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Global Sensitivity Analysis of a Rabies Epidemic Model involving Dog Vaccination and Dog Population Management

Wahyudin Nur[1,*], Darmawati[2]

[1,2] Department of Mathematics, Universitas Sulawesi Barat, Majene 91412, Indonesia

Corresponding email: wnalafkar93@gmail.com*

Abstract

Rabies is a zoonotic disease which is spread by animals mostly carnivores. Rabies regards as tropic disease. In this article, we construct a mathematical model for rabies involving dog vaccination and dog population management, namely sterilization and monitoring of dog movements. The model has rabies-free equilibrium point and endemic equilibrium point. We determine the effective reproduction ratio using next generation matrix. Our dynamical analysis shows that rabies-free equilibrium point is conditionally stable. A global sensitivity analysis is performed to investigate which intervention is the most crucial among the two interventions considered in the model. We use Latin hypercube sampling method to generate parameter space. To investigate the parameter sensitivity, we calculate the partial rank correlation coefficient. We provide numerical experimental results related to stability and global sensitivity analysis. The results show that the effective reproduction ratio is more sensitive to dog population management than vaccination intervention. This suggests that dog population management intervention significantly reduces the effective reproduction ratio compared to vaccination programs. In addition, the number of infectious dogs has a strong correlation with dog culling actions.

Keywords: *rabies model, global sensitivity analysis, Latin hypercube sampling, partial rank correlation coefficient*

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1. Introduction

Rabies is a neglected zoonotic disease tha can infect all mammals, including humans [1] and spread by animals mostly carnivores [2]. Rabies (mad dog disease) is a severe infection of the central nervous system by the rabies virus (family Rhabdoviridae, genus Lyssavirrus) [3]. Rabies is a zoonotic disease which is. The more frequent means of contagion is through bites of infected mammals (especially dogs, but also bats, skunks, foxes, raccoons and wolves) [4]. Dogs, the main rabies reservoir species, usually infect by an unprovoked bite [5]. Rabies is spread on almost all continents except the Antarctic continent. More than 150 countries have been impacted by this disease [6]. The incidence is higher in Africa and South East Asia, nearly double in men than in women, with a higher peak in childhood [4]. Over 90% of human rabies deaths today occur in Asia and Africa [7]. Every year more than 55,000 people die from rabies [6].

Rabies is one of the few communicable diseases that can possibly be controlled by currently available tools for veterinary and public health interventions. ASEAN guides several interventions as actions to eliminate rabies, including vaccination, animal movement control, and dog population management [7]. Approaches to manage dog populations include culling, fertility control, and sheltering [8]. In this article, a mathematical model of the spread of rabies among dogs that takes into account vaccination and dog population management is discussed.

Mathematical models have long been used to study the dynamics of the spread of rabies [9]–[14]. In [14], a rabies epidemic model is constructed involving populations of stray dogs, domestic dogs and humans. The author considered the intervention of vaccination and culling of stray dogs. However, the author only focused on dynamical analysis and does not provide a description of research results regarding

the impact of vaccination programs and culling of stray dogs on the spread of rabies. In 2022, Astuti [9] developed a rabies epidemic model that only involved the dog population. Vaccination and quarantine interventions were considered in the model. The findings are that vaccination and quarantine can decrease the number of exposed dogs and infected dogs. Nonetheless, the author does not deliver an explanation concerning which intervention is more sufficient in controlling the spread of rabies in the dog population. Meanwhile, a mathematical model related to the spread of rabies in human and dog populations are discussed in [10]. The model constructed involves vaccination interventions in dogs and humans. The authors' findings are that combining vaccination interventions and dog population management is a way to control the spread of rabies. Reducing the stray dog population can make it easier to achieve vaccination coverage targets.

Broadly speaking, the articles mentioned above have considered the vaccination and culling of dogs. However, there are still few authors who have studied in more depth what interventions are most effective in controlling the spread of rabies. One method that can be used to identify which interventions are most effective is to carry out sensitivity analysis. Sensitivity analysis is divided into two, namely local and global sensitivity analysis. Global sensitivity analysis is usually performed by calculating the partial rank correlation coefficient (PRCC) from the parameter space generated using the Latin hypercube sampling (LHS) technique as done in [15]–[22]. LHS permits an unbiased estimate of the average model output, with the advantage that it needs fewer samples than simple random sampling to achieve the same accuracy [23]. In this article, we develop a model of a rabies epidemic in a dog population. We considered dog vaccination and dog population management interventions (sterilization, culling of infectious dogs, and monitoring of dog movements). To examine which interventions were most effective, we conduct a global sensitivity analysis.

2. Methods

The study is conducted by doing the following steps:

- ❖ Formulating a mathematical model of rabies spread among dogs incorporating vaccination and dog population management.
- ❖ Determining the equilibrium points of the model and the conditions for its existence.
- ❖ Determining the effective reproduction ratio employing the next-generation matrix [24].
- ❖ Analyzing the stability of equilibrium point.
- ❖ Performing global sensitivity analysis as conducted in [16], [17], [20], [25], [26].

3. Results and Discussion

4.1 Model Formulation

In this section, we describe the model construction procedure. The assumptions used in building the model are as follows:

- The dog population is divided into four subpopulations, namely the susceptible dog (D_s), the latent dog (D_l), the infectious dog (D_i), and the vaccinated dog (D_v);
- Vaccination for susceptible dog only;
- The recruitment, vaccination, transmission, and natural death rate is constant;
- The dog population is not closed.

