Mathematical models for dog rabies that include the curtailing effect of human intervention

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Abstract

Rabies is a zoonotic viral disease that is responsible for an estimated 55,000 human deaths per year, where dogs are the primary source of human cases. The current strategy to combat human rabies is to eliminate rabies from domestic dogs and wildlife via mass vaccination and education campaigns. For some countries, such as Turkey and most of Asia, this has never been a successful approach and rabies remains endemic there. For other countries, such as Greece, rabies is currently reemerging in wildlife and causing sporadic cases in the domestic dog population. Educational campaigns raise the awareness of rabies, such that people are more likely to restrain or kill a dog if they witness unusual aggressive behaviour. This effect of human intervention is absent from existing mathematical models for dog rabies. We use a stochastic simulation model to investigate the impact of human intervention on the dynamics and persistence of rabies. Our simulations show that elimination of rabies occurs when the likelihood of human intervention increases above a certain threshold. We also explore the effect human intervention has on the distribution of the infectious period of rabies, and conclude that human intervention is not merely equivalent to a reduction in the average infectious period. We thus, gain more insight into future rabies outbreaks containment.

1 Introduction

Rabies is a zoonotic viral disease that is transmitted via the saliva of an infected animal. An estimated 55,000 people die every year from rabies, and in almost all cases transmission occurs through a dog bite. A common measure of an infectious disease is R_0, or the basic reproduction number, which represents the expected number of secondary infections arising from a single infected individual in a fully susceptible population. The R_0 for rabies is estimated to be between 1 and 2, depending on location [1]. In general, an infectious disease must have an $R_0 > 1$ to survive in a population.

While rabies is a worldwide issue, many countries today are considered rabies-free (with no human cases) as a result of mass vaccination programs [1]. Greece had been rabies-free since 1987 until rabies re-emerged in 2012, leaving public health officials scrambling to contain the outbreak [2]. Current strategies to stop rabies include mass vaccination, sterilisation, and educational campaigns. While vaccination and sterilisation are often included in existing rabies models, the "educational campaign" is not. As more humans become more aware of the impact of rabies through the educational campaigns, they are more likely to remove a dog as they witness a dog's uncharacteristic aggression. However, this mechanism of human intervention is unobserved in existing rabies models.

We examine the impact of this mechanism of human intervention in the emergence of dog rabies, and how the addition of human intervention changes the distribution of the infectious period of dog rabies.

2 The Model

2.1 The SEIR model: deterministic vs. stochastic

In a deterministic SEIR model for rabies in domestic dogs, the dog population is divided into susceptible (S), exposed (E), infectious (I), and removed (R) classes, also called compartments. Dogs move between these compartments at set rates. This model may be represented as a system of ordinary differential equations:

$$\frac{dS}{dt} = \mu N - \mu S - \beta S \frac{I}{N}$$
$$\frac{dE}{dt} = \beta S \frac{I}{N} - (\mu + a)E$$
$$\frac{dI}{dt} = aE - (\nu + \mu)I$$
$$\frac{dR}{dt} = \nu I - \mu R$$

where μ is the birth rate, β is the transmission rate, and $1/a$ and $1/\nu$ are the average exposure and infectious periods, respectively.

Deterministic models produce the same results every time given the same set of initial conditions. Stochastic models take chance into account, an element that deterministic models lack. To model the chance of human intervention deterministically, the system of differential equations must contain a large number of equations such that each equation represents a time step small enough to transform the

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probability of human intervention into a definite event at the appropriate small time step. Thus, the complexity required increases significantly. Additionally, implementing a spatial layer to the system would drive the complexity higher. Thus, we chose to study a stochastic model based on the set rates stated in Hampson's paper [3].

2.2 Modelling transmission with human intervention

Uncharacteristic aggression is a telltale sign of rabies. It is this characteristic that prompts humans to intervene. Thus, human intervention is modelled as a function of aggressive behaviour, where the probability of human intervention increases with observations of aggressive behaviour from the dog. This aggressive behaviour is described by the event of biting in the model, and only infectious dogs can bite. Let:

$$H = \text{the event of human intervention}$$
$$x = \text{the number of times a dog has bitten}$$
$$k = \text{the mean number of bites where } \Pr(H) = f(k) = 0.5$$
$$n = \text{the slope at } \Pr(H) = 0.5$$

The probability of human intervention can then be modelled by:

$$\Pr(H) = \frac{x^n}{x^n + k^n}$$

In this function, as shown in Figure 1, $\Pr(H)$ increases with x, such that as $n \to \infty$, $\Pr(H)$ becomes the step function, and k shifts the function along the x-axis.

