \pi_{\lambda_1}\left(\frac{\lambda_1}{T_0}\right)\right\rvert$
0.25	−181.45	−0.71	181.45	0.71
0.35	−92.58	−0.63	92.58	0.63
0.45	−56.00	−0.58	56.00	0.58
0.55	−37.49	−0.53	37.49	0.53
0.65	−26.84	−0.48	26.84	0.48
0.75	−20.16	−0.45	20.16	0.45
0.85	−15.69	−0.42	15.69	0.42

Table 2. Sensitivity and relative sensitivity values of MST(T_0) with transition rate (λ_2)

λ_2	$\pi_{\lambda_2} = \frac{\partial(T_0)}{\partial\lambda_2}$	$\delta_{\lambda_2} = \pi_{\lambda_2}\left(\frac{\lambda_2}{T_0}\right)$	$\left\lvert\pi_{\lambda_2} = \frac{\partial(T_0)}{\partial\lambda_2}\right\rvert$	$\left\lvert\delta_{\lambda_2} = \pi_{\lambda_2}\left(\frac{\lambda_2}{T_0}\right)\right\rvert$
0.25	−72.47	−0.53	72.47	0.53
0.35	−40.11	−0.50	40.11	0.50
0.45	−25.42	−0.45	25.42	0.45
0.55	−17.54	−0.42	17.54	0.42
0.65	−12.83	−0.39	12.83	0.39
0.75	−9.78	−0.36	9.78	0.36
0.85	−7.71	−0.34	7.71	0.34

Table 3. Sensitivity and relative sensitivity values of MST(T_0) with transition rate (λ_5)

λ_5	$\pi_{\lambda_5} = \frac{\partial(T_0)}{\partial\lambda_5}$	$\delta_{\lambda_5} = \pi_{\lambda_5}\left(\frac{\lambda_5}{T_0}\right)$	$\left\lvert\pi_{\lambda_5} = \frac{\partial(T_0)}{\partial\lambda_5}\right\rvert$	$\left\lvert\delta_{\lambda_5} = \pi_{\lambda_5}\left(\frac{\lambda_5}{T_0}\right)\right\rvert$
0.25	−24.92	−0.166	24.92	0.166
0.35	−12.71	−0.124	12.71	0.124
0.45	−7.69	−0.099	7.69	0.099
0.55	−5.15	−0.083	5.15	0.083
0.65	−3.69	−0.071	3.69	0.071
0.75	−2.77	−0.062	2.77	0.062
0.85	−2.16	−0.055	2.16	0.055

Table 4. Sensitivity and relative sensitivity values of MST(T_0) with transition rate (λ_7)

λ_7	$\pi_{\lambda_7} = \frac{\partial(T_0)}{\partial\lambda_7}$	$\delta_{\lambda_7} = \pi_{\lambda_7}\left(\frac{\lambda_7}{T_0}\right)$	$\left\lvert\pi_{\lambda_7} = \frac{\partial(T_0)}{\partial\lambda_7}\right\rvert$	$\left\lvert\delta_{\lambda_7} = \pi_{\lambda_7}\left(\frac{\lambda_7}{T_0}\right)\right\rvert$
0.25	−25.74	−0.159	25.74	0.159
0.35	−18.99	−0.174	18.99	0.174
0.45	−14.59	−0.179	14.59	0.179
0.55	−11.56	−0.181	11.56	0.181
0.65	−9.39	−0.178	9.39	0.178
0.75	−7.77	−0.175	7.77	0.175
0.85	−6.54	−0.170	6.54	0.170

Table 5. Sensitivity and relative sensitivity values of MST(T_0) with transition rate (λ_8)

λ_8	$\pi_{\lambda_8} = \frac{\partial(T_0)}{\partial\lambda_8}$	$\delta_{\lambda_8} = \pi_{\lambda_8}\left(\frac{\lambda_8}{T_0}\right)$	$\left\lvert\pi_{\lambda_8} = \frac{\partial(T_0)}{\partial\lambda_8}\right\rvert$	$\left\lvert\delta_{\lambda_8} = \pi_{\lambda_8}\left(\frac{\lambda_8}{T_0}\right)\right\rvert$
0.25	−10.48	−0.075	10.48	0.075
0.35	−8.06	−0.083	8.06	0.083
0.45	−6.39	−0.086	6.39	0.086
0.55	−5.19	−0.087	5.19	0.087
0.65	−4.29	−0.086	4.29	0.086
0.75	−3.62	−0.085	3.62	0.085
0.85	−3.09	−0.083	3.09	0.083

