AGENT-BASED MODELING OF RACCOON RABIES EPIDEMIC AND ITS ECONOMIC CONSEQUENCES

DISSERTATION

Completed in Partial Fulfillment of the Requirements for

the Degree Doctor of Philosophy in the Graduate

School of The Ohio State University

By

Pirouz Foroutan, M.A.

The Ohio State University

2003

Dissertation Committee:

Professor Mario Miranda, Adviser

Professor Brian Roe

Professor Alan Randall

Doctor Martin Meltzer

Approved by

Adviser

Department of Agricultural, Environmental and Development Economics

ABSTRACT

In the United States, rabies strains that infect raccoons have been responsible for the largest increase animal rabies in the past 3 decades. This work includes three articles that analyze: 1) the cost of 8 distributions of oral rabies vaccine (ORV) with strains known to infect raccoons in Ohio between 1997 and 2000, 2) an agent-based simulation of uninterrupted raccoon rabies epidemic in a hypothetical area, and 3) the costs and benefits of different ORV distribution strategies.

Article 1 documents the estimated cost of implementing an ORV program to provide a more efficient use of resources to control and limit the spread of rabies. Accurately measured distribution costs can be used to perform an economic cost-benefit analysis for alternative ORV programs. The existing ORV procedure consists of distributing fishmeal bait containing ORV through various means. The cost of personnel, vehicles, and helicopter and aircraft use and other associated expenses were obtained from field records and interviews with personnel and agencies involved in the ORV program.

Article 2 examines the major characteristics and behavior of raccoon agents and their relation to their environment. Under different parameter values, the models are simulated and results of a hypothetical raccoon rabies event is obtained in terms of the rate of disease movement, shape of the epidemic front and intensity of new infections. The results indicate that model results are sensitive to certain parameters (e.g., aggressiveness

of the epidemic regime, or nutrient regeneration capability of spatial units). Results on the shape of epidemic front proved to be invariant to different selection of model parameters.

In article 3, different ORV distribution strategies were devised to assess the effectiveness of ORV distribution strategies under different assumptions and their potential costs. Based on raccoon rabies literature, incidences of new infections were mapped to economic costs. These costs were used in conjunction with distribution costs obtained in Article 1 to conduct cost-benefit analyses. Results of cost-benefit analysis indicate while ORV distribution is not economically justifiable for the scope of hypothetical model space, the potential for justification of the program in a larger and real space is possible. Dedicated to Parichehreh Ghafouri

ACKNOWLEDGEMENTS

I wish to thank my adviser, Mario Miranda, for his support and encouragement in my choice of methodology, his guidance throughout the writing of my dissertation, and his always inspiring sense of humor.

I am grateful to Brian Roe for his significant contribution in reviewing many drafts of my research, his useful comments, and for persevering with me as my mentor throughout the time it took me to complete this research and write the dissertation.

I thank Martin Meltzer for his intellect and for sharing with me his vast knowledge of health economics. I am thankful for his major contribution in writing the first article of this dissertation and for his continued support in procuring funding for me throughout my graduate career.

I must also thank Alan Randall for teaching me the importance of critical thinking and ethical standards as a professional, and for his continued guidance in my research.

I also wish to thank Elena Irwin for introducing me to the field of agent-based modeling and for her guidance. My thanks go also to Kathleen Smith for providing valuable information from the Ohio Department of Health, and her major contribution in the first article of this dissertation.

This work would not have been possible without the continual support of my wife, Jacquelyn Spangler, and my sisters, Parisa and Pardis, and the inspiration of my son, Cyrus.

v

VITA

December 28, 1963. Born – Bushehr, Iran

1997-2003..... Fellow, The Centers for Disease Control and Prevention

Publications

Foroutan, Pirouz. "Costs of Distributing Oral Raccoon Rabies Vaccine in Ohio: 1997-2000," with Martin I. Meltzer and Kathleen A. Smith, Journal of the American Veterinary Medical Association, 220(2002): 27-32.

Fields of Study

Major Field: Agricultural, Environmental, and Development Economics

TABLE OF CONTENTS

		<u>Page</u>
Abstra	act	. ii
Dedic	cation	. iv
Ackno	owledgements	V
Vita		. vi
List of	f Tables	viii
List of	f Figures	xiii
Articl	les:	
1.	Costs of Distributing Orally Administered Raccoon-Variant Rabies Vaccine in Ohio: 1997-2000	1
Refere	ences: Article 1	. 15
2.	Predicting Movement Of An Infectious Disease: An Agent-Based Modeling Approach	.22
Refere	ences: Article 2	. 57
3.	Economic Analysis of A Raccoon Rabies Abatement Program: An Agent-Based Modeling Approach.	. 97
Refere	ences: Article 3	.112
Biblio	ography	.122
Apper	ndix: Basis for the values of ecological and epidemiological parameters of the model	.127

