

## Threshold conditions for global stability of disease free state of COVID-19

Muhammad Zamir<sup>a</sup>, Kamal Shah<sup>b,\*</sup>, Fawad Nadeem<sup>a</sup>, Mohd Yazid Bajuri<sup>c</sup>, Ali Ahmadian<sup>d,\*</sup>, Soheil Salahshour<sup>e</sup>, Massimiliano Ferrara<sup>f</sup>

<sup>a</sup> Department of Mathematics, University of Science and Technology, Bannu, Khyber Pakhtunkhwa, Pakistan

<sup>b</sup> Department of Mathematics, University of Malakand, Chakdara, Dir(L), Khyber Pakhtunkhwa, Pakistan

<sup>c</sup> Department of Orthopaedics and Traumatology, Faculty of Medicine, Universiti Kebangsaan Malaysia(UKM), Kuala Lumpur, Malaysia

<sup>d</sup> Institute of IR 4.0, The National University of Malaysia, 43600, UKM, Bangi, Malaysia

<sup>e</sup> Faculty of Engineering and Natural Sciences, Bahcesehir University, Istanbul, Turkey

<sup>f</sup> ICRIOS – The Invernizzi Centre for Research in Innovation, Organization, Strategy and Entrepreneurship, Bocconi University, Department of Management and Technology Via Sarfatti, 25 20136 Milano (MI), Italy

### ARTICLE INFO

#### Keywords:

Mathematical model  
Basic reproduction number  
Next generation matrix  
Sensitivity analysis  
Global stability  
Threshold condition

### ABSTRACT

This article focus the elimination and control of the infection caused by COVID-19. Mathematical model of the disease is formulated. With help of sensitivity analysis of the reproduction number the most sensitive parameters regarding transmission of infection are found. Consequently strategies for the control of infection are proposed. Threshold condition for global stability of the disease free state is investigated. Finally, using Matlab numerical simulations are produced for validation of theoretical results.

### Introduction

The pandemic of viral infection, causing COVID-19, initiated in China. COVID-19 is highly infectious disease. The causative agent of the disease is a virus called severe acute respiratory syndrome coronavirus 2, or SARS-CoV-2. Very rapid viral transmission occur in human population, whenever they are in close contact. The transmission probability is high when the contact range is less than 2 meters. In such a circumstances the virus spreads by respiratory droplets released when an infected individual coughs, sneezes or talks. These droplets can be inhaled or directly reach the mouth or nose of a nearby person with medium of air. However if a susceptible human is not close range, the shredded virus contaminate the nearby surfaces. These contaminated surfaces help the viral transmission in community, however this isn't considered to be a main way it spreads through [1].

Coronaviruses represents a big family. This family causes different types of infections. The infection ranges from common cold/flu to the most severe infection like severe acute respiratory syndrome and MERS; middle east respiratory syndrome [2]. The novel COVID-19 first emerged in December, 2019, Wuhan, China, in the form of severe cases of pneumonia and respiratory problems. The correct etiology of the

infection could not be traced that time. WHO reported the virus as a novel coronavirus (2019-nCoV). The disease was named as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). The virus was first identified from a single individual. Subsequently the virus was verified in sixteen more cases [4,5].

It is expected that the virus might be bat origin [3], and the infection transmission might be initiated from a seafood market (Huanan Seafood Wholesale Market) of China [6]. Currently 7,597,304 cases of the disease as been confirmed and 423,844 deaths has occurred as of June 12, 2020, world wide [7].

About 75% of the victims of COVID-19 don't develop symptoms of the disease and recovered naturally [8]. 20% of the exposed individuals develop symptoms. The most common symptoms of COVID-19 are tiredness, fever and dry cough. Some patients may have aches and pains, runny nose, nasal congestion, Muscle aches, Chills, Loss of taste or smell or both, Headache, Chest pain and sore throat. Other less common symptoms have been reported, such as rash, nausea, vomiting and diarrhea. These symptoms are usually mild and starts slowly and gradually. Most symptomatic individuals (about 80%) recover from the disease without needing special treatment. In children and young adults, COVID-19 is generally minor. However, for some people it can cause

\* Corresponding authors.

E-mail addresses: [kamalshah408@gmail.com](mailto:kamalshah408@gmail.com) (K. Shah), [yb@ppukm.ukm.edu.my](mailto:yb@ppukm.ukm.edu.my) (M.Y. Bajuri), [ahmadian.hosseini@gmail.com](mailto:ahmadian.hosseini@gmail.com) (A. Ahmadian), [soheil.salahshour@eng.bau.edu.tr](mailto:soheil.salahshour@eng.bau.edu.tr) (S. Salahshour), [massimiliano.ferrara@unirc.it](mailto:massimiliano.ferrara@unirc.it) (M. Ferrara).

<https://doi.org/10.1016/j.rinp.2020.103784>

Received 24 September 2020; Received in revised form 23 December 2020; Accepted 24 December 2020

Available online 6 January 2021

2211-3797/© 2021 The Author(s).

Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

serious illness. This type of severe attack of the virus may cause death. In some cases the attack may result SARS (severe acute respiratory syndrome) or pneumonia. The symptoms of infection appears in 2–14 days [9,10]. The recovery time of mild cases is approximately 2 weeks and in severe/critical cases the recovery may take 3–6 weeks [11]. The individuals who developed severe form of disease, the medium time to dyspnea ranges from 5–8 days. The average time to acute respiratory distress syndrome (ARDS) varies from 8 days to 12 days. The average time to intensive care at vent bol (ventilated class) ranges from 10–12 days [27,26,28,29].The recovered individuals of disease can have antibodies for at least two weeks, long-term data are still lacking [12].

The coronavirus (2019-nCoV) is genetically related to the coronavirus that caused the SARS-2003, however the diseases they caused are quite different [13]. The genetic features and some clinical findings of the infection have been reported recently [14–16]. International air travel contributed the international spread of the infection. The infection has got global attention regarding its elimination and control [17].

The whole world is highly concerned with drastic future forecast of the disease. The scientists and researchers, therefore focus the development of mathematical model. The model not only helps estimating dynamics of the transmission of the virus but other important forecasts. Recent mathematical modeling includes [18–23]. These models mainly focused the transmission/spreading of coronavirus or basic reproduction number of coronavirus, ( $R_0$ ). The authors followed intrinsic growth rate and the serial intervals. *Wu et al.* in their study focus the forecasting and Newscasting of the novel coronavirus both nationally and internationally. The authors used Markov Chain Monte Carlo methods in their study [24].

However, these models don't discuss the origin(bat) and the route of transmission/spreading (seafood market). *Chen et al.* extended this work. The authors in their work presented a comprehensive model of novel coronavirus [25]. Some more detailed information about the said infection can be found in [26,27,29,30]. In this study, we focus the effect

of different intervention on the transmission of the disease with help of sensitivity analysis of the parameters of the model. We combine different interventions in particular ratio and formulate a strategy. The effect of different strategies on disease control is shown graphically to facilitate strategy selection for the agencies fighting against COVID-19. Lastly we find a threshold condition for global stability of the disease free state in the community.

**Model formulation**

The total human population is divided in nine sub-classes: susceptible humans class ( $S$ ), the quarantine humans class ( $Q$ ), exposed humans class ( $E$ ), symptomatic infected humans class ( $I_1$ ), asymptomatic infected humans class ( $I_2$ ), isolated human class ( $I_S$ ), mild human class ( $I_M$ ), critical human class ( $I_C$ ) and recovered humans class ( $R$ ).  $W_i$  denote the class of contaminated surfaces/stuff shedded/stained with coronavirus.

The susceptible human population can catch infection from infected humans (both symptomatic and asymptomatic), exposed humans and also from the stuff stained/contaminated with coronavirus at different rates. All those susceptible individuals are quarantined who got contact with infectious human in the last 14 days. The quarantined individuals are passed through laboratory tests and accordingly move to susceptible class or exposed class. The exposed individuals after completing latency or incubation period move to symptomatic infectious class  $I_1$  or asymptomatic infectious class  $I_2$ . The symptomatic infectious individuals are isolated in isolation class  $I_S$ . After completing transition period at  $I_S$  some of the individuals move to mild class  $I_M$  and the rest move to critical class  $I_C$ . Most of the individuals at mild class recover and about 49% of the infected individuals at critical class die due to disease. The symptomatic and asymptomatic infectious individuals contaminate both the stuff and environment close to them at the rate called shedding coefficient. The class of such stuff is denoted by  $W_i$ .

The following system (1) of coupled nonlinear differential equations represents the model of COVID-19:

$$\begin{cases} \dot{S} = \Lambda - (\beta_1(I_1 + c_2I_2 + c_4E) + \beta_2W_i)S - \mu S + k_2Q + \beta R \\ \dot{Q} = (\beta_1(I_1)S - (k_1 + k_2 + \mu)Q \\ \dot{E} = (\beta_1(c_2I_2 + c_4E) + \beta_2W_i)S - (\kappa_E + \mu)E + k_1Q \\ \dot{I}_1 = r_1\kappa_E E - (k_I + \mu)I_1 \\ \dot{I}_2 = (1 - r_1)\kappa_E E - (r_n + \mu)I_2 \\ \dot{I}_S = k_I I_1 - (r_i + \mu)I_S \\ \dot{I}_M = \delta r_i I_S - (k_4 + \mu)I_M \\ \dot{I}_C = (1 - \delta)r_i I_S - (k_5 + D_2 + \mu)I_C + k_3 r_n I_2 \\ \dot{R} = k_4 I_M + k_5 I_C + (1 - k_3)r_n I_2 - (\mu + \beta)R \\ \dot{W}_i = \xi_1 I_1 + \xi_2 I_2 - (\epsilon + e_x)W_i \end{cases} \tag{1}$$

The following table (1) contains the values of the different parameters used in the model (1).

In this section properties of the model including Disease-Free-Equilibrium, Invariant region and the Basic Reproduction Number are addressed.

