IS4250 Project Report [DRAFT]
Healthcare Analytics

An Evaluation of Rabies Vaccination Rates among Canines and Felines Involved in Biting Incidents within the Wellington–Dufferin–Guelph Public Health Department

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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 worldwide[1], 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 often 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 Organization (WHO) and the Global Alliance for Rabies Control (GARC), coordinated actions have been taken for eliminating human rabies through the canine rabies control.

(lead to paper research purposes etc, and interest in the paper/how the paper can contribute to current situation)

[1] See Appendix A for a geographical impact of rabies

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 particles[2] 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.

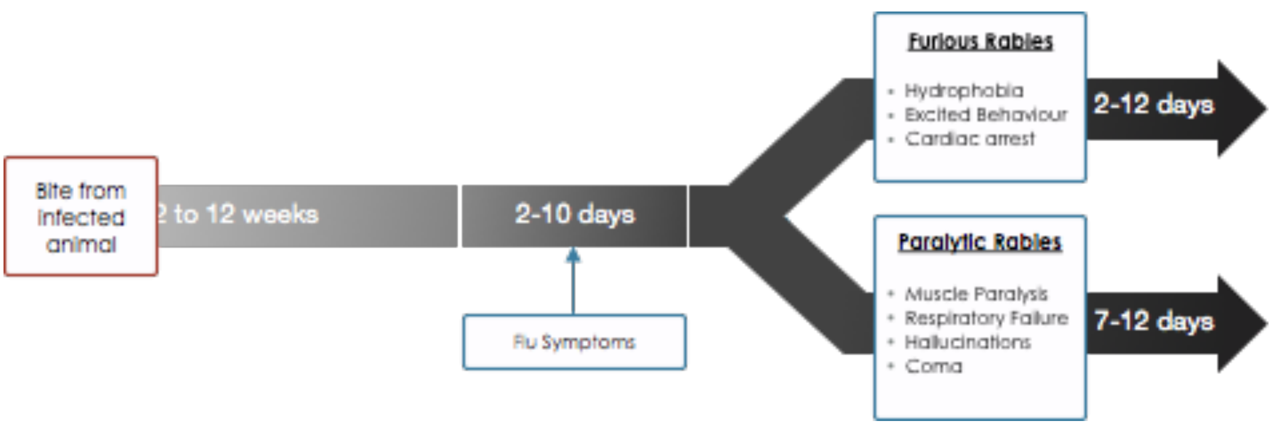


Figure 1. An illustration of Rabies Symptoms.

[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)[3], 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 time 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.

[3] Contains rabies virus grown on MRC-5 human diploid cell culture, concentrated by ultrafiltration, and inactivated with ß-propiolactone (Wiktor et al., 1980)

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 are 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 to get a reply, we decided to simulate the dataset as an alternative.

The descriptive variables in the paper that were initially obtained from Wellington–Dufferin–Guelph (WDG) health department's database were stimulated using Java (Appendix B) and Excel. 718 bite reports that contain the variables: gender of animal, species (feline or canine), season of bite, vaccination status and municipality were generated, while taking the overall percentage for each category in the original paper into consideration. This is to ensure that the generated dataset aligns closely with the summary data given.

Population size of each municipality was first taken from the Canadian population census of 2011. It was then used to get the number of dog bites and animal bites in a year by multiplying (population size/1000) to animal bites per 1000 residents and dog bites per 1000 residents. The number of dog bites and animal bites were then multiplied by 2 to make up for 2 years of incident; both 2010 and 2011. Finally, the value were rounded using the round function in excel to the nearest integer. 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.

Population size was also multiplied to the percentage of unvaccinated animal and percentage of unvaccinated dogs to get the number of unvaccinated and number instead of percentage values. The round function in excel was used again to round 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 are 5 variables: Gender, Species, Season, Vaccination Status and Municipality. Since specific number of bite incidents of specific species (dog or cat), of specific vaccination status, specific and of specific municipality, the Java code only needs to randomly assign gender and season which the bite incidents happen. A random number generator from 1 to 100 was used to determine assignment for both variables based on their percentage makeup. For example, if 60% are males and 40% are females, if the dice roll is from 1 to 40, the gender will 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 adheres closely to their division of municipalities, where urban areas have a percentage of urbanized area above 88%, and rural areas have a percentage urbanized area 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 differs greatly from the data in the original article.