Now we will explain the model construction process based on the above assumptions. The susceptible dogs is decreased due to dog vaccination which results in vaccinated dogs leaving the susceptible dog class and moving into the class of vaccinated dogs with a constant vaccination rate, namely ω. In addition, the subpopulation of susceptible dogs is also reducing due to new infections with constant transmission rates (γ). Afterward, the dog subpopulation was reduced due to natural mortality with constant natural death rate (μ). In contrast, the subpopulation of susceptible dogs grows with a constant recruitment rate

(α) and the presence of vaccinated dogs leaving the vaccinated class and entering the susceptible class due to loss of immunity at rate of τ. The dynamics of the susceptible dogs is represented by the following equation.

$$\frac{dD_S}{dt} = (1-u)\alpha + \tau D_V - \gamma D_S D_I - (\omega+\mu)D_S, \tag{1}$$

where $u \in [0,1)$ is a parameter related to the control of the presence of new dogs (sterilization and monitoring dog movement).

The latent dog subpopulation increases due to the presence of newly infected dogs leaving the susceptible class and entering the latent class. The subpopulation of latent dogs decreases due to natural death and there are dogs that have passed the latent period and thus move to the infectious class at rate of β. The dynamics of the latent dogs is represented by the following equation.

$$\frac{dD_l}{dt} = \gamma D_S D_I - (\beta+\mu)D_l. \tag{2}$$

The subpopulation of infectious dogs rises due to the presence of dogs that have passed the latent period leaving the latent class and entering the infectious class. In contrast, the infectious dog subpopulation declined due to natural deaths, deaths due to rabies at rate of δ, and deaths due to culling intervention at rate of κ. The subpopulation of vaccinated dogs increases due to vaccination and conversely decreases due to natural death and loss of immunity at a rate of τ. The following equations represent the dynamics of the infectious dog and vaccinated dog subpopulation, respectively.

$$\begin{aligned} \frac{dD_I}{dt} &= \beta D_l - (\delta+\mu+\kappa)D_I, \\ \frac{dD_V}{dt} &= \omega D_S - (\tau+\mu)D_V. \end{aligned} \tag{3}$$

The flow diagram of the constructed model can be seen in Figure 1.

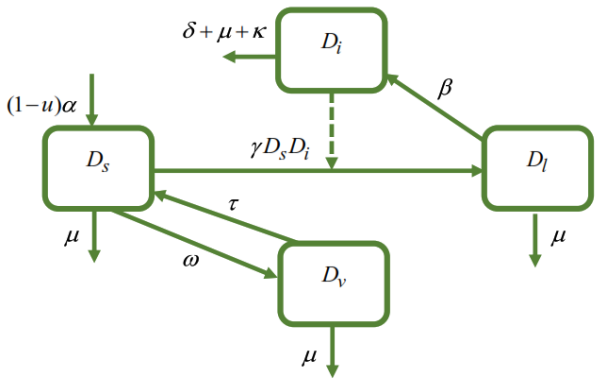


Figure 1. Compartment diagram of the model

Based on equations (1), (2), and (3), the following model is obtained.

$$\begin{aligned}
\frac{dD_s}{dt} &= (1-u)\alpha + \tau D_v - \gamma D_s D_i - (\omega+\mu)D_s,\\
\frac{dD_l}{dt} &= \gamma D_s D_i - (\beta+\mu)D_l,\\
\frac{dD_i}{dt} &= \beta D_l - (\delta+\mu+\kappa)D_i,\\
\frac{dD_v}{dt} &= \omega D_s - (\tau+\mu)D_v.
\end{aligned} \tag{4}$$

4.2 Equilibrium Points and Effective Reproduction Ratio

After solving system equation (4) when $\frac{dD_s}{dt}=\frac{dD_l}{dt}=\frac{dD_i}{dt}=\frac{dD_v}{dt}=0$, we get rabies-free equilibrium point that is $E_0=\left(D_s^*,D_l^*,D_i^*,D_v^*\right)=\left(\frac{(1-u)\alpha(\tau+\mu)}{(\tau+\omega+\mu)\mu},0,0,\frac{(1-u)\alpha\omega}{(\tau+\omega+\mu)\mu}\right)$ which always exists and the endemic equilibrium point $E_1=\left(D_s^{**},D_l^{**},D_i^{**},D_v^{**}\right)$, where

$$\begin{aligned}
D_s^{**} &= \frac{(\tau+\mu)}{(\tau+\omega+\mu)\mu}\left[\frac{\beta(1-u)\alpha-(\beta+\mu)(\delta+\mu+\kappa)D_i^{**}}{\beta}\right],\\
D_l^{**} &= \frac{(\delta+\mu+\kappa)D_i^{**}}{\beta},\\
D_i^{**} &= \frac{(R_e-1)(\tau+\omega+\mu)\mu}{(\tau+\mu)\gamma},\\
D_v^{**} &= \frac{\omega}{(\tau+\omega+\mu)\mu}\left[\frac{\beta(1-u)\alpha-(\beta+\mu)(\delta+\mu+\kappa)D_i^{**}}{\beta}\right],
\end{aligned}$$

and $R_e=\frac{\beta\gamma(1-u)\alpha(\tau+\mu)}{(\beta+\mu)(\delta+\mu+\kappa)(\tau+\omega+\mu)\mu}$. Clearly, the equilibrium E_1 exists if $R_e>1$.

