USE OF RACCOON RABIES SPATIAL PATTERNS TO OPTIMIZE EFFICIENCY OF ORAL RABIES VACCINE INTERVENTIONS

by

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A Dissertation

Submitted to the University at Albany, State University of New York

in Partial Fulfillment of

the Requirements for the Degree of

Doctor in Public Health

Dissertation Advisor:

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School of Public Health

2006

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ABSTRACT

The objective of this dissertation is to describe the spatial-temporal characteristics of the raccoon rabies epizootic in NYS and analyze factors associated with the distribution of raccoon rabies cases and the costs of oral rabies vaccine (ORV) intervention. For this dissertation, all terrestrial rabies cases were determined to be, or assumed to be, raccoon rabies variant.

To achieve this objective this dissertation presents three sequential studies. In the first study the factors associated with raccoon rabies distribution in NYS are investigated through the use of a Poisson regression model. In the second study the spatial and temporal patterns of raccoon rabies in NYS are explored with a spatial scan statistic. In the third study the cost of ORV is modeled for an intervention of enzootic and newly epizootic areas in NYS.

A higher number of raccoon-variant rabies cases in a census tract during 1997-2003 was associated with a higher proportion of low intensity residential areas (those with a lower concentration of housing units), lower land elevation, a lower proportion of wetlands, and a lack of rivers/lakes and major roads.

Statistically significant clusters of terrestrial rabies cases were identified particularly in the Albany, Finger Lakes, and South Hudson areas. The clusters were generally persistent in the Albany area, but demonstrated cyclical changes in rabies activity every few years in the other areas. Cluster adjustments allowed the discussion of possible causes for the high risk raccoon rabies areas identified.

Modeling the ORV bait purchase costs by applying the Poisson regression model to stratify rabies risk resulted in a reduction of costs compared with uniform ORV baiting strategies. The proportion of savings with distribution of ORV baits based on the expected number of cases per km^2 was 29.57% for the NYS enzootic region and 38.9% for the Long Island newly epizootic zone.

This study concluded that ORV baiting interventions for raccoon rabies can be modeled and applied considering differential risk to reduce costs by at least 30% compared with uniform baiting strategies.

ACKNOWLEDGMENTS

I would like to thank Dr. Millicent Eidson for being the chair of my doctoral committee, for her guidance and wisdom during my entire doctoral program, and for the great support she provided during this important part of my academic life that made possible the completion of my degree.

I would also like to thank the members of my doctoral committee, Dr. Bryan Cherry, Dr. Glen Johnson and Dr. Martin Kulldorf. They worked as true scientific collaborators during these studies. I thank them for being part of the committee and providing insightful advice to improve the dissertation studies.

I also thank the NYSDOH Wadsworth Center's Rabies Laboratory for the data on rabid animals used in the dissertation studies; the staff of local health departments for rabies reporting; April Ellis from the New York State Department of Health (NYSDOH) Zoonoses Program and the University at Albany School of Public Health student interns for their geocoding work; Sarah Crowe for the LHD follow-up survey on incomplete and inaccurate addresses; Dr. Laura Bigler for providing information on ORV programs of Cornell University; Dr. Amy Willsey and Brian Laniewicz from the NYSDOH-Zoonoses program for providing information on ORV interventions used in NYS; and all the NYSDOH Zoonoses Program staff members for their support during my dissertation work and their friendship which I will never forget.

Finally, I would like to acknowledge the support of Dr. Mary-Jane Schneider and the professors of the School of Public Health in the University at Albany for their support during my six years as a public health student.

DEDICATION

I wish to dedicate this dissertation to my mother, Susana Cabrera, who inspired me to follow the public health path. She may be physically absent, but her memory and teachings are alive forever.

I also want to dedicate this dissertation to the health workers, nurses, and community volunteers that work in the most local level of my country, Peru. I always recall their dedication and effort to protect public health in the face of the most unthinkable difficulties.

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1.1. The problem of raccoon rabies

Rabies is a disease with worldwide distribution affecting mankind since antiquity. Rabies is produced by a Lyssavirus and is usually 100% fatal following serious neurological symptoms and great suffering.[1] The rabies virus has several variants named according to the reservoir species. The present dissertation addresses the raccoon rabies variant. Raccoon rabies was first identified in Florida in the 1940's and subsequently spread to the Mid-Atlantic States and the Northeast.[2,3] Raccoon rabies has impacted New York State (NYS) since 1990. A rabid raccoon can transmit the disease to other mammal species, including pets and other wildlife. Humans can be exposed to raccoon rabies through contact with saliva of an infected animal. The spread of raccoon rabies to NYS has resulted in high costs for human rabies prevention and control.[4,5]

There have been efforts to reduce raccoon rabies with oral rabies vaccine (ORV) programs targeting raccoons.[6] The expenses of ORV programs are high, making it difficult to usefor large regions. At present, there are many enzootic areas in the US without any ORV interventions, including most of NYS, Pennsylvania, and other eastern states.[7] Thus, there is a need for the development of innovative strategies to make ORV intervention more efficient and economically feasible.

Areas affected by raccoon rabies are not uniform in land use, environmental features (rivers, mountains, elevation), and human population density. Although the raccoon population distribution may be unknown in many areas, previous studies indicate it is not uniform, with a greater concentration of raccoons where there is more food availability, and in woodland forests.[8-11] Therefore, ORV baiting programs should consider these differences, and program different bait densities according to raccoon rabies risk and risk of transmission to people and other mammals. These factors have been informally utilized in planning ORV baiting, visually assessing maps, and deciding in the field to increase intensity of the baiting based on habitat conditions. With raccoons being very adaptable to different habitats and very mobile, and other factors interacting with the risk of rabies transmission,[9,12] simple assessments for raccoon potential habitats may be insufficient for identifying risk areas for raccoon rabies when planning ORV interventions. There is a need to understand raccoon rabies patterns in space and time under various scenarios to support decisions regarding the number and pattern of ORV baits per area, and optimize cost-efficiency of ORV interventions.

This dissertation presents the development of alternatives strategies for ORV interventions that could be executed at lower than the current economic cost using a rational approach based on raccoon rabies associated factors and rabies risk assessment for different locations. Raccoon rabies in the NYS enzootic region was studied with different statistical and spatial analysis methods. The research study presented here is important to provide knowledge for better planning and cost modeling for ORV interventions in the epidemiological scenarios in which ORV is currently used (point-source infection control strategies for control in an epizootic scenario, and establishment of immune barriers) and to improve ORV feasibility for large enzootic regions. Although the studies in this dissertation are presented in independent chapters, the data produced in each study were used to build upon the previous one. The studies are prepared in journal format to allow their submission for scientific publication.

1.2. Raccoons and rabies

Raccoons *(Procyon lotor)* are mammals widely distributed in the Northeastern U.S.[11] Typical raccoon habitat has been described as woodlands, agricultural fields, and wetlands.[10-11] Raccoons avoid open land and pastures, and travel along lake shores or streams.[13] Raccoons live in hollow trees, close to water sources, but adapt very well to any place that they can use as a den.[10,13] Raccoons change homes very often according to food source availability, and for this reason are common in suburban residential areas.[14] Raccoon home ranges (size of area used by a raccoon) have been described from <0.2 km^2 in urban areas of Ohio to 49 km^2 in rural areas of North Dakota, and population densities range from 0.5 raccoons per km^2 in rural areas of North Dakota to 100 raccoons per km^2 in urban areas of Ohio.[12] Distribution of food resources affects raccoon population densities and movements. A recent study in Illinois demonstrated that raccoons have smaller home ranges and live more closely together in urban areas with more food availability than in rural areas where they are more dispersed.[9] This study used radiotelemetry to trace raccoon mobility. It was found that a raccoon's mobility from the center of its current home area is smaller in urban areas (mean = 113 meters, range: 47-1543) than in suburban areas (mean = 129 meters, range: 67-365) and in rural areas (mean = 241 meters, range: 43-575); and that urban raccoon home ranges are more stable than rural home ranges. Raccoon mobility is believed to have a role in rabies transmission and the spatial pattern of raccoon rabies.[12]

The incubation period for rabies in raccoons inoculated under laboratory conditions was 50 days (range: 23-92 days).[2] The incubation period in the wild was estimated as 5-6 weeks.[15] Due to a combined effect of raccoon mobility and the incubation period, the location where a rabid raccoon is found dead or trapped may not be the place where the raccoon was infected with rabies, but it would be reasonable to assume that in urban areas the location of infection is closer to the site where the raccoon was found than in rural and suburban areas.

In the United States, 92.5% of the rabid animals in 2004 were wild animals, with raccoons the most frequently reported species, representing 37.5% of all reported rabid animals.[16] For NYS, the raccoon rabies variant is believed to account for 92% of the animal rabies cases from 1990 to 2004.[17] The remaining 7% are primarily bats infected with bat variants, with the exception of a few fox-variant cases in the early part of the 1990's. In addition, 99.9% of the rabid terrestrial animals in the State in recent years have been infected with raccoon-variant rabies, due to the predilection for the raccoon variant to spill over to other terrestrial species, as compared with bat variants.

Rabid raccoons interact with each other and with other animals, including other wildlife, livestock, and pets, leading to spillover of the raccoon variant to non-reservoir species.[2] A study in Canada found that a raccoon bites another raccoon once every 3 nights while feeding.[14] The species most frequently affected by spillover of raccoon rabies in NYS are skunks, foxes, cats, and cattle.[17] It is unclear whether skunks have less interaction with other species compared to raccoons. The current ORV baits have not been demonstrated as effective for skunks. The large number of raccoon-variant infected skunks in NYS and elsewhere has led to concerns about skunks acting as a reservoir of raccoon variant virus, even if ORV has successfully eliminated the variant in raccoons.[18] In the eleven eastern states from New York to North Carolina, 82% of the counties reported the presence of rabid raccoons during 1977-1997. [19] In those states the raccoon rabies epizootic also led to an epizootic of rabies in skunks (with evidence that it can be attributed to the raccoon rabies variant). Epizootics in both species have the same geographical direction from 1990 to 2000.[18]

Raccoon rabies spreads with a velocity of approximately 46 km per year.[20] Environmental barriers such as large rivers slow the transmission as much as seven-fold from township to township, acting as a semipermeable barrier.[20-21] Paved roads may also represent a barrier for mammal movement.[22] A study in raccoons found that in rural and suburban areas, raccoons crossed paved roads often, while raccoons living in urban areas crossed less often.[9] Regarding land use, a study during an epizootic of raccoon rabies in Maryland found single-unit residential areas were associated with raccoons trapped alive. For road-killed raccoons the distribution was more equitable in all land types. There were less than expected trapped and road-killed raccoons in multi-unit residential and commercial-industrial-institutional areas. Open land areas had significantly fewer raccoons trapped but road-killed raccoons were in expected numbers.[23] A recent study modeled raccoon rabies risk using land use and human demographics in an enzootic area.[24] This Maryland study found that a high percentage of agricultural land and high water coverage in combination with a low human population density were positively associated with large epizootics. Mixed forest was inversely associated with the risk that a county would experience a large epizootic.

1.3. Rabies significance for public health

Due to the ~100% case fatality rate for rabies, the disease and potential human exposures are of high concern to the public. The presence of raccoon rabies leads to high management expenses to prevent human cases.[5] Human postexposure prophylaxis (PEP) in the U.S., consists of a series of five doses of cell culture-derived rabies vaccine plus a single dose of rabies immune globulin.[25] PEP is expensive and may be overused in areas with raccoon rabies, due to fears about the disease.[4,26]

An average of $941 per PEP was calculated for the biologics costs in NYS in a recent study.[27] Rabies costs can include patient and non-patient costs. The number of incidents and treatments can be reduced lowering both types of costs if raccoon rabies is controlled. A study in five heavily populated counties in NYS documented an increasing trend of rabies expenses through time and identified rabies postexposure treatment as the highest documented rabies-associated expense.[27] However, that study also revealed differences in the number of human treatments and specimens tested for rabies by county, suggesting the need for further research of the geographic and environmental factors influencing raccoon rabies risks.

During 1993 to 1998 in NYS (excluding New York City), 18,238 people received PEP after a suspected or confirmed rabies exposure. In the same time period, documented rabies prevention costs were $13.9 million, for specific items such as PEP, specimen shipment, and vaccination clinics.[5] Although the costly PEPs have been effective in the U.S. at preventing human cases, 56 human cases were reported in untreated persons during 1980 to 2004.[16] In 2003, the first human case of raccoon-variant rabies was reported. The death occurred in Virginia and the exposure was not identified;

rabies was not suspected and postmortem tests confirmed infection with raccoon rabies variant.[28]

1.4. Raccoon rabies control: Oral rabies vaccine

U.S. raccoon ORV programs, currently use a vaccinia-rabies glycoprotein recombinant vaccine (V-RG). Vaccinia is a virus used as a vector (transporter) for the DNA code of the rabies virus antigenic glycoproteins. This recombinant produces an antigenic response resulting in immune protection without disease.[29] The use of ORV is recommended by the Centers for Disease Control and Prevention (CDC) in selected situations and is restricted to use in state and federal rabies control programs and specific studies.[30] The vaccine is administered as a fishmeal coated sachet or with the sachet inserted into a fishmeal polymer matrix. The fishmeal coating/matrix was chosen to provide smells and flavors differentially preferred by raccoons, in order to minimize uptake by non-target species. The ORV baits can be delivered from the air by plane or helicopter,[31-32] or from the ground by hand-baiting or distribution from a moving vehicle. The efficacy of ORV has been demonstrated for raccoons,[33,34] and its use for the reduction or elimination of the raccoon variant is intended to reduce rabies-associated prevention and control costs.

ORV initiatives have been developed to reduce or eliminate rabies in certain animal species as a mechanism to reduce rabies-associated costs and prevent further spread of raccoon rabies to previously unaffected areas.[35] In Ontario, Canada where the fox rabies variant and the raccoon rabies variant are present, the use of ORV between 1990 and 2000 reduced laboratory-confirmed animal rabies cases by 90%. This effect was simultaneous with a reduction of 50% in human PEP.[36] Although the efficacy of ORV has been demonstrated in Canada, the administration of ORV programs is very expensive.[37]

NYS began an ORV program for raccoon rabies control in 1994, which continues to this day in cooperation with the United States Department of Agriculture (USDA) Wildlife Services (WS) and Cornell University,[31,38] Areas involved in the NYSDOH ORV project are the sections of the Adirondack Mountains in Clinton County and northeastern Essex County.[39] In 1996 Cornell University, in collaboration with the NYSDOH, NYS Department of Environmental Conservation (NYSDEC), and the Ontario Ministry of Natural Resources, Canada, began an additional program to distribute ORV baits in Niagara, Erie and St. Lawrence counties.[40] Results to date have indicated good levels of seroconversion among raccoons trapped after ORV baits are distributed.[20] Efficacy of the NYSDOH ORV project was recently reported to be approximately 45-60%, based on seroconversion data.[33] A study on the use of ORV vaccine in Massachusetts found that for free-ranging raccoons, a vaccination rate of 63% (percentage of raccoons trapped with titers ≥ 1:5 to rabies virus) was sufficient to stop the spread of rabies for suburban areas.[34] However, recently the immune barrier in Massachusetts has been breached.[41] Fortunately for the NYSDOH ORV project, the serologic evidence of efficacy has been supported by the lack of raccoon rabies cases in the baited area, allowing NYSDOH to extend the barrier down into the enzootic area.

The factors to be considered in developing the cost components for ORV programs include: size of area baited, bait density per area, bait cost per unit (e.g., $1.30), aerial distribution cost per area, ground distribution cost per area, and program evaluation costs.[35] Thus in developing ORV cost models for immune barriers and point source infection interventions, ORV costs are dependent on the density of baits per area applied and the size of the baited area.[35,42,43] Because the area for intervention would be fixed, and the cost of the bait can be assumed stable, the number of baits is the component that can be modified to optimize efficiency of ORV interventions. One set of models for an ORV immune barrier considered uniform baiting for the intervention area (baits distributed at uniform intervals or flight lines in a grid type pattern), at a constant density.[35] However, as indicated above, raccoon density and rabies cases may vary according to land type, and transmission rates can be influenced by natural barriers such as large rivers and roads. Therefore, the most cost-effective ORV baiting pattern should not be assumed to be uniform. In Massachusetts, higher vaccination rates were obtained by habitat targeted bait distribution as compared to uniform bait distribution.[34] To optimize ORV use, it may be valuable to identify and measure the differences in raccoon rabies risk by land type and the other factors. Program optimization may be accomplished by adjusting the number of ORV baits per area and the type of bait distribution based on the epidemic scenarios, land type and proximity to large rivers and roads. An improved understanding about where and how to bait may help in the prevention of future immune barrier breaches. In addition, reducing the number of baits in immune barriers through optimization of their distribution may enable their availability for other areas requiring point source infection control emergency interventions.

A previous study identified a reduction of the observed number of raccoon rabies cases by 30% after ORV programs started in the State.[44] However, ORV baiting is an expensive intervention and the cost-benefits of ORV intervention are still under evaluation.[45-46] ORV baiting interventions can be administered to eliminate the variant in newly infected areas, to form an immune barrier at the edge of enzootic areas to prevent spread to new areas, or in a widespread baiting program in large areas to reduce rabies incidence.[34-35,42,47,48]

In this study, two epidemiological scenarios (epizootic and enzootic/post-epizootic) were examined in assessing costs associated with ORV baiting. For the introduction of raccoon rabies into a new area distant from the enzootic area (for example, due to raccoon translocation), a point-source infection control strategy has been previously proposed involving high bait density (144 baits/km^2) to be administered in a 3.25 miles radius from the epidemic edge.[42] In a recent control program for a raccoon rabies outbreak in Long Island, New York, 118 baits/km^2 were used. The efficacy of these baits densities are yet to be evaluated. For ORV baiting in an immune barrier along an enzootic front, the number of baits frequently considered is 75/km^2, about half of the number for emergency point source control programs. Barriers usually are in uninfected areas abutting infected areas,[35] although they may be widened to include some infected areas as well. Ohio used 77 baits/km^2 for its immune barrier in 2003, and New York State 75 baits/km^2.[31,47] The optimal number of ORV baits for raccoon rabies control is derived from research assessing control program efficacy.[31,47-48] Immune barriers in Ohio and Massachusetts have been breached, requiring emergency response and additional baiting.[41,47] New York studies on ORV baiting efficacy for an enzootic area suggest that 50 baits/km^2 may be the minimum bait density to control rabies in raccoon rabies enzootic areas.[31,39]

Initial cost estimates for a NYS wildlife rabies control campaign that would include ORV were $10.7 million per year, and $73 million for a 10-year campaign.[38] Identification of the areas of risk and understanding the reasons for differences in risk by place and time can provide clues to maximize the benefits and reduce the costs of preventive interventions such as ORV. Specifically, in decision making and planning of ORV baiting interventions, baits can be targeted to areas of greater likelihood for raccoon rabies transmission (where there is a susceptible population of raccoons and other mammals that interact with each other, in addition to other favorable conditions for transmission).

1.5. The use of GIS in rabies and public health

The distribution of any infectious disease varies by place and time. Geographical information systems (GIS) and spatial epidemiology methods can describe and identify patterns of health events by place and thus may help to elucidate rabies epizootic patterns.[18] Recent technologic advancements in computer hardware and software allow sophisticated analyses of disease data to uncover spatial and temporal patterns. Statistical tests have been developed for geographical analysis of various types of heath events.

A GIS allows the combination of different types of data in space and creation of enriched data for spatial analysis. In spatial analysis, health events can be studied at the individual level (point analysis) or area-level (aggregated data). The levels of resolution for area-level analyses may be country, state, county, town, zip code, or census tracts. Data can also be aggregated in time by year, month, week or days.[49-50] However, boundaries are artificial and using a large resolution for spatial analysis may dilute or hide the spatial patterns. Because the raccoon rabies cases are reported by address it is possible to geocode the addresses to geographical coordinates and place the geocoded addresses into a GIS to combine rabies case information with place information. Commercial software can be used to geocode large number of addresses automatically assigning a certain level of precision (if the software does not find the address, it assigns a "close" match) or manually.[51] Automatic geocoding can introduce error if the level of precision is relaxed.[51,52] Comparisons of coordinates of geocoded addresses in Western NYS processed by commercial software were compared to coordinates determined by a GPS (Global Positioning Systems) satellite receiver, considered the true coordinates. The median distance from the geocoded point to the true location was 28 meters (90% CI: 34m-46m), and this error was larger for non-urban areas (mean: 52 meters; 90% CI: 44m-61m) than for urban areas(mean: 32 meters, 90% CI: 28m-37m), and errors as big as 800 meters were found.[53] Another study used digitally enhanced aerial orthoimagery for the same comparison of addresses in the Albany, Schenectady, Saratoga and Rensselaer Counties in NYS. [52] The positional error increased as population decreased--the positional error was less than or equal to 21 meters for 95% of the addresses in urban areas, ≤ 39 meters for suburban areas, and ≤ 195 meters for rural areas. Geocoding precision can be improved using the additional support of internet engines for telephone numbers and names, when this information is available.[54]

Spatial analysis can be conducted for raccoon rabies using point coordinates--having the coordinates for each case allows the analysis of the point patterns and the use of small areas in the analysis, such as census tract or ZIP code. Frequently, raccoon rabies cases are digitized at the town level, and published studies of raccoon rabies spatial patterns in NYS used county or town level for spatial resolution.[17-18,44] Spatial analyses can also help to identify the optimal pattern for bait dispersal (e.g., targeted to habitat vs. uniformly distributed). Factors that may reduce the risk, and thus the need for costly ORV baiting, are those that may potentially slow transmission, including natural or manmade barriers.