Hence our group has to generate the number of vet clinics per 1000 people randomly using R. The number of vet clinics per 1000 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 in unacceptable is 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 1000 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. Following the methodology described by the paper, the two outcomes pertaining to bite incidents, a poisson regression model was first used to fit the data. It was then compared to the negative binomial regression model using the log likelihood ratio test. If the p-value of the log likelihood ratio test is less than 0.05, the negative binomial regression is then favoured; else the poisson regression model is then used. The actual R screenshots are enclosed in the appendix and the R script is attached. Below is a summarised table of the model simulation.

5. Limitations

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 are a result of under-reported bite incidents and other factors which would make it very difficult to be accounted for in the paper.

5.1 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 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 in 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.

5.2 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.

5.3 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 1000 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.

6. Areas for future exploration

Though the study and its findings are limited, it is enough for organisations such as the CDC enough to act on.

Organizations can target those high risk areas; those of high number of bite incidents and high proportion of unvaccinated animals. A pilot project can be introduced to reduce bite incidents and increase vaccination rate through education campaigns and other efforts can be carried out in the high risk areas. Results from the pilot project must then be evaluated. Findings from the pilot project may assist in the revision of the initial study and further studies can be conducted.

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. However, the model should be extrapolated out of Canada with caution as the model might not be a good fit for other countries which is structurally different from Canada.

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. Organizations can focus their efforts on increasing vaccination rates to areas with high proportion of unvaccinated animals. Measures include increased education and more policing of mandatary vaccinations. WHO claims that at least 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; more prediction factors can be added to model to make it a better fit.

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 prevent animal bites and and increase vaccination rate.

Further research on factors that affect to the owner’s decision or willingness to vaccinate their pet can be conducted to give further insights on how to increase vaccination rates. With a greater understanding on pet owners’ decision to vaccinate their pets, organizations can focus on the factors affecting pet owners’ decision instead of just educating them about the perils of not vaccinating their pets.

All in all, this study has given us some insights about rabies and the factors correlated to it. However, further research and study have to be conducted before it can be extended to Africa and rural Asia where rabies is a significant public health issue.

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.

Canadian Communicable Disease Report. (2002). A survey of knowledge, attitudes, and practices of dog and cat owners with respect to vaccinating their pets against rabies. Retrieved from: http://publications.gc.ca/collections/Collection/H12-21-28-1.pdf

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. Retrieved from: 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

Harper, T. K. (2004). TKH Virology Notes: Rabies. Retrieved from http://www.tarakharper.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

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.

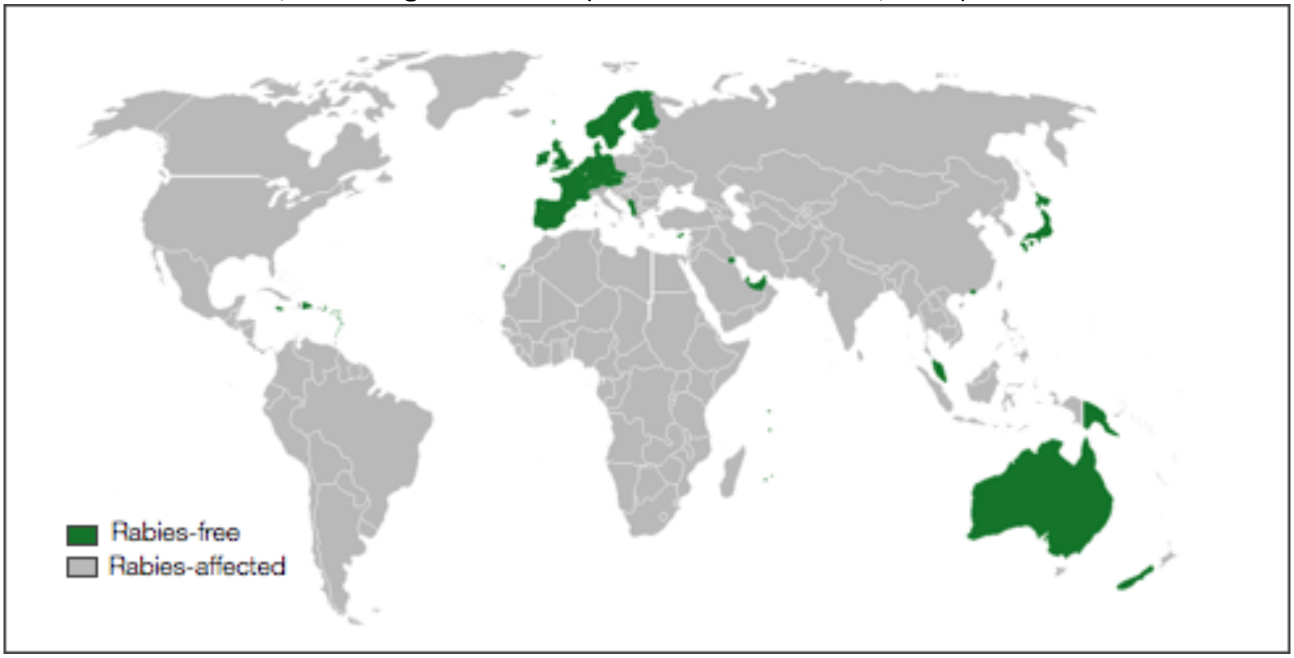
World Health Organization. (2016). Human rabies. Retrieved from: http://www.who.int/rabies/human/en/