LIST OF TABLES

<u>Table</u>	Page
1.1	Ohio oral rabies vaccine distribution effort: 1997-2000
1.2	Ground distribution costs of the Ohio oral rabies vaccine (ORV) program
1.3	Air Distribution Costs of the Ohio ORV Program
1.4	Distribution and Financial Costs of the Ohio ORV Program
2.1	Ranking of raccoon habitats
2.2	Models: Article 2
2.3	Average pre-epidemic population densities by land use category65
2.4	Major categories of average population densities for models with Simple nutrient grow back algorithm
2.5	Major categories of average population densities for models with Urban nutrient grow back algorithm
2.6	Comparison of major categories of population densities for models with Simple versus Urban nutrient grow back algorithm
2.7	Comparison of major categories of population densities for models with Uniform versus Normal home range distribution: <i>t</i> statistics67
2.8	Comparison of major categories of population densities for pairs of models with uniform versus normal home range distribution: Z statistics
2.9	Comparison of major categories of population densities for pairs of models with 13-week versus 21-week mating season: Z statistics

<u>Table</u>	<u>P</u>	age
2.10	Consistency of models with Simple nutrient grow back algorithm, uniform home range distribution and 13-week mating season: Z statistics	69
2.11	Consistency of models with Simple nutrient grow back algorithm, uniform home range distribution and 21-week mating season: Z statistics	59
2.12	Consistency of models with Simple nutrient grow back algorithm, normal home range distribution and 13-week mating season: Z statistics	.70
2.13	Consistency of models with Simple nutrient grow back algorithm, normal home range distribution and 21-week mating season: Z statistics	.70
2.14	Consistency of models with Urban nutrient grow back algorithm, uniform home range distribution and 13-week mating season: Z statistics	.71
2.15	Consistency of models with Urban nutrient grow back algorithm, uniform home range distribution and 21-week mating season: Z statistics	.71
2.16	Consistency of models with Urban nutrient grow back algorithm, normal home range distribution and 13-week mating season: Z statistics	.72
2.17	Consistency of models with Urban nutrient grow back algorithm, normal home range distribution and 21-week mating season: Z statistics	.72
2.18	Number of weeks lapsed after onset of rabies until its appearance by quadrant (1 through 8) in models with Simple nutrient grow back algorithm: aggressive vs. non-aggressive epidemic regimes	73
2.19	Number of weeks lapsed after onset of rabies until its appearance by quadrant (1 through 8): in models with Urban nutrient grow back algorithm aggressive vs. non-aggressive epidemic regimes	74
2.20	Order of infection by quadrant (1 through 8) in models with Simple nutrient grow back algorithm: aggressive vs. non-aggressive epidemic regimes.	75

<u>Table</u>	Page
2.21	Order of infection by quadrant (1 through 8) in models with Urban nutrient grow back algorithm: aggressive vs. non-aggressive epidemic regimes
2.22	Number of infections by quadrant in models with Simple nutrient grow back algorithm: comparison of aggressive vs. non-aggressive epidemic regimes
2.23	Number of infections by quadrant in models with Urban nutrient grow back algorithm: comparison of aggressive vs. non-aggressive epidemic regimes
2.24	Number of weeks lapsed after onset of rabies until its appearance by quadrant (1 through 8) in models with aggressive epidemic regime: Simple versus Urban nutrient grow back
2.25	Number of weeks lapsed after onset of rabies until its appearance by quadrant (1 through 8) in models with non-aggressive epidemic regime: Simple versus Urban nutrient grow back
2.26	Order of infection by quadrant (1 through 8) in models with aggressive epidemic regime: Simple versus Urban nutrient grow back algorithm 81
2.27	Order of infection by quadrant (1 through 8) in models with non-aggressive epidemic regime: Simple versus Urban nutrient grow back algorithm
2.28	Number of infections by quadrant in models with aggressive epidemic regime: Simple versus Urban nutrient grow back algorithm
2.29	Number of infections by quadrant in models with non-aggressive epidemic regime: Simple versus Urban nutrient grow back algorithm 84
2.30	Speed of epidemic front in models with aggressive epidemic regime: uniform versus normal home range distribution
2.31	Speed of epidemic front in models with non-aggressive epidemic regime: uniform versus normal home range distribution
2.32	Order of infection by quadrant (1 through 8) in models with aggressive epidemic regime: uniform versus normal home range distribution

Table

Page

2.33	Order of infection by quadrant (1 through 8) in models with non-aggressive epidemic regime: uniform versus normal home range distribution
2.34	Number of infections in models with aggressive epidemic regime: uniform versus normal home range distribution
2.35	Number of infections in models with non-aggressive epidemic regime: uniform versus normal home range distribution
2.36	Speed of epidemic front in models with aggressive epidemic regime: 13-week versus 21-week mating season
2.37	Speed of epidemic front in models with non-aggressive epidemic regime: 13-week versus 21-week mating season
2.38	Order of infection by quadrant (1 through 8) in models with aggressive epidemic regime: 13-week versus 21-week mating season
2.39	Order of infection by quadrant (1 through 8) in models with non- aggressive epidemic regime: 13-week versus 21-week mating season94
2.40	Number of infections in models with aggressive epidemic regime: 13 weeks versus 21 weeks mating season
2.41	Number of infections in models with non-aggressive epidemic regime: 13 weeks versus 21 weeks mating season
2.42	Summary of effects of model variables with respect to speed and shape of epidemic front
3.1	Estimated incremental raccoon rabies cost of an epidemic year in two counties in NJ in 1990
3.2	Estimated cost of administration of pre-exposure prophylaxis and PEP in Massachusetts
3.3	Estimated number of rabies prophylaxis patients and its incremental unit cost per km^2 in epidemic years in Massachusetts: 1991-1995116
3.4	Estimated number of rabies patients, PEP biologics cost, and additional unit cost per km ² in epidemic years in Connecticut: 1990-1994 117

