

## Modeling of transmission pathways on canine heartworm dynamics

Sat Byul Seo\*

Department of Mathematics Education, Kyungnam University, Changwon 51767, Korea

**Abstract:** Canine heartworm disease is a vector-borne disease that is transmitted from dog to dog by mosquitoes. It causes epidemics that disrupt the health environments of dogs and are burdensome for many dog owners. Recent trends of changing temperatures and weather conditions in South Korea may have an impact on the population of mosquitoes, and it affects the population of dogs at risk of heartworm infection. Mathematical modeling has become an important measure for analyzing the epidemiological characteristics of infectious diseases. However, canine heartworm infection transmission has not been reported yet through mathematical modeling. We develop a mathematical model of canine heartworm infection to predict the population of infected dogs depending on the vector (mosquito) population using a susceptible, exposed, infected, and recovered model. Simulation results show that after 1 year, 3,289 dogs out of 73,602 (about 4.5%) are exposed and 134 (about 0.2%) are infected. Only 0.2% of susceptible dogs become infected after 1 year. However, if all exposed dogs are maintained in the same circumstances without any treatment, then the number of infected subjects will increase over time. This may increase the possibility of other dogs, especially dogs that live outside, being infected.

**Keywords:** *Dirofilaria immitis*, vector-borne disease, mathematical model, epidemiology

\*Corresponding author

Sat Byul Seo  
Department of Mathematics Education, School  
of Education, Kyungnam University, 7  
Kyungnamdaehak-ro, Masanhappo-gu,  
Changwon 51767, Korea

Tel: +82-55-249-6445  
Fax: +82-505-999-2149  
E-mail: sbseo@kyungnam.ac.kr

ORCID:  
Sat byul Seo  
<https://orcid.org/0000-0002-9110-271X>

Conflict of Interest  
There is no conflict of interest.

Received: October 11, 2019  
Revised: December 1, 2019  
Accepted: December 16, 2019

### Introduction

*Dirofilaria immitis*, called canine heartworm, is a vector-borne disease, and it is a parasitic roundworm that causes dirofilariasis. It is spread from host to host through the bites of mosquitoes, and it inhabits the right ventricle and pulmonary arteries of canines. Hosts diagnosed with heartworm infection may have serious complications, and the disease typically culminates in death after secondary congestive heart failure. The definitive host is the dog, but it can also infect other animals such as cats, wolves, coyotes, foxes, and, under rare circumstances, humans [1].

The Companion Animal Parasite Council in the U.S. has reported that over 100,000 dogs are diagnosed with heartworm infection annually [2]. In South Korea, 25.1% of households have pets, and 75.3% of those have dogs [3]. Changes in perceptions of pets have occurred in recent years in South Korea, but dogs have traditionally been recognized as guards, so the majority of dogs live outside. In addition, as the popularity of pets increases, the number of dogs abandoned is increasing year by year. These outside dogs, rescue dogs, and dogs that become wild dogs after being abandoned are exposed to heartworm infections. Climate and weather conditions affect the vector ecology and dogs' exposure to infection [4]. In the last 30 years, temperatures have increased 1.4°C, and the highest average annual temperature was 14.1°C in the 2010s (2011–2017). Precipitation in the last 30 years has increased 124 mm. In this period, summer has become 19 days longer, and winter has become 18 days shorter [5]. The ongoing trends of increasing temperature and more variable weather affect the dog population at risk of infection.

Prediction of the population of infected dogs depending on the vector (mosquito) population can serve as a blueprint for the prevention of diseases such as quantifying of drug preparation. Mathematical modeling has become an important measure for analyzing the epidemiological characteristics of infectious diseases. These epidemiological models provide the population that remains in the absence of disease, called a disease-free equilibrium (DFE) [6]. Coyne et al. [7] proposed a susceptible, exposed, infected, and recovered (SEIR) model, and one study described the population dynamics of a rabies epidemic in raccoons using the SEIR model. Moreover, transmission path-

ways of mosquito-borne disease dynamics for humans have been actively analyzed through mathematical approaches [8,9]. However, canine heartworm infection transmission has not been reported yet through mathematical modeling.

