



IS4250 Project Report

Healthcare Analytics

An Evaluation of Rabies Vaccination Rates among Canines and Felines
Involved in Biting Incidents within the Wellington–Dufferin–Guelph Public
Health Department
Semester 2, 2015/2016

Prepared for: Prof Chan Wai Mun, Raymond

Prepared by:

Project Group 26: Catalytics

Chik Jun Qi (A0099141A)

Ong Yi Quan (A0100058X)

Yap Zi Xuan (A0105763R)

BComp Information Systems
National University of Singapore

CONTENTS

1	An Introduction to Rabies	3
2	Background	4
3	Clinical Descriptions and Vaccinations	5
	3.1 Vaccinations for Humans	6
	3.2 Vaccinations for Animals	6
4	Paper Study	7
	4.1 Dataset Simulation	7
	4.2 Analysis of Univariate Data	9
	4.3 Model Simulation	12
5	Limitations of Original Paper.....	16
6	Areas for future exploration	18
7	Conclusion	19
	Appendix A	23
	Appendix B	24
	Appendix C	25
	Appendix D	26
	Appendix E	27
	Appendix F	28
	Appendix G	36

1. An Introduction to Rabies

Rabies is a viral disease that affects the central nervous system, progressively leading to a fatal brain inflammation. Although pre-exposure immunisation and prevention methods have been developed, rabies continue to be a substantial threat worldwide¹, with a high fatality rate each year. An estimate of 60,000 human deaths are caused by rabies annually, most of which occurring in South Asia and Africa (World Health Organisation, 2016).

Despite being recognised as a pervasive global threat, the severity of the disease is often neglected in developing countries, where priority is given to other diseases such as malaria, tuberculosis and Ebola virus disease. A few factors that contributed to the situation in these countries include poor community participation in local programmes, cultural and religious beliefs, a lack of social awareness, and limited access to proper health facilities and medications (Hemachudha, Laothamatas & Rupprecht, 2002). Through the collaborative effort of World Health Organisation (WHO) and the Global Alliance for Rabies Control (GARC), coordinated actions have been taken for eliminating human rabies through the canine rabies control.

Among the different measures taken in rabies elimination programmes, a recent study by Bottoms et al. (2014) conducted in Canada, Ontario, examines the rate of animal bite incidents with unvaccinated, domestic canines and felines. With a better understanding of the paper and the analyses conducted, similar investigations can be conducted on rabies-affected areas to identify the root problem in rabies persistence.

This paper seeks to replicate the various analyses conducted to assess its findings, determine possible limitations, while looking into variables or additional information that can be taken into account when targeting other rabies-affected areas.

¹ Visual representation of the geographical Impact of Rabies can be found in [Appendix A](#).

2. Background

A zoonotic disease with a long history, rabies can be transmitted between animals and to humans, usually through the saliva of a rabid animal into a bite or scratch wound. Rabies is caused by viruses belonging to the genus *Lyssavirus*, the two most prominent being the classical rabies virus (RabV) that is responsible for most human rabies cases, and the Australian bat lyssavirus (ABLV), which is the sole *Lyssavirus* member found in Australia (Garg, 2014). While carriers of the virus may differ according to geographical location, domestic dogs have been identified to be the main carriers of RabV, contributing to 99% of human rabies cases (World Health Organisation, 2016). It is important to note that canine rabies also predominates in both India and Africa, the two developing regions with the highest death toll from human rabies.

While the near 100% fatality rate in rabies victims may sound severe, a vaccine for the disease have been developed since 1885 (Baer, 2007). Rabies is entirely preventable through immediate vaccination to bite victims, and strict guidelines in vaccination of domestic dogs have proven effective in reducing or eliminating the threat of rabies. Factors that have contributed to the unrelenting situation in greatly affected areas mainly stem from their limited access to healthcare, as well as a lack of public awareness of the disease. The disease also faces issues of underreporting in these areas, coupled with a lack of proper surveillance and response systems in rabies control efforts (Taylor & Knopf, 2015). Various studies have also highlighted the overall impact associated with rabies — economic burden from direct costs, public health budgets, livestock and human losses (Hampson et al., 2015), emphasising the urgency of controlling the rabies situation in developing countries.

In the December 2015 International Conference hosted by WHO, a new campaign have been launched with the goal of eliminating dog-transmitted rabies by 2030 (End Rabies Now, n.d.). One of the first measure taken in the initiative is to address the problem of underreporting and negligence of animal bite incidents, while educating the public about preventive and control programmes. The control programme encourages close monitoring of the vaccination status of domestic pets, and assists developing countries by subsidising the cost of educational efforts and vaccines.

3. Clinical Descriptions and Vaccinations

The rabies virus enters the victim's body through an open wound to the muscle nerve cells, where viral replication occurs. The replicated virus proceeds to travel towards the victim's spinal cord to the brain, eventually leading to coma and death. The incubation period of rabies is highly dependent on the distance between the bite location and the brain, as well as the amount of rabies viral particles² present in the victim's body (Garg, 2015). The duration between the animal bite and initial symptoms varies between 2 to 12 weeks, and flu symptoms are the first sign of an infection. Victims usually experience tingling at the site of the wound, muscle weakness, headaches and fever. During this phase, however, the symptoms are non-specific and may not raise suspicions, making the illness hard to diagnose (Linscott, 2012). The following phase may vary, depending on the two different forms of rabies (Figure 1). Paralytic rabies appears in around 30% of human cases, and usually occur in victims with post-exposure vaccination (Ghosh, Roy, Lahiri, & Bala, 2009). 17% to 80% of victims also experience hydrophobia (Harper, 2004), regardless of the form of rabies infection. Hydrophobic episodes last around 5 minutes each, where victims may experience painful muscle spasms in the throat that causes foaming of saliva and an inability to swallow.

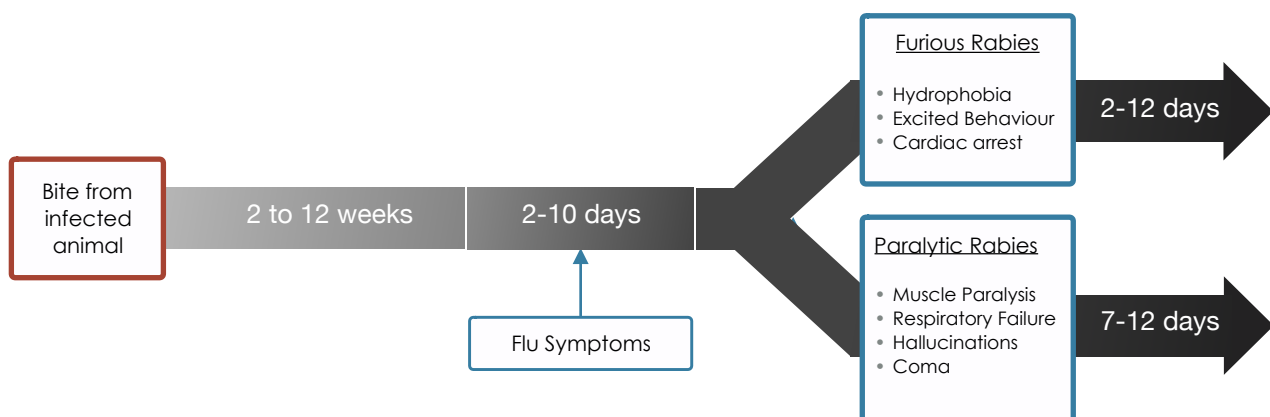


Figure 1. An illustration of Rabies Symptoms

² Usually measured as *viral load*: the quality of virus in a given volume, which correlates with the severity of infection

3.1 Vaccinations for Humans

The most commonly administered vaccine for human rabies is the human diploid cell vaccine (HDCV), which is available for both pre-exposure (preventive) and post-exposure vaccination. The preventive vaccination is usually given in three doses, containing 1 ml of HDCV each. Post-exposure vaccination usually consists of both the rabies vaccine and an injection of human rabies immune globulin (HRIG), and is referred to collectively as post-exposure prophylaxis (PEP) (CDC, 2015). PEP should be given to victims immediately after thorough wound cleansing, and given four times to non-immunised victims, and twice to victims who are previously vaccinated.