<u>Table</u>		Page
3.5	Estimated number of rabies patients, PEP biologics cost, and additional unit cost per km ² in epidemic years in four counties in NY: 1992-1994	117
3.6	Estimated incremental raccoon rabies unit cost estimates in epidemic years	. 118
3.7	A possible raccoon rabies cost schedule in epidemic and endemic years	.118
3.8	Models: Article 3	. 119
3.9	Number of weeks lapsed after onset of rabies until its appearance by quadrant (1-8)	.119
3.10	Number of infections by quadrant (1-8)	.120
3.11	Net present value of alternative ORV strategies versus an uninterrupted rabies epidemic	.121

LIST OF FIGURES

<u>Figure</u>	Page
1.1	Detection of rabies in raccoons (by year) in the United States and Canada
1.2	Area covered and density of oral rabies vaccine distributed in Ohio; May, 1997 to April, 2000
2.1	Factors relating to the raccoon population density
2.2	Probability distribution of age in wild raccoon population
2.3	Representation of model's space with 7 different land use categories and 16 quadrants
2.4	Home range potential of a raccoon agent with home range of 7 units (2.25 km^2) in a 100 m ² cell lattice
2.5	Two possible home range distributions for the raccoon agents 63
3.1	Representation of model's space with 7 different land use categories and 16 quadrants
3.2	Assumed relationship of vaccine uptake and intensity of ORV bait distribution
3.3	Proportion of susceptibles vaccinated in ORV barrier with different baiting strategies and effectiveness distribution
3.4	Designation of quadrants and ORV barrier in the model's space 115

ARTICLE 1

Costs of Distributing Orally Administered Raccoon-Variant Rabies Vaccine in Ohio: 1997-2000

OBJECTIVE

Analysis of the economic costs of 8 distributions of orally administered rabies vaccine (ORV) with strains known to infect raccoons in Ohio between 1997 and 2000.

INTRODUCTION

In the past 3 decades, rabies in raccoons has spread north from states where it has been enzootic (eg, Florida, Georgia) to Virginia and Maine in the eastern portion of the United States and recently westward into the northeastern portion of Ohio.¹⁻⁸ The western boundary of the current rabies epidemic in raccoons includes the northeastern portion of Ohio, western Pennsylvania, and northwestern West Virginia along the Ohio River (Figure 1.1).⁹ One result of such enzootics of rabies in wildlife can be economic losses.^{1, 2, 10, 11} Aubert¹⁰ estimated that the economic costs of a rabies epidemic in red foxes for a 12-month period in France were in excess of \$25,000,000. Using this cost estimate as a base, Aubert predicted the cost of rabies in red foxes in France to have been over \$400,000,000 in a 15-year period.¹⁰ Uhaa et al¹ estimated that money used to prevent rabies in humans and domestic animals for 2 counties in the New Jersey

(area: 2,137 km²) increased from \$768,500 in 1988 (pre-epizootic year) to \$1,952,000 in 1990 (an epizootic year).

One method used to control and limit the spread of rabies is to vaccinate wildlife hosts with orally administered rabies vaccine (ORV).^{4, 12} An ORV program consists of seasonal distribution of vaccine placed inside baits. The bait for raccoons is made of fishmeal, with a hollow core in which a small plastic bag containing liquid vaccine is placed.^a Baits are distributed over the designated area so that the healthy, susceptible portion of the population that serve as hosts will consume the bait and vaccine and become protected against lethal infection. By immunizing a critical proportion of the raccoon population, the disease is controlled or eliminated.^{6, 13} Torrence et al⁶ defined this critical proportion of immunized animals needed to stop the spread of the disease as either the threshold (or minimum) ratio of vaccinated to susceptible animals, or the minimum density of vaccinated animals per unit area. As an example of the critical portion, empirical observations indicate that a minimum of one fox per km² must be vaccinated to prevent the spread of rabies in red foxes in Europe.¹³ Oral rabies vaccine programs have substantially reduced the prevalence of rabies in foxes in western Europe, rabies in raccoons in Cape Cod, Massachusetts, and Ohio, and rabies in covotes in south Texas.^{3, 8, 10, 14, 15}

Despite these apparent successes, few studies have thoroughly examined the economics of using ORV.¹⁶ One problem preventing such studies is lack of suitable economic

2

data.¹⁶ In the study reported here, an analysis of the costs of distributing ORV baits—to prevent rabies carried by raccoons from spreading westward into Ohio—is conducted.