## Materials and Methods

Heartworms can be transmitted from dog to dog by mosquitoes. Microfilariae (young heartworm) enter the system of the mosquito when an infected dog is bitten by a mosquito, called the first larval stage (L1). In the second larval stage (L2), the microfilariae develop into infective larvae inside the mosquito within two weeks, and in the infective third larval stage (L3), they can be transmitted to other dogs. After 1–2 weeks, they enter the fourth larval stage (L4). Then, they migrate to the muscles of the chest and abdomen, entering the fifth stage (L5). It takes approximately 6 months for the infective larvae to mature into adult heartworms, which is known as the “prepatent period.” During the first 3 months, the larvae migrate through the dog’s body, eventually reaching the blood vessels of the lung, and during the last 3 months, the immature worms grow to adults to lengths of up to 35 cm. The blood vessels are destroyed by the worms, which causes severe lung and heart disease. When the worms mature, the adult worms mate and produce new microfilariae, which can cause damage to the other organs of dogs. This lifecycle continues and repeats when a mosquito bites an infected animal, becoming infected by the microfilariae. Adult heartworms can survive in dogs for 5 to 7 years [10]. To determine the dynamic transmission route of canine heartworm infection, we utilize a system of nonlinear ordinary differential equations (ODEs) as the deterministic mathematical model. We consider two subpopulation transmission models of canine heartworm in dogs: dogs and mosquitoes. The dog population has four categories: susceptible dogs  $S_D$ , exposed dogs  $E_D$ , infected dogs  $I_D$ , and partially immune dogs  $R_D$ . The total dog population is denoted by  $N_D = S_D + E_D + I_D + R_D$ . Mosquitoes acting as the vector are categorized into susceptible mosquitoes  $S_v$ , exposed mosquitoes  $E_v$ , and infected mosquitoes  $I_v$ . The total number of mosquitoes is given by  $N_v = S_v + E_v + I_v$ . Recovered mosquitoes are not considered in this model. The list of the state variables used in this model is shown in Table 1. A schematic of heartworm infection transmission is illustrated in Fig. 1.

The model is a system of ODE as follows:

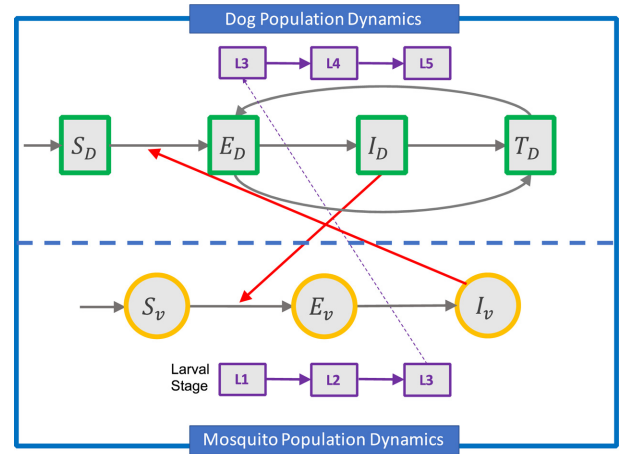
$$\frac{dS_D}{dt} = a(N) - b\left(\beta_{vD}\frac{I_v}{N_v}\right)S_D$$

$$\frac{dE_D}{dt} = b\left(\beta_{vD}\frac{I_v}{N_v}\right)(S_D + T_D) - \delta_D E_D - \gamma E_D$$

$$\frac{dI_D}{dt} = \delta_D E_D - \gamma I_D$$

**Table 1.** Epidemiological classes

State variable	Description
$S_D$	Susceptible dogs
$E_D$	Exposed dogs (L3)
$I_D$	Infected dogs (L4)
$T_D$	Treated dogs
$N_D$	Total number of dogs
$S_v$	Susceptible mosquitoes
$E_v$	Exposed mosquitoes (L1-L2)
$I_v$	Infected mosquitoes
$N_v$	Total number of mosquitoes