*Invariant Region*

The state variables and parameters used in the model are always non-negative because the model is concerned with the living population. Adding all the compartments related to human population we have:

$$\dot{N} = \Lambda - \mu N - D_2 I_C, \tag{2}$$

From Eq. (2) we have

**Table 1**  
Parameters and their description.

Notation	Parameter definition	Value	Source
$\Lambda$	Humans recruitment rate	0.0015875 day <sup>-1</sup>	[31]
$\mu$	Humans natural mortality rate	0.00004 day <sup>-1</sup>	[31]
$c_2$	Transmission multiple of $\beta_1$ with $I_2$	0.24666	[8]
$\beta_1$	Disease transmission probability from $I_1$	0.65 day <sup>-1</sup>	[25]
$c_4$	Transmission multiple of $\beta_1$ with $E$	0.31666	[8]
$\kappa_E$	Inverse of disease incubation period	5–14 day	[32]
$k_I$	Disease clinical detection period	5–10 day	[8]
$k_0$	Quarantine period	14 days	[33]
$\beta_2$	Disease transmission probability from contaminated stuff	0.165 day <sup>-1</sup>	[25]
$r_n$	Transition period in $I_2$	14–22 days	[34]
$r_i$	Transition period in $I_S$	14–21 days	[34]
$r_1$	The ratio of exposed moving to symptomatic	25%	[8]
$\xi_1$	Shedding coefficient of $I_1$	0.5	[25]
$\xi_2$	Shedding coefficient of $I_2$	0.5	[25]
$D_2$	Disease induced death ratio of critical class	0.49%	[35]
$\epsilon$	The life time of virus on stuff	1–10 days	[25]
$e_x$	Expiry period of contaminated stuff	30 days	assume
$k_1$	Ratio of quarantine moving to $I_S$	66%	assume
$k_2$	Ratio of quarantine moving to $S$	33%	assume
$k_4$	Recovery ratio of mild class	99%	[36]
$k_5$	Recovery rate of critical class	47%	[37]
$k_3$	Ratio of asymptomatic moving to $I_C$	4%	[38,39]
$\delta$	Ratio of isolated moving to $I_C$	15%	[40]
$\beta$	Immunity loosing period	15 days	[41]

$$\dot{N} \leq \Lambda - \mu N.$$

Solving the above equation we have:

$$N \leq N(0)e^{-\mu t} + \frac{\Lambda}{\mu}(1 - e^{-\mu t}) \Rightarrow N \leq \frac{\Lambda}{\mu} \text{ when } t \rightarrow \infty.$$

On the basis of above discussion we claim the following result:

**Proof.**  $\Omega$ ; the region of the proposed model, defined by

$$\Omega = \left\{ (S, Q, E, I_1, I_2, I_S, I_M, I_C, R, W_I) \in R_+^{10}, N \leq \frac{\Lambda}{\mu} \right\}$$

is positively invariant domain, and the model is epidemiologically and mathematically well posed [42] and all the trajectories are forward bounded.  $\square$

**Reproductive number**

The number of secondary infections caused by a single primary infection in completely susceptible population is called reproduction number denoted by  $R_0$ . The reproduction number is found by next generation matrix [44,43] as:

$R_0 = \rho(-FV^{-1})$ , where  $\rho$  is spectral radius, where  $F = \mathcal{F}_f$ ; the jacobian of  $f$  and

$$f = \begin{pmatrix} f_1 \\ f_2 \\ f_3 \\ f_4 \\ f_5 \\ f_6 \\ f_7 \end{pmatrix} = \begin{pmatrix} (\beta_1 c_4 E + \beta_2 W_I) S \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

The column in matrix  $f$  denotes the individuals who get infected. Similarly.

$V = \mathcal{F}_v$ ; the jacobian of  $v$  and

$$v = \begin{pmatrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \\ v_6 \\ v_7 \end{pmatrix} = \begin{pmatrix} -(\kappa_E + \mu)E + k_1 Q \\ r_1 \kappa_E E - (k_I + \mu)I_1 \\ (1 - r_1) \kappa_E E - (r_n + \mu)I_2 \\ k_I I_1 - (r_I + \mu)I_S \\ \delta r_I I_S - (k_4 + \mu)I_M \\ (1 - \delta) r_I I_S - (k_5 + D_2 + \mu)I_C + k_3 r_n I_2 \\ \xi_1 I_1 + \xi_2 I_2 - (\epsilon + e_X)W_I \end{pmatrix}.$$

The column of matrix  $V$  denotes the individuals that enter the infected class or leave the infected class, excluding those coming from susceptible class.

The dominant Eigenvalue of  $(-FV^{-1})$  and hence  $R_0$  is:

$$R_0 = \frac{\beta_1 c_4 \Lambda}{\mu(\kappa_E + \mu)} + \frac{\beta_2 \Lambda((r_n + \mu)(1 - r_1) \kappa_E \xi_1 + (k_I + \mu) r_1 \kappa_E \xi_2)}{\mu(\kappa_E + \mu)(k_I + \mu)(r_n + \mu)(\epsilon + e_X)}.$$

**Stability analysis**

In this part, the threshold condition for global asymptotic stability of Disease Free State of the system (1) is studied. The following theorem would be used in the upcoming results, stated here for convenience:

**Theorem 3.1.** ([45]) *Let the given model be presented as*

$$\begin{cases} \dot{\tilde{\mathcal{Y}}}_1 = \tilde{\mathcal{B}}_1(\tilde{\mathcal{Y}})(\tilde{\mathcal{Y}} - \tilde{\mathcal{Y}}_1^*) + \tilde{\mathcal{B}}_{12}(\tilde{\mathcal{Y}})\tilde{\mathcal{Y}}_2 \\ \dot{\tilde{\mathcal{Y}}}_2 = \tilde{\mathcal{B}}_2(\tilde{\mathcal{Y}})\tilde{\mathcal{Y}}_2. \end{cases}$$

Then the DFS (Disease free state) is GAS (globally asymptotically stable) if the following holds.

- (a<sub>1</sub>): All the populations involved in the model are forward bounded and hence the system is mathematically well posed.
- (a<sub>2</sub>): The sub-system of non infected classes  $\dot{\tilde{\mathcal{Y}}}_1 = \tilde{\mathcal{B}}_1(\tilde{\mathcal{Y}}_1, 0)(\tilde{\mathcal{Y}}_1 - \tilde{\mathcal{Y}}_1^*)$  is globally asymptotically stability at the origin.
- (a<sub>3</sub>): The matrix of non infected compartments denoted by  $\tilde{\mathcal{B}}_2(\tilde{\mathcal{Y}})$  is both metzler and irreducible.
- (a<sub>4</sub>): The matrix of infected classes,  $\tilde{\mathcal{B}}_2$  is bounded by some matrix  $\overline{\mathcal{B}}_2$  and  $\tilde{\mathcal{N}} = \{ \tilde{\mathcal{B}}_2(\tilde{\mathcal{Y}}), \tilde{\mathcal{Y}} \in \Omega \}$ . Then  $\overline{\mathcal{B}}_2$  may or may not belong to  $\tilde{\mathcal{N}}$ . However if  $\overline{\mathcal{B}}_2 \in \tilde{\mathcal{N}}$  then for any  $\tilde{\mathcal{Y}} \in \Omega$  such that  $\overline{\mathcal{B}}_2 = \tilde{\mathcal{B}}_2(\tilde{\mathcal{Y}})$ ,  $\tilde{\mathcal{Y}} \in R^{n_1} \times \{0\}$
- (a<sub>5</sub>): The spectral radius of  $(\overline{\mathcal{B}}_2)$  is less than or equal to zero.

To prove the global stability of the disease free equilibrium let  $Y =$  (The column vector of all the state variables). Let  $Y_s$  be the sub class of  $Y$ , containing all noninfected compartments of the total population.  $Y_I$  be the sub class of  $Y$  containing infected human population. That is

$Y_s =$  (The column vector of all non infected classes of the model)

and

$Y_I =$  (column vector of all infected state variables of the model).

**Theorem 3.2.** *Given sub system of non-infected population*

$$\begin{cases} \dot{S} = \Lambda - (\beta_1(I_1 + c_2 I_2 + c_4 E) + \beta_2 W_I)S - \mu S + k_2 Q + \beta R \\ \dot{R} = k_4 I_M + k_5 I_C + (1 - k_3) r_n I_2 - (\mu + \beta) R \end{cases} \quad (3)$$

This system of non-infected classes is GAS at the domain  $G$ , where  $G = \{ \mathcal{Y} \in \Omega; \mathcal{Y}_s \neq 0, \mathcal{Y}_I = 0 \}$ .

**Proof.** We re-write the above system as:

$$\dot{\mathcal{Y}}_s = \mathcal{E}_s(\mathcal{Y})(\mathcal{Y}_s) + \mathcal{F}_s$$

At the Domain  $G$ , the above system reduces to the form.

$$\begin{cases} \dot{S} = \Lambda - \mu S \\ \dot{R} = -\mu R \end{cases} \quad (4)$$

Here

$$C_s = \begin{pmatrix} -\mu & 0 \\ 0 & -\mu \end{pmatrix} \Rightarrow \mathcal{F}_s = (\Lambda, 0)^T.$$

All the entries  $j_{(i,i)}$  of the matrix  $C_s$  are  $-ve$ , Hence the said system is GAS at Disease Free equilibrium (DFE).

The DFE point is  $(\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0, 0)$ .  $\square$

The sub system of infected population is:

$$\dot{\mathcal{Y}}_I = \mathcal{B}_I(\mathcal{Y})\mathcal{Y}_I,$$

where

$$\dot{\mathcal{Y}}_1 = \begin{cases} \dot{E} = (\beta_1 c_4 E + \beta_2 W_1)S - (\kappa_E + \mu)E \\ \dot{I}_1 = r_1 \kappa_E E - (k_I + \mu)I_1 + k_1 Q \\ \dot{I}_2 = (1 - r_1) \kappa_E E - (r_n + \mu)I_2 \\ \dot{I}_S = k_I I_1 - (r_t + \mu)I_S \\ \dot{I}_M = \delta r_t I_S - (k_4 + \mu)I_M \\ \dot{I}_C = (1 - \delta) r_t I_S - (k_5 + D_2 + \mu)I_C + k_3 r_n I_2 \\ \dot{W}_1 = \xi_1 I_1 + \xi_2 I_2 - (\varepsilon + e_X)W_1 \end{cases} \quad (5)$$

**Theorem 3.3.** In the system (5),  $\mathcal{B}_1$  is irreducible and metzler  $\forall \mathcal{Y} \in \Omega$ . Further more there exist some  $\overline{\mathcal{B}}_1$  as

$$\mathcal{B}_1(\mathcal{Y}) \leq \overline{\mathcal{B}}_1(\mathcal{Y}) \text{ for } \mathcal{Y} \in \Omega. \quad (6)$$

Also

$$\overline{\mathcal{B}}_1 \in \mathcal{N} = \{ \mathcal{B}_1(\mathcal{Y}), \mathcal{Y} \in \Omega \} \quad \overline{\mathcal{B}}_1 = \mathcal{N}_{\max \Omega}. \quad (7)$$

$$q(\overline{\mathcal{B}}_1) \leq 0. \quad (8)$$

$q$  is modulus of stability and denotes the dominant real part of the eigenvalues of  $\overline{\mathcal{B}}_1$ .