MATERIALS AND METHODS

<u>Program Description</u>—The Ohio ORV program was implemented by the Ohio Department of Health (ODH) in May 1997, 2 months after a raccoon-variant rabies epizootic was confirmed in Mahoning County in northeastern Ohio. Since its inception, seasonal baitings (ORV distributions) have been performed in the spring and fall of each year in an effort to create a barrier of immune raccoons. To date (Spring 2000), 6 seasonal baitings have been performed. In addition, 2 smaller emergency baitings were carried out in May 1997 (the initial distribution effort) and in June 1999 (in response to a breach of the immune barrier; Table 1.1).

In the first 2 baitings, ground vehicles and a helicopter were used. In subsequent bait operations, fixed-wing aircraft were also used. The ground delivery method, used in urban and other residential areas, typically includes teams of 2 people distributing baits from an automobile; however, in many areas, baits are distributed on foot. Bait delivery by helicopter requires 2 people: the pilot and a crew member to throw baits from the craft. The crew of each fixed-wing aircraft typically includes the pilot, a navigator, and 3 crew members to operate the automatic bait-dispensing machine. Two crews per airplane alternate their flight duties. Typically, each airplane can carry out 4 flights per day, with each flight lasting 2 to 3 hours. Each seasonal bait distribution lasted approximately 1 week, whereas each emergency baiting lasted about 3 days. The target

bait density for all methods of distribution was set at 75 baits/km², with the exception of the April 1999 baiting, when a bait density study was performed (Table 1.1).

<u>Cost Data</u>—Distribution cost data from each of the 8 baitings carried out from May 1997 to April 2000 were obtained (and, in some instances, estimated) by interviews, field observations, and data provided by agencies involved in bait distribution efforts. Costs were categorized by method of distribution (ground or air) and calculated in dollars per square kilometer covered. In some instances, the areas baited with the use of fixed-wing aircraft and helicopter overlapped; hence, the aerial distribution cost could not be divided between these 2 delivery methods.

Ground distribution costs included automobile cost, valued at \$0.31/mile, and the cost of personnel who participated in the ground baiting. The personnel cost was calculated by using the total amount of time each person spent on baiting and other ORV-related tasks (driving to and from baiting areas, doing agency paperwork, etc.) multiplied by his or her hourly wages, plus benefits. The amount of time that each person spent during the ORV effort and his/her hourly wage rate was obtained from interviews.

The air distribution costs included helicopter cost, cost of fixed-wing aircraft (collected in dollars per hour of flight time, including maintenance and insurance), cost of flight crews, fuel cost, cost of administrative and support personnel, and miscellaneous costs. Helicopter services including the aircraft and its pilot and fuel were contracted from the Ohio Department of Transportation at a lump-sum rate. The cost of administrative and support personnel supplied by ODH and other state and local agencies was recorded separately.

The USDA Wildlife Services (USDA-WS) procured fixed-wing aircraft services from the Ontario Ministry of Natural Resources (OMNR) at a fixed contract price. The contract included the use of twin-engine fixed-wing^b aircraft, each fitted with an ORV bait-delivery mechanism. Contract price for each fixed-wing aircraft included the salaries of 2 pilots, 1 engineer, and 2 bait specialists. However, after discussion with the USDA-WS personnel who arranged the contract, it was decided that the negotiated contract price may include an indirect subsidy, in that the USDA-WS may not be charged the full cost of the services provided. To capture the true economic cost, or opportunity cost, of fixed-wing aircraft services, it was estimated by obtaining hourly rental rates of aircraft similar to those used in the bait distribution. The hourly rate charged to rent an aircraft, including operation and maintenance costs, was quoted at \$1000 (Canadian) per hour (an average of \$0.684 US per \$1 Canadian was used for calculation) by a private contractor.^c Personnel cost was calculated by multiplying the total time each person spent on the ORV project or was compensated for (ie, overtime, time off) by his or her hourly wage. The wages of the flight crew and other payments to them such as car rentals, hotel costs, per diem, and compensation time, were estimated or obtained by interviews and field observation.

The ODH paid for the fuel used in the aircraft and also provided personnel for administration of and participation in the ORV program. Wages, travel costs (mileage, hotel, and per diem), and compensation time for ODH personnel and other local, state, and federal agency employees who participated in the aerial distribution effort were included in the aerial distribution costs. Data for such costs were collected by interviewing each person involved and by field observation. Miscellaneous costs were also collected using the same methods and included equipment rental, purchases, and incidental costs for each of the baiting events.

The cost of the ORV, delivered to the ODH in bait form, was not included in the estimates of distribution costs because it represented a fixed cost for the program, but it was included in the calculations for the total cost. The cost of ORV was obtained from the ODH, and the vaccine was purchased directly from the producer.^a The overall bait density was targeted at no less than 75 baits/km², although local area modifications were made by field staff because of variations in raccoon habitats. During the April 1999 baiting, a 1-time study was performed to determine the efficacy of different bait densities, with some areas having a density as high as 300 baits/km². Such densities would not be considered "typical" and it was reasoned that the costs of bait distribution associated with the experiment would be considerably higher than nonexperimental distributions. Therefore the data collected during the April 1999 distribution was considered as having the potential to distort the statistical analysis of the cost data (ie, the April 1999 data are potential outliers). This conclusion led to adding an additional set of calculations to the data analysis.