The model assumes random mixing and the contact rate per dog to increase linearly with the density of the population. Transmission is modelled by asking a series of questions (see Figure 2) for each dog in a population of 2000 dogs, and for each time step, where one time step represents six hours. For each question, a uniform random number is generated such that if the random number were less than a particular set rate, the dog proceeds to the next question, and when the dog successfully "passes" the last question, a new dog is infected with rabies.

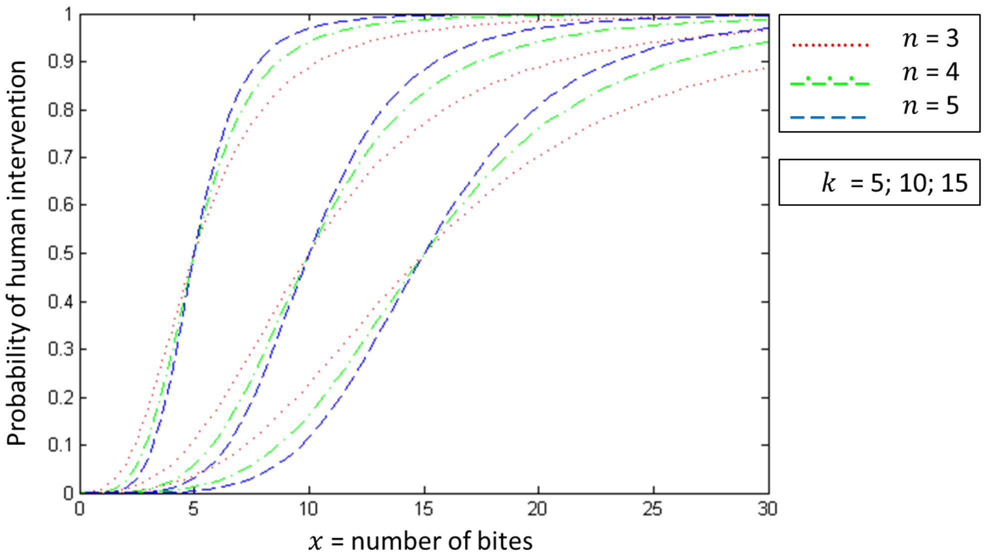

Figure 1: Probability of human intervention for different parameter values

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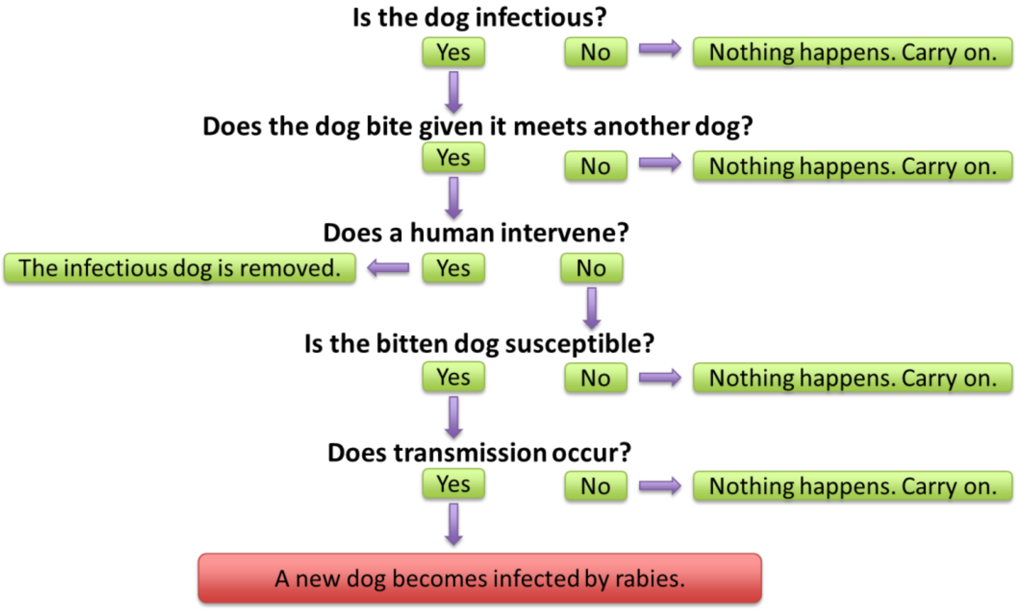