Now, we determine the effective reproduction ratio. Based on model (4), we get the following regeneration and transition matrix, respectively

$$f=\begin{pmatrix}\gamma D_s D_i\\0\\0\end{pmatrix} \text{ and } v=\begin{pmatrix}(\beta+\mu)D_l\\(\delta+\mu+\kappa)D_i-\beta D_l\\(\tau+\mu)D_v-\omega D_s\end{pmatrix}. \tag{5}$$

Therefore, the Jacobian matrix of (5) at E_0 are as follows

$$F=\begin{pmatrix}0 & \gamma D_s^* & 0\\0 & 0 & 0\\0 & 0 & 0\end{pmatrix} \tag{6}$$

and

$$V=\begin{pmatrix}\beta+\mu & 0 & 0\\ -\beta & \delta+\mu+\kappa & 0\\ 0 & 0 & \tau+\mu\end{pmatrix}.$$

It is straightforward to show that

$$V^{-1}=\begin{pmatrix}\dfrac{1}{(\beta+\mu)} & 0 & 0\\ \dfrac{\beta}{(\beta+\mu)(\delta+\mu+\kappa)} & \dfrac{1}{(\delta+\mu+\kappa)} & 0\\ 0 & 0 & \dfrac{1}{(\tau+\mu)}\end{pmatrix}. \tag{7}$$

Hence, from (6) and (7), we obtain the following next generation matrix

$$FV^{-1}=\begin{pmatrix}J_1 & J_2 & 0\\ 0 & 0 & 0\\ 0 & 0 & 0\end{pmatrix},$$

where $J_1=\dfrac{\beta\gamma(1-u)\alpha(\tau+\mu)}{(\beta+\mu)(\delta+\mu+\kappa)(\tau+\omega+\mu)\mu}$ dan $J_2=\dfrac{\gamma(1-u)\alpha(\tau+\mu)}{(\delta+\mu+\kappa)(\tau+\omega+\mu)\mu}$. It is clear that the effective reproduction ratio is $R_0=\rho\left(FV^{-1}\right)=\dfrac{\beta\gamma(1-u)\alpha(\tau+\mu)}{(\beta+\mu)(\delta+\mu+\kappa)(\tau+\omega+\mu)\mu}$. It is easy to see that $R_0=R_e$. Hence, the equilibrium E_1 exists if $R_0>1$.

4.3 Stability Analysis and Numerical Simulation

We now provide the results of stability analysis of the rabies-free equilibrium point.

Theorem 1. *The rabies-free equilibrium point* (E_0) *is locally asymptotically stable if* $R_0<1$ *and unstable if* $R_0>1$

Proof. The Jacobian matrix of system (4) at E_0 is

$$J(E_0)=\begin{pmatrix}-(\omega+\mu) & 0 & -\gamma D_s^* & \tau D_v^*\\ 0 & -(\beta+\mu) & \gamma D_s^* & 0\\ 0 & \beta & -(\delta+\mu+\kappa) & 0\\ \omega & 0 & 0 & -(\tau+\mu)\end{pmatrix}.$$

Therefore, the eigen values of matrix $J(E_0)$ are solutions of the following equation

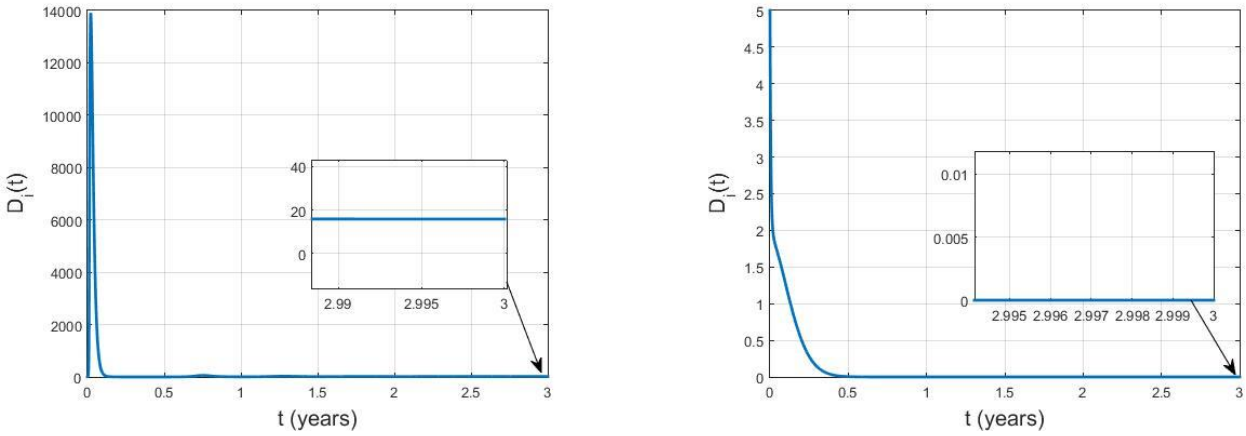
$$\left|\lambda I_{4\times 4} - J\left(E_0\right)\right| = \begin{vmatrix} \lambda+(\omega+\mu) & 0 & \gamma D_s^* & -\tau D_v^* \\ 0 & \lambda+(\beta+\mu) & -\gamma D_s^* & 0 \\ 0 & -\beta & \lambda+(\delta+\mu+\kappa) & 0 \\ -\omega & 0 & 0 & \lambda+(\tau+\mu) \end{vmatrix},$$
$$= P_1(\lambda)\times P_2(\lambda)$$
$$= 0,$$

where $P_1(\lambda) = \lambda^2 + p_1\lambda + \left([\omega+\mu][\tau+\mu] + \omega\tau D_v^*\right)$, $P_2(\lambda) = \lambda^2 + p_2\lambda + \left([\beta+\mu][\delta+\mu+\kappa] - \beta\gamma D_s^*\right)$, $p_1 = \omega+\tau+2\mu$, and $\beta+\delta+\kappa 2\mu$. It is clear that all roots of polynomial $P_1(\lambda)$ have negative real part. Furthermore, all zeros of polynomial $P_2(\lambda)$ have negative real part also if $[\beta+\mu][\delta+\mu+\kappa] > \beta\gamma D_s^*$ or $\dfrac{\beta\gamma(1-u)\alpha[\tau+\mu]}{[\beta+\mu][\delta+\mu+\kappa][\tau+\omega+\mu]\mu} = R_0 < 1.$ Thus, E_0 is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$ ■