**Fig. 1.** Flowchart of heartworm transmission dynamics between dogs and mosquitoes.

$$\frac{dT_D}{dt} = -b\left(\beta_{vD}\frac{I_v}{N_v}\right)T_D + \gamma I_D + \gamma E_D \quad (1)$$

$$\frac{dS_v}{dt} = -b\left(\beta_{Dv}\frac{I_D}{N_D}\right)S_v$$

$$\frac{dE_v}{dt} = b\left(\beta_{Dv}\frac{I_D}{N_D}\right)S_v - \delta_v E_v - \mu E_v$$

$$\frac{dI_v}{dt} = \delta_v E_v - \mu I_v$$

All parameter values are shown in Table 2. Since a mathematical model of heartworm infection has never been studied, we assume parameters of mosquito biting rate  $b$ , incubation rate in mosquitoes  $\delta_v$ , and natural mortality rate of mosquitoes  $\mu$  from other research in Zika dynamics or rabies. Recruitment rates of dogs  $a(N)$  are estimated from recent (2017) data from South Korea [11].  $\beta_{vD}$ , the infected mosquito-to-dog transmission rate, is taken as the same value as the infected mosquito-to-human transmission rate in [8]. The incubation rate in dogs is approximated to  $0.005(\text{days}^{-1})$ , since the prepatent period is normally 4–7 months [10]. The

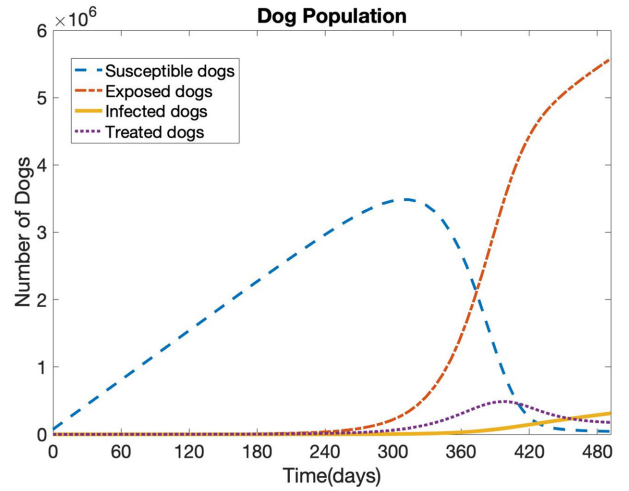
**Table 2.** Model parameter values

Parameter	Description	Unit	Standard value	Source
$a(N)$	Recruitment rates of dogs	dimensionless	$7.3 \times 10^4$	[11]
$b$	Mosquito biting rate	days <sup>-1</sup>	0.5	[8,9]
$\beta_{vD}$	Infected mosquito-to-dog transmission rate	dimensionless	0.30	[8,9]
$\beta_{Dv}$	Infected dog-to-mosquito transmission rate	dimensionless	0.30	[8,9]
$\delta_D$	Incubation rate in dogs	days <sup>-1</sup>	0.005(180 days)	Assumed
$\delta_v$	Incubation rate in mosquitoes	days <sup>-1</sup>	0.10	[12]
$\gamma$	Recovery rate	days <sup>-1</sup>	0.05(45-90 days)	Assumed
$\mu$	Natural mortality rate of mosquitoes	days <sup>-1</sup>	0.07	[13]