3.2 Vaccinations for Canines and Felines

As mentioned in the previous section, vaccination of domestic pets are crucial in eliminating rabies. Vaccines are available in both injection and oral forms, and more countries are regulating the administration of mandatory rabies vaccinations. The required interval between each vaccination differs among countries and states, and the vaccination schedule is usually tracked with a rabies vaccination certificate. An animal is considered vaccinated and immunised 28 days after initial vaccination, or if booster vaccinations are given according to schedule.

4. Paper Study

The severity of rabies, coupled with the high number of animal bite incidents across the world highlight the importance of pet vaccination. In most of the affected countries, the risk of rabies usually differs across each municipality. It is often a dilemma to organisations and the health departments when considering the first measure to take that would play the most significant role in lowering the risk of rabies — educational campaigns, stricter monitoring for pet vaccinations, sponsoring or lowering the price of vaccinations, or setting up more veterinary clinics and hospitals.

In the study of rabies vaccination rates in several municipalities of Canada by Bottoms et al. (2014), several outcomes and variables were analysed to identify possible associations linked to the demographics of unvaccinated cats or dogs. In this paper, the analyses conducted are replicated in an attempt to find possible limitations to the paper, while studying their use of models to determine the models that would be useful for research conducted out of Canada. This study also aim to identify additional variables that can be looked into for enhanced effectiveness in rabies control.

4.1 Dataset simulation

Since the analyses conducted were based on smoothed values of the original dataset, we tried to contact the original authors of the paper in hopes of obtaining the raw dataset. Due to unsuccessful attempts in getting a reply, we decided to simulate the dataset as an alternative.

The descriptive variables mentioned in the paper that were initially obtained from Wellington–Dufferin–Guelph (WDG) health department's database were stimulated using Java ([Appendix B](#)) and Excel. As a result, 718 bite reports containing the variables: (1) gender of animal, (2) species (feline or canine), (3) season of bite, (4) vaccination status and (5) municipality were generated. In addition, the overall percentage for each category in the original paper were taken into consideration. This helped to ensure that the generated dataset is similar to the summary data described in the paper.

The population size for each municipality was taken from the Canadian population census of 2011 (Statistics Canada, 2015). Information on the number of dog bites and number of animal bites per year were obtained by multiplying ($\text{population size}/1000$) with the number of animal bites per 1,000 residents, as well as the number of dog bites per 1,000 residents. The number of dog bites and animal bites were then multiplied by 2 to make up for 2 years worth of estimated incident

counts: 2010 and 2011. Finally, the values were rounded off to the nearest integer using the `round()` function in Excel. In total, 714 animal bites were derived after the previous steps. 4 new dog bite cases were then created and assigned to the 4 biggest cities each to skew the data to the minimum.

The population size for each municipality was also multiplied by the percentage of unvaccinated animals, and the percentage of unvaccinated dogs, to get the count number of unvaccinated animals and count number of unvaccinated dogs respectively. The `round()` function in Excel was also used here to round off the raw values to integer count values.

The Java code was then used to create the CSV file enclosed. For each of the 718 bite incidents, there were 5 variables: Gender, Species, Season, Vaccination Status and Municipality. Since the number of both dogs and cat bite incidents of specific vaccination status and of specific municipality has been determined, the Java code only had to assign gender and season randomly for each bite incident occurrence. A random number generator from 1 to 100 was used to determine the assignment for both variables based on their percentage makeup. For instance, if 60% of the subjects were males and 40% were females, and the random number is from 1 to 40, the gender would be female. Else, it will be male if it is from 41 to 100.

Other relevant information used in the paper such as the population frequency and density of each municipality were obtained from the WDG community health status report (WDG Public Health, 2012). Municipalities were categorised as urban and rural based on the paper's classification — the proportion of urbanized area in each municipality. Our paper adhered closely to their division of municipalities, where urban areas had a percentage of urbanized area above 88%, while rural areas had a percentage urbanized area that were less than 7%. Although the paper stated its sources for information regarding the number of veterinary clinics and mobile practices in each municipality, the search function in the database was only able to return results for cities, while several of the 16 municipalities listed in the paper are considered towns or townships. Zero results were returned for searches for several municipalities ([Appendix C](#)), which differed greatly from the data in the original article.

4.2 Analysis of Univariate Data

The authors considered the following variables for statistical analysis:

- (1) number of animal bite incidents per 1,000 residents per year,
- (2) number of dog bite incidents per 1,000 residents per year,
- (3) proportion of unvaccinated animals involved in the bite incidents
- (4) proportion of unvaccinated dogs involved in the bite incidents

Animals referred to the inclusion of both cats and dogs. In addition, an animal was considered unvaccinated if it had never been vaccinated against the rabies virus or if its rabies vaccination was outdated. Though the authors included a separate analysis for bite incidents involving just dogs, bite incidents involving cats were not analysed separately due to missing data. This was because they were unable to obtain vaccination status for any of the cats in 5 municipalities, and no cats were involved in the reported bite incidents for 6 of the municipalities over the 2-year period. Likewise, for our simulation, we analysed the bite incidents involving all animals (cats and dogs), and dogs alone, but not for cats alone.

A statistical summary of the simulated number of bites per 1,000 residents per year and the percentage of unvaccinated animals for each of the 16 municipalities was generated using R. This was quickly done by running `summary (X)`, which readily gave us summary statistics such as the mean, median, mode and quartiles for a univariate X. Statistical summaries for the three univariates are described in the table below. The overall mean for the three univariates were quite close to the means described in the original paper. However, the paper did not cover additional statistics such as the min, 1st quartile, median and 3rd quartile.

	No. of animal bites per 1000 residents per year	No. of dog bites per 1000 residents per year	Percentage of unvaccinated animals
Min	0.880	0.710	18.00
1st Quartile	1.220	0.945	32.97
Median	1.385	1.155	39.35
Mean (simulated)	1.551	1.238	43.02
Mean (paper)	1.550	1.240	43.0
3rd Quartile	2.040	1.560	45.12
Max	2.220	2.020	100.00

Two histograms are plotted to illustrate the frequency of both simulated animal bite incidents and dog bite incidents, as shown in Figure 4.2.1. Quite notably, the histogram for dog bites is skewed to the right as it followed a Poisson distribution. The number of dog bites per 1,000 residents mostly fell in between 1.0 to 2.0 for majority of the municipalities. On the other hand, the histogram for all animal bites had a bimodal (double-peaked) distribution. The code snippets used to generate the histograms in R Studio may be found in the [Appendix D](#).