Figure 2: A flow chart of the transmission process with human intervention

Human intervention occurs only after a dog has bitten another dog. If a human intervenes, the infectious dog immediately enters the removed state. Dogs may also enter the removed state through natural death.

Simulations were run with and without human intervention in the statistical program R, and differences were noted in the simulations where outbreaks occurred.

3 Results

The number of biting events from each infected dog (over the period it was infectious) and the average infectious period (in days) were recorded and displayed as histograms (See Figure 3). For simulations run without human intervention, the histogram of biting events appears to show a geometric distribution, and the histogram of the average infectious period appears to show an exponential distribution. However, when the same simulation was run with human intervention included, the distributions of the number of bites no longer looked to be from a geometric distribution. Similarly, when run with human intervention, the distribution of the average infectious period no longer looked to be exponential. This change in distribution is more pronounced as the human intervention parameter $k \to 0$.

At $k = 5$ where outbreaks are sustained, the mean number of exposed and infectious dogs at any given time are 56.57 and 9.16, respectively. Similarly, for $k = 4$ where outbreaks are sustained, the respective means are 18.84 and 2.85. For $k = 4$, it seems that outbreaks cannot be sustained long-term.

4 Discussion

4.1 Memoryless distributions

It was logical that the average infectious period and the mean number of biting events from an infected dog would be smaller when human intervention was introduced. A

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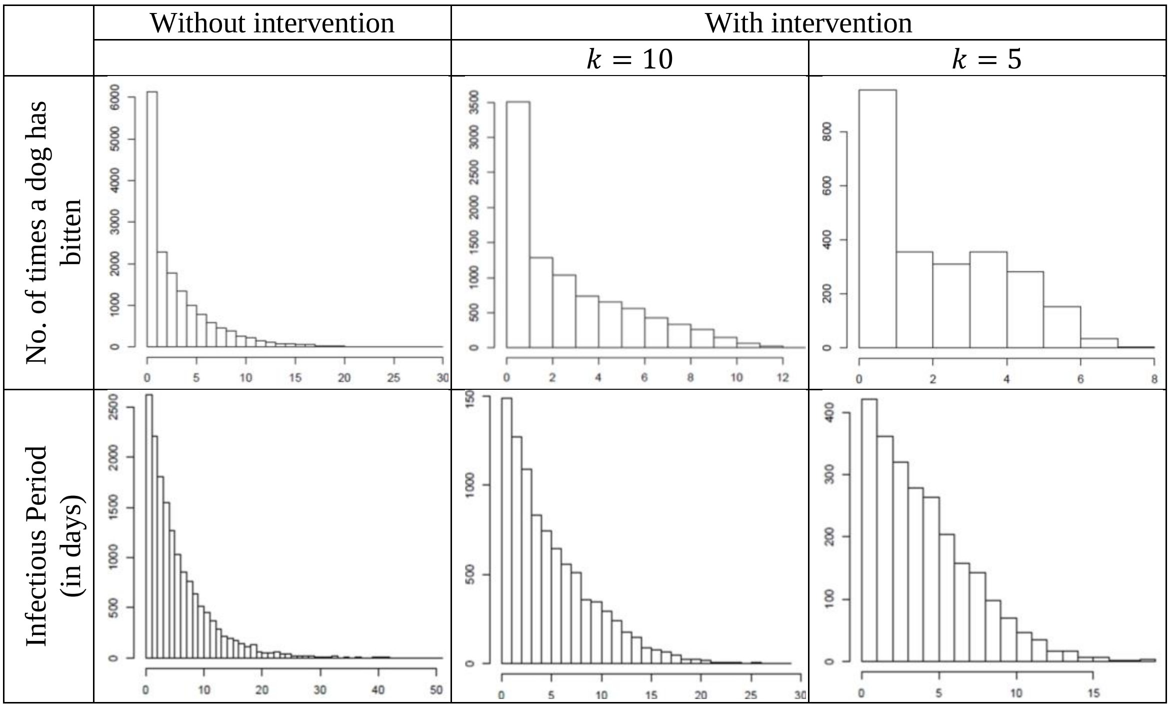