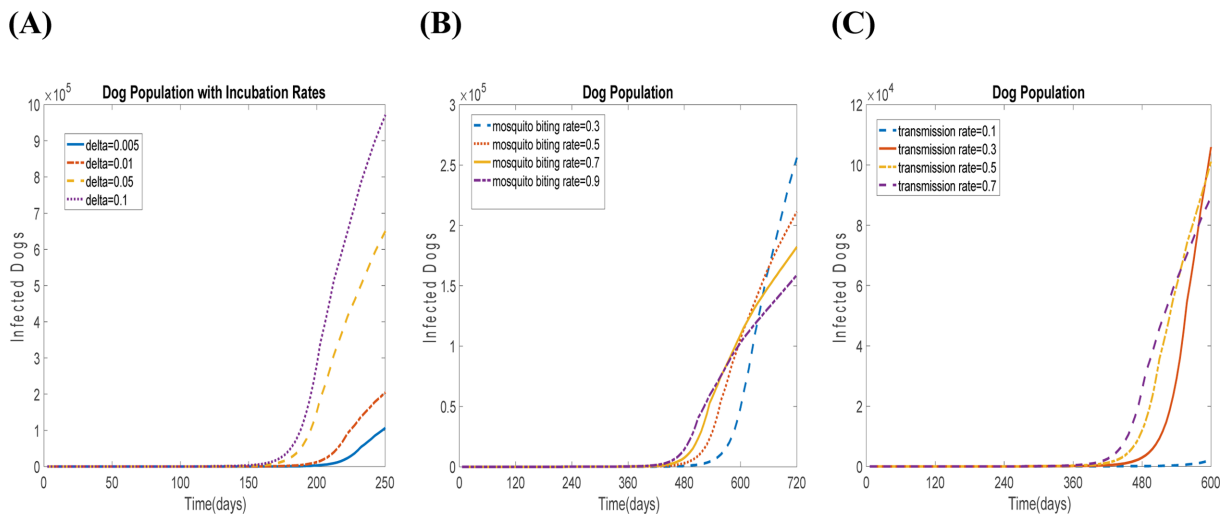
system of ODE as shown in Equation (1) was implemented in MATLAB, and the code is available at [https://github.com/venusseo12/Mathematical\\_Modeling\\_of\\_Dirofilaria\\_immitis.git](https://github.com/venusseo12/Mathematical_Modeling_of_Dirofilaria_immitis.git).

## Results

To understand the transmission pathways on the heartworm transmission dynamics between dogs and mosquitoes, we construct the model as a system of ODE, as shown in (1). MATLAB is used to obtain the numerical results, which are the different stage populations of dogs and mosquitoes (susceptible, exposed, infected, and treated). We do not consider the final stage, treated, for mosquitoes. We take all parameter values as shown in Table 2 for the base model. Fig. 1 shows the simulation results that represent the four different stages (susceptible, exposed, infected, and treated) of the dog population without control for 1 year. We assume that the number of recruited dogs (homeless, sheltered, or outdoor dogs) is 73,602 [11]. Simulation results show that after 1 year, 3,289 dogs out of 73,602 (about 4.5%) are exposed and 134 dogs are infected, as shown in Fig. 2. Only 0.2% of sus-



**Fig. 2.** Simulation results of model represent four different stages (susceptible, exposed, infected, treated) of dog population without control for 1 year. All parameter values are applied from Table1.



**Fig. 3.** Population of infected dogs from simulation of model with control: (A) shows the infected dog population with different incubation rates. We take 0.005 as the base parameter value that corresponds to 180 days for the prepatent period. (B) represents the number of infected dogs considering the different mosquito biting rates from 0.3 to 0.9. The value of 0.5 was taken as the base model from [8]. (C) shows the infected dog population with different infected dog-to-mosquito (or vice versa) transmission rates.

ceptible dogs become infected after 1 year, which seems low. However, this is because it takes about 6 months for exposed dogs to be infected through the procedure of the young worms maturing into adults and then migrating through the dog's lungs and other organs. Thus, if all exposed dogs are maintained in the same circumstances without any treatment, then the number of infected subjects will increase over time. This may increase the possibility of other dogs, especially dogs that live outside, being infected.

In order to estimate the accuracy of the parameters, we also experiment numerically with various values of incubation rate, mosquito biting rate, and infected dog-to-mosquito (or vice versa) transmission rate (see Fig. 3). As the mosquito biting rate is higher, the number of infected dogs also increases in the first 600 days. However, the growth rate of the mosquito biting rate 0.3 is the highest after 600 days. This implies that the parameter of mosquito biting rate is not significantly important for infection in the long term. Fig. 3C shows the infected dog population with different infected dog-to-mosquito transmission rates. The value of 0.1 is not applicable for our simulation, as shown in Fig. 3 (C, blue-dashed line).