Tabel 1. Parameter values

Parameter	***Value***	**Unit**	**Source**
α	10.01	$\text{dog}\times\text{day}^{-1}$	Estimated using the data given in [27]
τ	2.7×10^{-3}	day^{-1}	Estimated using the data provided in [28]
γ	6×10^{-5}	$\text{dog}^{-1}\times\text{day}^{-1}$	Estimated using data in [29]
ω	3.3×10^{-3}	day^{-1}	Estimated using the data delivered in [27]
μ	2.1×10^{-4}	day^{-1}	Estimated using the data given in [30]
β	0.2	day^{-1}	Estimated using the data in [2]
δ	0.1	day^{-1}	Estimated using the data in [31]
κ	0.2	day^{-1}	Assumed
u	0.5	unitless	Assumed

To support the results of the dynamical analysis, we conduct numerical simulations. The initial values of the simulation are $[D_s(0) \quad D_l(0) \quad D_i(0) \quad D_v(0)] = [47531 \quad 0 \quad 5 \quad 0]$. We set $\gamma = 6\times10^{-4}$ and other parameters as given in Table 1. These parameter values give $R_0 = 22.404 > 1$. According to Theorem 1, E_0 is unstable. This indicates that D_i does not go to 0. This result is in accordance with the solution plot of $D_i(t)$ in Figure 2(a). The second simulation is carried out by choosing a smaller transmission rate, namely $\gamma = 6\times10^{-6}$ which resulted in $R_0 = 0.22404 < 1$. Theorem 1 guarantees E_0 is asymptotically stable which suggests D_i goes towards 0. This result agrees with the solution plot of $D_i(t)$ given in Figure 2(b).



(a) (b)

Figure 2. Solution curve of $D_i(t)$: (a) $R_0 = 22.404 > 1$ and (b) $R_0 = 0.22404 < 1$

4.4 Global Sensitivity Analysis

In this subsection, we discuss the results of global sensitivity analysis. The baseline values of parameter used for the global sensitivity analysis correspond to those given in Table 1. We obtain the parameter space using the LHS technique. 10,000 models are simulated by generating the value of τ, ω, κ and u following a uniform distribution. Parameter $u \in [0,1]$ while with minimum and maximum values of τ, ω, κ are 10% below and above of the baseline values, respectively. The other parameters are set to be fixed.

4.4.1. *Global sensitivity on* R_0.

As revealed in the previous section, namely in Theorem 1, R_0 can be used to determine whether the disease will disappear from the population or not. The smaller the R_0, the closer the goal of achieving rabies elimination. Hence, we provide the outcomes of a global sensitivity analysis on R_0. This investigation is carried out to examine the control parameters that have the most impact on R_0. The parameters investigated are parameters related to the duration of immunity provided by the vaccine (τ), vaccination rate (ω), culling rate of infectious dogs (κ), and parameters associated to sterilization and monitoring dog movement (u).

Based on the results of the global sensitivity analysis in Figure 3(a), three parameters, namely $u, \kappa,$ and ω have negative PRCC values, while τ has positive PRCC value. These results indicate that increasing of $u, \kappa,$ and ω values can reduce R_0, while decreasing τ values can increase R_0. The effect of changing the value of each control parameter on the R_0 is statistically significant because the p-value of each control parameter is less than 0.01 (see Figure 3(b)). It can be seen that u is the control parameter that has the most influence on the R_0. These results suggest that the critical key to managing the spread of rabies is controlling dog births and dog movements. One intervention that can be done to control dog births is to enforce a mass sterilization program for dogs.