<u>Data analyses</u>—For each of the 8 bait operations and for each type of distribution (ground or air), cost and input data were distributed into categories representing the most important cost components (ie, wages, automobile mileage, helicopter fees). Costs were then added and divided by the total area covered to provide a mean cost per km^2 for each bait operation. Means and SD were then calculated for the 8 bait operations. Further, because the first seasonal operation (September 1997) and the April 1999 operation (Table 1.1) may both be described as atypical, the means and SD were recalculated, excluding the data from those operations. All data are reported as mean \pm SD.

RESULTS

<u>Ground distribution costs</u>—For ground distribution, 72 (\pm 22) people were used, representing 744 (\pm 290) total personnel hours (Table 1.2). The September 1997 distribution had the highest mean costs because that operation used the most personnel hours used for ground distribution. Personnel costs for the September 1997 distribution accounted for approximately 30% of all ground distribution costs (\$19.24/km² \pm \$6.35/km²). When the September 1997 and April 1999 data were removed (because they were atypical), the cost for ground distribution was \$16.34/km² (\pm \$0.82/km²).

<u>Air distribution costs</u>—Air distribution required 32 (\pm 14) people, representing a mean of 1,310 hours (\pm 476; Table 1.3). The data analyzed include the personnel flying and staffing the helicopter and fixed-wing aircraft, who were paid under contracts. The largest single cost was for the fixed-wing aircraft, at \$40,248 (\pm \$17,560) per baiting,

which accounted for approximately 37% of the total costs, or $24.71/\text{km}^2$ (± $4.65/\text{km}^2$). When the September 1997 and April 1999 data were removed (atypical), the cost for air distribution was $22.47/\text{km}^2$ (± $2.93/\text{km}^2$).

<u>Total distribution costs</u>—The total distribution costs ranged from $17.17/\text{km}^2$ (May 1997) to a maximum of $32.11/\text{km}^2$ (September 1997), with a mean of $23.23/\text{km}^2$ (± $5.20/\text{km}^2$; Table 1.3). When the September 1997 and April 1999 data were removed (atypical), the cost for total distribution was $20.58/\text{km}^2$ (± $2.78/\text{km}^2$). Most of the costs were for aerial distribution (mean, 81,025; Table 1.3), which were 5.1 times greater than ground distribution costs (mean, 15,766; Table 1.2).

The number of baits distributed ranged from 99,154 in May 1997 to a maximum of 751,404 in April 1999 (Table 1.4). When the cost of these baits was added to distribution costs, the total cost for a single bait operation was 153.20/km² (± 44.16/km²). The cost of the bait accounted for a mean of 85% of the total financial cost per km² baited.

<u>Area baited and bait densities</u>—The area designated for seasonal ORV baiting had increased from 3,872 km² in September 1997 (1,100 km² by ground; 2,772 km² by air) to 6,497 km² in April 2000 (830 km² by ground; 5,667 km² by air; Figure 1.2). The expansion in area covered was achieved with a major change in the way bait was distributed. In May 1997, 79% of the area covered was done by the hand baiting method but in April 2000, 87% of the area baited was done from the air. It was not possible to subdivide the area baited from the air into areas baited exclusively by helicopter and those baited exclusively by fixed-wing aircraft, because in some areas, to ensure a higher density of baits, helicopters covered the same ground (ie, increased the bait density) covered by fixed-wing aircraft.

A bait density of $91.00/\text{km}^2$ (± $32.10/\text{km}^2$) was achieved, with higher bait densities by aerial distribution (Figure 1.2). When the April 1999 data were removed (atypical), the bait density was $79.94/\text{km}^2$ (± $14.11/\text{km}^2$)

DISCUSSION

The ORV program for wildlife is the first immunologic tool to fight rabies in animal hosts since vaccination of dogs became widely available in the 1940s. Although successful application of ORV for rabies in foxes in Europe is well recognized, its use for rabies in raccoons in the United States is still emerging.^{1, 3, 4, 10, 14} The lack of data regarding the long-term effectiveness of the orally administered rabies vaccine used in situations such as those described here prevents one from comparing the cost of various distribution methods to the reduction of rabies (ie, performing a cost-effectiveness analysis of the various distribution methods).

These distribution costs can be used to perform an economic cost-benefit analysis of an ORV program.^{1, 2, 16, 17} In addition, the distribution costs can help determine the most efficient means of distributing ORV in the future.