### Discussion

We created a mathematical model of heartworm infection transmission dynamics in dogs and mosquitoes. Mathematical models for infectious disease dynamics have been used for a variety of diseases, and they suggest problems to solve for disease-free environments. Vector-borne diseases whose vector is the mosquito, such as Zika and Dengue, are especially actively studied by academic institutes. However, epidemic models with the dog as the host have rarely been studied. Some African and Chinese research teams have suggested models of rabies related to transmission from dogs to human [14,15]. To date, research with mathematical epidemic modeling has focused on diseases related to human beings. In the past, the number of dogs in South Korea and the number of dogs with diseases were not officially reported. It is expected that research on these pets will be actively conducted by the national dog registration system in South Korea. Prediction of the population of infected dogs depends on the vector (mosquito) population, and it will serve as a blueprint for the prevention of diseases as well as quantifying of drug preparation. We have some goals for future studies to develop the best model of heartworm infection transmission dynamics that predicts the optimal way of preventing deaths among dogs. First, we will continue to perform stability analyses to determine the locally and globally asymptotically stable DFE. Second, we will create a model with respect to the death rate, birth rate, and other parameter estimations for dogs and mosquitoes. It is desirable to esti-

mate the effective and optimal use of vaccinations in dogs for eliminating the disease in South Korea.

### References

1. American Heartworm Society. FAQs. American Heartworm Society, Wilmington, 2014. Available from: <https://www.heartwormsociety.org/>.
2. Bowman DD, Liu Y, McMahan CS, Nordone SK, Yabsley MJ, Lund RB. Forecasting United States heartworm *Dirofilaria immitis* prevalence in dogs. *Parasit Vectors* 2016;9:540.
3. Hwang WK, Chung GS, Kim DY. Pet Reports 2018: Pet Related Industries and Parenting Status. KB Financial Group Inc., Seoul, 2018.
4. Campbell-Lendrum D, Manga L, Bagayoko M, Sommerfeld J. Climate change and vector-borne diseases: what are the implications for public health research and policy? *Philos Trans R Soc Lond B Biol Sci* 2015;370:370.
5. Kim JW, Bu KO, Choi JT, Byun YH. Climate Change in the Korean Peninsula for 100 Years. National Institute of Meteorological Sciences, Jeju, 2018.
6. van den Driessche P, Watmough J. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. *Math Biosci* 2002;180:29-48.
7. Coyne MJ, Smith G, McAllister FE. Mathematic model for the population biology of rabies in raccoons in the mid-Atlantic states. *Am J Vet Res* 1989;50:2148-2154.
8. Manore CA, Hickmann KS, Xu S, Wearing HJ, Hyman JM. Comparing dengue and chikungunya emergence and endemic transmission in *A. aegypti* and *A. albopictus*. *J Theor Biol* 2014;356:174-191.
9. Olawoyin O, Kribs C. Effects of multiple transmission pathways on Zika dynamics. *Infect Dis Model* 2018;3:331-344.
10. American Veterinary Medical Association. Heartworm Disease. American Veterinary Medical Association, Schaumburg. Available from: <https://www.avma.org/public/PetCare/Pages/Heartworm-Disease.aspx>.
11. Ji IB, Kim HJ, Kim WT, Seo GC. Development Strategies for the Companion Animal Industry. Korea Rural Economic Institute, Naju, 2017. Available from: [www.krei.re.kr](http://www.krei.re.kr).
12. Shutt DP, Manore CA, Pankavich S, Porter AT, Del Valle SY. Estimating the reproductive number, total outbreak size, and reporting rates for Zika epidemics in South and Central America. *Epidemics* 2017;21:63-79.
13. Yang HM, Macoris ML, Galvani KC, Andrighetti MT, Wanderley DM. Assessing the effects of temperature on the population of *Aedes aegypti*, the vector of dengue. *Epidemiol Infect* 2009;137:1188-1202.
14. Asamoah JK, Oduro FT, Bonyah E, Seidu B. Modeling of rabies transmission dynamics using optimal control analysis. *J Appl Math* 2017;2017:2451237.
15. Zhang J, Jin Z, Sun GQ, Zhou T, Ruan S. Analysis of rabies in China: transmission dynamics and control. *PLoS One* 2011;6:e20891.