An infectious agent can produce cases of a disease that group in space, in time, or in both. The pattern of this grouping is a process called clustering. A disease is clustered when there is a residual spatial variation in risk, variation due to known or unknown factors in the clustering area. Clusters are areas with an excess of cases (high residual risk).[55,56] Modern methods for cluster analysis can identify clusters in space and time, and provide information about where and when the cluster occurs. Statistical tests can also be applied to assess the probability of the cluster to be a random event.[57] The spatial scan statistic is a method currently available and used in previous studies.[58,59] The process involves drawing circular windows (purely spatial analysis) or cylinders (space-time analysis) around a point and increasing window size to include a certain proportion of cases in a given period and area. The scan statistic identifies the areas and time where the points cluster; calculates likelihood ratios through comparison with a population (Poisson model) or a control group (Bernoulli model); and calculates *p-values* for the cluster areas using a Monte Carlo simulation.[57,60] The spatial scan statistic allows adjustment for multiple covariates, and recent improvements included the use of a space-time permutation model, which requires case data only (no comparison group is used in this model).[57] The Poisson model is beneficial when population data is available for the spatial resolution required in the study (e.g., state, county, town, etc). The Bernoulli model has the advantage that a control group can be selected to comply with the characteristics under study, which is important for many epidemiological exposure studies. The space-time permutation model allows for cluster analysis when population data is not available, and control groups can not be selected.[57] To study raccoon rabies, an important consideration is that raccoon and other mammal population data is not available, comparing with human population data can be problematic, and control groups are difficult to select.

The software that performs cluster analysis is SaTScan, free licensed software developed by the National Cancer Institute that is available online. [56] SaTScan provides likelihood ratios, relative risks, coordinates of the cluster center, radius of the cluster, and it identifies clusters by both time and place. The spatial scan statistic has been used to study events in the fields of medicine, veterinary medicine, forestry, neuroscience, and criminology.[57] The scan statistic has been used to study several infectious diseases and wildlife diseases. [58-59,61,-71] Rabies has not been studied yet with this method. This study intends to identify raccoon rabies clusters in NYS using a spatial scan statistic. Identification of case clusters can help locate areas of excess of risk and factors associated with that risk including land use, human population density, and natural barriers. Landscape features can influence the velocity of rabies spread. A study of raccoon rabies in Connecticut found that large rivers act as a barrier with a 7-fold reduction of the rabies propagation rate from township to township.[21] Several studies modeled raccoon rabies in the Northeast of the U.S. and in NYS, using information on rabid raccoons by town and time of first appearance. Those studies demonstrated the possibility of modeling raccoon rabies in time and space, and suggested the influence of environmental features and the need for further research.[20-21,44,72-73]

Using GIS and spatial analysis, for example, a study compared eleven eastern states from New York to North Carolina, with 82% of the counties reporting the presence of rabid raccoons during 1977-1997.[72] Another study using GIS and other types of spatial statistics with county-aggregated data found that the raccoon rabies variant circulating in skunks was not independent from the raccoon rabies variant circulating in raccoons.

Previous studies aggregated the number of raccoon rabies cases by county. In the research studies presented in this dissertation, the pattern of raccoon rabies cases is examined using the geographical coordinates of the case location and aggregating the cases at census tract level, to provide better precision in the results.

1.6. Research question and objectives

The overall research question for the presented studies is: Can the temporal and spatial patterns of the raccoon rabies epizootic in NYS be used to estimate costs and optimize the benefits of ORV in enzootic areas and in newly epizootic areas?

In the first study the specific research question is: What are the factors associated with raccoon rabies in an enzootic region? The specific research question for the second study is: How are the raccoon rabies variant cases distributed in space and time for an enzootic region? For the third study the research question is: How can data produced by statistical, spatial and temporal analyses of raccoon rabies be used to produce lower cost models compared to uniform bait distribution? NYS is used in this dissertation as a model for a raccoon rabies enzootic area.

The objective of this dissertation is to describe the spatial-temporal characteristics of the raccoon rabies epizootic in NYS and analyze factors associated with raccoon rabies patterns, distribution, exposures, and costs of ORV intervention.

To achieve this objective, this dissertation presents three sequential studies. In the first study, the factors associated with raccoon rabies distribution in NYS are investigated through the use of a Poisson regression model. In the second study, the spatial and temporal patterns of raccoon rabies in NYS are explored with a spatial scan statistic. In the third study, the cost of ORV for intervention of an enzootic area and epizootic area in NYS is modeled.

The specific objectives for the studies contained in this dissertation are:

1. Identify environmental conditions and other factors that may influence the epidemiology of raccoon rabies.
2. Develop a Poisson regression model for raccoon rabies to determine which risk factors are most significant to the epidemiology of raccoon rabies.
3. Analyze rabies data using a spatial scan statistic technique, incorporating both observed cases and the predicted distribution of cases based on the Poisson regression model.
4. Identify the high risk clustering areas in the NYS enzootic region.
5. Model ORV bait numbers and cost at different levels of raccoon rabies risk for an enzootic region.
6. Explore the use of an ORV cost model for areas susceptible to the introduction of raccoon rabies.

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Chapter 2:

Factors associated with enzootic raccoon rabies, New York State

2.1. Abstract

New York State (NYS) has been a large raccoon rabies-enzootic area for 15 years. Using a Poisson regression model, a higher number of raccoon-variant rabies cases in a census tract during 1997-2003 was associated with a higher proportion of low intensity residential areas (those with a lower concentration of housing units), lower land elevation, a lower proportion of wetlands, and a lack of rivers/lakes and major roads. The model was adjusted for county, ecoregion, and latitude to help control for unknown spatially dependent covariates. The model may be used in prioritizing areas for rabies control based on differential risk, including use of costly intervention methods such as oral rabies vaccine.

Keywords: raccoon rabies; rabies vaccine; rabies epidemiology; landscape epidemiology

2.2. Introduction

Raccoon rabies has seriously impacted the East Coast of the United States, reaching New York State (NYS) in 1990. Rabies was laboratory-confirmed in 14,892 terrestrial animals in NYS from 1990 to 2004; 10,980 (74%) of these cases were raccoons.[1] The New York State Department of Health (NYSDOH) received reports of 20,031 people receiving rabies treatment due to attacks and bites by suspected rabid terrestrial animals or by wildlife that could not be tested for rabies, from 1993 to 2004.[2]

Studies have documented high and increasing economic costs for the health care system to respond to rabies exposures.[3,4]

The use of oral rabies vaccines (ORV) is one strategy recommended by the Centers for Disease Control and Prevention to reduce raccoon variant rabies, exposures to humans, and spread to new areas. Although costly, ORV has been utilized with some success in the last decade.[5,6,7] The vaccine is contained in baits that can be dropped by air or distributed by hand.[8] ORV containment barriers at the epizootic ‘wavefront’ are in place in many states in the U.S.[8-11] Because of the high bait purchase and distribution costs, factors influencing costs and benefits have been under study.[10-13] Persistence of the raccoon rabies epizootic in NYS for more than 15 years indicates that there are probably many factors associated with maintaining the disease even with natural depopulation of the reservoir species due to the disease. Evidence of the association of land use and human demographics in rabies epizootics has been previously reported.[14,15] Identification of these factors and others that may influence rabies spread in an enzootic area can help to assess risk for rabies and provide the opportunity for improved planning and efficient application of ORV or any other raccoon rabies control programs.

NYS is a large enzootic area for raccoon rabies that includes diverse land use types, elevation, and human population distribution that can be used to study the association of raccoon rabies and these types of factors. Previous studies have identified factors of interest at the regional, state, and county levels.[3,4,16-20] In the present study raccoon rabies is modeled at the census tract level to provide more local estimates of risk.

2.3. Materials and methods

Study area

The study included upstate New York counties (excluding NYC and Long Island) that had not been exposed to ORV during the study period. Counties exposed to ORV programs during the study period were excluded, including portions of some counties that were exposed during the study period and adjacent to large ORV exposed areas in neighboring counties (see Figure 2.1). Although a few census tracts of Albany and Rensselaer counties in eastern New York were exposed to ORV in 1997, those two counties were not excluded due to the small area of the exposure and the absence of exposure during the following years included in the study. Census tracts of 47 counties were included in the study, totaling 1,639 census tracts and 90,846.4 km^2 of land.

Data collection

The *rabies specimen history forms* (form DOH-487z) for terrestrial animal specimens that tested positive for rabies and were submitted from upstate New York during the years 1997 to 2003 were selected. The cases selected for the study were assumed to be infected with raccoon rabies variant because there are no other terrestrial rabies variants in New York State during the study period, and spillover of bat variants to terrestrial mammals is very rare (14 cases in 20 years).[1] The *rabies specimen history forms* are documents attached to the specimens submitted for rabies testing to the Rabies Laboratory at the NYSDOH Wadsworth Center, and contain information about the rabies suspect animal and the incident that prompted specimen submission. Animal location, species, and date of submission of 5,305 forms that met the study criteria were computerized.

A total of 4,932 addresses were processed with commercial software (MapMarker Plus 10.2™ from MapInfo Corporation) to obtain geographical coordinates. To improve the quality of address information, the local health departments (LHDs) were provided a list of the addresses that required more complete information or correction. Through this process an additional 114 addresses could be geocoded. Once geocoded, each rabies case was assigned to the corresponding census tract and the number of cases by census tract was calculated. The 373 addresses that could not be geocoded to provide street level coordinates were excluded. This exclusion was done to reduce the possibility of misclassification when cases were assigned to the census tract. An additional 484 cases were excluded because the geographical coordinates were located outside the study area. A final total of 4,448 animal rabies cases were included in the study.

Land Use

To study the association of different land use types, the proportion of each land use type was obtained for each census tract. The *NYS Land Cover Data 2000-U.S. Geological Survey (USGS)* from the National Land Cover Data (NLCD) was used to extract land use data for the study area. The USGS-NLCD is based on 30 meter pixel resolution LANDSAT satellite imagery and provides 21 land use types for NYS.[21] For this study the land use types were reduced to eight based on grouping of similar types. The eight land use categories for this study are: agricultural, barren, commercial/industrial/ transportation, forest, high intensity residential (i.e, areas with a high concentration of housing units), low intensity residential, water, and wetlands.

Polygonal maps representing the shapes of land use types were created from the NLCD raster image covering the study area by merging adjacent pixels of the same type. Using ArcView™ 8.3 geographical Information System (GIS) software, the area of each land use type was obtained for each census tract. The percentage of each land use type within each census tract was then obtained in SAS® 9.1. software (SAS Institute, Inc., Cary, North Carolina).

Statistical analysis

A Poisson regression model was used to examine the spatial and temporal patterns of raccoon-variant rabies with respect to explanatory variables.[22] A database was built where each record represented a unique census tract-year. Variables included area in square kilometers, year, count of cases, both county and ecoregion that contained the tract, latitude of the tract centroid, proportion of the tract covered by each land use type, elevation, presence of major roads, presence of lakes and/or rivers, protection from rabies by an adjacent ORV exposed area, and human population density (number of people per area). Modeling was performed with SAS© 9.1 using PROC GENMOD.[23]

The observed number of rabid terrestrial animals in the census tract for a given year was modeled as a Poisson distribution. With area of the census tract in square kilometers as an offset, the independent variables discussed above were evaluated for their linear relationship with the log of the Poisson rate. Adjustments for overdispersion were performed by multiplying the covariance matrix by the Pearson's chi-square statistic, with the option SCALE=PEARSON in SAS© 9.1.[23-24] A quadratic term was explored for population density, and dropped when no significance was obtained.

Because rabies cases are the result of direct transmission from animal to animal, it is characteristic for rabies cases to have positive spatial dependence. To help adjust for unknown spatially dependent variables that may co-vary with rabies, a model adjusted for large scale geographical variation (LSGV) was developed to introduce three "latent" variables in the model--latitude, county, and ecoregion. Latitude of the census tract centroid point also served to control for the temporal spread of the disease from the south to the north observed during the study period.[1] County was included to adjust for spatial variation among counties, utilizing the variability among census tracts within the same county for the regression parameter estimations. Ecoregion or ecozones are areas similar in soil, climate and vegetation, representing natural delimited spaces inside the study area. The United States Environmental Protection Agency (US-EPA) developed a national map for EPA Ecoregions Level IV.[25] The ecoregion data for NYS was extracted from that map and processed for use in the study. Results for a Poisson regression model adjusted for overdispersion with and without adjustment for LSGV are presented. The fit of the models was evaluated with the deviance and Pearson Chi-Square of each model.[24]

Independent variables

Because land use values were proportions that summed to one within each census tract, one of the land use types had to be removed from the model in order to maintain a design matrix that is of full rank. "Forest" was removed because it is the generally expected natural vegetation throughout New York and is associated with raccoon habitat,[26] therefore leaving the other categories to represent different types of deviations from background forested conditions.

Data on land elevation above sea level was obtained from the National Elevation Dataset (NED) produced by the United States Geological Service.[27] Raster grids for the study area were used to extract the values of land elevation in meters for the centroid of the census tract.

The presence of major roads in a census tract was included to model their potential barrier effect on wildlife mobility and rabies transmission. Vehicle traffic has been reported to limit mobility of raccoons more on urban roads than on rural roads.[28] Major roads in this study included limited access highways (freeways) and US highways and State highways, coded in the series A1* and A2* in the Highway Framework Classification Code (FCC). Road data was extracted from the U.S. Major Roads data provided by ESRI®.[29] The factor 'major roads' in this study is dichotomous, and it was considered present (coded as "yes") when at least one major road segment was within or along the boundaries of the census tract.

The presence of rivers and lakes in the census tract was included in the study because they are major features in the landscape that may act as a barriers for spread of a rabies epizootic, although they may also provide raccoon habitat along their boundaries.[30-31] Presence of rivers/lakes is a dichotomous variable, and it was considered present (coded as "yes") when at least one segment of the water body was within or along the boundaries of the census tract. An exception was made for Lake Ontario, one of the Great North American lakes located in the northwestern edge of the study area, and the Atlantic Ocean in the southern part of the study area, that were excluded in coding this variable because they are water bodies located outside of the study, and their large size prevents natural spread of raccoon rabies. Linear and polygonal data of rivers and lakes were extracted from commercial databases provided by ESRI® based on the U.S. National Atlas.[29]

Although the areas exposed to ORV had been excluded in order to examine factors associated with risk in areas without control programs, some areas in the cluster study are adjacent to the ORV exposed areas. Some degree of protective influence for raccoon rabies may be possible because immunized raccoons can move freely through census tract boundaries. The dichotomous variable “protected census tract neighboring an ORV area” was created to represent the influence described above. A census tract was considered “protected” if located adjacent to an ORV exposed area, or it was within a 12.5 km buffer from an ORV exposed area with at least 20% of its area included in this buffer. This buffer area was defined based on 12.5 km being the average distance that a raccoon was found from its home range center, as reported in a Canadian study.[32]

Information about ORV exposure in NYS was gathered from published reports and scientific communications,[6,33] and information provided by the NYSDOH Zoonoses Program and Cornell University’s ORV Project. To adjust for changes in the ORV exposure areas during the study period, values of the variable “protected” were assigned according to ORV exposure each year.

Human population density was included to model the association of raccoon rabies with human population, and also to control for observation bias when assessing the significance of the environmental variables. Values of the census tract population provided by the Census 2000 were utilized to calculate the population density in thousands of people per km^2.

2.4. Results

In the study area, 59% of the 1,639 census tracts reported at least one of the 4,448 terrestrial mammal rabies cases during the 7-year study period. The average number of cases was 2.71/census tract. The maximum number of cases in a census tract was 72 for the 7-year period. Almost two-thirds (63.67%) of the cases were raccoons, 22.76% were skunks, 5.97% were domestic animals, and 7.6% were other wild animals.

Figure 2.1 maps the EPA ecoregions and the density of terrestrial rabies cases by census tract. The regions with the highest rabies densities are the Hudson Valley counties along the eastern region of the study area, the central NYS region including the Finger Lakes and the northwest corner of the Western region. Although clear-cut associations between ecoregion and density or rabies cases are not apparent from the map, it does appear that many census tracts in the Northeastern Highlands and North Central Appalachians ecoregions had a lower density of rabies cases than other ecoregions with higher rabies case density occurring in only a few census tracts along their borders with adjacent ecoregions.

The average census tract size was 55.43 km^2 (95% CI: 49.88, 60.77). The largest census tract in the study was 2,205.63 km^2, located in Herkimer County, centrally located in the Adirondack Mountains (Northeastern Highlands ecoregion). In the study area, 99% of the census tracts were smaller than 446.64 km^2.

Forest land type represented 63.8% of the study area, agricultural land represented 26.72% of the study area, and all other land types individually represented less than 3% of the study area (Table 2.1). Although most of these land types represented only a small proportion of the total study area, most were represented in at least part of the majority of the census tracts. Agricultural, commercial/industrial/transportation, forest, high intensity residential, and low intensity residential land types were present in more than 97% of the census tracts. Water areas were present in 77% of the census tracts, wetlands in 58%, and barren areas in 31%.

The proportion of these land use types within each census tract, in terms of the mean, median, and quartile proportions, are provided in Figure 2.2. Census tracts varied the most in the proportion forested (range 0% to 100%). Census tracts varied the least in their proportion of barren, water, and wetlands land types. All land use type proportion distributions were skewed to the right.

Land elevation in the study area varied from sea level to 841.8 meters above sea level. The average land elevation was 194.23 meters above sea level (95% CI: 187.02, 201.44). About 94.2% (1,544) of the census tracts were located below 500 meters above sea level, and these census tracts included 92.3% (4,106) of the terrestrial rabies cases included in the study.

An average of 39 (2.4%) census tracts per year were considered "protected" for being adjacent to an ORV exposed area (although the number varied from 17 in 1998 to 122 in 1997). In the study area, 1,128 (69 %) of the census tracts had at least a major road within or along the boundaries. Water bodies (rivers or lakes) were present or along the boundaries in 986 (60%) of the census tracts.

Results of the Poisson regression modeling, adjusted for overdispersion but unadjusted for LSGV are presented in Table 2.2. This model fit the data reasonably (Deviance/DF= 1.0038). Without adjustment for LSGV, rabies cases were significantly ($p \leq 0.05$) negatively associated with the proportion of water or wetlands, and less likely to occur in areas that were not protected by an adjacent ORV exposed areas, and in census tracts at higher elevation or with higher human population densities (Table 2.2). Rabies cases were significantly positively associated with land types classified as low or high intensity residential, commercial/industrial/transportation or agriculture, and were more likely to occur in areas without major roads or rivers/lakes. After adjusting for LSGV, the significance of many covariates was reduced or nullified; however, rabies cases were still significantly negatively associated with a high proportion of wetlands and higher elevation, while also still significantly positively associated with a high proportion of land classified as low intensity residential, or those without major roads or rivers/lakes (Table 2.3). This model also fit the data reasonably (Deviance/DF= 0.7850).

In the model without adjustment for LSGV (Table 2.2), wetlands in particular had a strong negative association with raccoon rabies (RR: $1.13x^{10-5}$). The factor "protected from being located adjacent to an ORV exposed area" was positively associated with rabies. Census tracts neighboring an ORV exposed area were found to be 33% (RR: 1.33; 95% CI: 1.11, 1.59) more associated with raccoon variant rabies than census tracts not neighboring ORV exposed areas. Having a higher human population density was negatively associated with rabies risk. Population increases of 1,000 people per km^2 in a census tract were found to be associated with a decrease by 16% of the number of raccoon rabies cases (RR: 0.84; 95% CI: 0.75, 0.95). Although the increase of land elevation of the census tract was negatively associated with rabies, the magnitude of this significant association was small (RR: 0.997; 95% CI: 0.996, 0.997).

In the same model (Table 2.2), a higher proportion of low intensity residential land use type had the strongest positive association (RR: 8.01; 95% CI: 5.28, 12.15) with the number of rabies cases. Also, a higher proportion of the high intensity residential land use type in a census tract had a similar positive association (RR: 7.84; 95% CI: 3.62, 17.00).

Not having major roads within or along the census tract boundaries was positively associated with a slight increase in the number of rabies cases (RR: 1.31; 95% CI: 1.20, 1.44). Not having rivers or lakes within or along the boundaries of the census tract also had similar positive association with a slight increase in rabies risk (RR: 1.2; 95%CI: 1.05, 1.37).

2.5. Discussion

This study found that raccoon variant rabies risk in an enzootic area could be defined at a geographical level as small as a census tract. Census tracts with a greater proportion of their area classified as ‘low intensity residential’ (i.e., lower concentration of housing units) and a smaller proportion of their area classified as wetlands were at increased rabies risk. Similarly, census tracts without a river or lake were at increased risk, as were census tracts at lower elevation, and without any major roads to serve as barriers to spread. This is the first study to examine the association of these factors using the geographical coordinates of rabid animals in NYS, and the first to develop risk estimates at the census tract level in NYS.

There were some changes in the association of factors with rabies when the model was adjusted for LSGV. These changes indicate that some other explanatory variables are missing, which are associated with place, and supported the appropriateness of controlling for latent spatial variables. Raccoon rabies cases occur by direct transmission;

therefore the numbers of cases in a census tract is influenced by the number of cases in neighboring census tracts, and confound the associations of rabies with the factors in the study. Another spatial effect that required control was the temporal advance of raccoon rabies in NYS from South to North during the study period. Latitude of the census tract centroid was the factor used to control this effect. Adjusting for LSGV allowed for removal of the associations that were modified by location, and permitted us to identify the associations that influence raccoon rabies independent of space. A model adjusted for LSGV is appropriate for modeling raccoon rabies risk in other regions. A comparison of both models helps to identify the factors that are influenced by geographical variation.