Uhaa et al¹ provided an estimate of \$100/km²/year for the "distribution systems costs," which they assumed include baiting by helicopter, fixed-wing aircraft and ground (similar to this study). They did not, however, describe how they arrived at such a figure. Moreover, in their sensitivity analyses, they did not alter this cost estimate even though they varied bait density. This implies that they assumed that the distribution cost is fixed. In this study, the mean cost of distribution in the Ohio ORV program is $23.23/\text{km}^2$ (\pm SD, $5.20/\text{km}^2/\text{distribution}$), well below the assumed value in the aforementioned study.¹ Results of this study also revealed that a number of factors, including differing bait densities, may cause the cost of distribution to change notably (Tables 1.1-1.3). Aubert¹⁰ provided the only other specific estimate for the cost of distribution: \$9/km² (bait delivery by helicopter of \$7/km²; surveillance systems cost of $2/km^{2}$ for distributing ORV to control rabies in red foxes in Europe. Unfortunately, that report did not contain an explanation of how the estimate was obtained. Furthermore, because the density of red foxes appears to be much lower than raccoons, the density of ORV needed to control rabies in red foxes is probably much lower than that needed to control rabies in raccoons.^{1, 10, 13, 14} And because these results demonstrated that differences in densities of ORV impact costs of distribution, these data cannot be directly compared with Aubert's estimate. Therefore these results can be considered to be the first explicit attempt to document the actual costs of distributing ORV to control rabies in raccoons.

The data collected from 8 baiting operations revealed that although the costs of distribution approximated only 15% of the total costs, they may vary considerably

(Table 1.4). For example, the September 1997 baiting had the highest distribution cost of \$32.11/km², whereas distribution costs in May 1997, June 1999, and September 1999 were less than \$20/km². The high cost in September 1997 may be attributed to the fact that it was the first large-scale ORV operation undertaken (double the area covered in May 1997; Figure 1.2) by the agencies involved, and certain inefficiencies in a start-up operation are expected. In addition, the entire air operation (2,772 km²) was performed by helicopter and proved to be costly at \$30.73/km² (Table 1.3).

Even the ground baiting in the September 1997 operation, although it covered a smaller area than the May 1997 ground baiting (Figure 1.2), was much more costly per square kilometer (\$35.58/km²) than the May 1997 baiting (\$15.32/km²). This finding may be attributable to the fact that the September 1997 baiting was more labor-intensive. A more highly populated area (Youngstown, Ohio, and suburbs) was baited in September 1997, compared with the area baited in May 1997, which focused on the main roads outside of Youngstown. Another potentially atypical baiting operation was performed in April 1999, when several variations in strategies were tested, then adopted or abandoned. Consequently, the April 1999 mean aerial baiting density (179 baits/km²) and ground baiting density (113 baits/km²) were much higher than the remaining baiting events (means: 81 baits/km² for air, 74 baits/km² for ground). This increased the total cost per square kilometer by more than \$100/km² to \$261/km² (Table 1.4).

The increase in area baited increased total costs and was attributable to cases of rabid raccoons within the immune barrier and breach of the immune barrier in June 1999.

Despite the higher distribution cost of aerial bait delivery, this method is indispensable in areas with large tracts of farmland and forests where ground support is limited or potential raccoon habitats are not easily accessible. In addition, to be fully effective, baits must be distributed in a timely manner at critical periods of the year to accommodate behavior of the raccoon population (ie, mating, foraging). Thus, despite the expense, bait distribution by use of fixed-wing aircraft will continue to be the most commonly used method of ORV distribution in Ohio.

Some economy of scale can be achieved by buying large quantities of baits. For example, the reduction of bait cost by \$0.15/unit (\$1.52 in May 1997 to \$1.37 in April 1999) resulted in savings of \$112,710 for the 751,404 baits purchased in April 1999. The net result is that the total cost of the Ohio ORV project seems to have stabilized at approximately \$140/km² (September 1999, April 2000; Table 1.4).

Distribution costs may be further decreased as an optimal bait density strategy is achieved. However, reduction in the amount of baits used per unit area will not affect distribution costs with the same magnitude as it affects the total costs. For example, increasing or decreasing aerial bait density will not substantially increase or decrease the amount of personnel, personnel hours, equipment, or material required to distribute bait.

Although changes in bait density may not have notably impacted distribution costs, it appeared that, as the strategy matured, more consistent distribution costs were evident,

12

in the range of \$18-\$22/km². Changes in distribution costs over time indicated that there was a "learning curve" for establishment of an ORV program and many local, state, and federal agencies and organizations need to collaborate. Cost estimates for the last 2 baitings (September 1999 and April 2000) are perhaps more representative of an established ORV program than earlier operations. The costs incurred in earlier operations, however, serve as a reminder to other agencies in other locales contemplating similar programs of the need to learn and improve upon delivery systems as a program progresses through time.

Rabies in wildlife is typically a regional and persistent health problem; therefore, the economic costs and benefits of an ORV program should be considered over a broad region and over a long period. Collaboration among different regions could result in several economies of scale, such as reduced price of ORV from purchasing large quantities of baits. Regional cooperation could also lead to economies of scale by hiring new personnel and purchasing new equipment and material, both of which are currently being contracted out to external agencies (eg, fixed-wing aircraft, pilots, etc.).