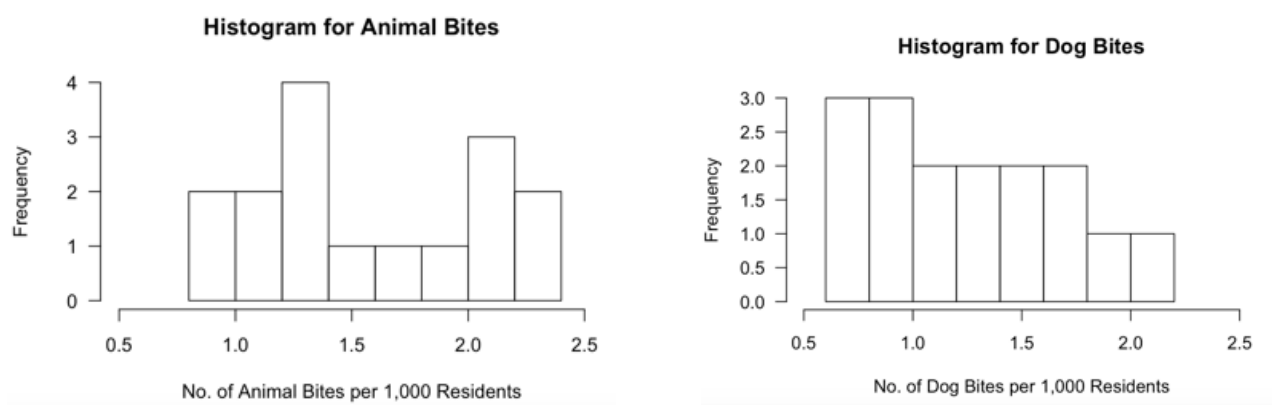


Figure 4.2.1 Histogram for Simulated Animal Bites and Dog Bites Respectively

Apart from the frequency of bite incidents, we were interested to know if our simulated municipality data was similar to what was presented in the original study. A scatter plot was generated using the number of bites per 1,000 residents per year and the percentage of unvaccinated animals for each of the 16 municipalities. This allowed us to compare our simulated municipality data to those presented in the authors' original scatter plot. The R code snippet below describes how our scatter plot was generated.

```
# Scatter Plot
plot(unvaccinated, bites, xlab="Percentage of
Unvaccinated Animals", ylab="No. of Bites per 1,000
Residents")
abline(v=mean(unvaccinated, na.rm=TRUE), col="orange")
abline(h=mean(bites, na.rm=TRUE), col="orange")
text(unvaccinated, bites, labels=name, cex=0.5, pos=1)
```

Figure 4.2.2 shows the scatter plot generated from our simulated dataset in R Studio. The horizontal orange line represents 1.385, the median value of the Y-axis variable (number of bites per 1000 residents per year) whereas the vertical orange line represents 39.35, the median value of the X-axis variable (percentage of animals that were unvaccinated).

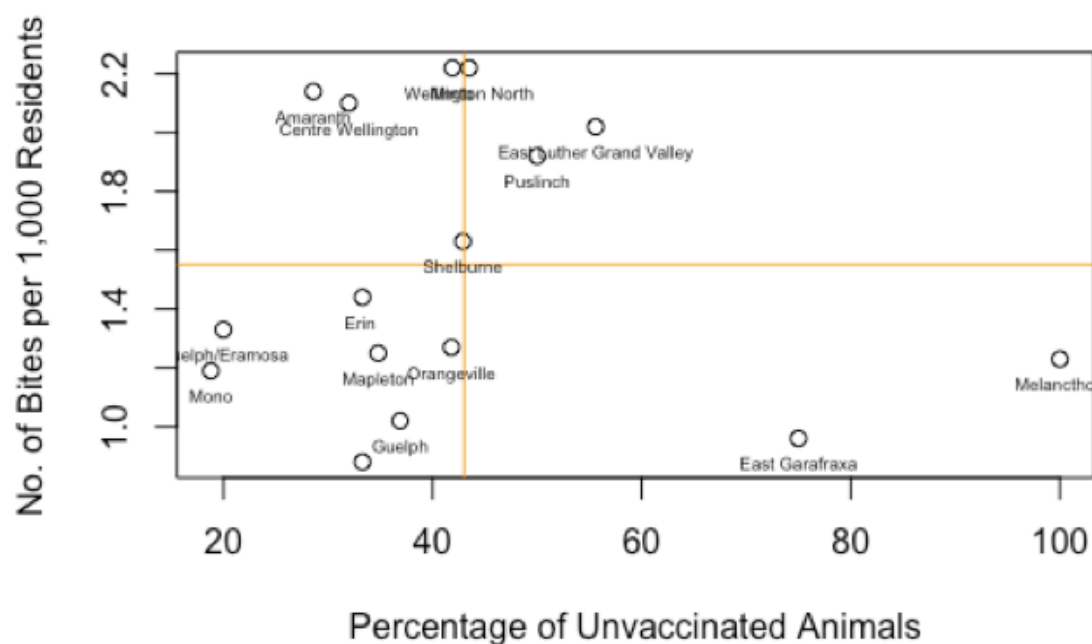


Figure 4.2.2 Scatter Plot displaying the number of animal bites per 1000 residents per year, and the proportion of those animals that were unvaccinated

By demarcating the scatter plot into four quadrants, we were able to observe municipalities with a higher than median number of bites per 1,000 residents, as well as a higher than median proportion of unvaccinated animals. These cities include Puslinch, East Luther Grand Valley, Wellington North, Minto and Shelburne, which were very similar to both results depicted in the raw and smoothed scatter plots in the original study. However, for our scatter plot's case, the data simulated for both Minto and Shelburne had a close to median proportion of unvaccinated animals. As a result, their data points were positioned very closely to the orange vertical line in the scatter plot.

4.3 Model simulation

Following the methodology described by the paper, a poisson regression model was first used to fit the data for the two outcomes pertaining to bite incidents. According to the paper, Pearson statistics were used to determine a good fit. There was a lack of details on the chi-square test; it can be used to compare the 2 different models or individual models in which full models and models with less variables are compared. In this paper, however, the log-likelihood test is a comparison between the negative binomial regression model and the poisson regression model.

Poisson model was chosen as the bite incidents are count data of incidents that occurred within a fixed interval of time (2010, 2011). An ideal poisson model should have its mean equal to its variance. Negative binomial model was chosen as the alternative if the count data distribution is over-dispersed; its variance being much higher than its mean. However, the variance of both animal bites incidents and dog bite incidents have variances much higher than their mean as shown earlier, implying that the poisson distribution is over-dispersed.

As explained earlier, the data on the number of veterinary clinics per 1,000 people was not complete and had to be generated randomly using R. The number of veterinary clinics per 1,000 people was assumed to have a normal distribution; its mean of 1.8 and standard deviation of 1.5 as obtained from the paper. Random variables were first generated using the `rnorm()` function in R. However, despite numerous attempts, negative values were always present, which was unacceptable in the context of number of vet clinics. Hence, the `runif()` function was used instead, with the setting of 0 as the minimum and 4.3 as the maximum. Both minimum and maximum values were also obtained from the paper.

For each municipality, an interaction term was derived by multiplying the number of vet clinics per 1,000 people to the boolean urban variable. A population offset was used for the poisson regression model and multiplied by 2 to make up for 2 years. The final set of values used to run the statistical models can be found in [Appendix E](#).

As the binomial negative regression model has less predictors, the H_0 for the log-likelihood test for the negative binomial model serves as a better fit. If the p-value of the log-likelihood ratio test is less than 0.05, H_0 can be rejected and the poisson regression model is favoured. Else, the negative regression model is then used. The actual R screenshots³ are in [Appendix F](#). Below is a summarised table of the model simulation.