Table 6. Sensitivity and relative sensitivity values of MST(T_0) with transition rate (λ_9)

λ_9	$\pi_{\lambda_9} = \frac{\partial(T_0)}{\partial\lambda_9}$	$\delta_{\lambda_9} = \pi_{\lambda_9}\left(\frac{\lambda_9}{T_0}\right)$	$\left\lvert\pi_{\lambda_9} = \frac{\partial(T_0)}{\partial\lambda_9}\right\rvert$	$\left\lvert\delta_{\lambda_9} = \pi_{\lambda_9}\left(\frac{\lambda_9}{T_0}\right)\right\rvert$
0.25	−5.43	−0.042	5.43	0.042
0.35	−3.57	−0.039	3.57	0.039
0.45	−2.53	−0.036	2.53	0.036
0.55	−1.88	−0.033	1.88	0.033
0.65	−1.46	−0.030	1.46	0.030
0.75	−1.16	−0.028	1.16	0.028
0.85	−0.95	−0.026	0.95	0.026

Table 7. Sensitivity and relative sensitivity values of MST(T_0) with recovery rate (β_1)

β_1	$\pi_{\beta_1} = \frac{\partial(T_0)}{\partial\beta_1}$	$\delta_{\beta_1} = \pi_{\beta_1}\left(\frac{\beta_1}{T_0}\right)$	$\left\lvert\pi_{\beta_1} = \frac{\partial(T_0)}{\partial\beta_1}\right\rvert$	$\left\lvert\delta_{\beta_1} = \pi_{\beta_1}\left(\frac{\beta_1}{T_0}\right)\right\rvert$
0.2	17.06	0.148	17.06	0.148
0.3	16.48	0.200	16.48	0.200
0.4	15.93	0.241	15.93	0.241
0.5	15.41	0.276	15.41	0.276
0.6	14.91	0.303	14.91	0.303
0.7	14.44	0.327	14.44	0.327
0.8	13.99	0.346	13.99	0.346
0.9	13.56	0.362	13.56	0.362

Table 8. Sensitivity and relative sensitivity values of MST(T_0) with recovery rate (β_5)

β_5	$\pi_{\beta_5} = \frac{\partial(T_0)}{\partial\beta_5}$	$\delta_{\beta_5} = \pi_{\beta_5}\left(\frac{\beta_5}{T_0}\right)$	$\left\lvert\pi_{\beta_5} = \frac{\partial(T_0)}{\partial\beta_5}\right\rvert$	$\left\lvert\delta_{\beta_5} = \pi_{\beta_5}\left(\frac{\beta_5}{T_0}\right)\right\rvert$
0.3	12.51	0.123	12.51	0.123
0.4	10.97	0.138	10.97	0.138
0.5	9.69	0.148	9.69	0.148
0.6	8.62	0.153	8.62	0.153
0.7	7.73	0.156	7.73	0.156
0.8	6.96	0.158	6.96	0.158
0.9	6.30	0.158	6.30	0.158

Table 9. Sensitivity and relative sensitivity values of MST(T_0) with recovery rate (β_7)

β_7	$\pi_{\beta_7} = \frac{\partial(T_0)}{\partial\beta_7}$	$\delta_{\beta_7} = \pi_{\beta_7}\left(\frac{\beta_7}{T_0}\right)$	$\left\lvert\pi_{\beta_7} = \frac{\partial(T_0)}{\partial\beta_7}\right\rvert$	$\left\lvert\delta_{\beta_7} = \pi_{\beta_7}\left(\frac{\beta_7}{T_0}\right)\right\rvert$
0.3	3.13	0.028	3.13	0.028
0.4	2.12	0.025	2.12	0.025
0.5	1.54	0.022	1.54	0.022
0.6	1.16	0.020	1.16	0.020
0.7	0.91	0.019	0.91	0.019
0.8	0.73	0.017	0.73	0.017
0.9	0.60	0.016	0.60	0.016