Previous reports on raccoon rabies and land use associations also identified the influence of some land use types, water, and roads on raccoon rabies dynamics, and the need for additional research.[14,15] However, the effect of ORV in the area was not assessed in those studies, and the simultaneous effect of those factors with land elevation and human population was not reported. In this study, the influence of ORV was specifically addressed by excluding the ORV treated areas in order to examine the associations with factors in an enzootic area without the influence of a large vaccination program, and by adjusting for any potential remaining influence for areas close to any of those ORV exposed areas. Also, additional environmental features were included in the current study. In our results, the land use types most associated with raccoon rabies were low intensity residential, and a lack of wetlands.

One of the previous studies reported that at the county level, larger initial raccoon rabies *epizootics* were associated with a high percentage of agricultural land, a high proportion of water combined with low population density, and a low proportion of water combined with high population density. Those results were not adjusted for LSGV.[15] Our study of rabies at the census tract level during the *enzootic* period identifies somewhat different factors associated with increased risk. In the Poisson regression model unadjusted for LSGV, the agricultural land type was significantly associated with higher rabies risk, a higher proportion of the census tract being water had a protective effect, and a higher human population density also had a protective effect, but those associations were not significant when adjustments for LSGV were applied. Possible explanations for the differences in study results include: inclusion of more factors in the current study, a more focal level of analysis (census tract), and the different phase of the rabies outbreak being assessed (factors associated with epizootic spread may be different than those associated with maintaining enzootic rabies).

Increased human population density was significantly associated with a lower number of terrestrial rabies cases before the adjustment for LSGV, but not after the adjustment. This change may reflect the presence of differential surveillance and reporting among local health departments. Reporting bias is a potential problem in spatial analysis of surveillance data.[34] Reducing the reporting effects is another benefit of adjusting the model for LSGV.

The finding that one of the strongest associations of enzootic raccoon rabies was with low intensity residential land use type was not surprising because this land use type of a low concentration of housing units combines food availability for raccoons due to human presence with natural areas that provide habitat for raccoons.[28] This combination ensures that the raccoon vector is close to humans, their pets and other wildlife, and makes it easier for rabies cases to be seen and reported. This finding also agrees with a study documenting reduced raccoon home ranges in low intensity residential areas by the provision of artificial food resources in those areas.[28]

The study also found that census tracts with higher levels of the wetlands land type, and the presence of rivers/lakes, were relatively protected against raccoon rabies. This association may be due to census tracts with large amounts of water and wetlands having less available raccoon habitat (if the land is underwater), and these bodies of water providing barriers to raccoon movement and transmission of rabies. Our study did not identify statistically significant associations for any of the other land use types in the model, when adjusting for LSGV. The "barren" land use type (land that cannot sustain vegetation) was poorly represented in the model. Barren covered only 0.1% of the study area and this small sample size may have influenced the results. Agricultural land, high intensity residential, commercial/industrial/transportation, and water were better represented than barren. Although the stability (confidence intervals) of the parameters for these land use types change minimally (water and agricultural land use types) or greatly improved (high intensity residential and commercial/industrial/ transportation land use types) after adjusting for LSGV, those factors were no longer significantly associated with rabies risk. Therefore, independent of other factors, those land types were not associated with raccoon rabies at the census tract level.

Higher land elevation was confirmed as a protective factor for raccoon rabies. Because raccoons are the primary animal reservoir for the raccoon rabies variant, a reduced raccoon presence due to altitude may minimize or interrupt rabies transmission. Although the relative risk is very close to one, the association is statistically significant, very stable, and is not modified by model adjustments LSGV. Some misclassification of rabies cases in regards to elevation is inevitable by using the elevations of the census tract centroids.

The increased risk in areas protected by being adjacent to ORV exposed areas (variable “protected”) was not sustained when adjusting for LSGV —the risk effect remained positive but became barely significant (p=0.0517). The sample size for this factor was very small. The finding of an increased risk effect associated with being adjacent to an ORV area was surprising. Because ORV is a control intervention, we might expect that being adjacent to ORV exposed areas would reduce the number of rabies cases. However, ORV is specifically used in epizootic rather than enzootic areas, to contain the spread of rabies. Thus, one possible explanation may be that the wave front of the areas bordering ORV exposed areas are more active for rabies than those areas further from the wave front that are truly enzootic. Additional studies of the influence of ORV specifically focused on these areas close to the epizootic front may help to clarify these findings.

The absence of major roads in the census tract was confirmed to be positively associated with raccoon rabies. Our results agree with the suggestion that major roads may act as barriers for raccoon rabies spread.[28] Our results also confirm that the absence of rivers and lakes in the census tract is positively associated with raccoon rabies. Previous studies reported that rivers act as barriers slowing transmission of raccoon rabies and limiting the area of rabies spread.[30-31] These associations remain after adjusting for LSGV of the raccoon rabies cases.

Some limitations of this study must be considered. First, 373 (8.4%) of the raccoon rabies cases were excluded due to incomplete or inaccurate address information that did not allow location geocoding. This reduction in cases may have resulted in a reduction of statistical power, and could have resulted in a differential impact if there were differential problems in address accuracy. A specific pattern for the excluded cases could not be determined. Although these excluded cases were widely distributed throughout the study area, it is possible that an important proportion of them were located in rural areas, because during the geocoding process rural addresses are less likely to obtain a match or a good level of precision in their geographical coordinates.[35] This situation may lower representation of rural environments in the model.

Due to differences in the population distribution across the study area, reporting bias may have affected the results in the study. Rabid raccoons are more likely to be found or expose people or pets when they live close to human populated areas, compared to areas not populated by humans. Reporting bias in this study may overestimate the risk for areas with high population density, and underestimate the risk for unpopulated areas. In this study including population density in the model helped to reduce the effect of this type of bias.

Also, the land use types and environmental features in NYS may not be applicable in all other areas with raccoon variant rabies; thus the factors identified in this model may not be the best ones to use in an area geographically diverse from NYS. However, this general approach of identifying risk factors at the census tract level may be of benefit for another area in its development of a model for prioritization of resources. Finally, ORV interventions were considered to be similar in intensity and characteristics in the areas excluded for this study. These interventions were conducted by different groups using different types of bait, bait densities, and application methods. These variations could not be factored into this study.

A generalized linear mixed model may be more appropriate, whereby the latent spatial variables would be treated as random effects. However, we wanted to develop a model that is simpler to understand and be less technically demanding so it can be used at the local and regional level as well by disease control agencies in their future rabies control decision-making.

This study has identified factors associated at the census tract level with increased and decreased risk of raccoon variant rabies cases in a large area of enzootic rabies. The primary purpose of this study was to identify factors that would allow a cost savings in the application of control programs such as ORV, by allowing agencies to prioritize areas for control and save control costs by reducing control activities in areas with less rabies risk.

These results have already been used to project the ORV costs in Long Island, New York, an area with a recent (late 2004) introduction of the raccoon variant. At a uniform bait density of 300 baits/km^2, 991,747 baits at a projected bait purchase cost of $1,289,271 would be required for a single ORV baiting of Long Island to control further raccoon rabies spread. On the other hand, if baiting by applying the factors identified in this study, and dividing Long Island census tracts into quartiles of risk, the number of baits could be reduced to 605,702 at a cost savings of $501,858 if distributed at 100 baits/km^2 for the lowest risk census tracts, 200 baits/km^2 for the middle two quartiles of risk, and 300 baits/km^2 in the highest risk census tracts.

The factors associated with raccoon rabies can be utilized to prioritize areas for rabies control. ORV baits can be applied with more intensity to areas of higher proportion of low intensity residential land type, less proportion of wetlands, absence of major roads and/or no presence of lakes or rivers. Because those high risk areas may also have larger raccoon populations, the same characteristics can be used as criteria to place raccoon traps for evaluation activities after an ORV application, and maximize the number of raccoon captures. Census tracts at greater risk due to the characteristics described above can be identified, and targeted for education on raccoon rabies prevention and handling of rabies exposures, and for pet vaccination programs to prevent raccoon rabies spillover to pets.

Additional studies applying this model to real-world ORV or other control decision-making are required, along with evaluation of its success in reducing costs while still reducing rabies risk. In addition, GIS statistical cluster analysis approaches may also improve identification of high and lower risk areas, and will be summarized in an additional study.

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Table 2.1. Land use type and area in 1,639 census tracts, New York, 1997-2003.

Land Use Type	Number and proportion of census tracts with each land use type		Proportion of state study area*	
	Number of census tracts	%	Area in km^2	%
Agricultural	1306	97.99	24271.40	26.72
Barren	508	30.99	89.60	0.10
Com./Ind./Transp.	1596	97.38	748.90	0.82
Forest	1636	99.82	57959.23	63.80
High intensity residential	1601	97.78	582.73	0.64
Low intensity residential	1626	99.21	2319.54	2.55
Water	1269	77.43	2712.60	2.99
Wetland	948	57.84	2162.10	2.38

**Excluding areas of state that were not part of the study: NYC, Long Island, and ORV exposed areas.*

Table 2.2. Factors associated with raccoon rabies, relative risks and 95% confidence intervals estimated with a Poisson regression model adjusted for overdispersion and unadjusted for large scale geographical variation, New York, 1997-2003.

Factor	RR	95% Confidence Interval	*p-value*
Higher proportion of land use type within census tract*			
Water	0.46	0.22, 0.95	0.0357
Low intensity residential	8.01	5.28, 12.15	<0.0001
High intensity residential	7.84	3.62, 17.00	<0.0001
Commercial/Industrial/Transportation	3.70	1.34, 10.22	0.0118
Barren	28.10	0.36, 2164.84	0.1323
Agricultural	1.28	1.02, 1.61	0.0370
Wetland	1.13×10^{-5}	0.13×10^{-5}, 10.10×10^{-5}	<0.0001
Land elevation (meters above sea level)	0.997	0.996, 0.997	<0.0001
Protection from adjacent ORV area			
Yes	1.33	1.11, 1.59	0.0023
No	*Reference*		
Presence of major roads within census tract			
No	1.31	1.20, 1.44	<0.0001
Yes	*reference*		
Presence of rivers/lakes within census tract			
No	1.32	1.15, 1.53	0.0001
Yes	*reference*		
Higher population density (thousands of people/km^2)	0.84	0.75, 0.95	0.0054

With forest land use type as background.

Table 2.3. Factors associated with raccoon rabies, relative risks and 95% confidence intervals estimated with a Poisson regression model adjusted for overdispersion and for large scale geographical variation *, New York, 1997-2003.

Factor	RR	95% Confidence Interval	*p-value*
Higher proportion of land use type within census tract**			
Water	0.55	0.26, 1.16	0.1173
Low intensity residential	7.68	5.11, 11.54	<.0001
High intensity residential	1.55	0.82, 2.90	0.1747
Commercial/Industrial/Transportation	0.38	0.13, 1.15	0.0856
Barren	0.84	0.004, 182.97	0.9506
Agricultural	1.3	0.87, 1.95	0.2042
Wetland	0.01	0.001, 0.09	<.0001
Land elevation (meters above sea level)	0.998	0.997, 0.999	<.0001
Protection from adjacent ORV area			
Yes	1.20	1.00, 1.45	0.0517
No	*reference*		
Presence of major roads within census tract			
No	1.10	1.00, 1.20	0.0473
Yes	*reference*		
Presence of rivers/lakes within census tract			
No	1.20	1.05, 1.37	0.0063
Yes	*reference*		
Higher population density (thousands of people/km^2)	1.02	0.98, 1.06	0.3139

Adjusted for county, latitude, and ecoregion.
*****With forest land use type as background.***

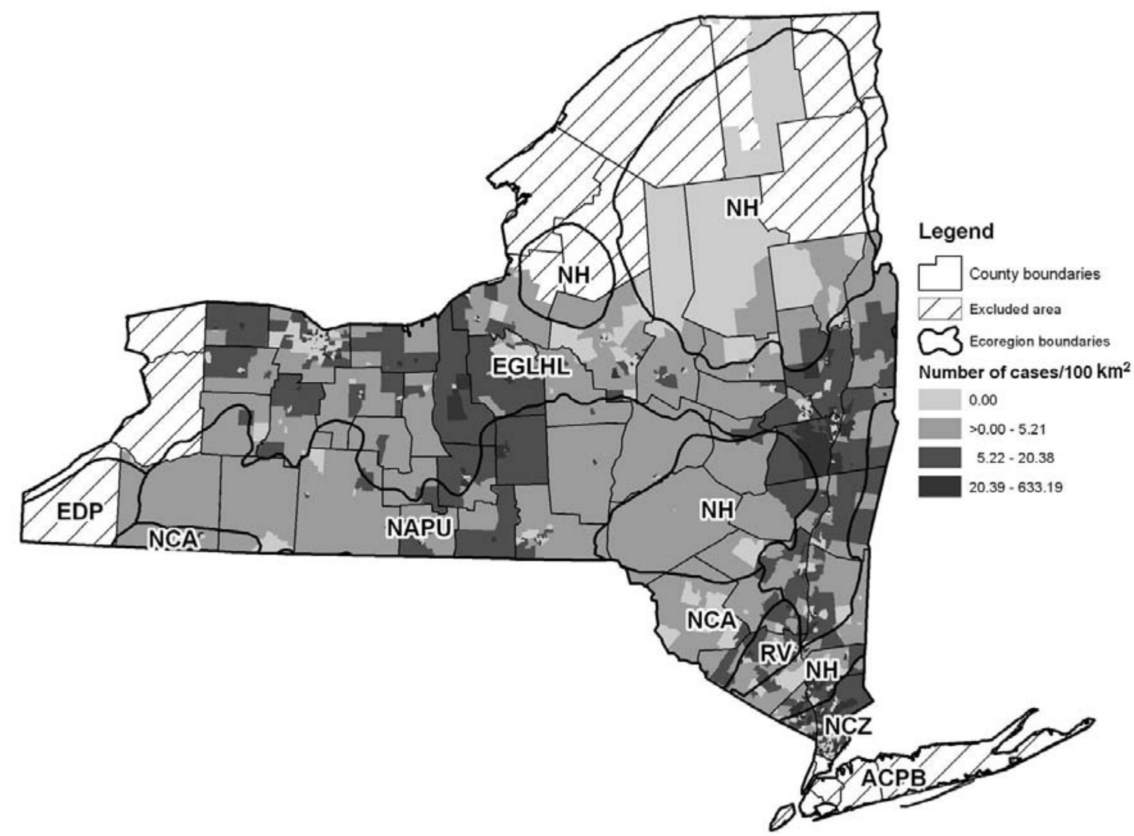

Figure 2.1. The density distribution of raccoon rabies variant cases by census tract in New York and its EPA ecoregions, 1997-2003. Density in number of rabies cases per 100 km^2 stratified by quantiles.

Ecoregions*: ACPB: Atlantic Coastal Pine Barrens; EDP: Erie Drift Plains; EGLHL: Eastern Great Lakes and Hudson Lowlands; NCA: North Central Appalachians; NAPU: Northern Appalachian Plateau and Uplands; NCZ: Northeastern Coastal Zone; NH: Northeastern Highlands; RV: Ridge and Valley.*

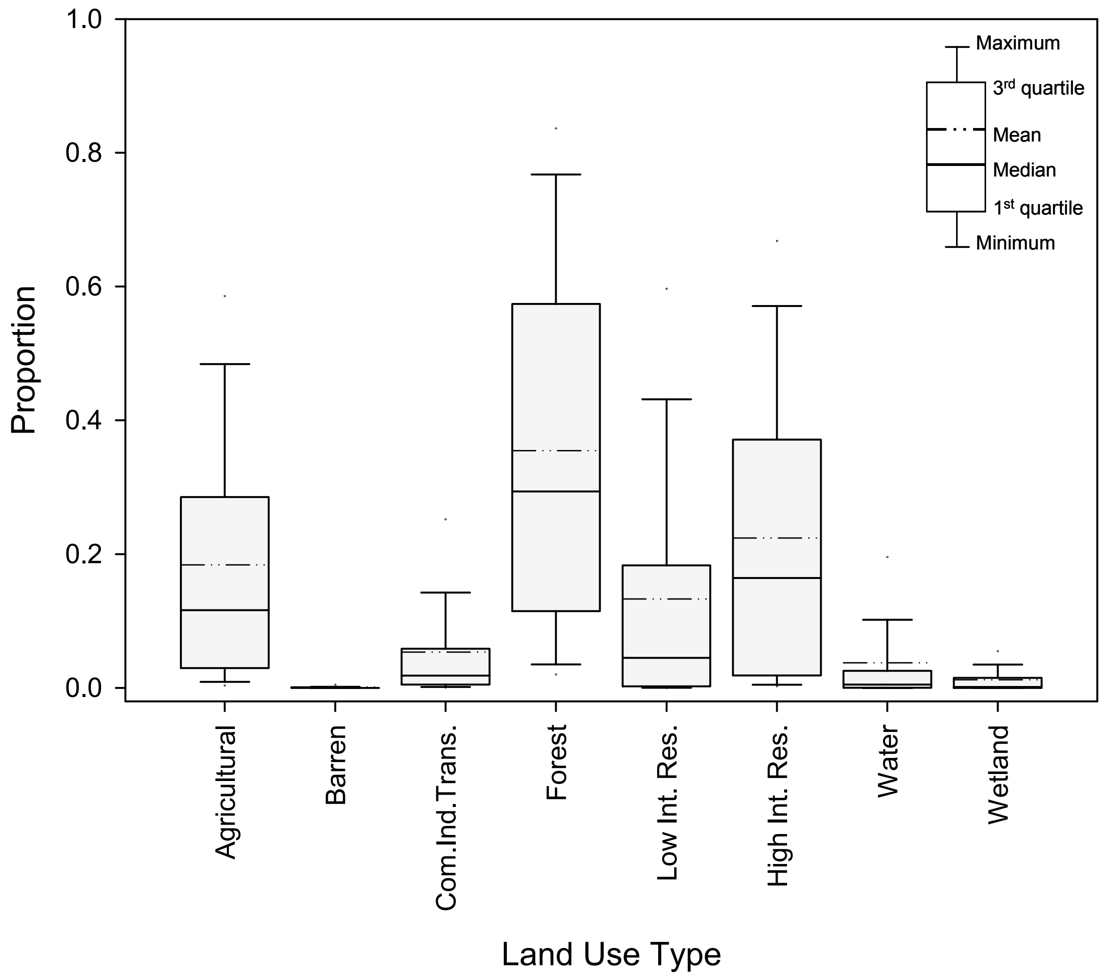

Figure 2.2. Proportion of land use types within 1,639 census tracts, New York, 1997-2003.

Chapter 3:

Spatial and temporal patterns of enzootic raccoon rabies adjusted for multiple covariates

3.1. Abstract

With the objective of identifying spatial and temporal patterns of enzootic raccoon variant rabies, a spatial scan statistic was utilized to search for significant terrestrial rabies clusters by year in New York in 1997-2003. Cluster analyses were unadjusted for other factors, adjusted for covariates, and adjusted for covariates and large scale geographic variation. Statistically significant clusters were identified particularly in the Albany, Finger Lakes, and South Hudson areas. The clusters were generally persistent in the Albany area, but demonstrated cyclical changes in rabies activity every few years in the other areas. Cluster adjustments allowed the discussion of possible causes for the high risk raccoon rabies areas identified.

Keywords: raccoon rabies; rabies epidemiology; spatial epidemiology; spatial scan statistic.

3.2. Introduction

Raccoon rabies is a disease that is prevalent in the eastern United States with impacts on other wildlife and domestic species, and poses a threat to the human population. Raccoon rabies has been present in New York State (NYS) since 1990.[1]

Raccoon rabies entered NYS from the south and spread out northward and eastward, reaching the northern part of the state by 1998.[2] Almost all of NYS is now a large enzootic area (with the exception of Long Island and the Adirondack Mountains). Efforts to contain the spread of the epizootic have been conducted since 1995 in the western, north and northeastern sections of the state by building immune barriers with oral rabies vaccine (ORV) targeting of raccoons.[3,4] Although ORV programs continue in 10 NYS counties neighboring Canada,[5] most of NYS has not received an ORV intervention to deter the raccoon rabies enzootic which has now been active for at least a decade in most areas. In an enzootic area the lethal effect of rabies usually reduces the population of the reservoir species. Rabies activity increases when the area is repopulated by new generations of susceptible hosts, creating cycles with peaks every few years. These raccoon rabies cycles are reflected in the raccoon rabies incidence oscillations recorded by the NYS Department of Health (NYSDOH) rabies surveillance system at the town and county level.[6]

The first ORV intervention in an enzootic area was reported in Albany and Rensselaer counties in NYS from 1994-1997. This pilot study demonstrated rabies suppression by ORV, but the area was small and the efforts were not continued after 1997.[7] Discussion of whether or not to intervene with ORV in enzootic areas has been ongoing,[8,9] but currently ORV has been primarily utilized in epizootic areas with immune barriers to contain rabies spread.[5] The high cost of ORV interventions, especially for large areas,[10] is an obstacle to considering large-scale applications of ORV to control enzootic raccoon rabies. To develop better control strategies using ORV or other interventions for raccoon rabies enzootic areas, it is necessary to examine the disease patterns in space and time and understand how those spatial and temporal patterns might provide scientific support for new approaches to use of ORV and other control programs. Analyses to determine whether and where significant geographical clustering of rabies cases occur after adjusting for geographic and human factors that may be associated with increased or decreased transmission would help to develop more efficient rabies control strategies.