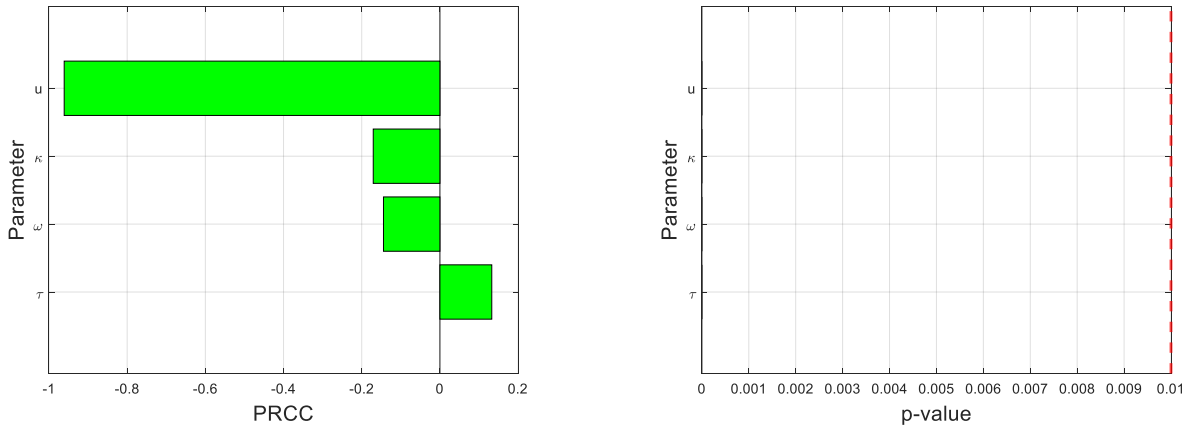


Figure 3. PRCC value of u, κ, ω, τ and its corresponding p-value

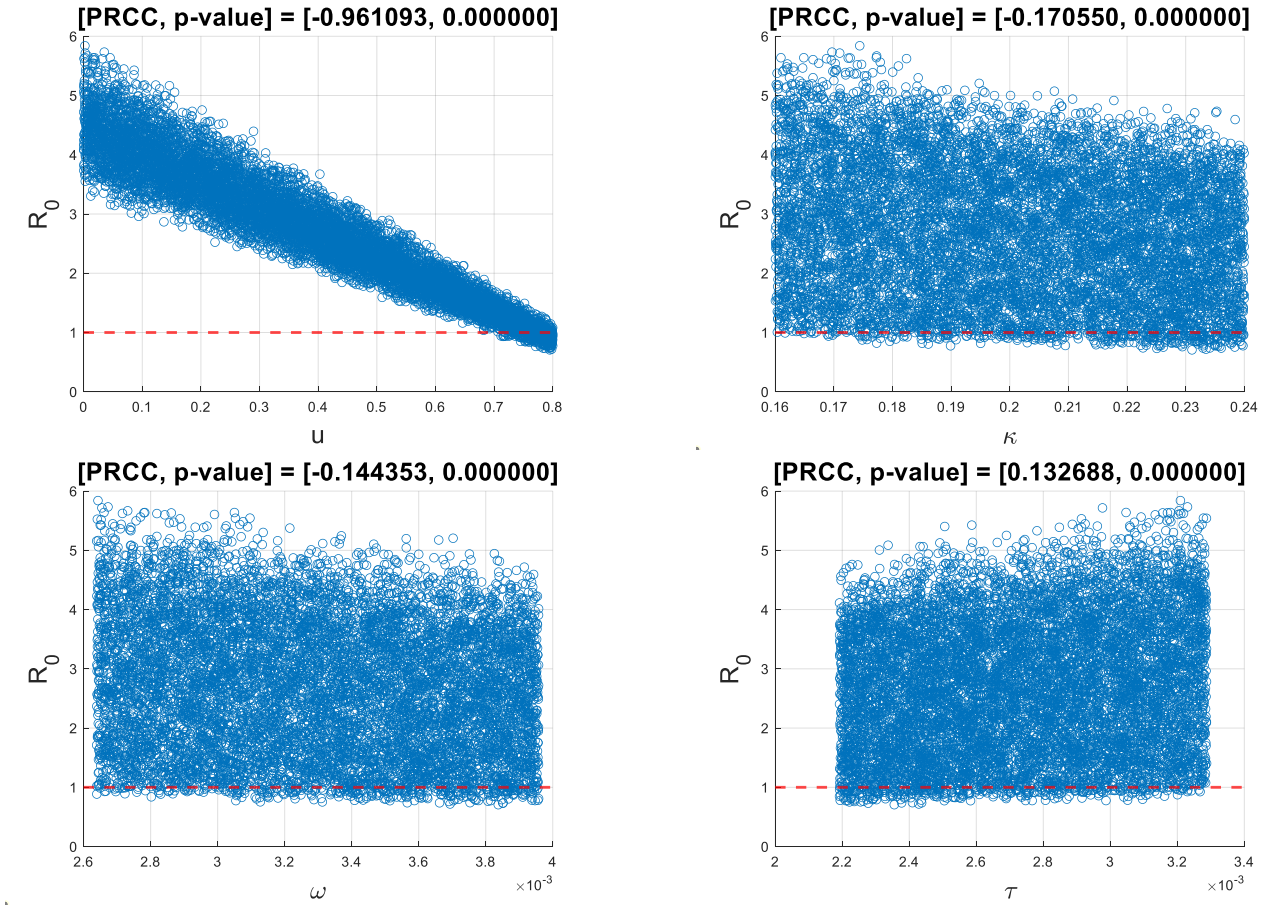


Figure 4. Scatter plot of the PRCC value of u, κ, ω, τ

The scatter plot results as shown in Figure 4 very clearly show the relationship between the four control parameters and R_0. However, the clearest pattern is the figure that shows the relationship between u and R_0 while the other images show more spreading pattern. It is obvious that there is a downhill pattern from left to right in the pictures which show scatter plot $u, \omega,$ and κ vs R_0. The results indicates that there is a negative correlation between $u, \omega,$ and κ with R_0. On the contrary, an uphill pattern from left to right can

be seen in the image which shows scatter plot τ vs R_0. This indicates that there is a positive correlation between τ and R_0. Based on the distribution of points in each scatter plot, it is clear that u has the strongest correlation with R_0. This result is in line with the results of the PRCC calculation. The results of the PRC calculation and scatter plot tell us that u is the most influential parameter on the R_0.

4.4.2. Global Sensitivity on D_i

We also perform a global sensitivity analysis on D_i. We are interested in studying what control parameter had the greatest effect on the number of infectious dogs at. Here, $PRCC-D_i(t)$ measures the correlation between the number of infectious dogs and the value of control parameters (u,κ,ω,τ) at time t. Figure 5 shows the $PRCC-D_i$ dynamics in the first 50 days. Most of the control parameters had fluctuating $PRCC-D_i$ in the first 50 days. Regardless, the $PRCC-D_i$ of κ is relatively constant. The parameters that do not have a statistically significant correlation with D_i (p-value > 0.01) have $PRCC-D_i$ in the range -0.0453 to 0.0453 (see gray shaded area). It can be seen that only κ whose $PRCC-D_i$ is outside the shaded area. This indicates that only κ has a statistically significant correlation with D_i. Furthermore, the $PRCC-D_i$ of κ is negative, indicating that the greater the κ, the smaller the D_i.