Table 10. Sensitivity and relative sensitivity values of MST(T_0) with recovery rate (p_1)

p_1	$\pi_{p_1} = \frac{\partial(T_0)}{\partial p_1}$	$\delta_{p_1} = \pi_{p_1}\left(\frac{p_1}{T_0}\right)$	$\left\lvert\pi_{p_1} = \frac{\partial(T_0)}{\partial p_1}\right\rvert$	$\left\lvert\delta_{p_1} = \pi_{p_1}\left(\frac{p_1}{T_0}\right)\right\rvert$
0.3	14.19	0.182	14.19	0.182
0.4	15.57	0.251	15.57	0.251
0.5	17.16	0.324	17.16	0.324
0.6	18.19	0.403	18.19	0.403
0.7	21.15	0.489	21.15	0.489
0.8	23.68	0.582	23.68	0.582
0.9	26.71	0.686	26.71	0.686

Table 11. Sensitivity and relative sensitivity values of MST(T_0) with recovery rate (p_2)

p_2	$\pi_{p_2} = \frac{\partial(T_0)}{\partial p_2}$	$\delta_{p_2} = \pi_{p_2}\left(\frac{p_2}{T_0}\right)$	$\left\lvert\pi_{p_2} = \frac{\partial(T_0)}{\partial p_2}\right\rvert$	$\left\lvert\delta_{p_2} = \pi_{p_2}\left(\frac{p_2}{T_0}\right)\right\rvert$
0.3	65.4	0.45	65.4	0.45
0.4	85.3	0.67	85.3	0.67
0.5	115.8	0.95	115.8	0.95
0.6	166.2	1.34	166.2	1.34
0.7	258.4	1.90	258.4	1.90
0.8	455.4	2.81	455.4	2.81
0.9	1007.5	4.59	1007.5	4.59

Table 12. Sensitivity and relative sensitivity values of MST(T_0) with recovery rate (r_5)

r_5	$\pi_{r_5} = \frac{\partial(T_0)}{\partial r_5}$	$\delta_{r_5} = \pi_{r_5}\left(\frac{r_5}{T_0}\right)$	$\left\lvert\pi_{r_5} = \frac{\partial(T_0)}{\partial r_5}\right\rvert$	$\left\lvert\delta_{r_5} = \pi_{r_5}\left(\frac{r_5}{T_0}\right)\right\rvert$
0.3	4.32	0.037	4.32	0.037
0.4	4.36	0.049	4.36	0.049
0.5	4.39	0.062	4.39	0.062
0.6	4.43	0.074	4.43	0.074
0.7	4.46	0.085	4.46	0.085
0.8	4.50	0.097	4.50	0.097
0.9	4.54	0.109	4.54	0.109

Table 13. Sensitivity and relative sensitivity values of MST(T_0) with recovery rate (s_4)

s_4	$\pi_{s_4} = \frac{\partial(T_0)}{\partial s_4}$	$\delta_{s_4} = \pi_{s_4}\left(\frac{s_4}{T_0}\right)$	$\left\lvert\pi_{s_4} = \frac{\partial(T_0)}{\partial s_4}\right\rvert$	$\left\lvert\delta_{s_4} = \pi_{s_4}\left(\frac{s_4}{T_0}\right)\right\rvert$
0.3	13.40	0.114	13.40	0.114
0.4	14.20	0.154	14.20	0.154
0.5	15.08	0.197	15.08	0.197
0.6	16.04	0.242	16.04	0.242
0.7	17.10	0.289	17.10	0.289
0.8	18.26	0.338	18.26	0.338
0.9	19.55	0.390	19.55	0.390

10. Conclusion

In the present paper, a general stochastic model for human lung disease progression considering two types of diagnostic tests has been introduced. The evaluated expressions for mean sojourn times of the model give estimates of the times for a lung disease patient to remain in different states. The investigations through the analyses of the model conclude that mean survival time of the lung disease patients reduces for higher rates of transition to different stages. It has been concluded that mean survival time improves with higher values of recovery rates at different stages of lung disease progression. Further, infection rate, ordinary clinical testing rate of symptomatic patients and damage rate at earlier stages of the lung disease have more effect on mean survival time of the patient. Also, recovery rate from initial lung disease stage and diagnose of lung infection in non-symptomatic patients have higher impact on their survivability.

Competing Interests

The authors declare that they have no competing interests.

Authors' Contributions

All the authors contributed significantly in writing this article. The authors read and approved the final manuscript.

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