The information presented here can be combined with knowledge on raccoon ecology and epidemiologic characteristic of rabies in raccoons to predict future spread of rabies as well as the economic impact of using ORV. Several scenarios may need to be evaluated, and they will be important in determining the feasibility of regional and national efforts and in designing future interventions to control this public health problem. ^a Raboral (Rhone Merieux), Merial Inc., Athens, Georgia.

^b De Havilland Corporation, Taylor, Michigan.

^c Rudy Kellar, First Air, Ottawa, Ontario, personal communication, May 1998.

REFERENCES: ARTICLE 1

- Uhaa LJ, Dato VM, Sorhage FE, et al. Benefits and costs of using an orally absorbed vaccine to control rabies in raccoons. *J Am Vet Med Assoc* 1992; 201:1873-1882.
- 2. Kreindel SM, McGuill M, Meltzer M, et al. The cost of rabies postexposure prophylaxis: One state's experience. *Public Health Rep* 1998; 13:247-251.
- Robbins AH, Borden MD, Windmiller BS, et al. Prevention of the spread of rabies to wildlife by oral rabies vaccination of raccoons in Massachusetts. *J Am Vet Med Assoc* 1998; 213:1407-1412.
- Winkler WG, Jenkins SR. Raccoon rabies. In: Baer GM, ed. *The natural history of rabies*. 2nd ed. Boca Raton, FL: CRC Press Inc.; 1991:325-340.
- Fischman HR, Grigor JK, Horman JT, et al. Epizootic of rabies in raccoons in Maryland from 1981 to 1987. *J Am Vet Med Assoc* 1992; 201:1883-1886.
- Torrence ME, Jenkins SR, Glickman LT. Epidemology of raccoon rabies in Virginia, 1984 to 1989. J Wildl Dis 1992; 28:369-376.
- Krebs JW, Rupprecht CE, Childs JE. Rabies surveillance in the United States during 1999. J Am Vet Med Assoc 2000; 217:1799-1811.
- 8. Smith KA. Update on rabies in Ohio. Ohio Vet Med Assoc Newslett 1998; 29:5.
- Wandeler A, Rosatte RC, Williams D, et al. Update: Raccoon rabies epizootic -United States and Canada, 1999. MMWR Morb Mortal Wkly Rep 2000; 49:31-35.
- Aubert, MFA. Costs and benefits of rabies control in wildlife in France. *Rev sci tech* 1999; 18:533-543.

- 11. Nelson RS, Cooper GH, Cartter ML, et al. Rabies postexposure prohylaxis— Connecticut, 1990-1994. *MMWR Morb Mortal Wkly Rep* 1996; 45:232-234.
- Rupprecht CE, Wiktor TJ, Johnston DH, et al. Oral immunization and protection of raccoons (*Procyon lotor*) with a vaccinia-rabies glycoprotein recombinant virus vaccine. *Proc Natl Acad Sci U S A* 1986; 83:7947-7950.
- Anderson RM, Jackson HC, May RM, et al. Population dynamics of fox rabies in Europe. *Nature* 1981; 289:765-771.
- 14. Wandeler AI. Oral immunization of wildlife. In: Baer GM, ed. *The natural history of rabies*. 2nd ed. Boca Raton, FL: CRC Press Inc., 1991; 485-503.
- 15. Fearneyhough MG, Wilson PJ, Clark KA, et al. Results of an oral rabies vaccination program for coyotes. *J Am Vet Med Assoc* 1998; 212:498-502.
- Meltzer MI, Rupprecht CE. A review of the economics of the prevention and control of rabies," *Pharmacoeconomics* 1998; 14:365-383.
- 17. Meltzer, MI. Assessing the costs and benefits of an oral vaccine for raccoon rabies: a possible model. *Emerg Infect Dis* 1996; 2:336-342.



Figure 1.1—Detection of rabies in raccoons (by year) in the United States and Canada⁹



Figure 1.2 - Area covered and density of oral rabies vaccine distributed in Ohio; May, 1997 to April, 2000.

Baiting	Date	Туре	Area Baited by Air (km ²)	Area Baited by Ground (km ²)	Total Area (km ²)	Bait Delivery Method
1	May-97	Emergency	365	1,415	1,780	Helicopter, Ground
2	Sep-97	Seasonal	2,772	1,100	3,872	Helicopter, Ground
3	Apr-98	Seasonal	3,297	690	3,987	Aircraft, Helicopter, Ground
4	Oct-98	Seasonal	3,310	677	3,987	Aircraft, Helicopter, Ground
5	Apr-99	Seasonal	3,757	705	4,462	Aircraft, Helicopter, Ground
6	Jun-99	Emergency	1,605	96	1,701	Aircraft, Helicopter, Ground
7	Sep-99	Seasonal	5,698	799	6,497	Aircraft, Helicopter, Ground
8	Apr-00	Seasonal	5,667	830	6,497	Aircraft, Helicopter, Ground