List of Abbreviations used in the paper

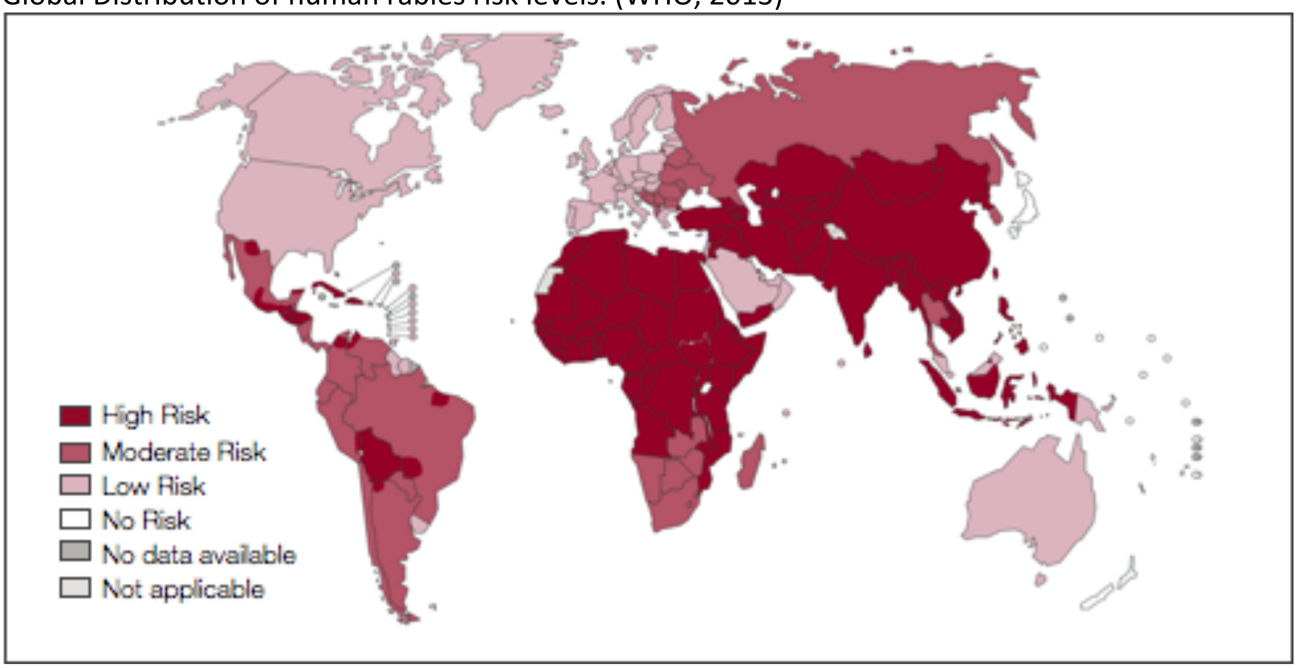
Abbreviation	Full Name	Definition
ABLV	Australian bat lyssavirus	A zoonotic virus closely related to rabies virus
CDC	Centers for Disease Control and Prevention	Leading national public health institute of US that focuses national attention on developing and applying disease control and prevention
GARC	Global Alliance for Rabies Control	The leading organization 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 Organization	An agency that plays a leading role in international public health

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: 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