The large NYS rabies enzootic area provides a unique opportunity to study raccoon rabies spatial patterns with respect to the natural and man-made environment in order to help explain raccoon rabies epidemiology in space and time. Raccoon rabies in NYS has been documented with a well-established surveillance system conducted by NYSDOH, local health departments (LHD), and other agency partners. Key features of this surveillance system include statutory reporting requirements, free laboratory testing of rabies-suspect animals, and partial reimbursement to local health departments for the cost of submitting animal specimens for testing. Available data include animal case reports, human exposures/incidents, human prevention treatments, cost of preventive activities, and laboratory test results. Rabies information from NYS has been utilized in national and regional rabies analyses, with data aggregated by town or county.[11-12] Recently, most of the terrestrial rabid animals reported to the NYSDOH have been geocoded to geographical coordinates, enabling the analysis of rabies patterns at a local level.[13] In this study, spatial and temporal patterns of the raccoon rabies epizootic in NYS are identified, and described with spatial cluster techniques, to assist in understanding the natural dynamics of raccoon rabies.

3.3. Materials and methods

Study area

The study area included the New York counties (excluding NYC and Long Island) that had not been exposed to ORV during the 1997-2003 study period. New York City does not participate in all aspects of the State's rabies surveillance program, and Long Island remained free of raccoon-variant rabies until 2004. The counties exposed to ORV programs during most of the study period were excluded. Those counties were Chautauqua, Clinton, Essex, Franklin, Jefferson, Niagara, and St. Lawrence. Counties exposed to ORV no more than once at the beginning (Albany and Rensselaer counties) or no more than twice at the end of the study period (Erie, Lewis, and Oswego counties) were not excluded. Because counties were included or excluded as a whole in the study, counties with small areas of ORV such as Oswego and Lewis were not excluded.[14] The selection criteria for the counties permitted maximizing the sample size for the raccoon rabies variant cases, and keeping the study area comparable through the 7-year study period. Forty-eight counties were included in the study containing a total of 1,873 census tracts and 94,996.68 km^2 of land area.

Data collection

The raccoon variant rabies cases were extracted from the geocoded rabies database of the Zoonoses Program, NYSDOH. This database was developed for a previous study, and included the geographical coordinates (latitude/longitude) of the addresses that were reported to the NYSDOH Wadsworth Center's Rabies Laboratory on its Rabies Specimen History form (DOH-487z).[13] The forms are included with the rabies suspect samples submitted for testing. Data from 4,690 terrestrial animals confirmed with rabies from the study area during 1997 to 2003 were selected.

The cases selected for the study are assumed to be infected with raccoon rabies variant because ongoing variant testing by the Rabies Laboratory has confirmed raccoon variant in terrestrial animals during the study period (fox variant was reported in the early 1990's), and spillover from bats is very rare (14 cases in 20 years).[1] Terrestrial animals confirmed with other rabies variants (bat variant, fox variant) were excluded. To increase the number of cases in the study and maximize the statistical power of the study, the addresses of any terrestrial rabies cases that were not previously geocoded to a street level were processed to obtain geographical coordinates at a zipcode level or better with commercial software (MapMarker Plus 10.2™ by MapInfo Corporation). After geocoding, 4,671 cases were included in the study and 19 cases were excluded because the zipcode could not be determined. The cases were assigned to the corresponding census tract using a geographic information system (GIS) developed with ArcView 8.3™.

Cluster analysis

Identification of significant rabies geographical clustering would be valuable for developing improved raccoon rabies control strategies. It would also be helpful to examine how clusters are modified after adjustment for geographic and human factors that may be associated with increased or decreased transmission, such as land use type, land elevation, human population density, presence of major roads, presence of rivers/lakes, and protection from being adjacent to an ORV exposed area.

In this study a spatial scan statistic was utilized to detect statistically significant clusters of terrestrial rabies cases. This method has been previously utilized for research and surveillance of other zoonotic diseases.[15-19] The spatial scan statistic uses a circular moving window (purely spatial cluster search) or a cylinder window (space-time cluster search) that goes from one census tract centroid to another across the study area, increasing its size from zero to a maximum size specified by the user. SaTScan™ v. 5.1.3 is the software that was used for cluster identification in this study. The SaTScan output provides data files with cluster locations (center and radius), number of cases and expected cases for each cluster area, statistical significance (*p-value*), and risk estimates for each location (RR). For space-time cluster searches, the software also provides the timeframe of the cluster.[20]

The cluster analysis was conducted separately for each year in the 7-year study period. Because raccoon populations can be reduced by rabies with its ~100% case fatality rate, changes in the population are expected.[21] Once a rabies epizootic has occurred, raccoon and other impacted wildlife populations may need several years to rebound as the enzootic state is established, and will likely never reach the levels before rabies was introduced. Raccoon population changes can impact rabies cluster locations each year across the 7-year study period.

For this analysis, it was assumed that the surveillance efforts to detect terrestrial rabies cases across the study area did not change through the study period. Sudden changes in surveillance efforts could potentially confound the results. To examine the issue of surveillance effort changes, the number of terrestrial animals tested for rabies by county and year was summarized, and reviewed for variations from one year to another that could be attributed to systematic changes in surveillance.

Cluster analyses were conducted considering census tracts as the unit of analysis. Purely spatial analysis was performed, scanning for clusters with high risks using the Poisson probability model,[22] which requires cases and population counts within each potential cluster. Because raccoon and wildlife population counts or estimations are not available, the area of each census tract was used in lieu of population. To apply the Poisson model we assumed that the raccoon rabies cases are Poisson distributed and the number of cases in a census tract is proportional to the census tract area. The size of the scanning window in the spatial scan statistic was allowed to increase until a maximum of 25% of the study area was reached. The statistical significance of the clusters was established by comparing the calculated likelihood ratio of each cluster to 999 Monte Carlo replications of the distribution where cases are assumed to be randomly distributed across space. A cluster was statistically significant when its *p-value* was equal to or less than 0.05. Clusters with larger *p-values* were considered nonsignificant.

With the objective of observing the effect on rabies spatial clustering when some factors associated with raccoon variant rabies are controlled, we conducted cluster analyses adjusting for covariates. A previous study developed a Poisson regression model for factors associated with raccoon variant rabies in NYS.[13] In that model the dependent variable was the number of terrestrial rabies cases in a census tract and the independent variables were proportion of land use type in a census tract, land elevation, human population density, presence of major roads in the census tract, presence of rivers/lakes in a census tract, and protection from being adjacent to an ORV exposed area. The model was also adjusted for county, latitude, and ecoregion to help adjust for possible unknown variables that co-vary spatially with the response, and control for large scale geographical variation (LSGV).

This Poisson regression model was utilized for our study area and the parameters obtained were used to calculate the expected number of terrestrial rabies cases in the census tract. The expected values were calculated for a model with the covariates and for a model adjusted for covariates and LGSV. The Poisson regression models were performed using SAS 9.1, with PROC GENMOD.[23] To obtain raccoon rabies clusters adjusted for covariates, the cluster analyses were repeated replacing the census tract area values in the spatial scan statistic with the expected number of raccoon rabies cases obtained from the Poisson regression model.[24] Cluster searches were repeated utilizing the expected values adjusted for associated covariates and the expected values adjusted for covariates and LSGV.

An additional space-time cluster analysis was performed using a space-time permutation model.[20,25] This approach is a recent feature of SaTScan that requires only cases, allowing for cluster analysis in the absence of population data. The space-time permutation cluster analysis was used to search for increases in enzootic activity across the study area during the seven-year study period. This cluster search was retrospective, with the space unit represented by census tracts and the time unit represented by months.

3.4. Results

Of the 4,671 terrestrial rabies cases included in the study, 2,974 (63.7%) were raccoons, 1,063 (22.8%) were skunks, and 634 (13.5%) were other animals including domestic and wildlife species. A review of the annual number of terrestrial animal tested for rabies from 1997 to 2003 in the 48 counties included in the study did not reveal systematic changes in surveillance efforts over time (Table 3.1).

The distribution of terrestrial rabid animals by year at the census tract level is presented in Figure 3.1. Grouping the census tracts in quartiles every year, the ones with the highest risk were located mainly in the eastern edge (Hudson Valley), in the center (Finger Lakes region), and northwest of the study area.

Table 3.2 summarizes the statistically significant ($p \leq 0.05$) clusters by year and region for the three types of cluster analyses: unadjusted for covariates or LSGV, adjusted for covariates, and adjusted for covariates and LSGV. These clusters are summarized with a timeline in Figure 3.2.

Cluster analysis unadjusted for covariates or LSGV

In the cluster analysis unadjusted for covariates or LSGV, 3 to 5 statistically significant clusters were detected each year, for a total of 24 in the 7-year study period (Table 3.2). Albany County had statistically significant rabies clusters in all years, and consistently had the highest relative risk for a rabies cluster in all years except 2000 (RR = 15.1, $p \leq 0.001$), when it was exceeded by the relative risk for the Niagara Falls area (RR = 33.26, $p \leq 0.001$). The persistence of the Albany County cluster can also be seen in the timeline summary of significant clusters (Figure 3.2). This cluster reduced in size progressively from 1997 to 1999, and then recovered its size progressively through the following four years of the study period (Figure 3.3).

No other areas had persistent and significant clusters in the same location for all seven years of the study period (Table 3.2, Figures 3.2-3.3). However, significant clustering was found in one or more locations of the Finger Lakes region (Broome, Cayuga, Cortland, Onondaga, Ontario, Oswego, Schuyler, Seneca, Steuben, Tioga, Tompkins, Yates, and Wayne counties) through the study period. A cluster in the Finger Lakes East area (in parts of Cayuga, Cortland, Onondaga, Seneca, Tompkins, and Wayne counties) increased its size and moved to the north from 1997 to 2000 (Figure 3.3). By 2000 there were two main clusters in the Finger Lakes region, one in the north and the other in the south. The northern cluster (in parts of Cayuga and Wayne counties) was smaller in 2001, but during the following two years it increased in size and became relocated in the same area as the beginning of the study period. The statistically significant cluster in the south east of the Finger Lakes area in 2000 (in parts of Broome, Chemung, Tioga, Tompkins counties) was preceded by a nonsignificant area of clustering in 1999. In 2001 the cluster was increased in size and then disappeared in 2002.

The Southern Hudson region (in parts of Dutchess, Orange, Putnam, Rockland, Sullivan, Ulster, Westchester) had a significant rabies cluster in 1997 that disappeared during the following three years (Table 3.2, Figures 3.2-3.3). This cluster reappeared in 2001 in the same location with a similar size and shape as in 1997, followed by an increase in size in 2002, and persistence through the end of the study period in 2003.

The Northwest region (Erie, Genesee, and Orleans counties) had a significant cluster of rabies in 1998 that was preceded by a nonsignificant cluster in the same area in 1997 (Table 3.2, Figures 3.2-3.3). The cluster persisted until 1999 when it appeared to split into two more focal areas, one area of significant clustering in Orleans County and another area of nonsignificant clustering in Erie County that included the area of Niagara Falls. An isolated small significant cluster was observed in the Niagara Falls area in

2000. An isolated small significant cluster was observed in Monroe County in 2001. In the same area, nonsignificant clusters were observed during the subsequent two years.

Cluster analysis adjusted for covariates

Adjusting for covariates (land use type, land elevation, presence of major roads, presence of rivers/lakes, human population density, and protection from adjacent ORV exposed area), 24 significant clusters were detected in the 7-year study period, with 3 to 4 clusters observed each year (Table 3.2). Albany County or its area had the highest risk of rabies clusters in alternate years (1997, 1999, 2001, and 2003). The cluster in the Niagara Falls area in 2000 was the area of highest relative risk (RR: 18.16, $p \leq 0.001$).

The Albany region had a statistically significant cluster of rabies in Albany County that persisted with a similar size throughout most of the study period (Figures 3.2, 3.4). This cluster was smaller in 2002, but in 2003 was at its maximum size. The highest relative risk for this cluster occurred in 2002 (Table 3.2) when it was the smallest in size. Another cluster in the Albany region was observed in Saratoga County only in 1997.

Persistent statistically significant clusters adjusted for covariates occurred in the overall Finger Lakes region through the study period (Table 3.2, Figures 3.2, 3.4). A cluster in the Finger Lakes East area (in parts of Cayuga, Cortland, Onondaga, Seneca, Tompkins, and Wayne counties) in 1997 and 1998 was reduced in size by ¾ in 1999. However, the cluster was back to its 1997-1998 size in 2000, and increased in size again to become a large rabies cluster covering most of the Finger Lakes region in 2001. This cluster was reduced in size again in the subsequent two years of the study period. Another significant cluster was observed in the Finger Lakes North East area (in parts of Cayuga and Wayne counties) in 1998 to 2000, and in 2002. This northern Finger Lakes cluster was located at the edge of Lake Ontario in 1998. By 1999, the cluster had moved inland, but by 2000 it was back again at the edge of Lake Ontario. In 2002, this cluster reappeared inland in a smaller size than previous years.

When adjusted for covariates, statistically significant rabies clusters were found in parts of the Southern region (Dutchess, Orange, Putnam, Rockland, Sullivan, Ulster, and Westchester counties) in four years of the study period (Table 3.2, Figures 3.2, 3.4). The significant cluster in the South Hudson area in 1998 appeared in a small portion of Westchester County in 1998, reappeared in a larger portion of the county in 2001, was reduced in size in 2002, and finally expanded in 2003 to its largest size of the study period, including Westchester and Putnam counties.

The Northwest region (Erie, Genesee, and Orleans counties) had two significant rabies clusters adjusted for covariates during the study period (Table 3.2, Figures 3.2, 3.4). In 1999 a small significant cluster was found in Orleans County, and in 2000 a small significant cluster was found in the Niagara Falls area of Erie County.

Cluster analysis adjusted for covariates and LSGV

In the cluster analysis adjusted for covariates and spatial covariates, 14 significant clusters were detected in the 7-year study period, with 1 to 4 clusters observed each year (Table 3.2, Figure 3.2). The cluster with the highest relative risk was located in the Niagara Falls area of Erie County (RR: 42.1) in 2000.

The Albany region had three significant rabies clusters during the study period (Table 3.2, Figures 3.2, 3.5). A cluster in Saratoga County was found only in 1997. A cluster in Albany, Rensselaer, and Columbia counties that began in 1998 became smaller in 1999, and even smaller in 2000, continuing through 2002. In 2002, a significant cluster appeared at the eastern edge of the study area along the Rensselaer and Columbia county boundaries, where a part of the large Albany area significant cluster had been located in 1998.

The Finger Lakes region had statistically significant rabies clustering adjusted for covariates and LSGV in 1997 and 2000 (Table 3.2, Figures 3.2, 3.5). A cluster in the Finger Lakes East area was found in 1997. In 2000, two significant clusters were found, with one in Wayne County of the Finger Lakes North area, and another in Tioga and Broome counties of the Finger Lakes South East area.

The Southern region had a significant cluster of rabies in 2001, in Westchester County (Table 3.2, Figures 3.2, 3.5). A larger significant cluster reappeared in 2003, covering seven counties.

The Northwest region had a significant cluster in 1998 in Orleans, Genesee and Erie counties (Table 3.2, Figures 3.2, 3.5). Nonsignificant clustering was observed in that area in the subsequent year. In 2000 a small significant cluster appeared in Erie County of the Niagara Falls area.

Comparison across types of cluster analyses

There are few differences in clustering in the Albany region depending on type of analysis, although persistent significant clustering is found for the unadjusted analyses and the analyses adjusted for covariates, whereas it does not occur at the beginning (1997) and end (2003) of the study period when adjusting for LSGV. This suggests that influence of the covariates and LSGV on the Albany region is small. In the Finger Lakes region the clustering is similar in the unadjusted analysis and the analysis adjusted for covariates. However, when adjusting for covariates and LSGV, the significant clustering disappeared in 1998, 1999, 2002 and 2003, suggesting that LSGV accounts for the clusters in those years. The Finger Lakes region has a unique land configuration in NYS, because the lakes divide the land into parallel valleys, acting as a natural barrier and keeping raccoon rabies movements within the valleys. Thus cases in this region may be more spatially dependent than in other areas of the state, and not able to build up to larger significant enzootic outbreaks.

Space-time permutation cluster analysis

The cluster search with the space-time permutation approach detected six statistically significant clusters during the study period (Table 3.3). Most of the significant clusters identified occurred in the first half of the study period, indicating increased enzootic activity in Albany, Albany North (Saratoga County), Finger Lakes East, Finger Lakes North, and Niagara Falls areas (Figure 3.6). One cluster was identified in the South Hudson at the end of the study period (2002-2003). This area was the only one with increased enzootic activity at the end of the study period. The average number of cases included in the clusters was 67.5 cases. The cluster including the largest number of rabies cases was located in the Finger Lakes East area in 1997, with 165 cases. The average duration of the clusters identified was 9.3 months. The cluster with the longest duration was located in the South Hudson area with 14 months (Table 3.3).

3.5. Discussion

The analyses in this study were able to identify statistically significant clusters of raccoon rabies in specific areas of New York from 1997 to 2003. Those clusters were persistent in the Albany region for most of the study period in all three types of purely spatial analyses. Significant clustering was also found in one or more parts of the Finger Lakes region for most of the study period in all three types of analyses, although the location of the significant clustering varied more than in the Albany region. Clustering in the South Hudson region was present in 3-4 of the study years depending on type of analysis. Clustering in the northwest region of the state was more sporadic. The space-time cluster analysis demonstrated increased enzootic activity in the first half of the study period in northern and western areas of NYS, and at the end of the study the increased enzootic activity was concentrated in the south, in the South Hudson area. This is the first study using the spatial scan statistic to identify terrestrial rabies clusters in an enzootic area using geocoded point data (latitude/longitude).

Although there are similarities in the size, distribution and location of some clusters in the unadjusted analyses with clusters in the adjusted analyses, the differences are worth noting. The unadjusted cluster analyses identify the areas of highest raccoon variant rabies activity each year of the study period, and thus provide a valuable picture of the disease during 1997 to 2003. However, it is useful to determine whether significant geographical clustering of rabies cases occurs even after adjusting for geographic and human factors that may be associated with increased or decreased transmission, such as land use type, land elevation, human population density, presence of major roads, presence of rivers/lakes, and protection from being adjacent to an ORV exposed area. Using a Poisson regression model, a previous study in New York found that elevated numbers of raccoon-variant rabies cases in census tracts were associated with a higher proportion of low intensity residential areas (those with a lower concentration of housing units), lower land elevation, a lower proportion of wetlands, and a lack of rivers/lakes and major roads, after adjusting for LSGV.[13] Because raccoon rabies transmission occurs directly from animal to animal, terrestrial rabies cases are also by definition related spatially to one another, and thus have influence over the occurrence of rabies in the subsequent year. Thus, the use of expected values adjusted for LSGV (county, latitude, and ecoregion) is also important in identifying truly significant geographical clustering of rabies separate from this phenomenon.

The South Hudson area presented significant clusters in an apparent cycle in the unadjusted cluster analysis. A significant cluster in 1997 was followed by three years without clusters. Significant clustering reappeared in 2001 with increasing size in 2002 and 2003. A somewhat similar cycle was seen in the adjusted analyses, but the clusters were smaller in size and more often statistically insignificant. The presence of a large cluster in 2003 even when adjusting for covariates and LSGV indicates an increasing risk for raccoon rabies in the South Hudson area that may not be explained by those factors. The South Hudson region is highly populated; however, population density was included as one of the covariates and thus cannot explain this large cluster. The South Hudson region borders the states of Connecticut to the east and New Jersey to the west, both states with current raccoon rabies enzootic activity. The rabies activity in the neighboring states may be influential in the South Hudson region cluster; such influenced was not modeled in this study.

The significant cluster found in 2001with the unadjusted analyses in Rochester, Monroe County disappeared with the adjustment for covariates. With population density as one of the covariates, the cluster's disappearance may indicate that there was no significant clustering of cases beyond the association with people being available to report them. However, this phenomenon might be expected to impact reporting of clusters in other years, and none were reported.

Orleans County, another county in the northwestern region of the state, had clustering in 1997 that became statistically significant in 1998 and 1999 with the unadjusted analyses, then reappeared as a large nonsignificant cluster in 2003. There are some small differences in the appearance, size, and significance of clustering in the adjusted analyses, but no clear pattern. Orleans County borders an ORV exposed area in Niagara County and was chosen to be a control area for the ORV program for two years before the study period. There were no large changes in surveillance efforts for Orleans County during the study period. The cluster was located in the Iroquois National Wildlife Refuge, and this habitat may play a role in increasing raccoon rabies activity in the area. The cluster in the Niagara Falls area (Grand Island, Erie County), was very small and occurred only in 2000 in all three types of cluster analysis.

Interpretation of the nonsignificant clusters is difficult. Their presence in years before or after significant clusters was inconsistent. The presence of a nonsignificant cluster may indicate an increase in rabies activity that could be statistically significant the following year. However, the evidence found in this study is inconclusive regarding the utility of nonsignificant clusters as announcements of subsequent significant clusters.

The locations of the clusters identified using the space-time permutation approach were similar to the location of the clusters identified using the Poisson model approach (purely spatial clusters). The space- time clusters demonstrated increased enzootic activity from 1997 to 2000, and identified the same foci of increased raccoon rabies activity at the end of the study period (South Hudson) as found by the purely spatial cluster analysis.

There are a number of additional factors that need to be considered in interpreting the results of these cluster analyses. The first factor is the potential influence of differential surveillance. The presence of significant clustering in the Albany area may be due to the presence of the NYSDOH Rabies Laboratory and the state (New York State Department of Health, Department of Environmental Conservation, Department of Agriculture and Markets) and federal (USDA Wildlife Services) agencies that participate in rabies surveillance and control. Similarly, the presence of the Cornell University Animal Health Diagnostic Center and College of Veterinary Medicine in the Finger Lakes region may influence the degree of rabies surveillance even though rabies testing is not available at those facilities. These agencies do not specifically target their surrounding towns and counties for increased rabies surveillance. However, their location facilitates specimen transport, and may also increase the public awareness of raccoon rabies. Areas with ORV are specifically targeted for increased surveillance. Although these areas were largely excluded from these cluster analyses, Albany and Rensselaer counties did receive ORV in early 1997 with increased active surveillance that year, with a possible influence on interest in specimen submissions in neighboring Saratoga County, which reported a significant rabies cluster only in 1997. Periodic significant clustering in the northwestern region of the State may also have been due to a ‘spillover’ effect of interest in surveillance due to the more active surveillance in the neighboring ORV areas that were excluded from the study (the ORV program in Niagara County started 1997 and continues to the present), although the variable appearance of these clusters by year is difficult to explain related to the consistent ORV work in that region.