**Proof.** Let us re-write sub system (5) as:

$$\dot{\mathcal{Y}}_1 = \mathcal{B}_1(\mathcal{Y}) \mathcal{Y}_1$$

$$\mathcal{B}_1(\mathcal{Y}) = \begin{pmatrix} E & F \\ G & H \end{pmatrix},$$

$$E = \begin{pmatrix} \beta_1 c_4 S - (\kappa_E + \mu) & 0 & 0 \\ r_1 \kappa_E & -(k_I + \mu) & 0 \\ (1 - r_1) \kappa_E & 0 & -(r_n + \mu) \end{pmatrix},$$

$$F = \begin{pmatrix} 0 & 0 & 0 & \beta_2 S \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}, G = \begin{pmatrix} 0 & k_I & 0 \\ 0 & 0 & 0 \\ 0 & 0 & k_3 r_n \\ 0 & \xi_1 & \xi_2 \end{pmatrix},$$

$$H = \begin{pmatrix} -(r_t + \mu) & 0 & 0 & 0 \\ \delta r_t & -(k_4 + \mu) & 0 & 0 \\ 0 & (1 - \delta) r_t & -(k_5 + D_2 + \mu) & 0 \\ 0 & 0 & 0 & -(\varepsilon + e_X) \end{pmatrix}.$$

Since the off diagonal entries are non-negative and the diagonal entries are negative. Therefore the matrix  $\mathcal{B}_1(\mathcal{Y})$  is irreducible and metzler for all  $\mathcal{Y} \in \Omega$ . Next let  $\overline{\mathcal{B}}_1$  be the upper bond of the matrix  $\mathcal{B}_1(\mathcal{Y})$ . Then,

$$\overline{\mathcal{B}}_1(\mathcal{Y}) = \begin{pmatrix} I & J \\ K & L \end{pmatrix},$$

$$I = \begin{pmatrix} \beta_1 c_4 S^0 - (\kappa_E + \mu) & 0 & 0 \\ r_1 \kappa_E & -(k_I + \mu) & 0 \\ (1 - r_1) \kappa_E & 0 & -(r_n + \mu) \end{pmatrix},$$

$$J = \begin{pmatrix} 0 & 0 & 0 & \beta_2 S^0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}, K = \begin{pmatrix} 0 & k_I & 0 \\ 0 & 0 & 0 \\ 0 & 0 & k_3 r_n \\ 0 & \xi_1 & \xi_2 \end{pmatrix},$$

$$L = \begin{pmatrix} -(r_t + \mu) & 0 & 0 & 0 \\ \delta r_t & -(k_4 + \mu) & 0 & 0 \\ 0 & (1 - \delta) r_t & -(k_5 + D_2 + \mu) & 0 \\ 0 & 0 & 0 & -(\varepsilon + e_X) \end{pmatrix}.$$

Since  $S \leq S^0$ . Therefore  $\overline{\mathcal{B}}_1(\mathcal{Y})$  is the upper bond of  $\mathcal{B}_1(\mathcal{Y})$ . This maximum is uniquely realized in  $\Omega$  if  $S = N = S^0$ . This corresponds to the DFE.

Also the matrix  $\overline{\mathcal{B}}_1(\mathcal{Y})$  is equal to  $J_2$ . Where  $J_2$  represent the Jacobian of the infected sub-system (3) at the DFE. Thus the assumption  $a_4$  of theorem (3.1) holds. This proves (7) and (6).  $\square$

Next we prove  $a_5$  or (8).

**Theorem 3.4.** The metzler matrix satisfy the axiom  $a_5$ ;  $q(\overline{\mathcal{B}}_1) \leq 0$ , if  $\xi < 1$ , where  $\xi$ , is given by:

$$\xi = \frac{\beta_1 c_4 \Lambda}{\mu(\kappa_E + \mu)} + \frac{r_1 \kappa_E \xi_1 \beta_2 \Lambda}{\mu(\kappa_E + \mu)(k_I + \mu)(\varepsilon + e_X)} + \frac{(1 - r_1) \kappa_E \xi_2 \beta_2 \Lambda}{\mu(\kappa_E + \mu)(r_n + \mu)(\varepsilon + e_X)},$$

where

**Proof.** We use the following decomposition of the matrix  $\overline{\mathcal{B}}_1$ .

$$\overline{\mathcal{B}}_1 = \begin{pmatrix} M & N \\ O & P \end{pmatrix}, \text{ where}$$

$$M = \begin{pmatrix} n_1 - (\kappa_E + \mu) & 0 & 0 & 0 & 0 \\ r_1 \kappa_E & -(k_I + \mu) & 0 & 0 & 0 \\ (1 - r_1) \kappa_E & 0 & -(r_n + \mu) & 0 & 0 \\ 0 & k_I & 0 & -(r_t + \mu) & 0 \\ 0 & 0 & 0 & \delta r_t & -(k_4 + \mu) \end{pmatrix},$$

$$O = \begin{pmatrix} 0 & 0 & k_3 r_n & 0 & (1 - \delta) r_t \\ 0 & \xi_1 & \xi_2 & 0 & 0 \end{pmatrix},$$

$$N = \begin{pmatrix} 0 & 0 \\ 0 & n_2 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \end{pmatrix}, P = \begin{pmatrix} -(k_5 + D_2 + \mu) & 0 \\ 0 & -(\varepsilon + e_X) \end{pmatrix}.$$

$$n_1 = \frac{\beta_1 c_4 \Lambda}{\mu}, \quad n_2 = \frac{\beta_2 \Lambda}{\mu}, \quad p_1 = (\kappa_E + \mu), \quad p_2 = (k_I + \mu),$$

$$p_3 = (r_n + \mu), \quad p_4 = (r_t + \mu), \quad p_5 = (k_4 + \mu) \quad p_6 = (k_5 + D_2 + \mu),$$

$$p_7 = (\varepsilon + e_X), \quad d_1 = r_1 \kappa_E, \quad d_2 = (1 - r_1) \kappa_E.$$

**Table 2**  
Sensitivity indices of parameters.

Parameter	value	index	Parameter	value	index
$r_n$	0.035714	-0.4869	$c_4$	0.31666	0.1623
$\Lambda$	0.0015875	1	$r_1$	0.25	0.3707
$e_x$	0.0333	-0.2093	$\beta_1$	0.65	0.1623
$\beta_2$	0.165	0.8377	$\mu$	0.00004	-1.0009
$k_E$	0.142857	-0.1620	$k_I$	0.1492537	-0.3501
$\xi_1$	0.5	0.3502	$\epsilon$	0.1	-0.6284
$\xi_2$	0.5	0.4875			

The stability of matrix  $\overline{B}_I$  depends on the stability of the matrix of  $M$  and  $P-OM^{-1}N$ .

Clearly all the entries  $m_{ij}$  of the  $M$  are non-negative for  $i \neq j$  and the eigenvalues are  $-ve$ . Hence the matrix  $M$  is metzler stable. Let  $G = P-OM^{-1}N$ .

Then the stability  $\overline{B}_I$  depends on the stability of  $G$ .

We know from Routh-Hurwitz [46] that in our case:  $\rho(\overline{B}_I) \leq 0$  only if

$$\frac{\beta_1 c_4 \Lambda}{\mu(\kappa_E + \mu)} + \frac{r_1 \kappa_E \xi_1 \beta_2 \Lambda}{\mu(\kappa_E + \mu)(k_I + \mu)(\epsilon + e_x)} + \frac{(1 - r_1) \kappa_E \xi_2 \beta_2 \Lambda}{\mu(\kappa_E + \mu)(r_n + \mu)(\epsilon + e_x)} - 1 > 0 \tag{9}$$

$$\frac{\beta_1 c_4 \Lambda}{\mu(\kappa_E + \mu)} + \frac{r_1 \kappa_E \xi_1 \beta_2 \Lambda}{\mu(\kappa_E + \mu)(k_I + \mu)(\epsilon + e_x)} + \frac{(1 - r_1) \kappa_E \xi_2 \beta_2 \Lambda}{\mu(\kappa_E + \mu)(r_n + \mu)(\epsilon + e_x)} > 1$$

Let us call the R.H.S of this equation as  $\xi$ . Then we have shown that the assumption  $a_5$  or (8) is satisfied for  $\xi < 1$ .  $\square$

In the above discussion we have proved all the assumptions of the theorem (3.1).

On the basis of above findings we claim the following theorem:

**Theorem 3.5.** : The DFE of Given system would be globally asymptotically stable If the parameters used in the given model satisfy  $\xi < 1$ , where  $\xi$  is as defined above.

*Sensitivity analysis of  $R_0$*

Different parameters used in the model effect the transmission of the disease differently. The role of the parameter  $K_t$  in the phenomenon  $Z_t$  is called sensitivity of  $Z_t$  w.r. t  $K_t$  and is given by [47,31].

$$\Upsilon_{Z_t}^{K_t} = \frac{\partial Z_t}{\partial K_t} \frac{K_t}{Z_t}$$

The sensitivity indices of parameters are given in the table (2).