Figure 3: Histograms of the number of times a dog has bitten (top row); histograms of the infectious period (bottom row)

geometric distribution for the number of times a rabid dog bites also makes sense since the event is discrete and the event of biting is memoryless – the probability that a rabid dog will bite given it meets another dog does not depend on whether the dog has bitten in the past. According to Feller [4], suppose we know that no success has occurred during the first m trials; the waiting time T from this mth failure to the first success has exactly the same distribution and is independent of the number of preceding failures.

Similarly, the probability of a success, i.e. the death of the rabid dog due to the virus, at the mth time step does not depend on the previous failures, i.e. the survival of the rabid dog, before the mth time step. The memoryless property of the distribution of the infectious period arises from this independence. Since the infectious period is the total waiting time until the first success, and time is continuous, it follows the continuous form of memorylessness – the exponential distribution.

4.2 Significance of human intervention

If the effect of human intervention were plainly that it shortens the average infectious period or the number of times a dog has bitten, then human intervention could be modelled by simply changing the appropriate parameters. The results showed that the addition of human intervention in a rabies model changed the shape of the distributions not just the expected values. This change cannot be mimicked by changing a parameter. The effect of human intervention in a rabies model is meaningful in that it changes the distribution of certain parameters. Furthermore, the change in distribution alters the way we make inferences about the data.

Human intervention shortens the infectious period, which in turn affects R_0. Sustained outbreaks are more difficult to obtain as k decreases, such that for some value $k = k^*$, where the estimated value of k^* is between 4 and 4.5, outbreaks can no longer be sustained and rabies is driven out of the population.

4.3 Challenges ahead

One challenge is to derive an equation for R_0 that accounts for human intervention. The difficulty lies in the combination of memoryless processes (such as the events of biting and death due to the virus) and processes with memory (human intervention following aggressive behaviour). The process of human intervention is not memoryless as humans remember the number of times a dog has bitten. It is this memory that warrants a human to act responsibly when he / she increasingly suspects a dog is rabid. Given an equation for the new R_0, new thresholds may be calculated to make realistic goals for educational campaigns.

Validation for rabies models is difficult due to the lack of data. It would be unreasonable and unethical to purposely infect dogs and set the rabid dogs free to collect data on their interaction in the wild. In addition, data on the frequency of human intervention is difficult to obtain as the event of human intervention is often unrecorded, and many animal shelters do not record down the number of animals that are euthanised or suspected of rabies infection.

Second, how human intervention may be integrated with existing mathematical models for rabies is unclear, but this would help guide public health officials on the best way to eliminate or contain rabies in the future.

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References

1. Hampson K, Dushoff J, Cleaveland S, Haydons D, Kaare M, Packer C, Dobson A. 2009. Transmission Dynamics and Prospects for the Elimination of Canine Rabies. *PLoS Biology*. 7(3):462-471.
2. Tsiodras S, Dougas G, Baka A, Billinis C, Doudounakis S, Balaska A, Georgakopoulou T, Rigakos G, Kontos V, Efstathiou P, Tsakris A, Hadjichristodoulou C, Kremastinou J. 2013. Re-emergence of animal rabies in northern Greece and subsequent human exposure, October 2012 – March 2013. *Euro Surveill*. 18(18)
3. Hampson K, Dushoff J, Bingham J, Bruckner G, Ali Y, Dobson A. 2007. Synchronous cycles of domestic dog rabies in sub-Saharan Africa and the impact of control efforts. *PNAS*. 104(18):7717-22.
4. Feller W. 1957. An Introduction to Probability Theory and Its Applications, 3rd edn, vol 1. *John Wiley & Sons, Inc.*, New York.

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