Surveillance may be influenced differentially by other diseases in certain areas, such as distemper.[21,26] Distemper may result in an increase of dead animals, and the numbers of raccoons submitted for rabies testing. However, this increase in submissions due to dead animals with distemper may not necessarily increase the number of raccoons confirmed with rabies. Separate from any influence on surveillance, a distemper outbreak could decrease the chance of rabies transmission by decreasing the size of the raccoon population.[26] The presence and effect of other raccoon diseases could not be assessed in this study and may be a confounding factor to be considered in future research.

There may also be misclassification of case location, because the addresses and the geocoded coordinates can be subject to errors.[27] In addition, animals may move between the time of infection and the time of death, so the locations reported for the dead animals may not represent the locations of transmission.[26] However, we have no evidence that these potential location errors are systematic, and they should be minimized by the use of census tracts as the unit of analysis rather than the specific geocoded address points.

This study analyzed raccoon variant rabies spatial and temporal patterns in NY that have not been previously described at a focal (census tract) level. Comparisons across the type of spatial analysis performed (purely spatial cluster search unadjusted, adjusted for covariates, and adjusted for covariates and LSGV) allow consideration of the potential influence of geographical factors for raccoon rabies and possible reasons for the highest risk areas (statistically significant clusters). This approach is one of several to more fully understand areas of greatest risk for raccoon variant rabies, in order to better target potential ORV or other control programs.[13] Further research targeting these hotspots may help to refine the results and identify other factors that influence raccoon variant rabies in those areas.

The cluster areas identified in this study should be considered for raccoon rabies control interventions. The areas of significant rabies clustering can be used as areas for piloting ORV program for enzootic zones, especially when there are insufficient resources to develop an ORV program for an entire large enzootic region. Sections of NYS can be prioritized using the clustering areas as centers of each section. The areas for intervention can be prioritized for intervention considering size; number of cases observed in the cluster; recent clustering activity; and proximity to a current ORV program (to consider the area an extension of those ORV areas). The cluster areas could also be used in developing the borders for immune barriers to surround and progressively isolate the largest clustering areas. Other raccoon rabies prevention activities could also benefit from using the clustering areas identified. Public education on raccoon rabies exposures and the need for increasing pet vaccination activities in areas where clusters were identified may be assessed when prioritizing those activities in such areas.

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Table 3.1. Annual number of terrestrial animals tested by the NYSDOH Rabies Laboratory for the 48 counties in the study area, New York, 1997-2003.

	YEAR						
County	**1997**	**1998**	**1999**	**2000**	**2001**	**2002**	**2003**
Albany	599	619	520	439	410	429	314
Allegany	53	35	32	47	49	35	40
Broome	107	115	73	120	104	99	80
Cattaraugus	76	62	55	59	67	59	45
Cayuga	271	184	173	160	130	121	83
Chemung	82	54	63	63	87	58	42
Chenango	53	55	39	27	33	24	37
Columbia	146	144	94	146	121	92	54
Cortland	202	139	110	111	80	71	55
Delaware	75	56	40	37	52	41	32
Dutchess	203	147	152	134	127	121	119
Erie	411	420	412	477	427	459	438
Fulton	19	14	15	11	14	16	18
Genesee	48	48	71	55	30	34	39
Greene	86	76	83	61	74	52	48
Hamilton	2	0	10	0	3	0	2
Herkimer	49	21	36	42	19	28	17
Lewis	107	55	36	45	50	41	41
Livingston	91	95	76	45	58	52	34
Madison	66	79	57	48	37	33	39
Monroe	92	122	132	100	99	104	89
Montgomery	47	31	26	30	25	21	18
Oneida	138	101	90	85	83	59	76
Onondaga	268	250	196	167	154	147	141
Ontario	140	91	78	74	80	50	65
Orange	157	157	152	144	124	125	145
Orleans	81	78	74	67	73	60	53
Oswego	118	139	101	93	86	93	56
Otsego	99	55	62	50	47	46	32
Putnam	43	45	50	34	48	44	45
Rensselaer	277	176	200	127	113	173	184
Rockland	168	129	122	122	111	110	87
Saratoga	241	129	137	84	98	85	84
Schenectady	134	106	103	102	97	78	73
Schoharie	56	39	35	37	46	38	49
Schuyler	34	23	30	22	23	22	32
Seneca	27	27	22	29	29	17	25
Steuben	106	103	103	74	92	65	80
Sullivan	73	78	62	40	27	34	37
Tioga	87	69	56	82	56	40	55
Tompkins	120	132	65	114	110	79	98
Ulster	161	191	188	117	115	136	122
Warren	42	44	44	47	33	26	34
Washington	107	102	86	64	54	75	59
Wayne	92	93	69	78	70	54	53
Westchester	465	412	282	385	390	312	267
Wyoming	31	43	40	39	45	39	32
Yates	54	51	44	47	41	35	26

Source: Rabies Laboratories –Wadsworth Center, NYSDOH

Table 3.2. Location of statistically significant (p≤0.05) terrestrial rabies clusters, New York, 1997-2003, for models unadjusted for covariates or large scale geographical variation, adjusted for covariates, and adjusted for covariates and large scale geographical variation. Not statistically significant clusters observed in the same significant cluster location trough adjustments are also shown. (Dash indicates no cluster found).

		Unadjusted			Adjusted for covariates			Adjusted for covariates and large scale spatial variation		
Year	**Cluster location**	**Cases observed**	**RR**	***p-value***	**Cases observed**	**RR**	***p-value***	**Cases observed**	**RR**	***p-value***
1997										
	Albany	203	6.81	≤0.001	112	4.8	≤0.001	28	2.24	0.418
	Albany North (Saratoga)	-	-	-	51	5.54	≤0.001	51	4.72	≤0.001
	Finger Lakes East	181	3.88	≤0.001	172	4.23	≤0.001	146	1.8	≤0.001
	South Hudson (Roc-Wes)	60	3.22	≤0.001	19	2.31	0.973	4	9.08	0.942
1998										
	Albany	172	14.98	≤0.001	148	5.65	≤0.001	117	2.24	≤0.001
	Finger Lakes East	107	2.86	≤0.001	97	2.62	≤0.001	6	7.68	0.470
	Finger Lakes North East	-	-	-	42	2.24	0.022	32	2.14	0.334
	Orleans	44	2.85	≤0.001	3	15.37	0.936	20	3.49	0.015
	South Hudson (Roc-Wes)	-	-	-	12	5.86	0.020	4	26.05	0.083
1999										
	Albany	80	46.06	≤0.001	102	7.81	≤0.001	80	2.3	≤0.001
	Finger Lakes East	89	2.41	≤0.001	28	7.32	≤0.001	3	1.09	0.998
	Finger Lakes North East	3	49.99	0.101	33	2.86	0.004	3	20.36	0.731
	Orleans	15	7.96	≤0.001	15	5.09	0.006	30	2.18	0.359
2000										
	Albany	100	15.1	≤0.001	90	6.8	≤0.001	24	4.67	≤0.001
	Finger Lakes North East	73	2.71	≤0.001	44	2.65	≤0.001	21	3.6	0.009
	Finger Lakes East	5	11.86	0.260	52	2.7	≤0.001	-	-	-
	Finger Lakes South East	21	3.63	0.008	-	-	-	22	3.32	0.015
	Niagara Falls	8	33.26	≤0.001	8	18.16	≤0.001	8	42.1	≤0.001
2001										
	Albany	95	21.25	≤0.001	93	9.31	≤0.001	33	3.45	≤0.001
	Finger Lakes East	68	6.4	≤0.001	-	-	-	-	-	-
	Finger Lakes Center/South	53	2.14	0.003	140	1.74	≤0.001	79	1.64	0.106
	Monroe	7	10.16	0.047	-	-	-	7	50.2	0.869
	South Hudson (Roc-Wes)	39	3.12	≤0.001	35	2.92	0.002	32	2.53	0.028
2002										
	Albany	81	7.18	≤0.001	39	6.77	≤0.001	13	6.63	0.002
	Albany South East (Rensselaer)	-	-	-	-	-	-	16	4.69	0.007
	Finger Lakes East	77	2.17	≤0.001	35	3.93	≤0.001	5	6.34	0.962
	South Hudson (Roc-Wes)	80	1.69	0.025	6	14.23	0.028	6	9.79	0.181
2003										
	Albany	34	6.42	≤0.001	24	3.18	0.007	-	-	-
	Finger Lakes East	48	2.41	0.002	43	2.61	≤0.001	14	2.86	0.813
	South Hudson (Roc-Wes)	68	3.23	≤0.001	33	2.55	0.009	71	2.04	0.002

Albany = Albany County
Albany North = parts of Albany, Saratoga, Schenectady counties
Albany South East = parts of Rensselaer, Columbia counties
Finger Lakes North East = parts of Cayuga, Oswego, Wayne counties
Finger Lakes East = parts of Cayuga, Cortland, Onondaga, Seneca, Tompkins, Wayne counties
Finger Lakes South East = parts of Broome, Chemung, Tioga, Tompkins counties
Finger Lakes Center/South = parts of Broome, Cayuga, Cortland, Onondaga, Ontario, Schuyler, Seneca, Steuben, Tioga, Tompkins, Yates counties
Monroe = Monroe County
Niagara Falls = Grand Island , northwest of Erie County
Orleans = Orleans County
South Hudson = parts of Dutchess, Orange, Putnam, Rockland, Sullivan, Ulster, Westchester counties

Table 3.3. Location of statistically significant (p≤0.05) terrestrial rabies clusters, New York, 1997-2003, for space-time permutation cluster search.

Cluster location	Time frame	Cases observed	RR	*p-value*
Albany	10/1998 - 4/1999	48	3.09	≤0.001
Albany North (Saratoga)	1/1997 - 12/1997	81	2.13	≤0.001
Finger Lakes East	2/1997 - 10/1997	165	1.78	≤0.001
Finger Lakes North	5/2000 - 8/2000	25	3.76	0.014
Niagara Falls	10/1999 - 7/2000	16	6.04	0.008
South Hudson (Roc-Wes)	10/2002 - 11/2003	70	2.13	0.006

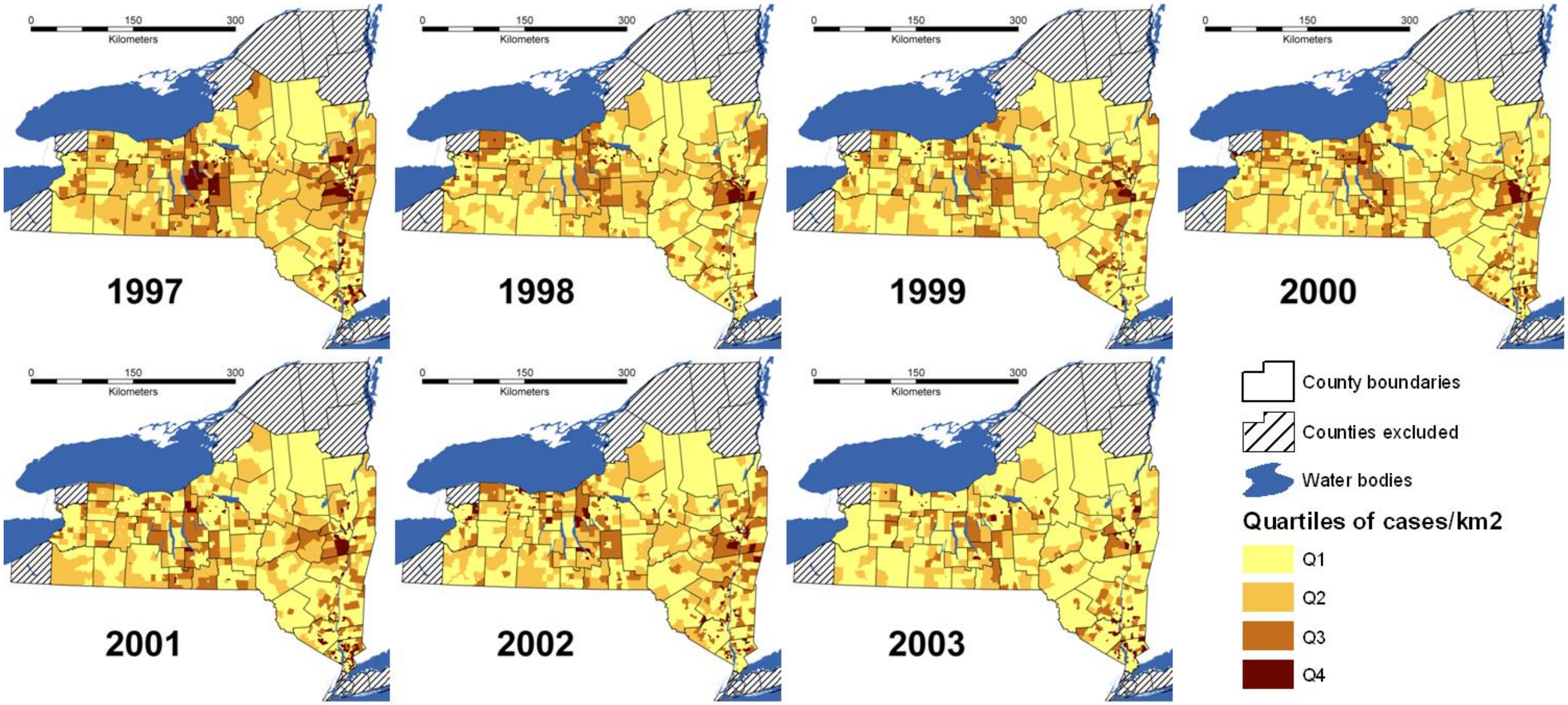

Figure 3.1. Terrestrial rabies cases per km^2 by year in quartiles strata at census tract level, NYS, 1997-2003.

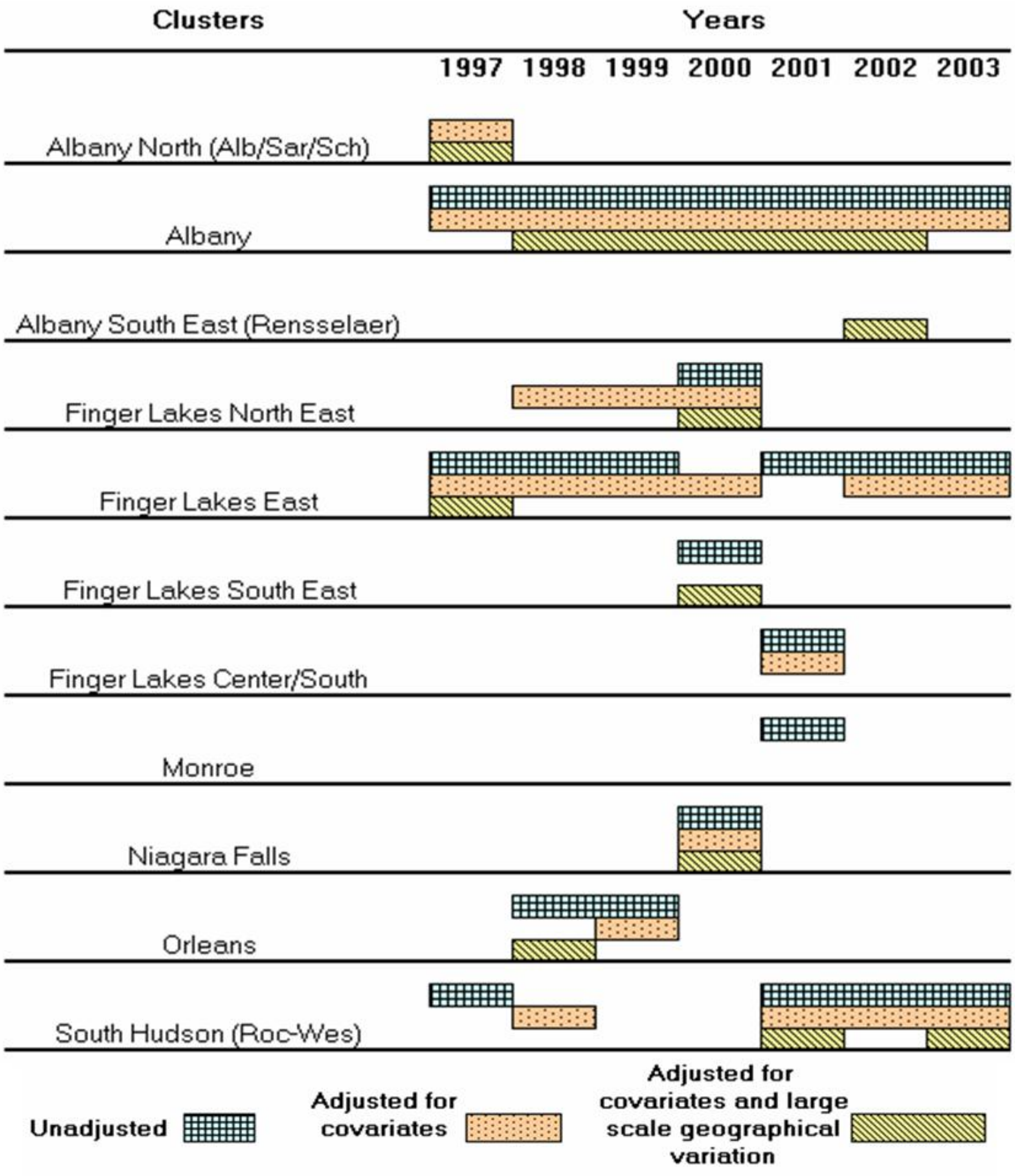

Figure 3.2. Timeline of statistically significant terrestrial rabies clusters, New York, 1997-2003, by type of purely spatial cluster analysis.

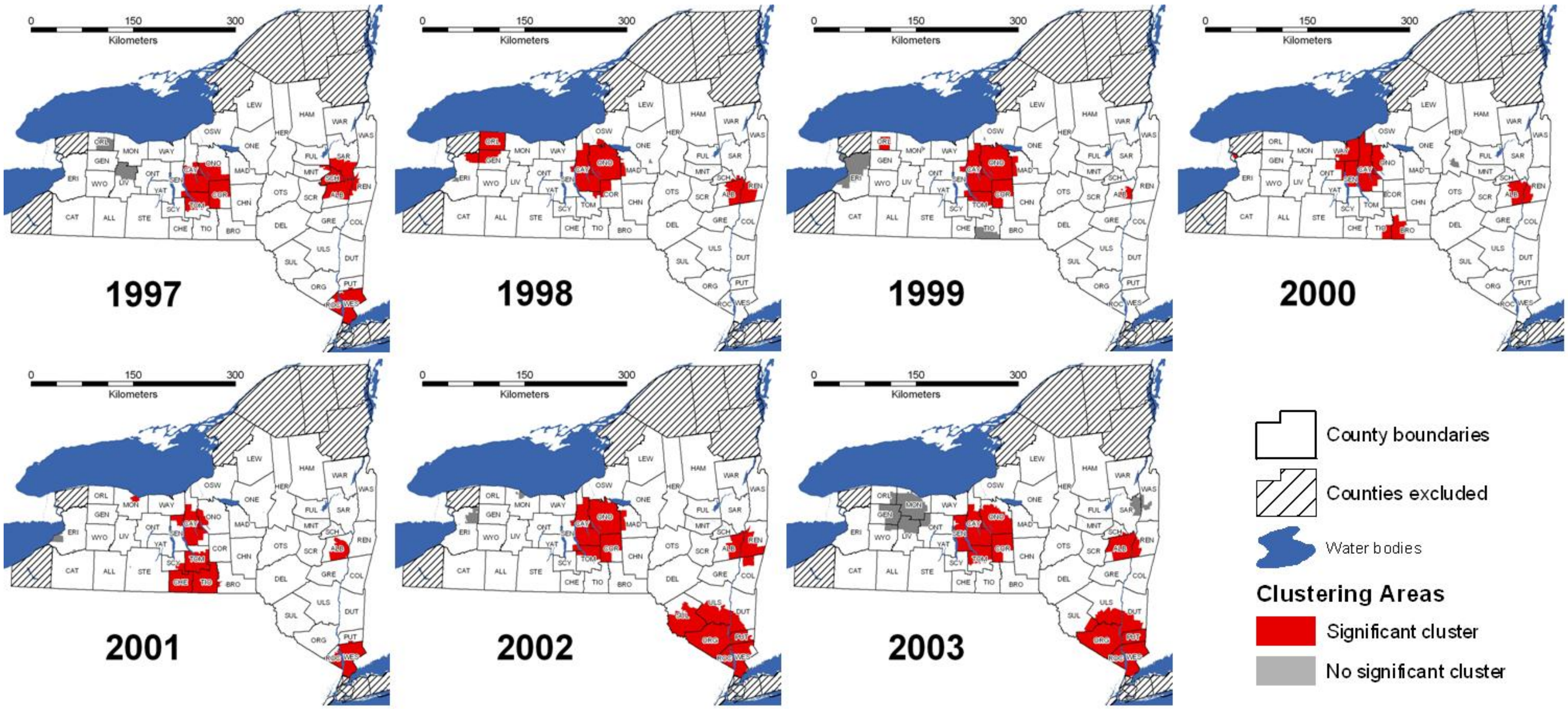

Figure 3.3. Terrestrial rabies clusters, unadjusted for covariates or large scale geographical variation, New York, 1997-2003.
County abbreviations: *ALB: Albany; ALL: Allegany; BRO: Brooome; CAT: Cattaraugus; CAY: Cayuga; CHE: Chemung; CHN: Chenango; COL: Columbia; COR: Cortland; DEL: Delaware; DUT: Dutchess; ERI: Erie; FUL: Fulton; GEN: Genesee; GRE: Greene; HAM: Hamilton; HER: Herkimer; LEW: Lewis; LIV: Livingston; MAD: Madison; MON: Monroe; MNT: Montgomery; ONE: Oneida; ONO: Onondaga; ONT: Ontario; ORG: Orange; ORL: Orleans; OSG: Oswego; OTS: Otsego; PUT: Putnam; REN: Rensselaer; ROC: Rockland; SAR: Saratoga; SCH: Schenectady; SCR: Schoharie; SCY: Schuyler; SEN: Seneca; STE: Steuben; SUL: Sullivan; TIO: Tioga; TOM: Tompkins; ULS: Ulster; WAR: Warren; WAS: Washington; WAY: Wayne; WES: Westchester; WYO: Wyoming; YAT: Yates.*