*Sensitivity based control strategies*

The parameter is directly proportional to initial transmission rate  $R_0$  if has got positive sensitivity index, like the sensitivity index of human birth rate,  $\Lambda$  is +1 and is inversely proportional to  $R_0$  if the index is negative. The parameter has more effective role in the transmission of the disease if its sensitivity index is high. However some parameters, though have got high sensitivity index but are beyond human control, like the natural mortality rate of human population or the disease incubation period.

We intervene 6 parameters,  $k_I$ ; the clinical detection of disease,  $\beta_1$ ; the disease transmission probability from human to human,  $\beta_2$ ; the disease transmission probability from contaminated surfaces,  $\xi_1$ ; the shedding coefficient of symptomatic infectious individuals,  $\xi_2$ ; the shedding coefficient of asymptomatic infectious individuals,  $\epsilon$  the life time of virus on the surface.

Non pharmaceutical interventions are,

**Table 2.2**

strategy	$k_I$	$\beta_1$	$\beta_2$	$\xi_1$	$\xi_2$	$\epsilon$
strategy 1	0.1492537	0.65	0.165	0.5	0.5	0.1
strategy 2	0.2492537	0.15	0.015	0.3	0.3	0.29
strategy 3	0.8492537	0.015	0.005	0.1	0.001	0.86

- Face mask; This intervention addresses  $\beta_1$ , the transmission from human to human and the shedding coefficients  $\xi_1$  and  $\xi_2$ .
- Wash hands; This intervention addresses both  $\beta_1$ , the transmission from human to human and  $\beta_2$ , the transmission from contaminated surfaces to human.
- Sanitizer; This intervention addresses both  $\epsilon$ , the life time of virus on different surface and  $\beta_2$ .
- smart lock down; This intervention addresses all the parameters.

The control strategies given in table 2.2 present the magnitudes of these interventions.

**Simulation results of the model**

We use RK-4 method for six set of values (called strategy) to generate numerical simulation, using matlab. Unit used is per day. The behavior of the disease is forecasted for 3000 days. For better visibility of disease's behavior some figures are split time wise, like Figs. 0001-3 shows the behavior of quarantine class, in the initial period, over all period and final period of 1500 days to 3000 days respectively.

*Discussion*

In this work, a mathematical model of COVID-19 was formulated. The focus of the study is the elimination of the disease and the global stability of the disease free state so obtained. For this the sensitivity of  $R_0$  was calculated and on the basis of sensitivity analysis, six parameter were chosen for intervention as shown in table (2.2). Three control strategies were designed for the mentioned six interventions. On the basis of the results obtained from numerical simulations, we recommend strategy 3rd.

Fig. (1) shows that as a result of strategy 3, the density curve of quarantined class is flattened as compared to that of strategy 1 and strategy 2. In fact this result is desired to reduce the burden of quarantine centers. Fig. (3) shows that the recommended strategy overcome the quarantined class in 2600 days completely.

Similarly the recommended strategy flattens the density curve of exposed class and succeed to eliminate it in 2200 days, as shown in Figs. (5) and (4). The density of symptomatic infectious class reduce to zero in 1400 days (See Fig. 6).

The behavior of asymptomatic infectious class is presented in Figs. (8) and (7). Since these infected individual do not develop signs and symptoms, so the control of this class takes about 1800 days (See Figs. 9-12).

The densities of the isolated and mild classes reduces to zero in about 2200 days, as shown in figures. The behavior of critical class is presented by Fig. (14), Figs. (15) and (13). The recommended strategy 3 reduces the density of this class in 2600 days as shown in Fig. (13). The effective use of sanitizer reduces the density of contaminated stuff in very short time, as shown in Figs. (16) and (17).

*Conclusion*

It is concluded that the disease can be eliminated with help of relax non phrenetical interventions (like smart lock down of Pakistan). However it may take from six to seven years in its complete eradication. The study also derive threshold condition for global stability of disease free state. The condition agrees that there will be no outbreak, once the disease was eliminated. However it is suggested not to focus just the

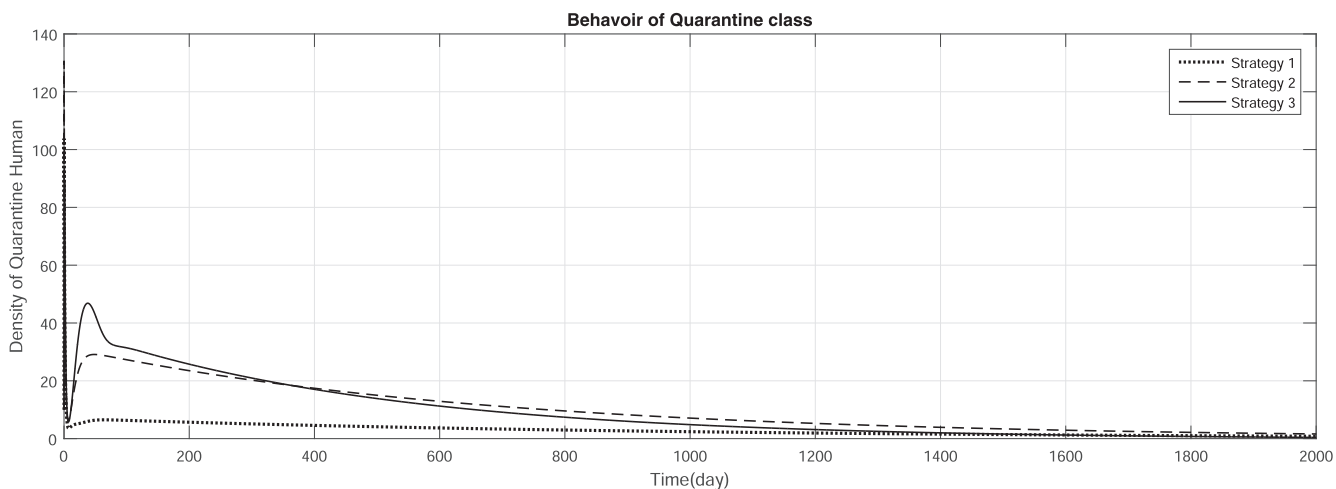


Fig. 1. The graph represents the comparison of the strategies regarding quarantine human population in initial period.

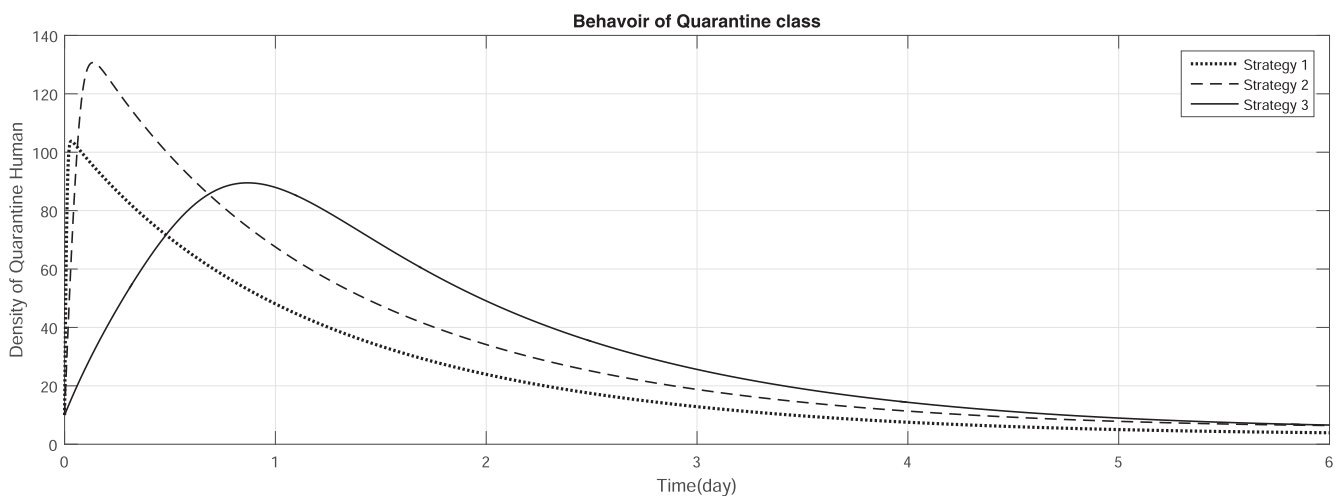


Fig. 2. The graph represents the comparison of the strategies regarding quarantine human population for the whole period of 3000 days.

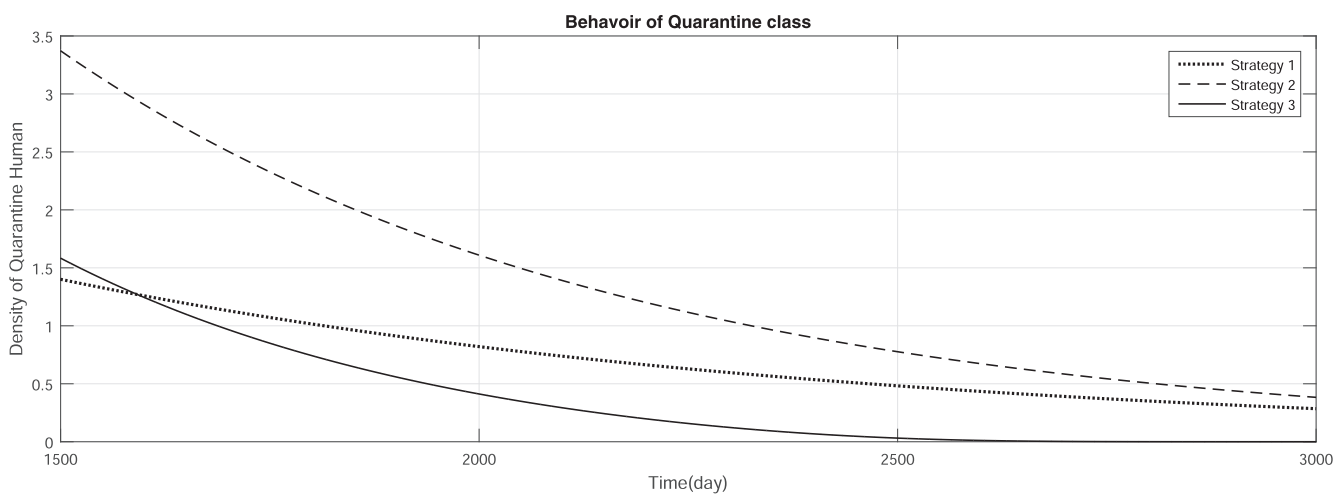


Fig. 3. The graph represents the comparison of the strategies regarding quarantine human population for 1500 days to 3000 days.