Outcome	Model	Variable	P-Value	Log Likelihood, Model1 over Model	R2/ Mcfadden's R
Animal Bites	Poisson Regression	Urban	1.18E+00	0.05114	0.7665267
		Vets per 10,000 people	0.0711		
		Interactio	0.0027		
Animal Bites	Negative Binomial Regression	Urban	0.09619	0.01915	0.6354646
		Vets per 10,000 people	0.00446		
		Interaction	0.000118		
Dog Bites	Poisson Regression	Urban	0.178795	Nil	0.6728997
		Vets per 10,000 people	0.002603		
		Interaction	0.02763		
Dog Bites	Negative Binomial Regression	Urban	0.00199	Nil	0.6901492
		Vets per 10,000 people	0.2475		
		Interaction	0.2708		
Unvaccinated Animals	Linear Regression	Urban	0.624	Nil	0.1175520
		Vets per 10,000 people	0.642		
		Interaction	0.1976		
Vaccinated Animals	Binomial Logistic Regression	Urban	0.1535	Nil	0.1048
		Vets per 10,000 people	0.568		
		Interaction	0.527		
Unvaccinated Dogs	Linear Regression	Urban	0.568	Nil	0.1448021
		Vets per 10,000 people	0.527		
		Interaction	0.527		

— Note: Highlighted cells are what this model simulation is trying to replicate from the paper

³ R script can be found in Github repository, named Model Simulation.R

A screenshot of the paper's statistically modelling is shown in Figure 4.3.1.

Table 3. Multivariable negative binomial model for the number of animal bites per 1000 residents and multivariable Poisson model for the number of dog bites per 1000 residents in Wellington–Dufferin–Guelph Public Health department in 2010 and 2011

Outcome	Risk factor	Incidence rate ratio	Confidence interval	P-value
Animal bites per 1000 residents	Urban municipality (baseline: rural)	0.687	0.530, 0.890	0.005
	Veterinary clinics per 10 000 people	1.095	0.996, 1.203	0.060
Dog bites per 1000 residents	Log likelihood = -52.46; LR (χ^2) = 6.83; P = 0.0329; likelihood ratio test of α = 0; P = 0.048			
	Urban municipality (baseline: rural)	0.352	0.214, 0.578	<0.0001
	Veterinary clinics per 10 000 people	1.052	0.958, 1.156	0.285
	Interaction term (urban & vet clinics)	1.373	1.080, 1.747	0.010
Log likelihood = -46.71; LR (χ^2) = 39.16; P < 0.0001				

Figure 4.3.1 Statistics for Multivariable Negative Binomial Model and Multivariable Poisson Model
Used in the Paper

Integer values for total animal bites and total dog bites are used instead of normalised values shown above as the R function that is used for both poisson regression and negative binomial regression throws an error when the dependent variable is a non-integer. This is due to both regression models are assumed to have a poisson distribution and hence only dependable count variables which are integers are only allowed.

For dog bites, the model simulation managed to achieved p-values not far off from what the paper has achieved. The model simulation has Urban as highly significant, has Interaction as significant and Vets per 10,000 people as not significant. The order of p-values are also retained. When a log-likelihood test is ran on both models, the p-value of 0.019 is obtained, favouring the poisson regression model as per the paper.

For the same set of randomly generated number of veterinary clinics per 10,000 people values, the model simulation is not able to achieve similar p-values for animal bites as in the paper. The order of p-values was inversed too; our model simulation had the number of veterinary clinics per 10,000 people as a more statistically significant variable instead. However, the p-value of the log-likelihood test was slightly above 0.5, which favoured the negative binomial model for animal bites. The above p-values are the closest our group was able to achieve through generating random values for 1 variable while not compromising on the other outcome, dog bites.

In addition, our group took a step further to include another test to determine which model was a better fit for the outcomes related to bite incidents. Mcfadden's Pseudo R-square was also used to access both poisson regression and negative binomial model. The formula for its calculation is shown below:

$$R^2 = 1 - \frac{\ln \hat{L}(M_{Full})}{\ln \hat{L}(M_{Intercept})}$$

M_{full} = Model with predictors

$M_{Intercept}$ = Model without predictors

\hat{L} = Estimated likelihood

The log-likelihood on the intercept model is treated as a total sum of squares, and the log-likelihood of the full model is treated as the sum of squared errors.

The Mcfadden's pseudo R-square, on the other hand, gave us contrasting results on which model should be favoured due to a better fit. The negative binomial model for dog bites and the poisson regression model for animal bites have higher R-square than their counterparts and should be the model favoured instead; this is the exact opposite results of the log-likelihood test using the anova chi-square function in R. However, this was not too surprising since the p-value of the likelihood tests for animals bites is 0.051, which marginally favoured the negative binomial model. If a more liberal p-value is set, for example 0.055, the poisson regression model will be favoured. Also, the difference of Mcfadden's R-square for dog bites models was a mere 0.018. However, our group did not manage to simulate the data perfectly, as explained earlier, using the p-values of the negative binomial of animal bites. The authors may have obtained more definitive results from their log-likelihood tests comparing the poisson model and negative binomial regression model.

5. Limitations of Original Paper

Though the authors have reached their objectives of identifying high-risk municipalities in the WDG area of study, there were still some unavoidable limitations and shortcomings. Most of these limitations were a result of under-reported bite incidents and other factors which would make it very difficult to be accounted for in the paper.

Under-Reporting of Bite Incidents

Firstly, the authors acknowledged that there were likely to be under-reported animal bite incidents that occurred within the time and area of study. There were several factors that may have influenced a victim to avoid reporting an incident. For instance, if a victim visits a veterinary clinic due to an animal bite, it will usually be reported to the local health department, as required by law. However, not all municipalities may have the same level of stringency. In cases where medical attention is not required and hence not pursued, under-reporting is likely to occur. Other possible reasons include the victim not being aware of the reporting process, or the process itself being too troublesome and thus deterring patients from taking action. A patient who was bitten by their own pet may also believe that their health is not being endangered, and hence avoided making a report due to complacency.

A complacent mentality among pet owners is not known to be uncommon. In a separate study conducted by the Ottawa-Carleton Health Department (Goodwin, Werker, Hockin, Ellis, Roche, 2002), researchers telephoned random Canadian residents to understand the attitudes and practices of dog and cat owners with respect to vaccinating their pets against rabies. The survey results found that even though more than 90% of respondents said they would call a doctor if they were bitten by a wild animal, only 39% said they would call a doctor if bitten by their own pet (CCDR, 2002). While this further highlights a high possibility of under-reported cases in other similar papers, it also indirectly reinforces the need for the public health department to continue to educate pet owners about rabies vaccination.

Unaccounted Biological Data

In addition, the study did not manage to account for pertinent biological information such as the breed and neuter status of each animal subject. This was due to the lack of knowledge resulting

from unreliable historical data and limited information of the reported animals. As a result, the authors excluded 350 reported bite incidents during their early stages of data exploration. Excluding such data may have introduced certain bias that could not be estimated or were unaccounted for in the study. For instance, certain breeds of canines, such as Pit bull or Rottweiler, are known to display more aggressive tendencies than other breeds. This unaccounted factor could have a causal effect on the overall bite rate of each municipality. It is possible that high-risk municipalities with more bite incident counts than other areas could have a relatively high percentage of pets from more aggressive breeds in the first place.