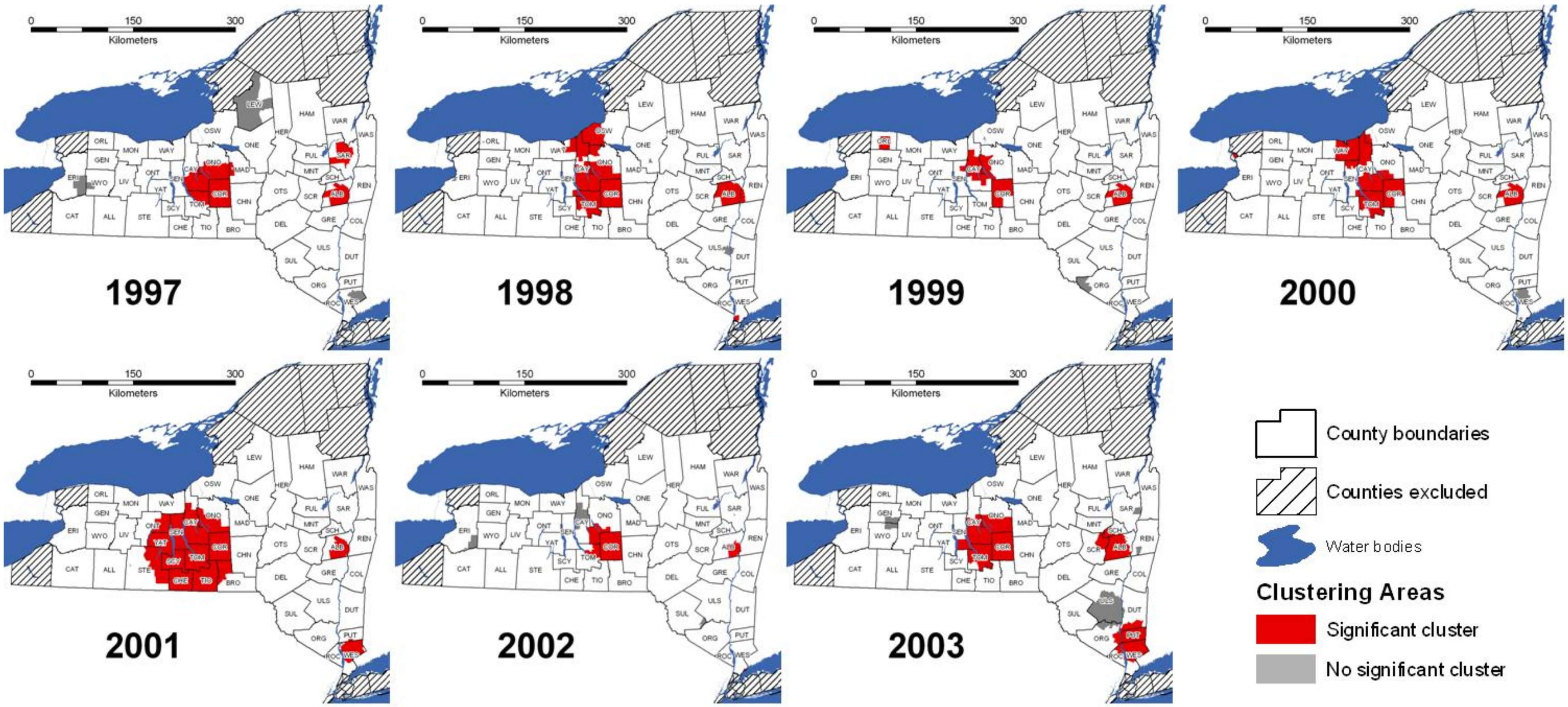

Figure 3.4. Terrestrial rabies clusters adjusted for covariates (land use type, land elevation, presence of major roads, presence of rivers/lakes, population density, and protection from adjacent ORV exposed area), New York, 1997-2003.

County abbreviations*: ALB: Albany; ALL: Allegany; BRO: Brooome; CAT: Cattaraugus; CAY: Cayuga; CHE: Chemung; CHN: Chenango; COL: Columbia; COR: Cortland; DEL: Delaware; DUT: Dutchess; ERI: Erie; FUL: Fulton; GEN: Genesee; GRE: Greene; HAM: Hamilton; HER: Herkimer; LEW: Lewis; LIV: Livingston; MAD: Madison; MON: Monroe; MNT: Montgomery; ONE: Oneida; ONO: Onondaga; ONT: Ontario; ORG: Orange; ORL: Orleans; OSG: Oswego; OTS: Otsego; PUT: Putnam; REN: Rensselaer; ROC: Rockland; SAR: Saratoga; SCH: Schenectady; SCR: Schoharie; SCY: Schuyler; SEN: Seneca; STE: Steuben; SUL: Sullivan; TIO: Tioga; TOM: Tompkins; ULS: Ulster; WAR: Warren; WAS: Washington; WAY: Wayne; WES: Westchester; WYO: Wyoming; YAT: Yates.*

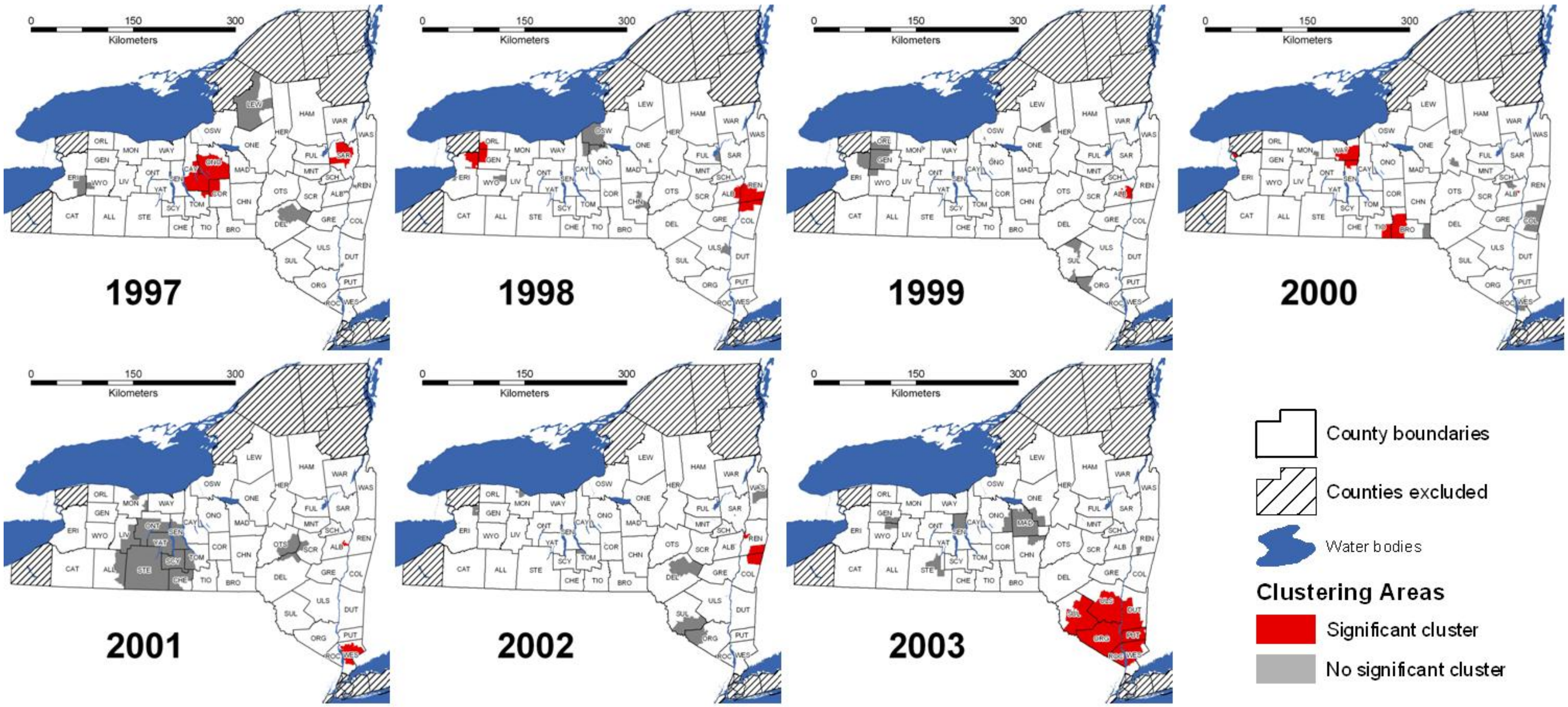

Figure 3.5. Terrestrial rabies clusters adjusted for covariates (land use type, land elevation, presence of major roads, presence of rivers/lakes, human population density, and protection from adjacent ORV exposed area) and large scale geographical variation (county, ecoregion, and latitude), New York, 1997-2003.

***County abbreviations**: ALB: Albany; ALL: Allegany; BRO: Brooome; CAT: Cattaraugus; CAY: Cayuga; CHE: Chemung; CHN: Chenango; COL: Columbia; COR: Cortland; DEL: Delaware; DUT: Dutchess; ERI: Erie; FUL: Fulton; GEN: Genesee; GRE: Greene; HAM: Hamilton; HER: Herkimer; LEW: Lewis; LIV: Livingston; MAD: Madison; MON: Monroe; MNT: Montgomery; ONE: Oneida; ONO: Onondaga; ONT: Ontario; ORG: Orange; ORL: Orleans; OSG: Oswego; OTS: Otsego; PUT: Putnam; REN: Rensselaer; ROC: Rockland; SAR: Saratoga; SCH: Schenectady; SCR: Schoharie; SCY: Schuyler; SEN: Seneca; STE: Steuben; SUL: Sullivan; TIO: Tioga; TOM: Tompkins; ULS: Ulster; WAR: Warren; WAS: Washington; WAY: Wayne; WES: Westchester; WYO: Wyoming; YAT: Yates.*

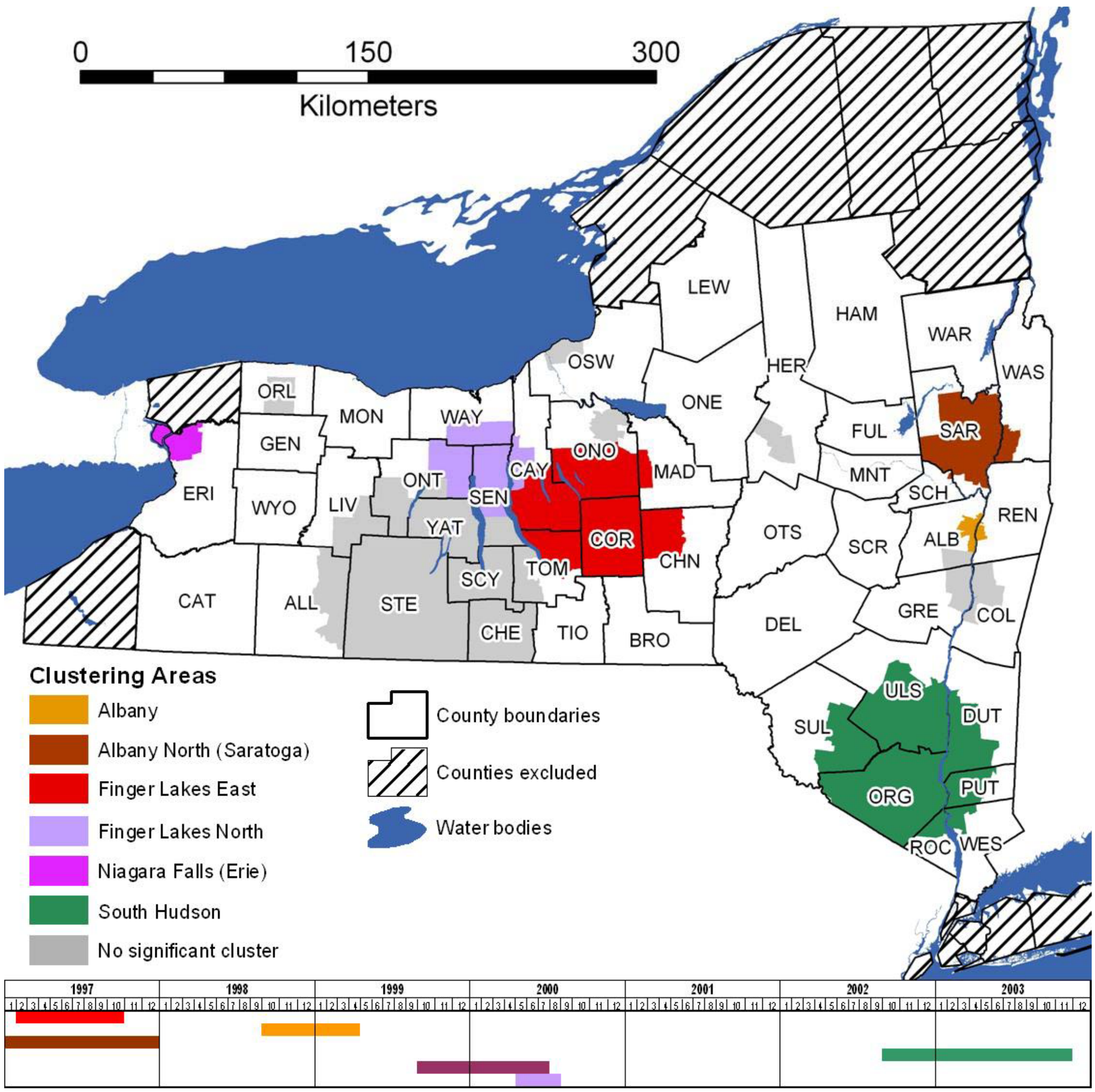

Figure 3.6. Location of statistically significant ($p \leq 0.05$) terrestrial rabies clusters, New York, 1997-2003, for space-time permutation cluster search.

Chapter 4:

Risk-based cost modeling of oral rabies vaccine interventions for raccoon rabies

4.1. Abstract

Oral rabies vaccine (ORV) is an effective but costly strategy to control raccoon rabies. Due to high costs, ORV for raccoon rabies in the U.S. has been limited to epizootic areas, with few and brief attempts to use ORV in enzootic areas, leaving extensive raccoon rabies regions without any ORV intervention.

Several cost scenarios for oral rabies vaccine (ORV) application in raccoon rabies enzootic and epizootic regions were modeled in New York State to obtain the total cost of ORV baits per scenario and potential savings compared with uniform ORV baiting strategies. These cost scenarios modeled application of ORV baits at different densities according to levels of risk defined by the observed number of raccoon rabies cases per km^2, and the expected number of cases per km^2 estimates calculated with a Poisson model, at the census tract level.

The cost scenarios resulted in lower bait purchase costs than uniform baiting, for both the NYS enzootic region and the Long Island epizootic zone. The proportion of savings for the NYS enzootic region was 29.57% (cost scenario based on expected number of cases per km^2). The proportion of savings for the Long Island epizootic zone was 38.9% (cost scenario based on expected number of cases per km^2).
Keywords: raccoon rabies; cost savings; risk assessment; Poisson regression.

4.2. Introduction

The currently licensed oral rabies vaccine (ORV), a vaccinia-rabies glycoprotein recombinant vaccine (V-RG), has been used to control the raccoon rabies variant in North America since 1990.[1] The vaccine, Raboral V-RG™, is manufactured by Merial, and has been demonstrated to be effective at reducing the number of raccoon rabies cases.[2-3] The vaccine is administered as liquid in packets placed inside oral baits made of fishmeal that is attractive to raccoons.[4] The ORV baits are dropped by air or distributed by manual baiting on the ground.[5-6] Most ORV interventions are intended to build immune barriers in unaffected areas to avoid spread of the epizootic[7-9] and to control point source introductions of rabies in new areas.[10] Although some ORV use in enzootic areas has been reported,[6,11-12] this use in large raccoon rabies enzootic areas has not been fully evaluated due to high costs and limited resources.[9,13-15] At a purchase cost of $1.30, the ORV bait is a major component of ORV program cost,[13] and reductions in the number of baits through prioritization of high and low risk areas can potentially have a large impact on the cost of an ORV program or allow coverage of wider enzootic areas for the same cost.

The number of ORV baits needed in an intervention depends on the intervention area size and the bait densities (number of baits per area).[16] There are no fixed rules for bait densities, but some studies have identified bait densities that produce acceptable raccoon seroconversion rates. For immune barriers, 50-75 baits/km^2 were reported effective in NYS.[7,12] Higher densities such as 144 baits/km^2 have been proposed for responding to rabies point source infection introductions,[10] and a density of 120 baits/km^2 was used in Nassau County, New York in an unsuccessful attempt to eradicate a point source introduction in 2004.[17] Enzootic raccoon rabies was reduced, but not eliminated, in New York State (NYS) with the use of 50-100 baits/km^2.[11-12] The total number of baits required in an ORV intervention equals the bait density times the intervention area. Although baits may not be applied homogeneously to the intervention areas, guidelines have not been developed for differential bait densities according to the risk for raccoon rabies.

This study models ORV bait numbers and costs at different levels of raccoon rabies risk. The models are explored in two study areas, the NYS enzootic region and the newly infected Long Island epizootic zone.

4.3. Materials and methods

Study parameters

In this study the primary requirement for an ORV intervention area, defined at the census tract level, was the need for raccoon rabies control. To target areas where ORV was needed, the following criteria were used: land elevation, presence of raccoon rabies risk, and absence of current ORV programs.

Elevation was included because raccoons are less likely to inhabit higher elevations.[18] In this study the elevation of the census tract centroid was used, even though some areas of the census tract would be at lower or higher elevations. Animal rabies case data from the NYS enzootic region not exposed to ORV was examined to confirm the role of land elevation in the distribution of raccoon rabies. The number of raccoon rabies cases in a census tract was plotted by elevation above sea level and it was found that 92.2% (4,096) of the cases occurred at or below an elevation of 500 meters, 7.2% (320)

occurred at elevations between 500 and 650 meters, and only 0.6% occurred at elevations higher that 650 meters. Based on this data, the elevation cut point for including census tracts in the intervention area was set at 650 meters. It was also observed that some census tracts between 500 and 650 meters did not have any reported raccoon rabies activity during 1997-2003 and may not need intervention; therefore a rule was created to exclude census tracts above 500 meters that did not report cases in the seven-year period prior to the intervention modeling.

For this study, the cost was set at $1.30, as previously reported.[13] This study modeled only the total cost of baits required for one ORV intervention using a bait density (number of baits per km^2) of 50 baits/km^2 for enzootic areas and 300 baits/km^2 for newly infected areas. Only areas without ORV programs were eligible for inclusion (see below).

Study areas

Two study areas were included: the raccoon rabies enzootic region in NYS and the recently infected zone in Long Island, New York. These regions are exclusive and are separated by New York City, which functioned as a man-made barrier protecting Long Island from spread of the disease in the last 15 years.

NYS raccoon rabies enzootic region. The cost scenarios described below were developed for the modeled ORV intervention area in the NYS enzootic region. The intervention area of the NYS enzootic region included upstate New York (excludes New York City and Long Island) and areas without any current ORV programs. The areas excluded due to the presence of ORV programs were: Clinton, Essex, St. Lawrence, Jefferson, Lewis, Niagara, Erie, and Chautauqua counties, the northeastern corner of

Oswego County, and the northwestern corner of Franklin County. Areas not exposed to ORV from Franklin County were isolated from the enzootic area by the Adirondack Mountains and the ORV exposed areas. Therefore, the remaining 11 census tracts in Franklin County would not require ORV in this model and were also excluded.

From the 1,628 census tracts remaining after the exclusion of ORV exposed areas and isolated census tracts, 11 census tracts with a centroid higher than 650 meters above sea level were excluded; those census tracts were located in Cattaraugus, Delaware, Greene, Hamilton, Schoharie, Ulster, and Warren counties. Thirteen more census tracts with a centroid 500-650 meters above sea level and without terrestrial rabies cases during 1997-2003 were also excluded; those census tracts were located in Cattaraugus, Delaware, Fulton, Herkimer, Hamilton, Oneida, Sullivan, Steuben, and Warren counties. Finally, 1,604 census tracts were included in the modeled intervention area with an average elevation of 185.96 meters above sea level (range: 0 – 646 m).