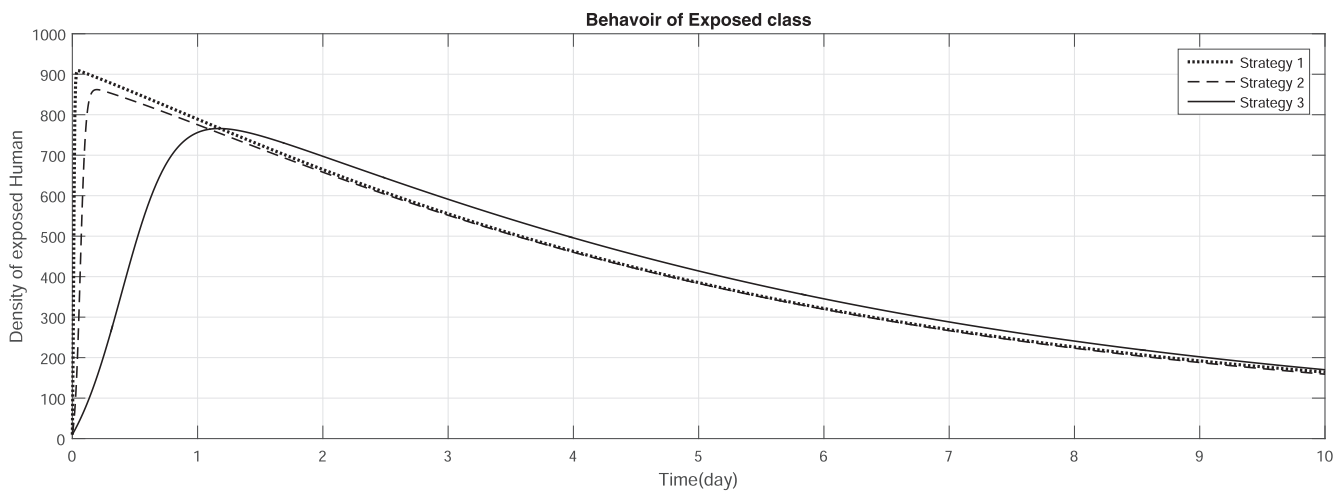


Fig. 4. The graph represents the comparison of the strategies regarding exposed human population.

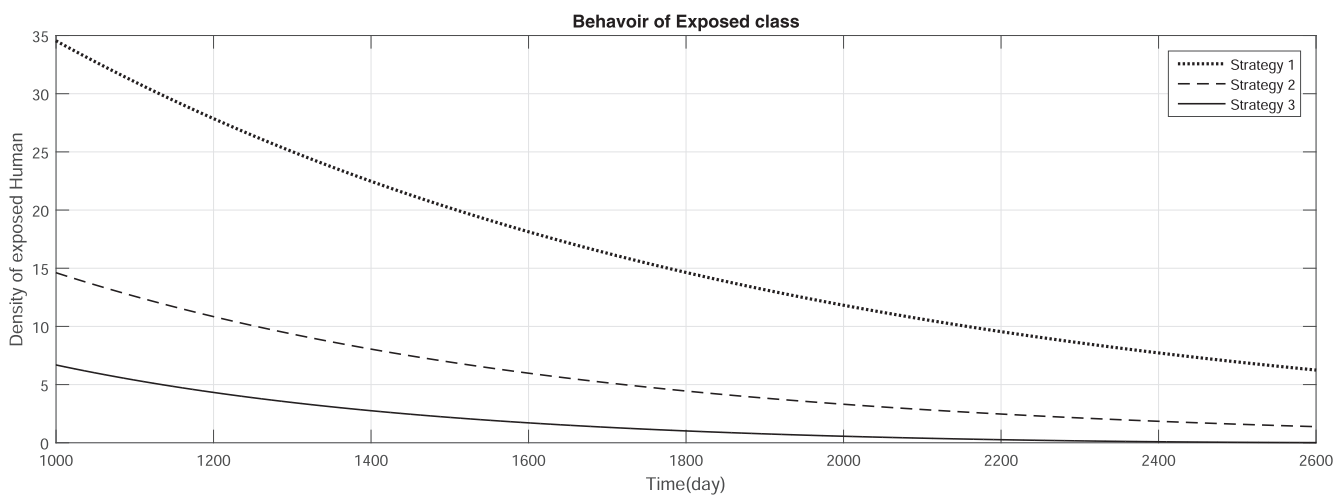


Fig. 5. The graph represents the comparison of the strategies regarding exposed human population for the initial period.

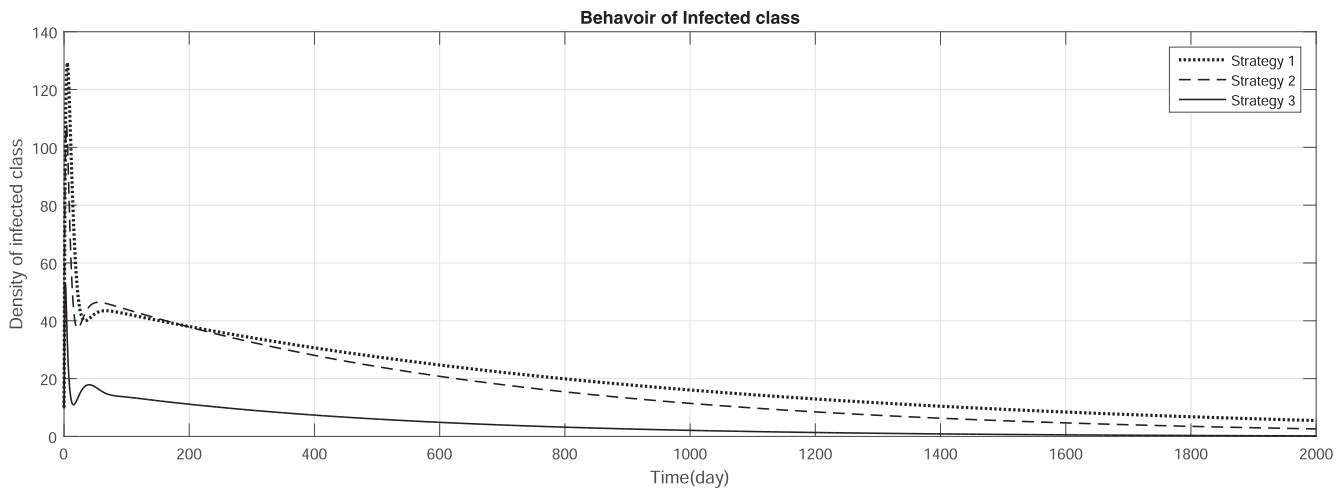


Fig. 6. The graph represents the comparison of the strategies regarding the density of infectious human population from 1000 days to 2000 days.

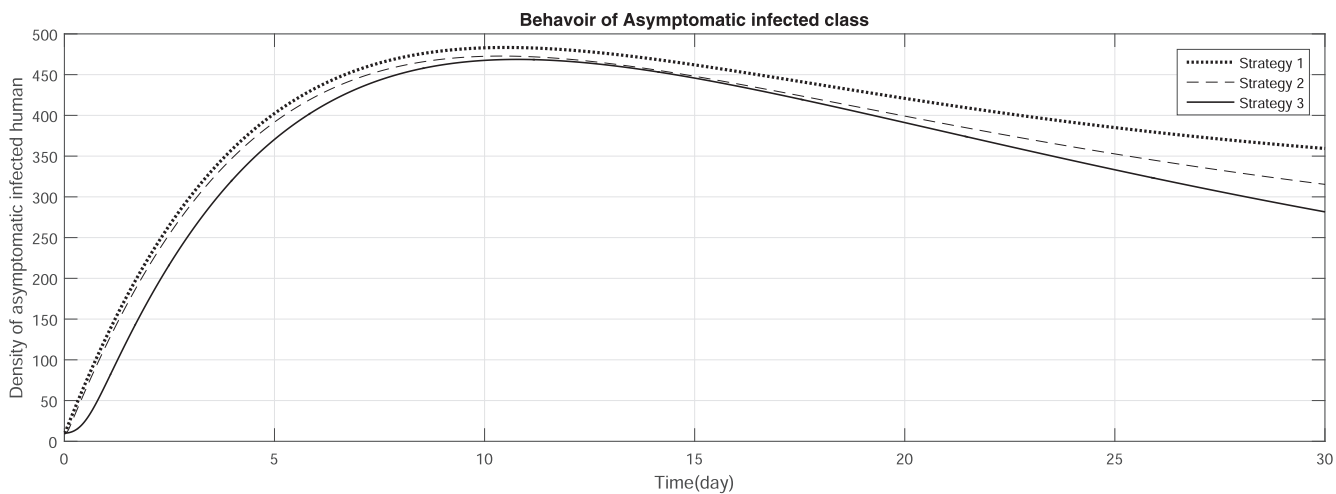


Fig. 7. The graph represents the comparison of the strategies regarding asymptomatic infectious human population in the initial period.