Unaccounted Reasons for Clinic Visitation

Lastly, if we were to consider the relationship between the number of veterinary clinics and number of bite incidents per 1,000 residents explored throughout the study, a boundary problem may have been unaccounted for in the paper's spatial analysis. The authors made an assumption where residents generally visit veterinary clinics in their own municipality. Realistically speaking, this may not always be the case. For instance, there may be clinics patronized by residents outside of the WDG area of study, and the exclusion of these clinics could have possibly skewed the authors' findings. Additionally, pet owners may not always choose their closest veterinary clinic as such decisions may be based on price, quality of service or public recommendations. Several pet owners may thus be willing to visit clinics in other municipalities due to these considerations. Though this would have greatly skewed the results of the study, it is still understandable that it would have been incredibly difficult for the authors to take all these human considerations into account.

Improvements to be made for further studies

The paper failed to develop a good fit multivariate model for the prediction of the proportion of the unvaccinated animals. Predicting the proportion of unvaccinated animals can significantly reduce the rate of rabies infection. Organisations can focus their efforts on increasing vaccination rates to areas with high proportion of unvaccinated animals. Measures include increased education and more policing of mandatory vaccinations. WHO claims that at least $\frac{1}{3}$ of the dog population must be vaccinated in order to break the cycle of transmission in dogs and to humans. Hence, further research can be done on predicting the proportion of unvaccinated animals, while more prediction factors can be added to the model to make it a better fit.

6. Areas for future exploration

Taking into account the various limitations of the study, several insights highlighted by the paper shows measures that can be taken by WHO and GARC to eliminate the global threat of rabies.

Target areas for educational outreach

CDC and WHO can target areas with high risk contracting rabies — those with a high number of bite incidents and a high proportion of unvaccinated animals. A pilot project can be introduced to educate the public on the risk of rabies transmission, and measures can be taken to reduce bite incidents and increase pet vaccination. More efforts can also be made to encourage pet owners to monitor vaccination statuses of their pets, while further research on factors that affect the owner's decision or willingness to vaccinate their pet can be conducted to give further insights on how to increase vaccination rates. A few possible reasons would be the cost of vaccination, the distance to the nearest vet, or the lack of awareness regarding the risk of rabies.

With a greater understanding on pet owners' decision to vaccinate their pets, organisations can focus on the factors affecting pet owners' decision instead of just educating them about the perils of not vaccinating their pets. Results from the pilot project must then be evaluated, and the findings from the pilot project may assist in the revision of the initial study. Further studies can be conducted on the participation rate of public on education campaigns, as well as the effectiveness in these campaigns.

Monitoring bite rate incidents

The prediction models developed in this study regarding the number of bite incidents per 1000 people can help identify areas that have potential to have high bite rate incidents. This is especially useful to areas where a lot of bite incidents go unreported. Taking into consideration that the model should be extrapolated out of Canada with caution — it may not be a good fit for other countries which is structurally different from Canada, similar prediction models can be conducted for other countries to grasp a clearer picture of the rabies situation in each region. With a better understanding of areas with higher bite incidents, organisations can look into different approaches to decrease bite incidents, such as educating pet owners on handling their pets, looking into reasons of animal aggressiveness, and monitoring pet vaccination statuses more closely.

High rate of bite incidents from strays

In the study, 37% of the bite incidents were excluded from the primary data as the animals come from a humane society or shelter; this is a significant amount that can be prevented. Further research can be followed up on shelters and humane societies, to minimise animal bites from strays and look into vaccination procedures for stray animals. Some possible measures that can be taken would be to look into stray animal aggressiveness, educating the public to handle stray animals with care, and looking into rabies vaccinations sponsoring for shelters and humane societies.

8. Conclusion

This study has presented us with several insights about the current situation of rabies, the importance of vaccinations, and the factors correlated to the persistent threat of rabies. The paper studied and the replication of several analyses also shown limitations to the current approach in rabies studies, as well as possible improvements that can be made. While the paper showed an interesting approach to understanding the rabies situation in an area of interest, it is important to note that further research and study have to be conducted before it can be extended to other countries, such as Africa and rural Asia where rabies is a significant public health issue. Several factors should also be looked into when conducting future research of unvaccinated pets. A different perspective at the number of unvaccinated animals would be to study variables related to their owners — their age group, household income, number of pets at home and how often they bring their pets to the vet. With various studies conducted to identify the root cause of unvaccinated pets, rabies campaigns can be made more efficient and effective.

References

- Baer, G. M. (2007). The History of Rabies In A. C. Jackson & W. H. Wunner (Eds.), *Rabies 2nd edition* (pp. 11-13). New York, NY: Academic Press Elsevier.
- Bottoms, K., Trotz-Williams, L., Hutchison, S., MacLeod, J., Dixon, J., Berke, O., & Poljak, Z. (2014). An Evaluation of Rabies Vaccination Rates among Canines and Felines Involved in Biting Incidents within the Wellington–Dufferin–Guelph Public Health Department. *Zoonoses and Public Health*, 61(7), 499-508. doi: 10.1111/zph.12101
- Centers for Disease Control and Prevention. (2013). Rabies-Free Countries and Political Units. Retrieved from: <http://www.cdc.gov/importation/rabies-free-countries.html>
- Centers for Disease Control and Prevention. (2015). Rabies Medical Care. http://www.cdc.gov/rabies/medical_care/
- End Rabies Now. (n.d.). About. Retrieved from: <https://endrabiesnow.org/about>
- Garg, S. R. (2014). *Rabies in Man and Animals*. Delhi, India: Springer Science & Business Media.
- Ghosh, J. B., Roy, M., Lahiri, K., & Bala, A. K. (2009). Acute flaccid paralysis due to rabies. *Journal of Pediatric Neurosciences*, 4(1), 33. doi:10.4103/1817-1745.49106
- Goodwin, R., Werker, D. H., Hockin, J., Ellis, E., & Roche, A. (2002). A survey of knowledge, attitudes, and practices of dog and cat owners with respect to vaccinating their pets against rabies, Ottawa-Carleton, Ontario, July 2000. Canada communicable disease report, 28(1), 1. Retrieved from: <http://publications.gc.ca/collections/Collection/H12-21-28-1.pdf>
- Harper, T. K. (2004). TKH Virology Notes: Rabies. Retrieved from http://www.tarakharpur.com/v_rabies.htm
- Hampson, K., Coudeville, L., Lembo, T., Sambo, M., Kieffer, A., Attlan, M., ... & Costa, P. (2015). Estimating the global burden of endemic canine rabies. *PLoS Neglected Tropical Disease*, 9(4), e0003709. doi:10.1371/journal.pntd.0003709