<u>Long Island epizootic zone</u>. The recently raccoon rabies-infected area in Long Island was chosen to apply the proposed methods to a new enzootic area where the raccoon rabies risk is unknown but can be estimated using geographical information, environmental features, man-made features and demographics of the area. To calculate the expected number of cases in the Long Island epizootic zone, the Poisson regression model previously developed for raccoon rabies in NYS was applied as previously described.[19]

The Long Island epizootic in this study included Queens, Nassau, and Suffolk counties. The ORV modeled intervention area covered all Long Island, and excludes most of New York City. Queens County belongs to the New York City area but was included because it is the easternmost part of New York City and westernmost end of Long Island, bordering Nassau County where the epizootic is active.[9,17] ORV Interventions in Queens County may be required to control rabies spread within the epizootic area. All the 1,255 census tracts in the three counties were included because none of the exclusion criteria were relevant. The average elevation for those census tracts was 20.4 meters above sea level (range: 0 – 94 m.).

Data

Baiting area. The area (km^2) of each census tract was calculated in ArcView 8.3™. The NYS USGS Land Cover satellite imagery data was used to calculate the area under water in each census tract. The net area for ORV baiting in a census tract was calculated by subtracting the areas under water from the census tract area, because baits are not dropped over water. The total intervention area and the area of each stratum were obtained by adding the net area for ORV baiting of all census tracts included in the intervention areas or in each of the corresponding strata.

Observed cases. The observed number of terrestrial rabies cases per census tract was extracted from the Zoonoses program-NYSDOH rabies geodatabase created for a previous study.[19] This database includes terrestrial rabies cases from NYS geocoded to geographical coordinates of the reported location of confirmed rabid terrestrial animals. The cases for 1997-2003 were matched to the corresponding census tracts in the ORV intervention area for the NYS enzootic region. The total number of cases by census tract was calculated and the observed number of cases per square kilometer at the census tract level (raccoon rabies cases/km^2) was also obtained.

Although some rabies case data of the Long Island epizootic zone were available from the initial phase of the outbreak, those cases were not used in this study The Long Island epizootic zone was modeled as it was pre-outbreak, as an example of an unaffected area and how baiting could be applied early in an outbreak with little case data.

Expected cases. The expected number of cases by census tract was calculated using a Poisson regression model previously developed to study raccoon rabies in NYS.[19] The Poisson model included as the dependent variable the number of raccoon rabies cases in a census tract in a year and as independent variables the proportion of land use types in a census tract, land elevation, human population density, presence of major roads, presence of rivers/lakes, and location adjacent to an ORV exposed area. This model also adjusted for overdispersion and included county, latitude, and ecoregion as large scale geographical variation (LSGV) adjustments. The Poisson regression model and predicted value calculations were performed with SAS PROC GENMOD,[20] for all census tracts in the intervention areas without excluding those at higher elevations. The predicted number of raccoon rabies cases for each census tract was utilized to calculate the expected number of cases per square kilometer (raccoon rabies expected cases/km^2).

Strata building

Rabies risk strata were built in Arcview 8.3™ for the observed number of cases, and the expected number of cases. For the observed and the expected number of cases per square kilometer, four risk strata were constructed by grouping the census tracts in quartiles by the number of observed or expected cases. The categories formed were for very low risk (first quartile), low risk (second quartile), moderate risk (third quartile), and high risk (fourth quartile).

Cost scenarios

Three cost scenarios are presented. The total cost for any scenario is obtained by multiplying the number of required baits and the cost of one bait ($1.30). The number of baits required is calculated by multiplying the bait density per square kilometer and the intervention area (excluding underwater area) in square kilometers, then rounded to the nearest whole bait. A first scenario and basis for the comparisons in this study is the "uniform baiting" scenario, in which ORV baits are applied with the same density to the whole intervention area.

The other two cost scenarios in this study apply bait according to calculated levels of risk. They are named according to the information used to build the risk strata. They are: observed number of cases per km^2, and expected number of cases per km^2. Bait density was then determined according to the risk level of each strata.

Enzootic Area: In an enzootic area such as New York with several years of rabies surveillance, all the data required to build the cost scenarios was available. Two cost scenarios based in differential risk were built, one using the observed number of cases per km^2 and the other using the expected number of cases per km^2.

To calculate the number of baits required for each risk strata, variations of 50% of the chosen bait density for enzootic regions (50 baits/km^2) are proposed in this study. The density of 50 baits/km^2 is the minimum density that was reported to reduce raccoon rabies.[11-12] Four strata were built grouping the census tract by quartiles. The bait density for the two middle strata (low risk and moderate risk) was set at 50 baits/km^2. The bait density for the upper strata (high risk) was 50% more (75 baits/km^2) than the two middle strata. The bait density for the lower strata (very low risk) was 50% less (25 baits/km^2) than the middle strata.

Epizootic zone: In newly infected areas, no previous surveillance data is available; therefore, only one differential cost scenario can be developed, the one using the expected number of cases per km^2. A theoretical expected number of cases per census tract can be obtained by applying the Poisson regression model previously developed for raccoon rabies.[19] Intense baiting may be required to control raccoon rabies risk in new areas, prior to the population reduction that occurs with rabies.[10,17] A bait density of 200 baits/km^2 was set for the two middle strata (low risk and moderate risk). Applying the 50% variations as above, 300 baits/km^2 was set for the upper stratum (high risk) and 100 baits/km^2 was set for the lower stratum (very low risk).

The total costs of the baits required for an ORV program in each cost scenario were compared with the costs for uniform baiting. The proportion of potential cost savings for choosing a differential baiting scenario versus the uniform baiting scenario was calculated.

4.4. Results

NYS raccoon rabies enzootic region

The intervention area in the NYS raccoon rabies enzootic region was 76,080.7 km^2, and 3,804,036 baits were needed to apply uniform baiting at a bait density of 50 baits/km^2 (Table 4.1). The cost for uniform baiting in this region was $4,945,246.80, the highest of all cost scenarios in the study. Total costs per scenario with differential levels of risk varied from a low of $3,482,719.07 (2,679,015 baits) in the cost scenario for expected number of case per km^2 (29.57% savings compared to uniform baiting) to a high of \$4,863,210.99 (3,740,932 baits) in the cost scenario for observed cases per km^2 (1.66% savings compared to uniform baiting). The size of the intervention areas and costs for the expected number of cases per km^2 cost scenario were highest in the very low risk strata and smaller in the high risk strata, wile in the cost scenario using the observed number of cases per km^2 the costs were highest in the low risk strata.

The spatial distributions of risk in the NYS raccoon rabies enzootic region for each cost scenario are presented in Figure 4.1. The spatial distribution of the high risk strata in the cost scenario for observed number of cases per km^2 is similar to the distribution in the cost scenario for expected number of cases per km^2 (Figure 4.1). However, the other strata had different distributions. In the observed number of cases per km^2 cost scenario, the very low risk strata was poorly represented, with 6.32% of the intervention area, while in the expected number of cases per km^2 cost scenario it accounted for 62.05% of the area (Table 4.1).

The strata in the cost scenarios were built grouping the number of cases per km^2 in quartiles, because census tracts are areas build on human population numbers, it is expected to observe ~25% of the population represented in each strata after grouping census tract by quartiles. The census tracts that had zero cases observed were 41% of all census tracts in the study, because all those census tracts have the same value, they were included in the lower quartile of the cost scenario based on the observed number of cases per km^2. The census tracts in the very low risk strata covered only a small area (6.3%) of the intervention, but concentrated 33.3% of the total population in the study area (2,107,367 people). For the cost scenario based on the expected number of cases per km^2

the population distribution across strata was more even, with proportions close to 25% population in each strata, as expected for a quartile distribution (Table 4.1).

Long Island epizootic zone

The intervention area in the Long Island epizootic zone was 3,305.82 km^2, and 991,747 baits were needed for uniform baiting at a bait density of 300 baits/km^2 (Table 4.2). The cost for uniform baiting in this zone was $1,289,271.10. In comparison, the total cost for the expected number of cases per km^2 cost scenario was $787,413.90, a cost savings of 38.93%. Across strata, the costs ranged from a low of $162,312.80 in the very low risk strata to a high of $270,636.60 in the high risk strata.

The spatial distribution of the risk strata for the expected number of cases per km^2 cost scenario in the Long Island epizootic zone is presented in Figure 4.3. The very low risk strata covered the largest proportion (37.77%) of the intervention area (Table 4.2), with the low risk strata covering the smallest proportion (17.40%). The moderate risk strata with 23.84% had coverage similar to that of the high risk strata with 20.99%. The high risk areas were concentrated in Nassau County and Queens, New York City, with the less densely populated areas of Suffolk County primarily in the very low risk category (Figure 4.2).

4.5. Discussion

This study modeled the cost of ORV baits to be used in raccoon rabies interventions in enzootic and epizootic areas. The study demonstrated that distributing ORV baits with a differential approach based on the risk for raccoon rabies can be a cost-savings strategy. All of the alternative cost scenarios modeled were less costly than uniform ORV baiting of the intervention area in both the NYS enzootic region and the Long Island epizootic zone.

The proportion of costs "saved" by using differential risk baiting ranged from the trivial (1.66%, for the cost scenario based on the observed number of cases per km^2) to the substantial (~30% for the cost scenario based on the observed number of cases per km^2) for the NYS enzootic region. The savings were even more substantial for the Long Island epizootic zone (38.9%). The results indicated that differential risk-based scenarios would be a beneficial choice when planning ORV interventions, in terms of reducing the bait purchase costs of an ORV program. However, the appropriateness of using a certain cost scenario may depend on the goals of the ORV intervention and the availability of the data required to estimate risk. The choice of the appropriate cost scenario will also make a difference in where higher bait densities will be applied, because the distributions of the risk areas were not the same across all cost scenarios.

The cost scenario based on the observed number of cases per km^2 may not be a good choice, not only because the cost savings obtained are small but because the risk distribution is potentially affected by reporting bias due to differences in human population densities and surveillance efforts across the modeled area. However, it may be possible that in some areas only raccoon rabies data are available and therefore expected values and spatial scan statistics cannot be calculated. In that case, only the cost scenario based on the observed number of cases per km^2 could be modeled. Although the savings in bait purchases using this cost scenario are small and the risk strata distribution may be biased, this strategy is still a better choice than a cost scenario that uses uniform baiting because more of the baits will be applied where more raccoon rabies cases were reported.

Previous studies have demonstrated that baiting targeted to raccoon habitat leads to higher seroprevalence rates than uniform baiting.[3]

The risk strata distribution in the cost scenario based on the expected cases per km^2 represent the risk adjusted for several factors present in the census tract that possibly influence raccoon rabies, and this approach may reduce the effect of reporting bias. This cost scenario is a good choice for an ORV intervention because it relies on an appropriate statistical description of the raccoon rabies risk distribution and additionally may generate a good proportion of cost savings. The expected number of cases per km^2 is especially appropriate for places where the number of cases across a specific area may not be available or reliable, because the intervention area had an inadequate surveillance system or because it is a new epizootic area with no background data on raccoon rabies (as exemplified by Long Island). In such instances only the cost scenario based on expected number of cases per km^2 would be modeled. Data availability on land use type, population density, presence of rivers/lakes, presence of major roads, and proximity to an ORV exposed area are required to model this cost scenario. Fortunately, these data are available in the U.S. and Canada where raccoon variant rabies is enzootic.

The large difference of savings between the costs scenario based in observed number of cases per km^2 (1.6%) and the cost scenario based on the expected number of cases per km^2 (29%) in the NYS enzootic region was dependent of the differences of in the distribution of the area across risk strata. Because the areas of the census tracts are variable, it is possible census tract with large areas resulted with expected number of cases per km^2 lower that the observed cases, therefore, those census tract were relocated in lower risk level than the one they were in the costs scenario based on observed cases per km^2 increasing greatly the area that would receive the lowest bait density.

Some limitations apply to this study. It cannot be guaranteed that the ORV intervention using the cost scenarios proposed will control or ultimately eliminate the spread of raccoon rabies. Efficacy studies should be conducted in any program for applying ORV with any of the cost scenarios presented, and this may add extra cost to the intervention. In addition, this study is based solely on the costs associated with purchasing ORV baits, and does not consider costs associated with bait distribution. This study presents a one-time baiting model. In the process of containing the spread of raccoon rabies, however, several years of baiting may be needed to reduce or eliminate raccoon variant rabies cases.

The bait densities utilized for an enzootic region in this study may not be appropriated. The reported attempt to control raccoon rabies in a enzootic area of NYS with 50-100 baits per km^2 demonstrated acceptable levels of seroconversion with 75 baits/km2,[11] which is the bait density used in our study for the high risk strata areas. The ORV intervention area for that report was surrounded for areas without intervention, allowing for the reinfection of the intervened area. Although, only reduction of cases was achieved in the reported intervention, it is possible that applying the bait densities used in our cost models may be effective to control or eventually eliminate raccoon rabies when the whole enzootic region is intervened avoiding to leave untreated areas that can preserve and reintroduce raccoon rabies to the intervened areas. Regarding with raccoon rabies reintroduction, the role of other species that can not be targeted for rabies vaccination and may act as a reservoir for the raccoon variant, as skunks, should be also considered.

Finally, different models and projected cost savings may be optimum in areas significantly different in geography, climate, and human presence from New York, although these modeling approaches may still be used to identify priority areas for intervention and achieve cost savings. In summary, the cost scenarios presented here contribute to the effort to improve decision-making when planning costly ORV interventions. The appropriate application of these cost scenarios may result in reducing the cost of ORV interventions. Although the efficacy of the interventions using the proposed cost scenarios remains to be tested, improved raccoon rabies control is expected because the models are based on a rational assessment of rabies risk that will allow the distribution of ORV baits to vary along with risk.

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Table 4.1. Bait costs by cost scenario and savings compared to uniform baiting, New York State enzootic area.

Cost Scenario	Strata	Human Population	Area in km^2 (Col A)	Proportion of intervention area	Bait density (n/km^2) (Col B)	Number of baits (A x B) (Col C)	Baits cost in US$ (C x $1.30)	Savings in US$	Proportion of savings
Uniform baiting		6,325,230	76,080.72	100.00%	50	3,804,036	$4,945,246.80	*reference*	*reference*
Observed number of cases per km^2	very low (Q1)*	2,107,367	4,806.80	6.32%	25	120,170	$156,221.00	*N.A.*	*N.A.*
	low (Q2)	1,351,275	48,323.72	63.52%	50	2,416,186	$3,141,041.80	*N.A.*	*N.A.*
	moderate (Q3)	1,544,821	20,667.58	27.17%	50	1,033,379	$1,343,392.70	*N.A.*	*N.A.*
	high (Q4)	1,321,767	2,282.62	3.00%	75	171,197	$222,556.10	*N.A.*	*N.A.*
total		6,325,230	76,080.72	100.00%		3,740,932	$4,863,211.60	$82,035.20	1.66%
Expected number of cases per km^2	very low (Q1)	1,491,434	47,205.03	62.05%	25	1,180,126	$1,534,163.80	*N.A.*	*N.A.*
	low (Q2)	1,658,780	18,407.06	24.19%	50	920,353	$1,196,458.90	*N.A.*	*N.A.*
	moderate (Q3)	1,518,674	8,264.47	10.86%	50	413,224	$537,190.77	*N.A.*	*N.A.*
	high (Q4)	1,656,342	2,204.16	2.90%	75	165,312	$214,905.60	*N.A.*	*N.A.*
total		6,325,230	76,080.72	100.00%		2,679,015	$3,482,719.07	$1,462,527.73	29.57%

** Q1, Q2, Q3, Q4 : Quartiles*
N.A. = not applicable

Table 4.2. Bait costs by cost scenario and savings compared to uniform baiting, Long Island epizootic zone.

Cost Scenario	Strata	Human Population	Area in km^2 (Col A)	Proportion of intervention area	Bait density (n/km^2) (Col B)	Number of baits (A x B) (Col C)	Baits cost in US$ (C x $1.30)	Savings in US$	Proportion of savings
Uniform baiting		4,712,602	3,305.82	100.00%	300	991,747	$1,289,271.10	*reference*	*reference*
Expected number of cases per km^2	very low (Q1)*	1,131,560	1,248.56	37.77%	100	124,856	$162,312.80	*N.A.*	*N.A.*
	low (Q2)	880,996	575.22	17.40%	200	115,045	$149,558.50	*N.A.*	*N.A.*
	moderate (Q3)	1,248,403	788.10	23.84%	200	157,620	$204,906.00	*N.A.*	*N.A.*
	high (Q4)	1,451,643	693.94	20.99%	300	208,182	$270,636.60	*N.A.*	*N.A.*
total		4,712,602				605,703	$787,413.90	$501,857.20	38.93%

** Q1, Q2, Q3, Q4 : Quartiles*
N.A. = not applicable

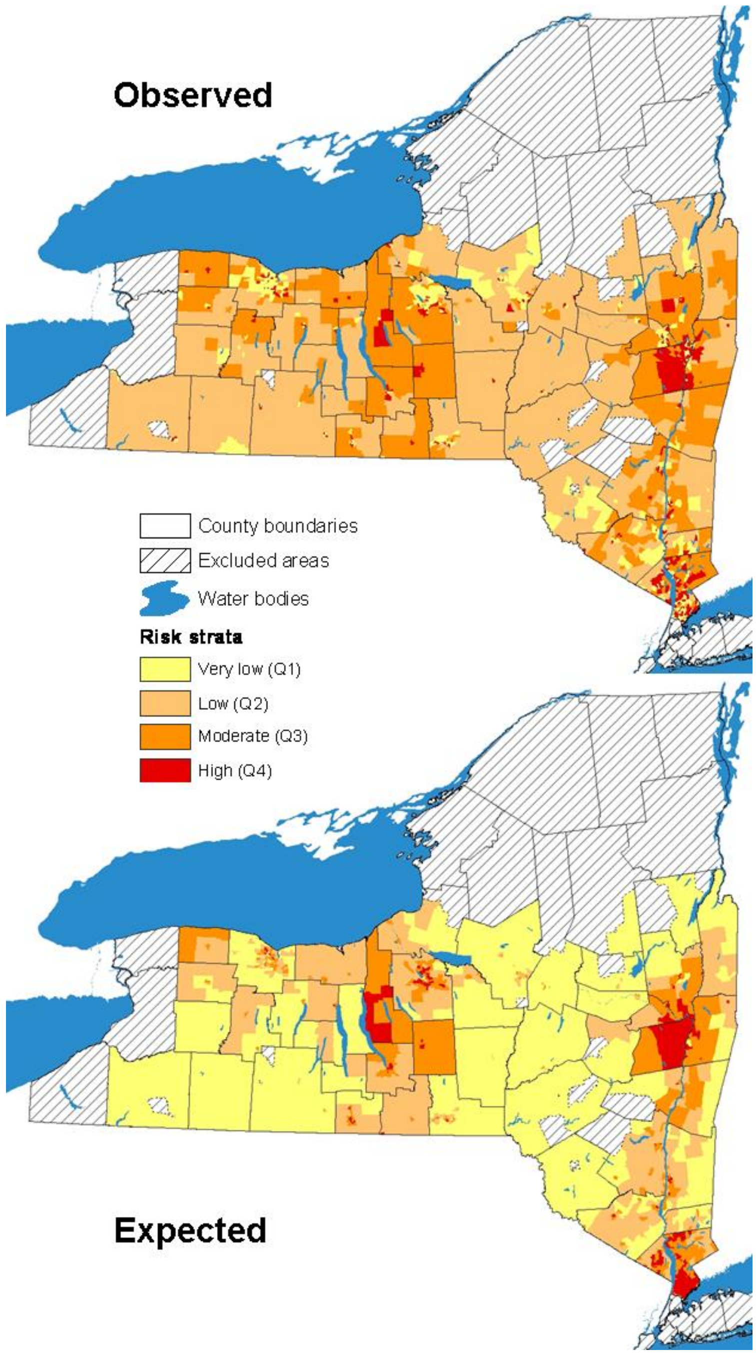

Figure 4.1. Spatial distribution of raccoon rabies risk by census tract modeled with the observed number of cases per km^2, and the expected number of cases per km^2 obtained with a Poisson regression model adjusted for covariates (land use types, population density, presence of major roads, presence of rivers/lakes, and influence of neighboring ORV exposed area) and large scale geographical variation (county, ecoregion, and latitude), NYS enzootic region, 1997-2003.
Q1, Q2, Q3, Q4.: First to fourth quartiles.

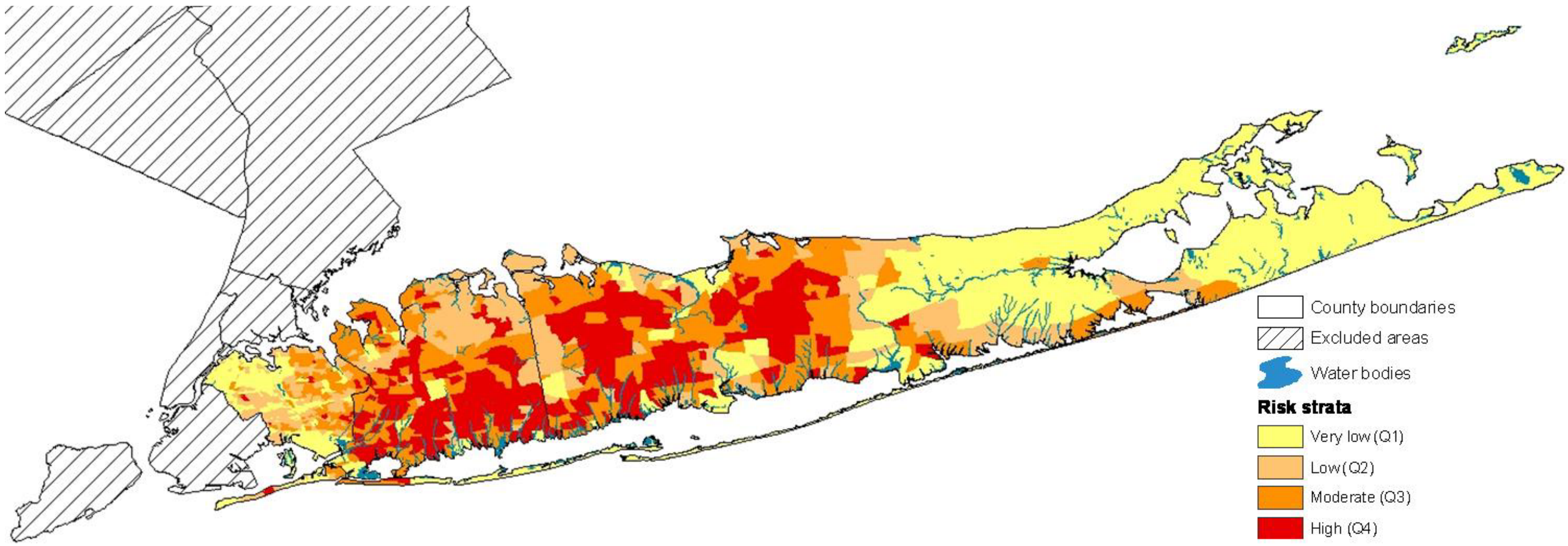

Figure 4.2. Spatial distribution of raccoon rabies risk by census tract modeled with the expected number of cases per km^2 obtained with a Poisson regression model adjusted for covariates (land use types, population density, presence of major roads, presence of rivers/lakes, and influence of neighboring ORV exposed area) and large scale geographical variation (county, ecoregion, and latitude), Long Island epizootic zone.