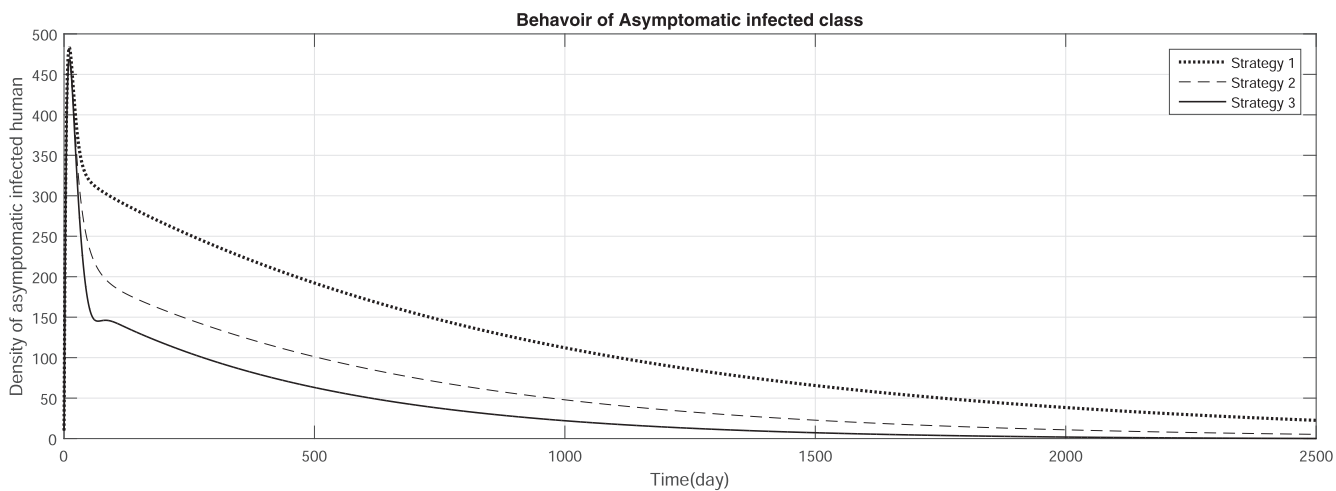


Fig. 8. The graph represents the comparison of the strategies regarding asymptomatic infectious human population.

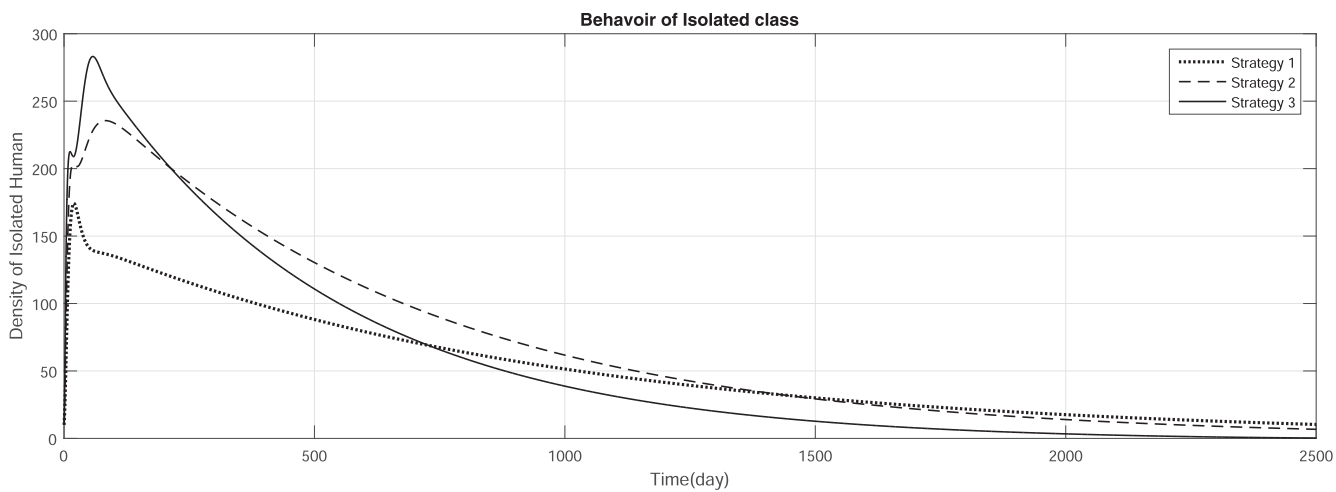


Fig. 9. The graph represents the comparison of the strategies regarding isolated class of human population.

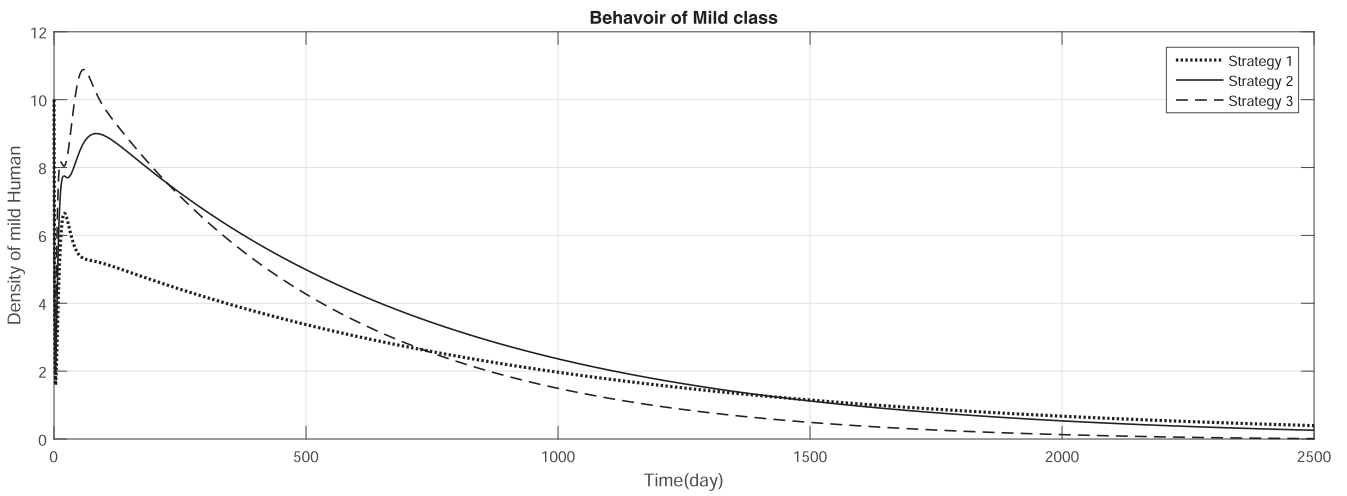


Fig. 10. The graph represents the comparison of the strategies regarding the density of the mild class of human population.

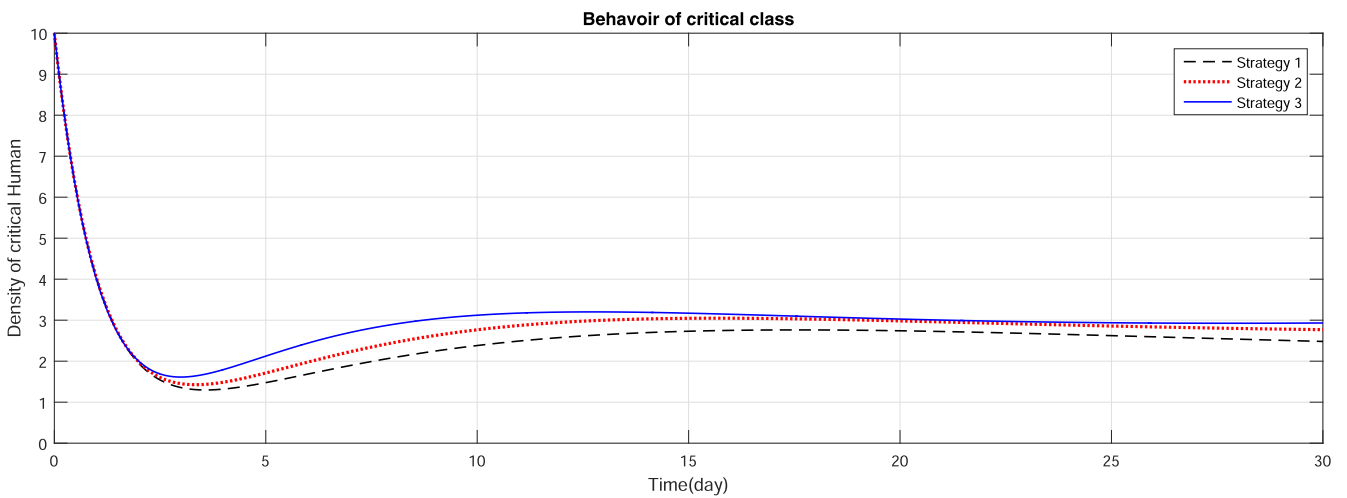


Fig. 11. The graph represents the comparison of the strategies regarding the density of the critical class of human in the initial period.

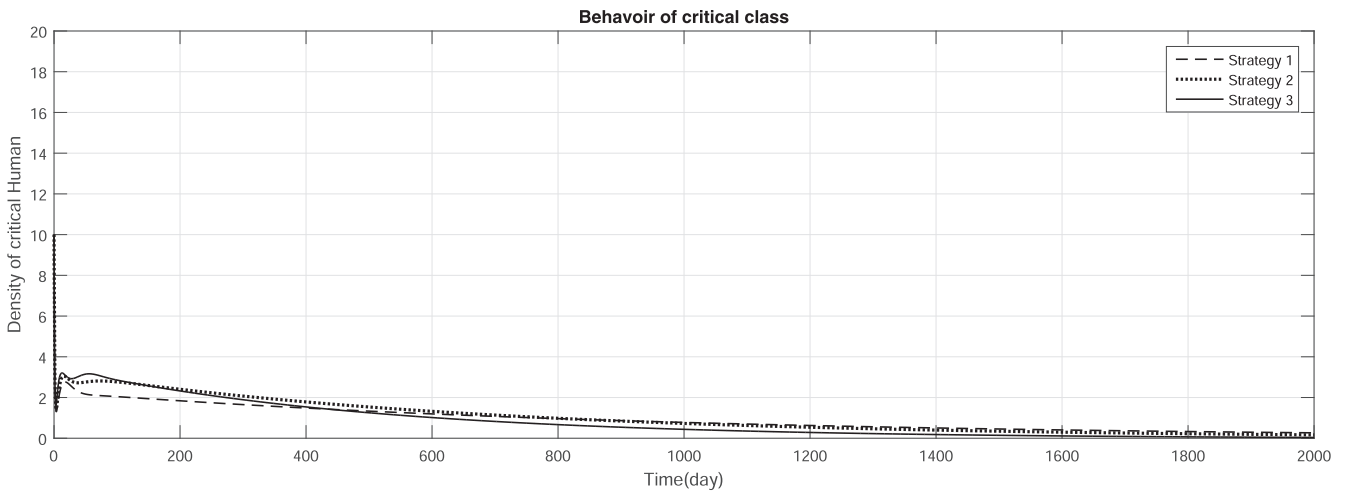


Fig. 12. The graph represents the comparison of the strategies regarding the density of the critical class of human for the whole period.