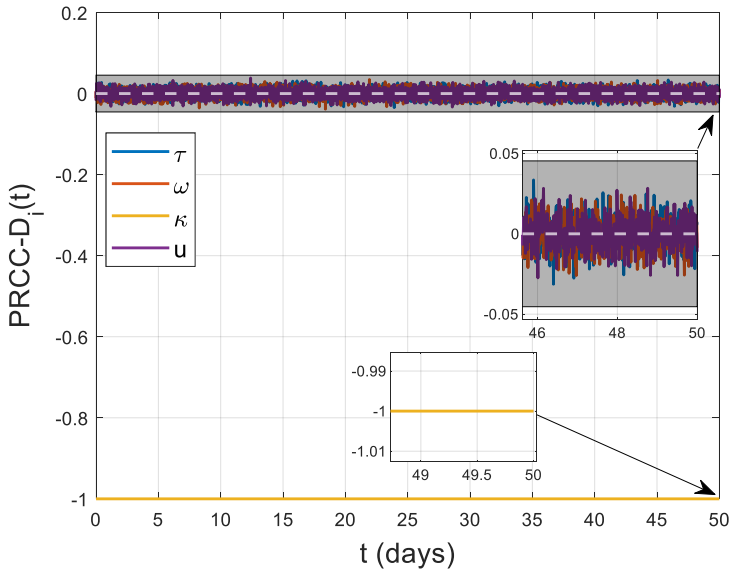


Figure 5. Time course of $PRCC-D_i$ of τ,ω,κ,u up to day 50

Figure 6 reveals that $u,\kappa,$ and ω are negatively correlated with the number of infectious dogs on day 50, $D_i(50)$. In contrast, τ is positively correlated with $D_i(50)$. Nevertheless, only $PRCC-D_i(50)$ of κ has p-value < 0.01. Thus, the negative correlation between κ and $D_i(50)$ is statistically significant, while the correlation of other control parameters is not statistically significant. These results are supported by Figure 7, which displays a clear pattern in the scatter plot of κ vs $D_i(50)$. This suggests that there is a strong correlation between κ and $D_i(50)$. On the other hand, the scatter plots of other control parameters reveal that there is no correlation (or weak correlation) between $u,\omega,$ and τ with $D_i(50)$. This result can be confirmed from the p-value of $PRCC-D_i(50)$ of $u,\omega,$ and τ.