Q1, Q2, Q3, Q4.: First to fourth quartiles.

Chapter 5:

New York Oral Rabies Vaccination Modeling Overview

The study focused on cost modeling of Oral Rabies Vaccine (ORV) in New York using methods and knowledge from epidemiology, statistics, geographic information systems (GIS), spatial analysis, infectious diseases, wildlife biology, health policy and management, geography, and ecology. The goal was to describe the spatial-temporal characteristics of the raccoon rabies epizootic in NYS, and to identify factors associated with raccoon rabies patterns, distribution, and costs of ORV intervention.

The results demonstrated that modeling bait purchase costs of ORV interventions using differential risk strata may provide cost-savings for ORV programs if the appropriate bait density can be determined based on the risk of rabies in a given area, and if raccoon rabies risk can be modeled at the census tract level using data of raccoon rabies cases, land elevation, land use type, population density, presence of major roads, presence of rivers/lakes, and proximity to an ORV exposed area. A Poisson regression model was developed that can be used to model the risk in the absence of good rabies surveillance data.

5.1. Public health implications

Several findings in the study have public health significance. Associations were found between a lower number of raccoon variant rabies cases and certain land use types, presence of major roads, presence of rivers/lakes, and land elevation. Census tracts with a greater proportion of their area classified as ‘low intensity residential’ (i.e., lower concentration of housing units) and a smaller proportion of their area classified as wetlands were at increased rabies risk. Similarly, census tracts without a river or lake were at increased risk, as were census tracts at lower elevation, and without any major roads to serve as barriers to spread. These factors can be used to prioritize areas for public health rabies planning and executing control activities, even in small areas such as census tracts or towns. ORV interventions can be intensified in areas with more low intensity residential land type, fewer wetlands, fewer major roads, and no lakes or rivers. Census tracts at greater risk for raccoon variant rabies also need to prevent spillover to pets;[1-2] therefore, towns with high risk census tracts could be chosen as preferential places for pet vaccination clinics. These factors can also help determine the location of raccoon traps to increase capture success for ORV seroconversion studies. This is particularly important when the number of captured raccoons needs to be maximized in trap-vaccination-release (TVR) and enhanced surveillance activities.[3-4]

The study also found that raccoon variant rabies cases cluster across an enzootic region, indicating that risk is not uniform in an enzootic region. Results of cluster analysis adjusted for multiple covariates indicated that risk is affected by factors of large scale geographical variation (LSGV) (county, ecoregion, latitude) and factors present in the environment (land use type, population density, presence of rivers/lakes, presence of major roads, and land elevation). Examination of clusters through time demonstrated that the highest risk clusters may persist with some variations through the years. The study also found residual clustering after adjusting for multiple covariates and for LSGV, suggesting the influence of unidentified factors increasing the risk.

These results indicate the need for further research and evaluation of unexplained cluster areas regarding raccoon ecology, area landscape, and the rabies case reporting system; and the need for increased rabies public education in the high risk cluster areas. Identification of areas with greater need for rabies education is important because having more raccoon rabies cases can lead to greater risk for human exposures.[5] Education for the general public on how to deal with potential rabies exposure and how to handle ill or dead wildlife can be prioritized, while at the same time not unduly causing alarm or an artificial increase in surveillance reports. The need for increased and subsidized pet vaccination clinics can be considered for the areas with animal case clusters, if there is a population group with pets and limited resources to pay for vaccinations.[6] Areas with persistent high risk clusters in the Albany and Finger Lakes regions, and areas with increasing risk such as the South Hudson area, need further investigation to clarify the factors that explain the clusters and their persistence. The cluster areas identified can be used as ORV pilot areas or ORV priority areas to intervene if a large ORV program is not possible in the NYS enzootic region.

The primary finding in this study was that distributing ORV baits with a differential approach based on the risk for raccoon rabies is a money-saving strategy. Compared with uniform baiting, about 30% to 40% of the ORV bait cost can be reduced by using differential baiting. The implication of this finding is that baiting can occur at reduced densities in some areas while still targeting rabies risk. The study provided different cost scenario alternatives for several situations in which risk strata can be built for rabies epizootic and enzootic areas. Our results indicate that use of ORV baits in an epizootic area can be optimized with a Poisson regression model based on environmental correlates of raccoon rabies risk. Risk stratification utilizing the expected number of cases obtained with that model is recommended. Application of differential baiting based on risk strata will be a new strategy; thus, efficacy studies should be conducted to determine whether this strategy will produce appropriate levels of seroconversion in response to vaccine distribution along with the cost savings.[4] Reducing the cost of ORV interventions will make ORV more feasible for large enzootic areas,[9-10] and would allow reallocation of resources for other raccoon rabies prevention activities. Large areas currently baited for immune barriers[10-12] can also benefit by applying differential baiting either to parts of the barrier or to emergency baiting of adjacent areas when a breach in the barrier occurs, as reported in recent years.[13]

Efficacy studies are a critical component of ORV interventions;[7-8] however, studies specific for the differential baiting strategy may initially increase costs if they are done more intensively to evaluate the new strategy. The use of a differential ORV baiting strategy implies that ORV evaluation activities such as raccoon trapping for serum tests and rabies specimen submission may increase inversely with the risk strata level, meaning that higher risk areas will require less trapping effort because of the larger number of raccoons and rabid animals, and lower risk areas will require more trapping effort, because there are likely to be fewer raccoons in lower risk areas.

This dissertation presented the first study that examined the association of these factors using the geographical coordinates of rabid animals in NYS, and the first to develop risk estimates at the census tract level in NYS. This is also the first study using the spatial scan statistic to identify terrestrial rabies clusters in an enzootic area using geocoded point data (latitude/longitude). Finally, this is the first attempt to model ORV bait purchase costs using a differential baiting approach based on risk.

The results presented help to increase understanding of enzootic raccoon rabies in its natural state. The use of the ORV cost models developed in this study potentially contribute to increase cost-efficiency and potential cost-benefits of ORV interventions for raccoon rabies, in epizootic and enzootic scenarios. These models can be used during the decision-making process when ORV interventions are planned, as technical tools to increase the feasibility of ORV interventions for large regions.

The study also provided a NYS raccoon rabies risk map at the census tract level that can be used for planning raccoon rabies prevention activities other than ORV. Those maps describe the raccoon rabies risk distribution before ORV intervention, and can be used as a baseline to compare improvement potentially associated with future ORV interventions.

The cost model was developed to save economic resources, improve the feasibility of ORV interventions, and ultimately to enhance control of raccoon rabies. If agencies use these models of raccoon rabies differential risk for planning ORV baiting interventions to produce better disease control, there will be a potential beneficial impact with a lower number of people exposed to rabid wildlife.[5] Human lives can be better protected and human rabies treatment costs can then be significantly reduced.[14]

5.2. Study strengths

The use of NYS to model factors associated with raccoon rabies and its spatial and temporal patterns is an important strength of this study. The results obtained have public health significance for enzootic regions in general because the NYS enzootic region included in this study was not exposed to ORV, is very heterogeneous in geographic features, is large in area, and is served by a good rabies surveillance system. Computerization of the surveillance system was established in 1994 and by 1997 was fully consolidated. This study used data from the years 1997-2003 that have been reviewed and are considered reliable by the Wadsworth Center. This study used seven years of rabies surveillance data to provide acceptable sample sizes for the analyses. Therefore, the results provide insights into the natural history of raccoon rabies, and the methods can be applicable to other similar enzootic regions.

Another strength of this study is the use of the census tract as a unit of analysis. Previous studies reported raccoon rabies at the county and town level.[15-18] This study geocoded raccoon rabies case addresses to the precise latitude/longitude point. Using addresses geocoded to the coordinate level not only provided a more precise description of the location of the incident, it also allowed us to correct the location of cases that would have been assigned to a reporting county that is different from the place of the rabies incident, and because town areas may cross county boundaries. Geocoding to geographical coordinates allowed assigning the case to the correct census tract.

A problem addressed in this study is the unavailability of raccoon population estimates. Most epidemiological disease analyses require population data. Because the raccoon population studies are few and restricted to small areas,[19-21] calculation of raccoon rabies rates (per 100,000 raccoons, for example) is not possible. This study demonstrated that in absence of raccoon population data, differential risk can be assigned to census tracts in modeling the raccoon rabies risk. The methods used in this study can be replicated for other zoonotic diseases in which wild animals are involved such as leptopirosis, and for wildlife diseases not transmissible to humans.

This study also presented the development of a Poisson model for raccoon rabies for an enzootic region, and its potential application in an epizootic region. The model allowed us to assess raccoon rabies risk in an area not yet infected or recently infected. The Long Island epizootic zone presented as a good example of the potential use of the model to improve planning and budgeting of ORV intervention in newly epizootic areas.[7,22]

5.3. Conclusion

The conclusion of this study is that ORV baiting interventions for raccoon rabies can be modeled and applied considering differential risk to reduce costs by at least 30% compared with uniform baiting strategies.

5.4. Study limitations

Some limitations apply to this study. The cost model can not be guaranteed to be effective. Efficacy studies are needed before confirming a specific cost scenario as optimal for ORV baiting protocols. The bait densities may need to be adjusted after efficacy studies and this may change the amount of bait costs saved.

The distribution of land use type in some rabies enzootic regions or areas susceptible for raccoon rabies may be very different from NYS; therefore, it is possible that applying the Poisson regression model developed from the NYS enzootic region would not be appropriate and new models would need to be developed. Similarly, the presence of unidentified factors in other regions may be more important and that may limit the applicability of the specific Poisson regression model developed in NYS. However, the general approach of this study may still be very applicable and useful in other areas.

The models and analysis in this study were specifically developed for raccoon rabies, and they may not be applicable to other rabies variants, although the study methodology may be helpful. Thus, the impact of applying the results of this study will be limited to raccoon rabies in North America.

5.5. Future research suggested

As mentioned previously, efficacy studies are the next step to assess the cost models presented in this study. The current Nassau County raccoon rabies outbreak in Long Island is an opportunity to test the efficacy of the cost model that used the expected number of cases per km^2 to stratify risk.

Further modeling of associated factors can also be done. In this study, a Poisson regression adjusted for LSGV was used to model the number of cases of raccoon rabies at the census tract level. In chapter 2, we mentioned that other statistical methods are available to study events that are spatially correlated as generalized linear mixed models.[23] A generalized linear mixed model can be used to replicate the modeling of factors associated with raccoon rabies and compare the results with the ones presented in this study.

Rabies remains an important zoonotic disease in the world that results in tens of thousands of deaths every year and has a large economic impact.[24-25] Although the study did not study other rabies variants, the principles used to assess risk can be modified in applications to other rabies variants, and in other countries with limited resources. Much of the data required for modeling other rabies variant is likely to be available. Currently, geographic data from satellite images is available online for the entire world, sometimes for free.[26] The World Health Organization maintains a rabies surveillance system at the regional level and supports many national surveillance systems for rabies and other diseases with information that can be used for modeling.[25]

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Appendix 1. Rabies specimen history, form DOH-487z

NEW YORK STATE DEPARTMENT OF HEALTH
Wadsworth Center

Rabies Specimen History

Instructions: Please type or print with black ink.
Completed history is required for specimen examination.

FOR LABORATORY USE ONLY

Lab No. ____________________

Date ____________________

1. Kind of animal	2. Breed/Species	3. Age	4. Sex ☐ M ☐ F

5. Animal location
   Town ____________ County ____________
   Exact location - Street address or route (road) and distance to nearest intersection (identify):
6. Submitted animal's rabies vaccination status: ☐ current ☐ not current ☐ unvaccinated ☐ unknown
7. Was the animal sick or acting strangely? ☐ yes ☐ no
   Signs of rabies: ☐ neurologic disorder ☐ paralysis ☐ difficulty swallowing ☐ unusual aggression
   Other, describe: ____________
8. Date of death: ____ / ____ / ____
9. If killed, how? ____________
10. Owner/complainant name ____________ Tel. No. (____) ____ - ____
    Address ____________
    No. & Street ____________ City ____________
11. Has any person been bitten by this animal?
    ☐ no ☐ yes date ____ / ____ / ____
    If yes, please give details including name, address and telephone number.
12. Was any person scratched or in direct contact with animal's saliva or nervous tissue?
    ☐ no ☐ yes date ____ / ____ / ____
    If yes, please give details including name, address and telephone number.
13. Was this animal in contact with a pet or domestic animal?
    ☐ no ☐ yes date ____ / ____ / ____
    If yes, Species ____________ Owner's name ____________
    Address ____________ Tel. No. (____) ____ - ____
    Exposed pet or domestic animal's vaccination status: ☐ current ☐ not current ☐ unvaccinated ☐ unknown
14. Specimen submitted by:
    Name ____________ Agency ____________
    Address ____________

FOR LABORATORY USE ONLY

LABORATORY REPORT

This is a FINAL report. Results of virus isolation tests will be reported only if they contradict the fluorescent antibody test.

☐ The fluorescent antibody test was negative for evidence of rabies.

☐ The specimen was unsatisfactory for examination due to: ☐ decomposition ☐ inappropriate tissue ☐ mutilation ☐ other ____________

☐ Other ____________

☐ EVIDENCE OF RABIES WAS FOUND BY THE FLUORESCENT ANTIBODY TEST. Container ☐

DOH-487z (5/95)

Appendix 2. Characteristics of NYS EPA ecoregions Level III

ATLANTIC COASTAL PINE BARRENS

• Grained soils and Oak-pine potential natural vegetation
• Moderately flat, but not too irregular surface

ERIE DRIFT PLAINS

• Farms, many associated with dairy operations.
• Low rounded hills, scattered end moraines, kettles, and areas of wetlands.
• Areas of urban development and industrial activity occur locally

E. GREAT LAKES & HUDSON LOWLANDS

• Irregular plains bordered by hills
• Less surface irregularity and more agricultural activity and population density than the adjacent ecoregions
• Orchards, vineyards, and vegetable farming
• Large percentage of the agriculture is associated with dairy operations

NORTH CENTRAL APPALACHIANS

• More forest covered than adjacent ecoregions
• Part of an elevated plateau composed of horizontally bedded sandstone, shale, siltstone, conglomerate, and coal
• Plateau surfaces, high hills, and low mountains
• Forestry and recreation

NORTHERN APPALACHIAN PLATEAU AND UPLANDS

• Much of this region is farmed and in pasture
• Hay and grain for dairy cattle are the principal crops
• Large areas are in forests of oak and northern hardwoods

NORTHEASTERN COASTAL ZONE

•Forests and residential development
•Great concentrations of human population
•Relatively nutrient poor soils
•Less surface irregularity than other ecoregions

NORTHEASTERN HIGHLANDS

•Nutrient poor soils blanketed by northern hardwood and spruce fir forests
•Relatively sparsely populated region
•Low mountains in the southwest and central portions to open high hills in the northeast

RIDGE AND VALLEY

•Forests cover about 50% of the region
•Springs and caves are relatively numerous
•Diverse aquatic habitats and species of fish

Source: http://www.hort.purdue.edu/newcrop/cropmap/ecoreg/descript.html

Appendix 3. NYS land use types from USGS-National Land cover data.

1. Water - All areas of open water or permanent ice/snow cover.

- **Open Water** - All areas of open water; typically 25 percent or greater cover of water (per pixel).
- **Perennial Ice/Snow** - All areas characterized by year-long cover of ice and/or snow.

2. Developed - Areas characterized by a high percentage (30 percent or greater) of constructed materials (e.g. asphalt, concrete, buildings, etc).

- **Low Intensity Residential** - Includes areas with a mixture of constructed materials and vegetation. Constructed materials account for 30-80 percent of the cover. Vegetation may account for 20 to 70 percent of the cover. These areas most commonly include single-family housing units. Population densities will be lower than in high intensity residential areas.

- **High Intensity Residential** - Includes highly developed areas where people reside in high numbers. Examples include apartment complexes and row houses. Vegetation accounts for less than 20 percent of the cover. Constructed materials account for 80 to100 percent of the cover.

- **Commercial/Industrial/Transportation** - Includes infrastructure (e.g. roads, railroads, etc.) and all highly developed areas not classified as High Intensity Residential.

3. Barren - Areas characterized by bare rock, gravel, sand, silt, clay, or other earthen material, with little or no "green" vegetation present regardless of its inherent ability to support life. Vegetation, if present, is more widely spaced and scrubby than that in the "green" vegetated categories; lichen cover may be extensive.

- **Bare Rock/Sand/Clay** - Perennially barren areas of bedrock, desert pavement, scarps, talus, slides, volcanic material, glacial debris, beaches, and other accumulations of earthen material.

- **Quarries/Strip Mines/Gravel Pits** - Areas of extractive mining activities with significant surface expression.

- **Transitional** - Areas of sparse vegetative cover (less than 25 percent of cover) that are dynamically changing from one land cover to another, often because of land use activities. Examples include forest clearcuts, a transition phase between forest and agricultural land, the temporary clearing of vegetation, and changes due to natural causes (e.g. fire, flood, etc.).

4. Forested Upland - Areas characterized by tree cover (natural or semi-natural woody vegetation, generally greater than 6 meters tall); tree canopy accounts for 25-100 percent of the cover.

- **Deciduous Forest** - Areas dominated by trees where 75 percent or more of the tree species shed foliage simultaneously in response to seasonal change.

- **Evergreen Forest** - Areas dominated by trees where 75 percent or more of the tree species maintain their leaves all year. Canopy is never without green foliage.

- **Mixed Forest** - Areas dominated by trees where neither deciduous nor evergreen species represent more than 75 percent of the cover present.

5. Shrubland - Areas characterized by natural or semi-natural woody vegetation with aerial stems, generally less than 6 meters tall, with individuals or clumps not touching to interlocking. Both evergreen and deciduous species of true shrubs, young trees, and trees or shrubs that are small or stunted because of environmental conditions are included.

- **Shrubland** - Areas dominated by shrubs; shrub canopy accounts for 25-100 percent of the cover. Shrub cover is generally greater than 25 percent when tree cover is less than 25 percent. Shrub cover may be less than 25 percent in cases when the cover of other life forms (e.g. herbaceous or tree) is less than 25 percent and shrubs cover exceeds the cover of the other life forms.

6. Non-natural Woody - Areas dominated by non-natural woody vegetation; non-natural woody vegetative canopy accounts for 25-100 percent of the cover. The non-natural woody classification is subject to the availability of sufficient ancillary data to differentiate non-natural woody vegetation from natural woody vegetation.

- **Orchards/Vineyards/Other** - Orchards, vineyards, and other areas planted or maintained for the production of fruits, nuts, berries, or ornamentals.

7. Herbaceous Upland - Upland areas characterized by natural or semi-natural herbaceous vegetation; herbaceous vegetation accounts for 75-100 percent of the cover.

- **Grasslands/Herbaceous** - Areas dominated by upland grasses and forbs. In rare cases, herbaceous cover is less than 25 percent, but exceeds the combined cover of the woody species present. These areas are not subject to intensive management, but they are often utilized for grazing.

8. Planted/Cultivated - Areas characterized by herbaceous vegetation that has been planted or is intensively managed for the production of food, feed, or fiber; or is maintained in developed settings for specific purposes. Herbaceous vegetation accounts for 75-100 percent of the cover.

- **Pasture/Hay** - Areas of grasses, legumes, or grass-legume mixtures planted for livestock grazing or the production of seed or hay crops.

- **Row Crops** - Areas used for the production of crops, such as corn, soybeans, vegetables, tobacco, and cotton.

- **Small Grains** - Areas used for the production of graminoid crops such as wheat, barley, oats, and rice.

- **Fallow** - Areas used for the production of crops that are temporarily barren or with sparse vegetative cover as a result of being tilled in a management practice that incorporates prescribed alternation between cropping and tillage.

- **Urban/Recreational Grasses** - Vegetation (primarily grasses) planted in developed settings for recreation, erosion control, or aesthetic purposes. Examples include parks, lawns, golf courses, airport grasses, and industrial site grasses.

9. Wetlands - Areas where the soil or substrate is periodically saturated with or covered with water as defined by Cowardin et al.

- **Woody Wetlands** - Areas where forest or shrubland vegetation accounts for 25-100 percent of the cover and the soil or substrate is periodically saturated with or covered with water.

Emergent Herbaceous Wetlands - Areas where perennial herbaceous vegetation accounts for 75-100 percent of the cover and the soil or substrate is periodically saturated with or covered with water.

Appendix 4. NYS land use type grouped categories and NYS EPA ecoregions.