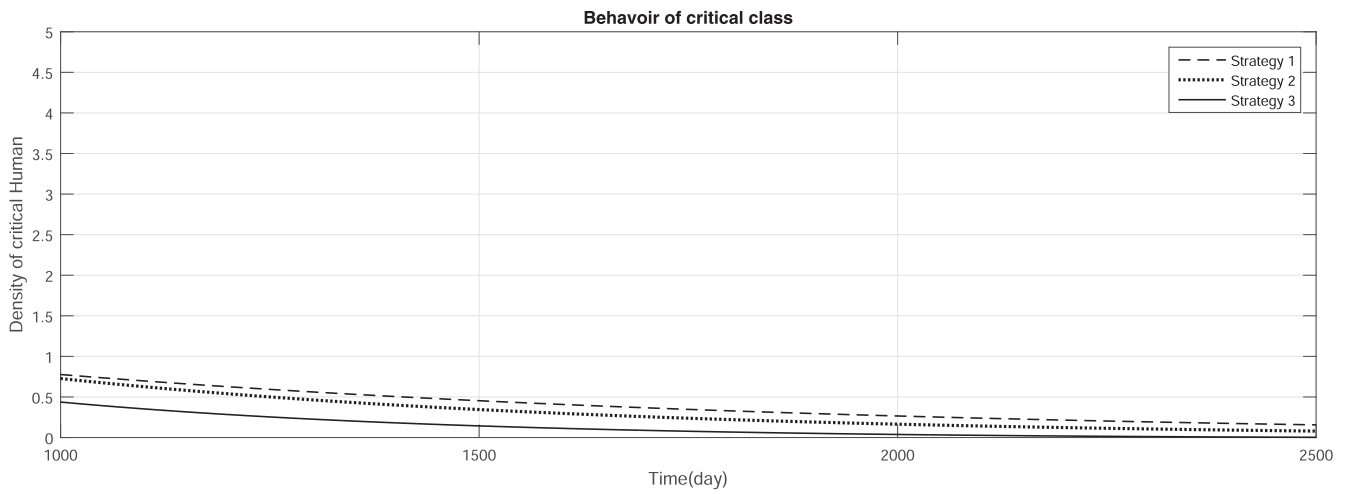


Fig. 13. The graph represents the comparison of the strategies regarding the density of the critical class of human for the final period.

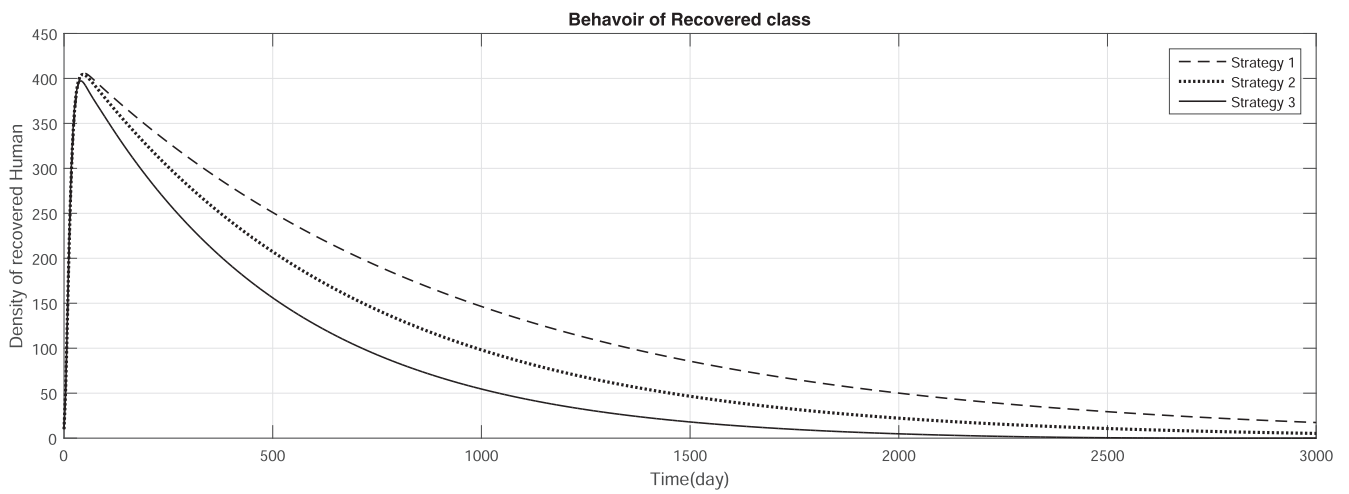


Fig. 14. The graph represents the comparison of the strategies regarding the density of the recovered class of human population.

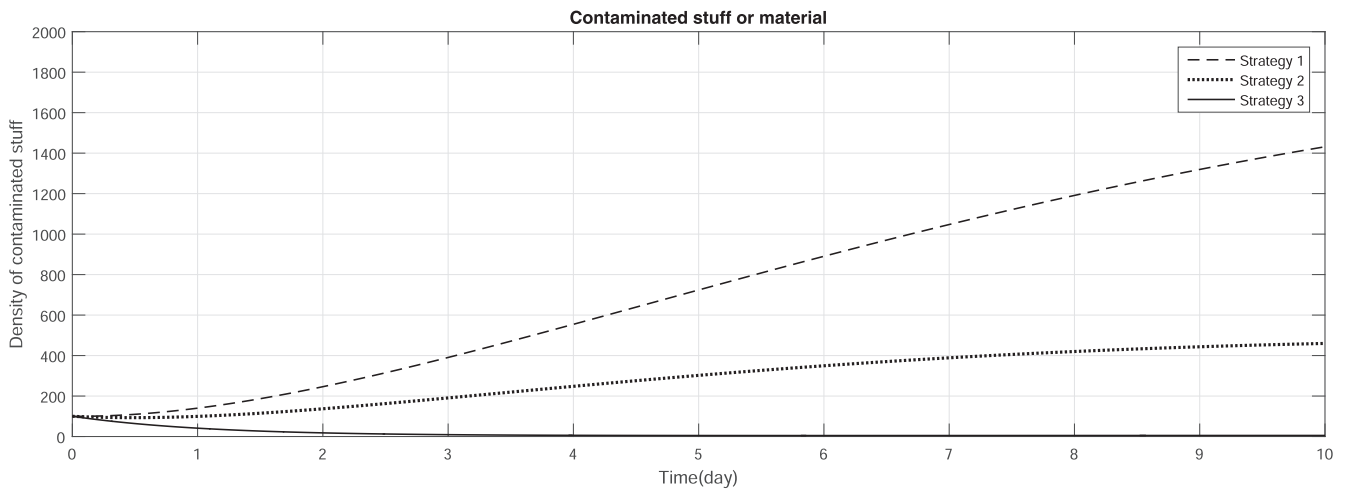


Fig. 15. The graph represents the comparison of the strategies regarding the density of the stuff stained/shedded with corona virus in the initial period.

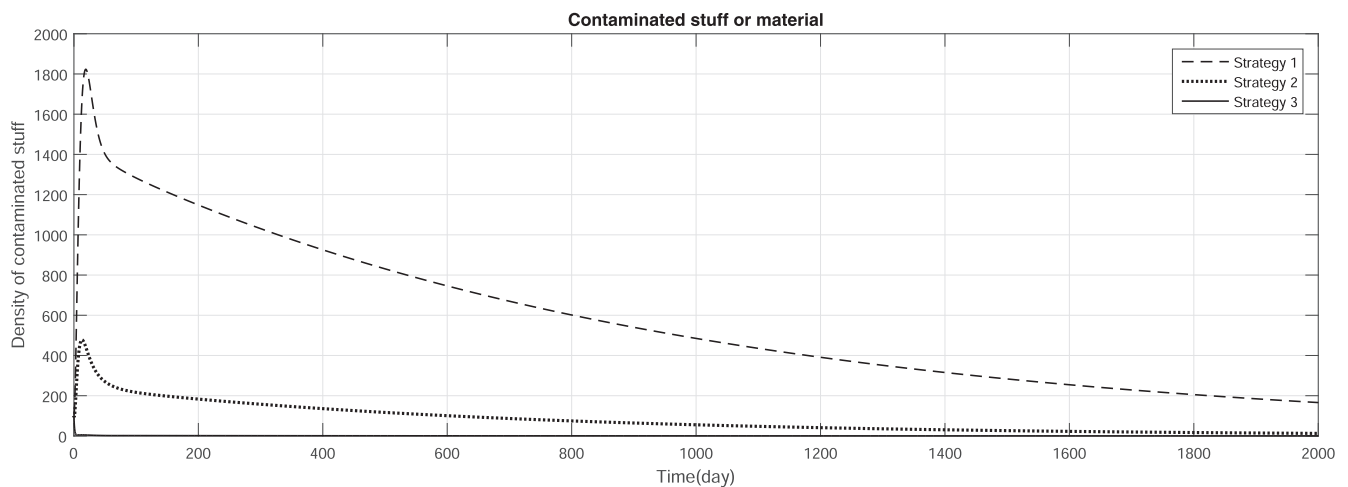


Fig. 16. The graph represents the comparison of the strategies regarding the density of the stuff stained/shedded with corona virus for the whole period.