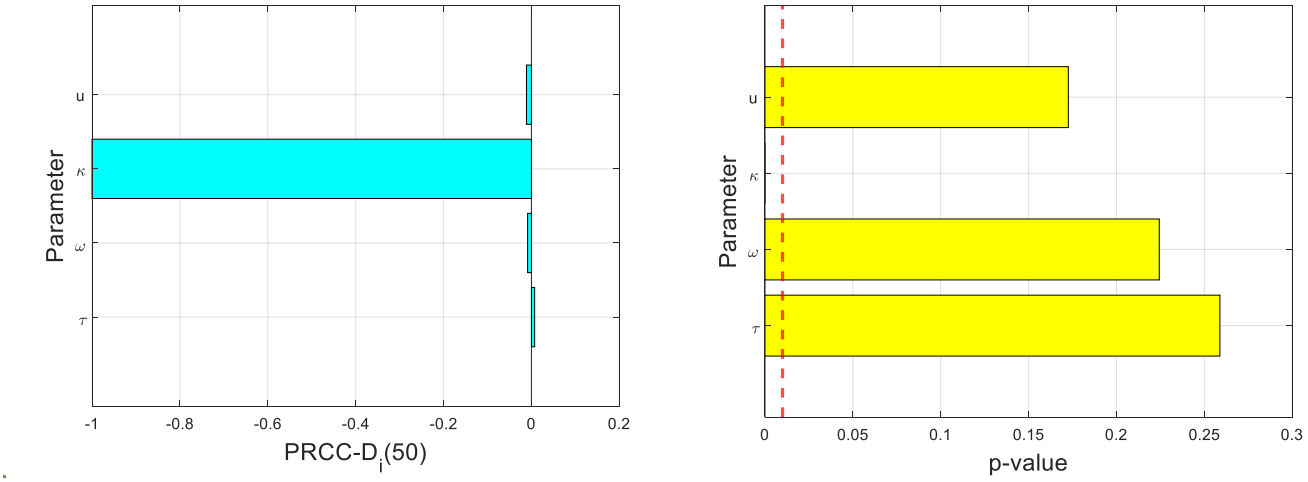


Figure 6. $PRCC - D_i(50)$ of u, κ, ω, τ and its corresponding p-value

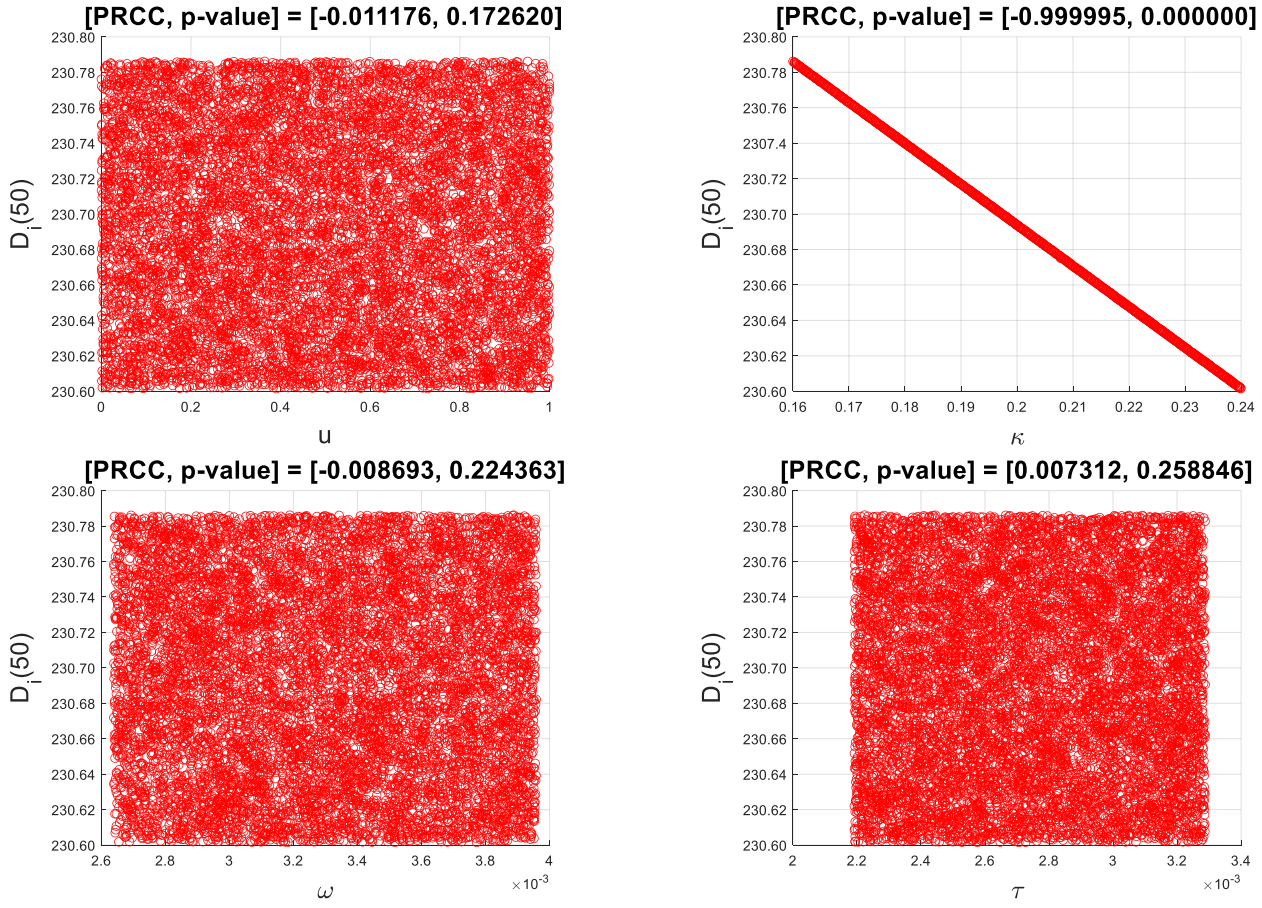


Figure 7. Scatter plot of the $PRCC - D_i(50)$ of u, κ, ω, τ

4. Conclusions

In this article, we construct a mathematical model for rabies involving dog vaccination and dog population management. The model has a conditionally stable rabies-free equilibrium point. A global sensitivity analysis is performed to investigate which intervention is the most crucial among the two interventions considered in the model. Our results show that the effective reproduction ratio is more sensitive to dog population management than vaccination intervention. This indicates that intervention in

the form of sterilization and strict monitoring of dog movements significantly reduces the effective reproduction ratio compared to vaccination programs. In addition, the number of infectious dogs has a strong correlation with dog culling actions.

References

[1] M. Y. Jane Ling *et al.*, "Rabies in Southeast Asia: a systematic review of its incidence, risk factors and mortality," *BMJ Open*, vol. 13, no. 5, p. e066587, May 2023, doi: 10.1136/bmjopen-2022-066587.

[2] A. Bilal, "Rabies is a Zoonotic Disease: A Literature Review," *Occup. Med. Heal. Afffairs*, vol. 9, no. 3, 2021.

[3] S. A. Maharani, I. L. Hilmi, and S. Salman, "Review : Efektivitas Vaksin Antirabies pada Manusia dan Cara Pemberantasan Kasus Rabies yang ada di Indonesia," *J. Ilm. Wahana Pendidik.*, vol. 9, no. 4, 2023, doi: https://doi.org/10.5281/zenodo.7684314.

[4] G. Lippi and G. Cervellin, "Updates on Rabies virus disease: is evolution toward 'Zombie virus' a tangible threat?," *Acta Biomed.*, vol. 92, no. 1, 2021, doi: https://doi.org/10.23750/abm.v92i1.9153.

[5] M. J. Warrell and D. A. Warrell, "Rabies: the clinical features, management and prevention of the classic zoonosis," *Clin. Med. (Northfield. Il).*, vol. 15, no. 1, pp. 78–81, Feb. 2015, doi: 10.7861/clinmedicine.14-6-78.

[6] Kementerian Kesehatan RI, *No Buku Saku Rabies: Petunjuk Teknis Penatalaksanaan Kasus Gigitan Hewan Penular Rabies di Indonesia*. Jakarta: Kementerian Kesehatan RI, 2019.

[7] ASEAN, "ASEAN Rabies Elimination Strategy," Jakarta, 2015.

[8] L. M. Smith, S. Hartmann, A. M. Munteanu, P. Dalla Villa, R. J. Quinnell, and L. M. Collins, "The Effectiveness of Dog Population Management: A Systematic Review," *Animals*, vol. 9, no. 12, p. 1020, Nov. 2019, doi: 10.3390/ani9121020.

[9] V. A. Astuti, "Analisis Dinamik Model Penyakit Rabies dengan Kekebalan Sementara," Universitas Sulawesi Barat, 2022.

[10] M.-M. Lv *et al.*, "Dynamic analysis of rabies transmission and elimination in mainland China," *One Heal.*, vol. 17, p. 100615, Dec. 2023, doi: 10.1016/j.onehlt.2023.100615.

[11] E. Ahmed, A. M. A. M. A. El-Sayed, and H. A. A. A. A. El-Saka, "Equilibrium points, stability and numerical solutions of fractional-order predator–prey and rabies models," *J. Math. Anal. Appl.*, vol. 325, no. 1, pp. 542–553, Jan. 2007, doi: 10.1016/j.jmaa.2006.01.087.