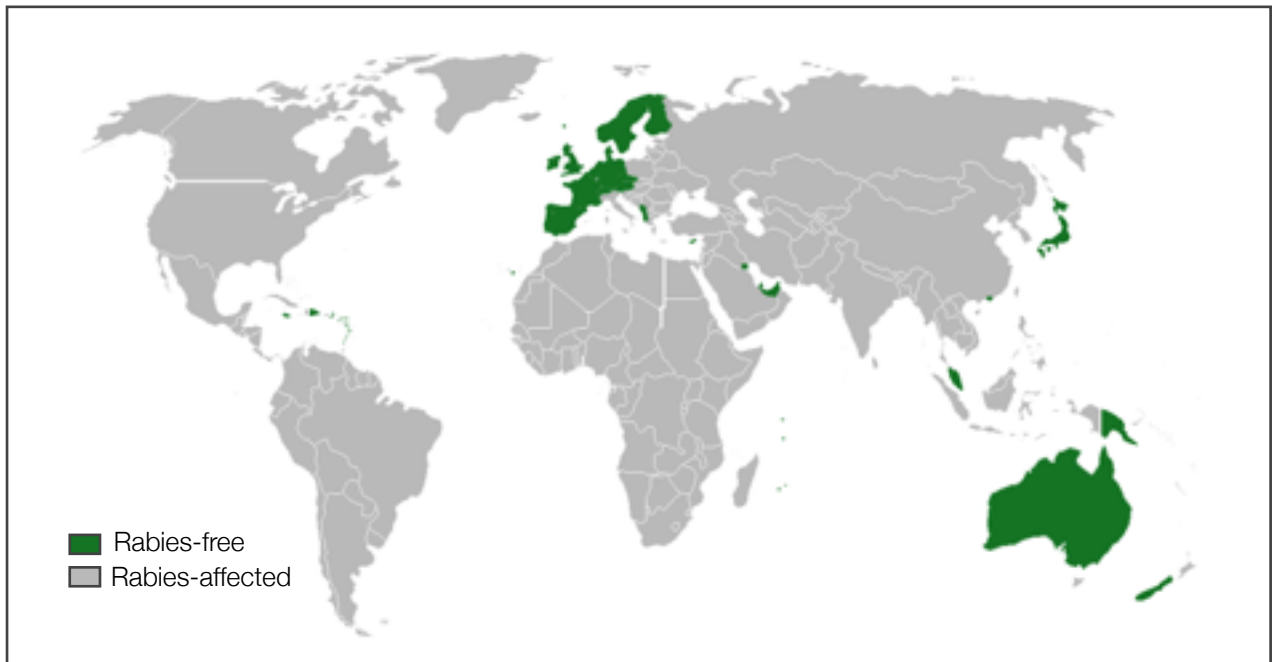
-
- Hemachudha, T., Laothamatas, J., & Rupprecht, C. E. (2002). Human rabies: a disease of complex neuropathogenetic mechanisms and diagnostic challenges. *The Lancet Neurology*, 1(2), 101-109.
- Linscott, A. J. (2012). Rabies. *Clinical Microbiology Newsletter*, 34(22), 177-180. <http://dx.doi.org/10.1016/j.clinmicnews.2012.10.003>
- Taylor, L. H., & Knopf, L. (2015). Surveillance of Human Rabies by National Authorities – A Global Survey. *Zoonoses and Public Health*, 62(7), 543-552. doi:10.1111/zph.12183
- The College of Veterinarians of Ontario. (2016). Information for the Public. Retrieved from: [https://cvo.org/For-the-Public/Find-a-Veterinarian-\(1\).aspx](https://cvo.org/For-the-Public/Find-a-Veterinarian-(1).aspx)
- Wellington-Dufferin-Guelph Public Health. (2012). *Community Picture Health Status Report*. Retrieved from: <https://www.wdgppublichealth.ca/sites/default/files/wdgpfiles/community%20picture%20health%20status%20report%202012.pdf>
- Wiktor, T. J., Plotkin, S. A., & Koprowski, H. (1977). Development and clinical trials of the new human rabies vaccine of tissue culture (human diploid cell) origin. *Developments in biological standardization*, 40, 3-9.
- World Health Organisation. (2016). Human rabies. Retrieved from: <http://www.who.int/rabies/human/en/>

List of Abbreviations used in the paper

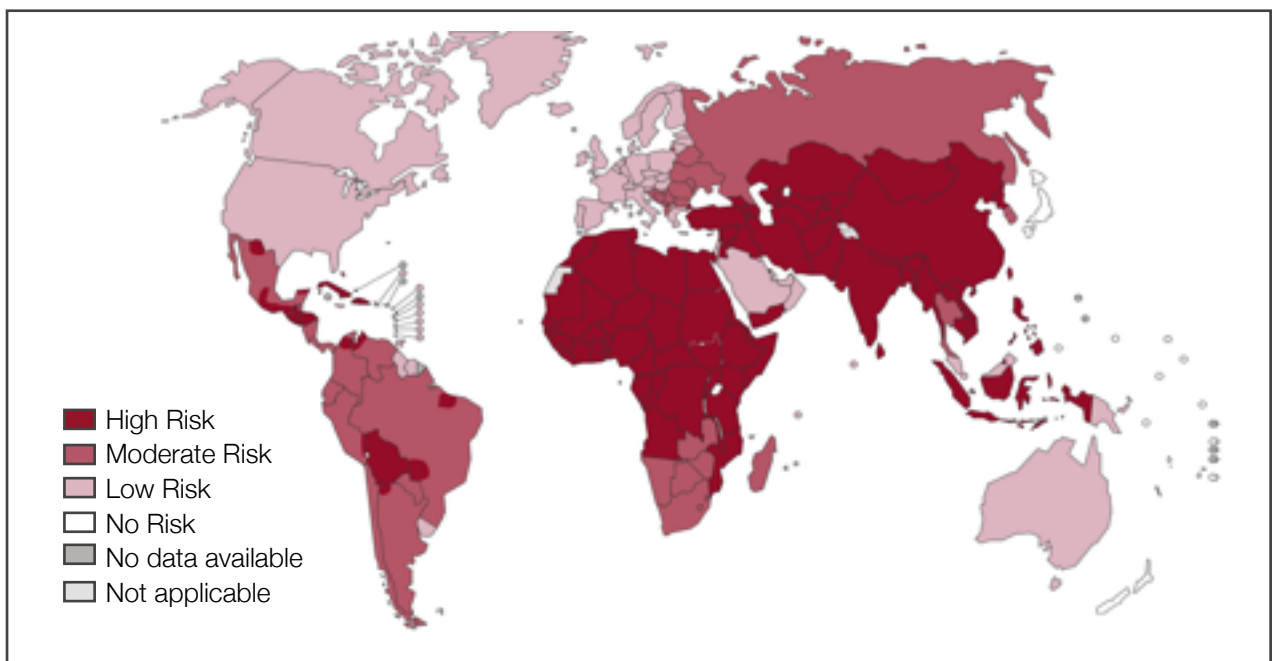
Abbreviation	Full Name	Definition
ABLV	Australian bat lyssavirus	A zoonotic virus closely related to rabies virus
CDC	Centers for Disease Control and Prevention	Leading national public health institute of US that focuses national attention on developing and applying disease control and prevention
GARC	Global Alliance for Rabies Control	The leading organisation working for the global prevention of rabies
HCDV	Human Diploid Cell Vaccine	Commonly used rabies vaccine, used for both pre-exposure and post-exposure
HRIG	Human Rabies Immune Globulin	Rabies antibodies to protect the victim from rabies virus
PEP	Post-exposure prophylaxis	Combination of rabies vaccine and HRIG
RabV	Rabies Virus	One of the most common lyssavirus member
WHO	World Health Organisation	An agency that plays a leading role in international public health
WDG	Wellington-Dufferin-Guelph	A public health non-profit agency serving 16 municipalities in Ontario, Canada

Appendix A: Geographical Impact of Rabies

Rabies-free countries, excluding bats rabies. (Information from CDC, 2013)



Global Distribution of human rabies risk levels. (WHO, 2013)