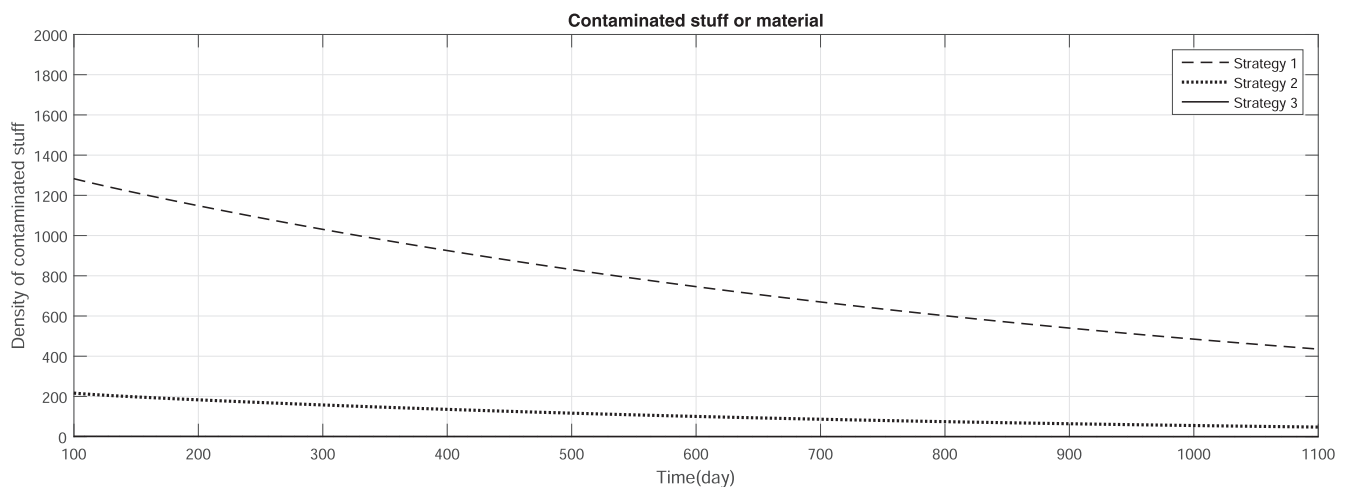


Fig. 17. The graph represents the comparison of the strategies regarding the density of the stuff stained/shedded with corona virus for the final period.

elimination but focus control too. Control means to flatten the curve of infection and elimination means to reduce density of the curve of infection to zero. Strategy-3 is best regarding flattening the curve of infection to reduce the burden of the hospitals, isolation and quarantine centers. Also the strategy eliminate the infection faster than the other two strategies.

### Funding

This work was supported by ICRIOS Bocconi University Grant “Dynamics of transmission and control of COVID-19: a new mathematical Modelling and numerical simulation” and Decisions LAB – University Mediterranea of Reggio Calabria, Italy Grant n. 2/2020.

### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### References

- [1] Adhikari SP, et al. Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: a scoping review. *Infect Dis Poverty* 2020;9(1):1–12.
- [2] Chiodini J. Maps, masks and media-Traveler and practitioner resources for 2019 novel coronavirus (2019-nCoV) acute respiratory virus. *Travel Med Infect Dis* 2020;33:101574.
- [3] Zhou P, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature* 2020;579(7798):270–3.
- [4] World Health Organization. WHO statement regarding cluster of pneumonia cases in Wuhan, China, Beijing: WHO 9; 2020.
- [5] Sohrabi C, et al. World Health Organization declares global emergency: a review of the 2019 novel coronavirus (COVID-19). *Int J Surg* 2020;76:71–6.
- [6] Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med* 2020;382:1199–207.
- [7] COVID-19 CORONAVIRUS/CASES: Available at: <https://www.worldometers.info/coronavirus/coronavirus-cases>, 20 May, 2020.
- [8] Ivorra B, Ferrandez MR, Vela-Perez M, Ramos AM. Mathematical modeling of the spread of the coronavirus disease 2019, (COVID-19) considering its particular characteristics. The case of China. *MOMAT 2020;2020:1–23*.
- [9] Abdulkareem EH. Poster 5: coronavirus COVID-19. *Dental Poster J* 2020;9(1):1–3.
- [10] Media Statement: Knowing the risks for COVID-19: <https://www.who.int-08-03-2020-knowing-the-risk-for-covid-19>, May 2020.
- [11] Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). <https://www.who.int-docs-default-source-WHO-China-joint>, March 2020.
- [12] Syal K. COVID-19: herd immunity and convalescent plasma transfer therapy. *J Med Virol* 2020. <https://doi.org/10.1002/jmv.25870>.
- [13] Wang Y, et al. Unique epidemiological and clinical features of the emerging 2019 novel coronavirus pneumonia (COVID-19) implicate special control measures. *J Med Virol* 2020;92(6):568–76.
- [14] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395(10223):497–506.
- [15] Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet* 2020. [https://doi.org/10.1016/S0140-6736\(20\)30154-9](https://doi.org/10.1016/S0140-6736(20)30154-9).

- [16] Zhu N, Zhang D, Wang W, Li X, Yang B, Song J. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med* 2020. <https://doi.org/10.1056/NEJMoa2001017>.
- [17] Bogoch II, Watts A, Thomas-Bachli A, Huber C, Kraemer MUG, Khan K. Pneumonia of unknown etiology in Wuhan, China: potential for international spread via commercial air travel. *J Travel Med* 2020;27(2):taaa008.
- [18] Zhao S, Lin Q, Ran J, Musa SS, Yang G, Wang W. Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: a data-driven analysis in the early phase of the outbreak. *Int J Infect Dis* 2020. <https://doi.org/10.1016/j.ijid.2020.01.050>.
- [19] Zhao S, Musa SS, Lin Q, Ran J, Yang G, Wang W. Estimating the unreported number of novel coronavirus (2019-nCoV) cases in China in the first half of January 2020: a data-driven Modelling analysis of the early outbreak. *J Clin Med* 2020. <https://doi.org/10.3390/jcm9020388>.
- [20] Atangana A. Extension of rate of change concept: from local to nonlocal operators with applications. *Results Phys* 19; 202: 103515.
- [21] Atangana A, Araz SI. Nonlinear equations with global differential and integral operators: existence, uniqueness with application to epidemiology. *Results Phys* 103593 [in press].
- [22] Atangana E, Atangana A. Facemasks simple but powerful weapons to protect against COVID-19 spread: can they have sides effects? *Results Phys* 2020;19: 103425.
- [23] Atangana A, Araz SI. Modelling the spread of COVID-19 with new fractal-fractional operators: can the lockdown save mankind before vaccination? *Chaos Solitons Fractals* 136; 2020: 109860.
- [24] Wu JT, Leung K, Leung GM. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. *Lancet* 2020. [https://doi.org/10.1016/S0140-6736\(20\)30260-9](https://doi.org/10.1016/S0140-6736(20)30260-9).
- [25] Chen TM, Rui J, Wang QP, Zhao ZY, Cui JA, Yin L. Amathematical model for simulating the phase-based transmissibility of a novel coronavirus. *Infect Dis Poverty* 2020;9(4). <https://doi.org/10.1186/s40249-020-00640-3>.
- [26] Huang C, Wang Y, Li X. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 395; 2020: 497–506.
- [27] Wang D, Hu B, Hu C. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA* 2020;323(11):1061–9.
- [28] Zhou F, Yu T, Du R. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020;395(10229):1054–62.
- [29] Pan L, Mu M, Yang P. Clinical characteristics of COVID-19 patients with digestive symptoms in Hubei, China: a descriptive, cross-sectional, multicenter study. *Am J Gastroenterol* 115; 2020.<https://doi.org/10.14309/ajg.0000000000000620>.
- [30] Yang C, Wang J. A mathematical model for the novel coronavirus epidemic in Wuhan, China. *Math Biosci Eng* 2020;17(3):2708–24.
- [31] Nadeem F, Zamir M, Tridane A, Khan Y. Modeling and control of zoonotic cutaneous leishmaniasis. *J Math* 2019;51(2):105–21.
- [32] Hiroshi N, et al. The extent of transmission of novel coronavirus in Wuhan, China. 330; 2020: 12.
- [33] Coronavirus-why 14 days quarantine period. <https://www.health24.com/Medical/Infectious-diseases/Coronavirus/coronavirus-why-the-14-day-quarantine-period-20200311-3>.
- [34] Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). <https://www.who.int/docs/default-source/coronavirus/who-china-joint-mission-on-covid-19-final-report.pdf>, April 2020.
- [35] Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a Report of 72314 cases from the chinese center for disease control and prevention. *Jama* 2020;323(13):1239–42.
- [36] Recovery rate in COVID-19. <https://www.webmd.com/lung/covid-recovery-overview1>, 2020.
- [37] Survival rate of sever infection. <https://www.theguardian.com/society/2020/mar/28/coronavirus-intensive-care-uk-patients-50-per-cent-survival-rate>; 2020.
- [38] Lavezzo E, Franchin E, Ciavarella C. Suppression of COVID-19 outbreak in the municipality of Vo, Italy.<https://doi.org/10.1101/2020.04.17.20053157v1.full.pdf>.
- [39] Covid-19: four fifths of cases are asymptomatic, China figures indicate. *BMJ* 369; 2020.<https://doi.org/10.1136/bmj.m1375>.
- [40] The percentage of Mild cases. <https://www.webmd.com/lung/qa/what-percent-age-of-covid19-cases-are-mild>; 2020.
- [41] Kwok KO, et al. Herd immunity-estimating the level required to halt the COVID-19 epidemics in affected countries. *J Infect* 2020;80(6):e32–3.
- [42] Zamir M, Zaman G, Alshomrani AS. Sensitivity analysis and optimal control of Anthroponotic Cutaneous Leishmania. *PloS One* 2016. <https://doi.org/10.1371/journal.pone.0160513,1-19>.
- [43] Zamir M, Zaman G, Alshomrani AS. Control strategies and sensitivity analysis of anthroponotic visceral leishmaniasis model. *J Biol Dyn* 2017;11(1):323–38.
- [44] Zamir M, Sultana R, Ali R, Panhwar WA, Kumar S. Study on the threshold condition for infection of visceral leishmaniasis. *Sindh Univ Res J (Sci Ser)* 2015;3(47): 619–22.
- [45] Kamgang JC, Sallet G. Computation of threshold conditions for epidemiological models and global stability of the disease-free equilibrium. *Math Biosci* 2008;213: 1–12.
- [46] Sundar S, Agrawal G, Rai M, Makharia MK, Murray HW. Treatment of Indian visceral leishmaniasis with single or daily infusion of low dose liposomal amphotericin, Randomised trial. *BMJ* 2001;323:419–22.
- [47] Ngoteya FN, Gyekye YN. Sensitivity analysis of parameters in a competition model. *Appl Comput Math* 2015;4(5):363–8.