[12] S. Ruan, "Modeling the transmission dynamics and control of rabies in China," *Math. Biosci.*, vol. 286, pp. 65–93, Apr. 2017, doi: 10.1016/j.mbs.2017.02.005.

[13] A. A. Ayoade, "Integer and fractional order models for rabies: a theoretical approach," *Math. Comput. Sci.*, vol. 3, no. 1, 2022, doi: 10.30511/mcs.2021.541111.1046.

[14] E. D. Wiraningsih *et al.*, "Stability analysis of rabies model with vaccination effect and culling in dogs," *Appl. Math. Sci.*, vol. 9, pp. 3805–3817, 2015, doi: 10.12988/ams.2015.53197.

[15] Fatmawati, F. F. Herdicho, Windarto, W. Chukwu, and H. Tasman, "An optimal control of malaria transmission model with mosquito seasonal factor," *Results Phys.*, vol. 25, p. 104238, Jun. 2021, doi: 10.1016/j.rinp.2021.104238.

[16] Darmawati and W. Nur, "Stability, cost-effectiveness, and global sensitivity analysis of COVID-19 model incorporating non-pharmaceutical interventions and indirect transmission," *Data Anal. Appl. Math.*, vol. 3, no. 1, pp. 28–41, Mar. 2022, doi: 10.15282/daam.v3i1.7594.

[17] L. K. Beay and N. Anggriani, "Dynamical Analysis of a Modified Epidemic Model with Saturated Incidence Rate and Incomplete Treatment," *Axioms*, vol. 11, no. 6, 2022, doi: https://doi.org/10.3390/axioms11060256.

[18] P. Yosyingyong and R. Viriyapong, "Global stability and optimal control for a hepatitis B virus infection model with immune response and drug therapy," *J. Appl. Math. Comput.*, vol. 60, no. 1–2, pp. 537–565, 2019, doi: 10.1007/s12190-018-01226-x.

[19] Z. Bai *et al.*, "Estimation and sensitivity analysis of a COVID-19 model considering the use of face mask and vaccination," *Sci. Rep.*, vol. 13, no. 6434, 2023, doi: 10.1038/s41598-023-33499-z.

[20] M. S. Alam, M. Kamrujjaman, and M. S. Islam, "Parameter Sensitivity and Qualitative Analysis of Dynamics of Ovarian Tumor Growth Model with Treatment Strategy," *J. Appl. Math. Phys.*, vol. 08, no. 06, pp. 941–955, 2020, doi: 10.4236/jamp.2020.86073.

[21] R. Viriyapong and W. Ridbamroong, "Global Stability Analysis and Optimal Control of Measles Model with Vaccination and Treatment," *J. Appl. Math. Comput.*, vol. 62, no. 1–2, pp. 207–237, 2020, doi: 10.1007/s12190-019-01282-x.

[22] Y. M. Rangkuti, Firmansyah, and A. Landong, "Sensitivity analysis of SEIR epidemic model of Covid 19 spread in Indonesia," *J. Phys. Conf. Ser.*, vol. 2193, no. 1, p. 012092, Feb. 2022, doi: 10.1088/1742-6596/2193/1/012092.

[23] S. Marino, I. B. Hogue, C. J. Ray, and D. E. Kirschner, "A methodology for performing global uncertainty and sensitivity analysis in systems biology," *J. Theor. Biol.*, vol. 254, no. 1, pp. 178–196, Sep. 2008, doi: 10.1016/j.jtbi.2008.04.011.

[24] P. van den Driessche and J. Watmough, "Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission," *Math. Biosci.*, vol. 180, no. 1–2, pp. 29–48, Nov. 2002, doi: 10.1016/S0025-5564(02)00108-6.

[25] M. Z. Ndii, B. S. Djahi, N. D. Rumlaklak, and A. K. Supriatna, "Determining the Important Parameters of Mathematical Models of the Propagation of Malware," in *Lecture Notes in Electrical Engineering*, 565th ed., Springer, 2019, pp. 1–9. doi: 10.1007/978-3-030-20717-5_1.

[26] Z. Ma *et al.*, "Modeling for COVID-19 with the contacting distance," *Nonlinear Dyn.*, vol. 107, no. 3, pp. 3065–3084, Feb. 2022, doi: 10.1007/s11071-021-07107-6.

[27] Kementerian Kesehatan RI, "One Health Roadmap Eliminasi rabies Nasional 2030," Jakarta, 2019.

[28] E. Wera, C. Warembourg, P. M. Bulu, M. M. Siko, and S. Dürr, "Immune Response After Rabies Vaccination in Owned Free-Roaming Domestic Dogs in Flores Island, Indonesia," *Front. Vet. Sci.*, vol. 9, Jun. 2022, doi: 10.3389/fvets.2022.868380.

[29] D. L. Knobel, T. Lembo, M. Morters, S. E. Townsend, S. Cleaveland, and K. Hampson, "Dog Rabies and Its Control," in *Rabies*, Third., Elsevier, 2013, pp. 591–615. doi: 10.1016/B978-0-12-396547-9.00017-1.

[30] R. S. Pratiwi and G. K. Wadrianto, "Berapa Lama Usia Hidup Anjing? Ini Penjelasannya," 2021. https://lifestyle.kompas.com/read/2021/03/27/170000020/berapa-lama-usia-hidup-anjing-ini-penjelasannya?page=all (accessed Oct. 20, 2023).

[31] Centers for Disease Control and Prevention, "Rabies," 2022. https://www.cdc.gov/rabies/index.html (accessed Oct. 20, 2023).