Appendix B: Java Code for dataset

```
import java.util.*;
import java.io.*;

class Data
{
    final public static int MAX_ROW = 718;
    final public static int MAX_COL = 5;

    public static int[] computeRowSums(int[][] arr, int row, int col)
    {
        int[] rowSum = new int[row];

        for (int i=0; i<row; i++)
        {
            for (int j=0; j<col; j++)
            {
                rowSum[i] += arr[i][j];
            }
        }
        return rowSum;
    }

    public static void main(String[] args)
    {
        int[] city = new int[]
{3963,26693,2595,2726,10770,120545,12380,9989,2839,8334,7546,3391,27975,7029,5846,114
77};

        int [] dogbites = new int[]{15,68,4,10,26,172,26,16,5,28,14,5,54,24,18,34};
        int [] catbites = new int[] {1,45,0,2,6,74,6,8,1,10,4,1,19,2,2,17};
        int [] unvacDogs = new int[] {5,14,3,6,9,51,3,6,6,7,4,2,19,11,8,14};
        int [] unvacAnimals = new int[] {5,36,3,7,11,91,6,8,6,16,3,2,31,13,9,22};
        int [] unvacCats= new int[16];
        int [] animalbites= new int [16];

        Random r = new Random();
        Random r2 = new Random();
        for(int i=0;i<16;i++){
            unvacCats[i]= unvacAnimals[i] - unvacDogs[i];
        }
        for(int i=0;i<16;i++){
            animalbites[i]= dogbites[i] + catbites[i];
        }
        int[][] results = new int[MAX_ROW][MAX_COL];
        int count =0;
        for(int i=0;i<16;i++){
            int Animalbites= animalbites[i];
            int Dogbites = dogbites[i];
            int UnvacDogs = unvacDogs [i];
            //Gender Species Season VaccinationStatus Municipality
            for(int j=0; j<Animalbites; j++){
                if (Dogbites!=0){
                    // 1 = Dog, 0 = Cat
                    results[count][1]= 1;
                    Dogbites--;
                }
                else{
                    results[count][1]= 0;
                }
            }
        }
    }
}
```



```

        if (UnvacDogs!=0){
            // 1 = Vaccinated, 0 = Unvaccinated
            results[count][3]= 0;
            UnvacDogs--;
        }
        else{
            results[count][3]= 1;
        }
        int gender = r.nextInt(90) +1;
        // Male = 1, Female = 2 , Unknown = 3
        if(gender<=45)
            results[count][0]=1;
        else if (gender<= 67)
            results[count][0]=2;
        else
            results[count][0]=3;

        int season = r2.nextInt(100)+1;

        // Spring=1, Summer=2, Autumn=3, Winter=4
        if(season<=28)
            results[count][2]=1;
        else if (season<=61)
            results[count][2]=2;
        else if (season<= 82)
            results[count][2]=3;
        else
            results[count][2]=4;

        results[count][4]=i+1;
        count++;
    }

}

try{
    PrintWriter writer = new PrintWriter("rabiesData.csv", "UTF-8");

    writer.println("Gender"+"," + "Species" + ","+"Season"+"," + "Vaccination"+","+"
Municipality");

    for (int i=0; i<718; i++){
        writer.println(String.valueOf(results[i][0])+"," +
String.valueOf(results[i][1])+"," +
        +String.valueOf(results[i][2])+"," + String.valueOf(results[i][3])+","+
String.valueOf(results[i][4]));
    }

    writer.close();
}

catch(IOException ex){
}

System.out.println("Done!!!!");
}
}

```

Appendix C: Municipalities and classifications and number of vets

Vet Information from The College of Veterinarians of Ontario (2016)

Municipalities	Settlement	County	Population Count	Characteristic	No. of Vets
Amaranth	Township	Dufferin County	3,845	Rural	0
Centre Wellington	Township	Wellington County	26,049	Rural	0
East Garafraxa	Township	Dufferin County	2,389	Rural	5
East Luther Grand Valley	Township	Dufferin County	2,844	Rural	0
Erin	Town	Wellington County	11,148	Urban	9
Guelph	City	City of Guelph	114,943	Urban	40
Guelph/Eramosa	Township	City of Guelph	12,380	Rural	1
Mapleton	Township	Wellington County	9,851	Rural	0
Melancthon	Township	Dufferin County	2,895	Rural	0
Minto	Town	Wellington County	8,504	Urban	0
Mono	Town	Dufferin County	7,071	Urban	17
Mulmur	Township	Dufferin County	3,318	Rural	0
Orangeville	Town	Dufferin County	26,925	Urban	31
Puslinch	Township	Wellington County	6,689	Rural	18
Shelburne	Town	Dufferin County	5,149	Urban	7
Wellington North	Township	Wellington County	11,175	Rural	0

Appendix D: Code snippets used to generate the histograms

Histogram for No. of Animal Bites per 1,000 Residents

```
animal_bites = municipalitiesData$Bites.per.1000.residents

hist(animal_bites,
     main="Histogram for Animal Bites",
     xlab="No. of Animal Bites per 1,000 Residents",
     xlim=c(0.5,2.5),
     las=1,
     breaks=5)
```

Histogram for No. of Dog Bites per 1,000 Residents

```
dog_bites = municipalitiesData$Dog.bites.per.1000.residents

hist(dog_bites,
     main="Histogram for Dog Bites",
     xlab="No. of Dog Bites per 1,000 Residents",
     xlim=c(0.5,2.5),
     las=1,
     breaks=5)
```

Appendix E: Set of values used to run the statistical models

Municipality	Population Count	Vets per 1000 people	Urban	Interaction term	Offset	Animal Bites	Dog Bites
Amaranth	3845	1.9254	0	0	7690	8	8
Centre Wellington	26049	2.1423	0	0	52098	55	33
East Garafraxa	2389	4.2885	0	0	4778	2	2
East Luther Grand Valley	2844	2.8734	0	0	5688	6	5
Erin	11148	3.1098	1	3.1098	22296	16	14
Guelph	114943	1.324	1	1.3240	229886	117	82
Guelph/ Eramosa	12380	1.3862	0	0	24760	16	13
Mapleton	9851	3.4247	0	0	19702	12	8
Melancthon	2895	3.2801	0	0	5790	4	3
Minto	8504	3.5326	1	3.5326	17008	19	14
Mono	7071	3.8477	1	3.8477	14142	8	7
Mulmur	3318	3.5276	0	0	6636	3	2
Orangeville	26925	1.3162	1	1.3162	53850	34	26
Puslinch	6689	1.8485	0	0	13378	13	11
Shelburne	5149	3.3178	1	3.3178	10298	8	8
Wellington North	11175	0.3911	0	0	22350	25	16

Appendix F: Regression Models

Model 1: Animal Bites - Poisson Regression

Call:

```
glm(formula = regression.data$Bites ~ regression.data$Urban +  
    regression.data$Vets + regression.data$interaction, family = "poisson",  
    offset = log(regression.data$offset))
```

Deviance Residuals:

Min	1Q	Median	3Q	Max
-1.75843	-0.57597	-0.08607	0.48620	1.40936

Coefficients:

	Estimate	Std. Error	z value	Pr(> z)
(Intercept)	-6.72390	0.18378	-36.587	< 2e-16 ***
regression.data\$Urban	-1.05959	0.24189	-4.380	1.18e-05 ***
regression.data\$Vets	-0.15212	0.08429	-1.805	0.07111 .
regression.data\$interaction	0.33977	0.11350	2.994	0.00276 **

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for poisson family taken to be 1)

Null deviance: 35.087 on 15 degrees of freedom

Residual deviance: 11.812 on 12 degrees of freedom

AIC: 89.822

Number of Fisher Scoring iterations: 4

Model 2: Animal Bites - Negative Binomial Regression

Call:

```
glm.nb(formula = regression.data$Bites ~ regression.data$Urban +  
        regression.data$Vets, init.theta = 2.740105061, link = log)
```

Deviance Residuals:

Min	1Q	Median	3Q	Max
-1.09997	-0.80990	-0.57630	0.01475	2.48185

Coefficients:

	Estimate	Std. Error	z value	Pr(> z)
(Intercept)	4.2720	0.4214	10.137	< 2e-16 ***
regression.data\$Urban	0.8278	0.3439	2.407	0.0161 *
regression.data\$Vets	-0.7114	0.1544	-4.607	4.08e-06 ***

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for Negative Binomial(2.7401) family taken to be 1)

Null deviance: 41.263 on 15 degrees of freedom

Residual deviance: 15.616 on 13 degrees of freedom

AIC: 122.91

Number of Fisher Scoring iterations: 1

Theta: 2.74
Std. Err.: 1.07

2 x log-likelihood: -114.907

Model 1 against Model 2 Log Likelihood test

Analysis of Deviance Table

Model 1: regression.data\$Dog.Bites ~ regression.data\$Urban + regression.data\$Vets + regression.data\$interaction

Model 2: regression.data\$Dog.Bites ~ regression.data\$Urban + regression.data\$Vets

	Resid. Df	Resid. Dev	Df	Deviance	Pr(>Chi)
1	12	9.2957			
2	13	14.7833	-1	-5.4875	0.01915 *

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Model 3: Dog Bites - Poisson Regression

Call:

```
glm(formula = regression.data$Dog.Bites ~ regression.data$Urban +  
    regression.data$Vets + regression.data$interaction, family = "poisson",  
    offset = log(regression.data$offset))
```

Deviance Residuals:

Min	1Q	Median	3Q	Max
-1.1378	-0.6674	0.0445	0.7202	1.3145

Coefficients:

	Estimate	Std. Error	z value	Pr(> z)
(Intercept)	-7.1117	0.2207	-32.217	< 2e-16 ***
regression.data\$Urban	-1.0996	0.2856	-3.850	0.000118 ***
regression.data\$Vets	-0.1352	0.1005	-1.344	0.178795
regression.data\$interaction	0.3955	0.1313	3.011	0.002603 **

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for poisson family taken to be 1)

Null deviance: 27.1755 on 15 degrees of freedom

Residual deviance: 9.2957 on 12 degrees of freedom

AIC: 83.571

Number of Fisher Scoring iterations: 4

Model 4 : Dog Bites – Negative Binomial Regression

Call:

```
glm.nb(formula = regression.data$Dog.Bites ~ regression.data$Urban +  
        regression.data$Vets, init.theta = 4.234700195, link = log)
```

Deviance Residuals:

Min	1Q	Median	3Q	Max
-1.2753	-0.7337	-0.4286	0.0484	2.4778

Coefficients:

	Estimate	Std. Error	z value	Pr(> z)
(Intercept)	3.7800	0.3572	10.581	< 2e-16 ***
regression.data\$Urban	0.9301	0.2971	3.130	0.00175 **
regression.data\$Vets	-0.6520	0.1340	-4.866	1.14e-06 ***

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for Negative Binomial(4.2347) family taken to be 1)

Null deviance: 47.665 on 15 degrees of freedom

Residual deviance: 14.783 on 13 degrees of freedom

AIC: 110.05

Number of Fisher Scoring iterations: 1

Theta:	4.23
Std. Err.:	1.89

2 x log-likelihood: -102.047

Model 3 against Model 4 : Log Likelihood Test

Analysis of Deviance Table

Model 1: regression.data\$Dog.Bites ~ regression.data\$Urban + regression.data\$Vets + regression.data\$interaction

Model 2: regression.data\$Dog.Bites ~ regression.data\$Urban + regression.data\$Vets

	Resid. Df	Resid. Dev	Df	Deviance	Pr(>Chi)
1	12	9.2957			
2	13	14.7833	-1	-5.4875	0.01915 *

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Model 5: Unvaccinated Animals – Multiple Linear Regression

Call:

```
lm(formula = unvaccinatedAnimals ~ Vets + Urban, data = regression.data)
```

Residuals:

	Min	1Q	Median	3Q	Max
	-23.009	-16.022	2.835	7.723	48.624

Coefficients:

	Estimate	Std. Error	t value	Pr(> t)
(Intercept)	33.957	13.200	2.572	0.0232 *
Vets	5.311	4.617	1.150	0.2708
Urban	-12.582	10.390	-1.211	0.2475

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 20.01 on 13 degrees of freedom

Multiple R-squared: 0.1628, Adjusted R-squared: 0.03403

F-statistic: 1.264 on 2 and 13 DF, p-value: 0.315

Model 6: Unvaccinated Animals – Logistic Binomial Regression

Call:

```
glm(formula = unvaccinatedAnimals/100 ~ Vets + Urban, family = "binomial",  
     data = regression.data)
```

Deviance Residuals:

Min	1Q	Median	3Q	Max
-0.48610	-0.32611	0.06281	0.16129	1.15175

Coefficients:

	Estimate	Std. Error	z value	Pr(> z)
(Intercept)	-0.6689	1.3677	-0.489	0.625
Vets	0.2224	0.4786	0.465	0.642
Urban	-0.5269	1.0763	-0.490	0.624

(Dispersion parameter for binomial family taken to be 1)

Null deviance: 2.9564 on 15 degrees of freedom
Residual deviance: 2.5375 on 13 degrees of freedom
AIC: 23.686

Number of Fisher Scoring iterations: 4

Model 7: Unvaccinated Dogs – Multiple Linear Regression

Call:

```
lm(formula = unvaccinatedDogs ~ Vets + Urban, data = regression.data)
```

Residuals:

Min	1Q	Median	3Q	Max
-24.931	-15.322	3.271	8.890	49.456

Coefficients:

	Estimate	Std. Error	t value	Pr(> t)
(Intercept)	26.968	13.554	1.990	0.0681
Vets	7.187	4.741	1.516	0.1535
Urban	-14.488	10.669	-1.358	0.1976

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 20.55 on 13 degrees of freedom
Multiple R-squared: 0.2242, Adjusted R-squared: 0.1048
F-statistic: 1.878 on 2 and 13 DF, p-value: 0.192

Model 8: Unvaccinated Dogs – Logistic Binomial Regression

Call:

```
glm(formula = unvaccinatedDogs/100 ~ Vets + Urban, family = "binomial",  
     data = regression.data)
```

Deviance Residuals:

Min	1Q	Median	3Q	Max
-0.55233	-0.31381	0.07841	0.18447	1.16319

Coefficients:

	Estimate	Std. Error	z value	Pr(> z)
(Intercept)	-0.9915	1.4169	-0.700	0.484
Vets	0.3125	0.4939	0.633	0.527
Urban	-0.6299	1.1043	-0.570	0.568

(Dispersion parameter for binomial family taken to be 1)

Null deviance: 3.3615 on 15 degrees of freedom
Residual deviance: 2.6860 on 13 degrees of freedom
AIC: 22.332

Number of Fisher Scoring iterations: 4

Appendix G: Variable Legend for Referencing rabiesData.csv File

City

- 1-Amaranth
- 2-Centre Wellington
- 3-East Garafraxa
- 4-East Luther Grand Valley
- 5-Erin-
- 6-Guelph
- 7-Eramosa
- 8-Maple ton
- 9-Melancthon
- 10-Minto
- 11-Mono
- 12-Mulmur
- 13-Orangeville
- 14-Puslinch
- 15-Shelburne
- 16 -Wellington North

Gender

- 1-Male
- 2-Female
- 3-Unknown

Season

- 1-Spring
- 2-Summer
- 3-Autumn
- 4- Winter

Species

- 1-Canine
- 2- Feline

Vaccination Status

- 1-Vaccinated
- 0- Not Vaccinated