Table 1.1—Ohio oral rabies vaccine distribution effort: 1997-2000

Cost	May 1997	Sep 1997	Apr 1998	Oct 1998	Apr 1999	Jun 1999	Sep 1999	Apr 2000	Mean (SD)
Wages	20,152	37,321	11,010	10,066	13,019	1,446	10,807	12,830	14,581 (9,833)
Automobile mileage	1,524	1,821	904	858	1,324	174	1,406	1,468	1,185 (484)
Ground distribution costs	21,675	39,142	11,914	10,923	14,343	1,619	12,213	14,297	15,766 (10,226)
No. of people participated	NA	73	92	73	85	20	75	87	72 (22)
No. of personnel hours	NA	1,057	738	689	872	93	818	945	744 (290)
Ground distribution costs/km ²	\$15.32	\$35.58	\$17.26	\$16.14	\$20.33	\$16.82	\$15.29	\$17.23	\$19.24 (6.35)

All costs are in US dollars. May 1997 data estimates were obtained from an external source. May 1997 and June 1999 baiting events took place as a result of the initial outbreak and breach of immune barrier (emergency baiting events). April 1999 baiting included a special bait density study.

NA = Data not available

Table 1.2—Ground distribution costs of the Ohio oral rabies vaccine (ORV) program

Cost	May 1997	Sep 1997	Apr 1998	Oct 1998	Apr 1999	Jun 1999	Sep 1999	Apr 2000	Mean (SD)
Helicopter (incl. fuel, pilot)	6,392	60,606	8,495	2,385	5,744	3,277	2,500	13,265	12,833 (18,372)
Administrative and support crew	2,500	21,472	31,487	32,338	28,423	5,019	28,250	34,682	23,021 (11.718)
Aircraft personnel (OMNR) cost	N/A	N/A	9,685	10,394	16,134	3,454	11,880	16,308	11,309 (4,355)
Aircraft	N/A	N/A	27,648	29,660	59,983	13,404	53,152	57,641	40,248 (17,559)
Aircraft fuel cost	N/A	N/A	5,445	7,574	9,641	3,149	8,890	9,292	7,332
Other costs	N/A	3,104	0	1,265	699	912	1,695	357	1,147 (952)
Total air distribution costs	8,892	85,182	82,761	83,617	120,624	29,215	106,366	131,545	81,025 (39,807)
No. of people participated	NA	10	25	41	41	14	48	45	32 (14)
No. of personnel hours	NA	908	1357	1416	1852	364	1557	1714	1,310 (476)
Air distribution costs/km ²	24.36	30.73	25.10	25.26	32.11	18.21	18.67	23.21	24.71 (4.65)

 $\overline{OMNR} = Ontario Ministry of Natural Resources, N/A = Not applicable.$ See Table 1.1 for key.

Table 1.3—Air Distribution Costs of the Ohio ORV Program

Cost	May 1997	Sep 1997	Apr 1998	Oct 1998	Apr 1999	Jun 1999	Sep 1999	Apr 2000	Mean (SD)
Unit Cost of bait	1.52	1.52	1.52	1.40	1.37	1.47	1.37	1.37	1.44
									(0.07)
No. of baits	99,154	233,577	354,222	371,581	751,404	151,653	569,998	549,691	385,160
									(210,895)
Aerial bait cost	31,733	260,741	455,211	437,535	919,866	212,142	682,452	669,709	458,674
									(271,570)
Ground bait cost	118,981	94,296	83,206	82,678	109,558	10,788	98,445	83,367	85,165
									(30,707)
Total bait cost	150,714	355,037	538,417	520,213	1,029,42	222,930	780,897	753,077	543,839
					3				(280,520)
Total distribution	30,568	124,324	94,674	94,541	134,967	30,834	118,579	145,842	96,791
cost									(41,596)
Distribution	17.17	32.11	23.75	23.71	30.25	18.13	18.25	22.45	23.23
cost/km ²									(5.20)
Total cost*	181,282	479,361	633,092	614,754	1,164,39	253,764	899,476	898,919	640,630
					0				(315,325)
Total cost/km ²	101.84	123.80	158.79	154.19	260.96	149.19	138.44	138.36	153.20
									(44.16)*

*Total cost = Total bait cost + total distribution cost.

See Table 1.1 for key.

Table 1.4 -Distribution and Financial Costs of the Ohio ORV Program

ARTICLE 2

Predicting Movement of an Infectious Disease: An Agent-Based Modeling Approach

OBJECTIVE

To implement agent-based modeling as an approach to predict movement of raccoon rabies across time and space.

INTRODUCTION

Prediction of movement of infectious disease across time and space can be an important tool for the basis of provision of funds and efficient use of resources available to the public health policy maker. Movement of disease has traditionally been modeled in the mathematics arena, typically through a system of ordinary differential equations.¹⁻⁴ These models use characteristics of highly aggregated groups of agents (e.g., susceptible or infected) to simulate the dynamics of the ecology and the epidemic process of the entire population. Extensions of these population-based models (PBMs) have distinguished fragments of the population by such characteristics and behaviors as gender, age, degree of dispersal, and mortality rate; however, none of these models have been inclusive of all these realisms.⁵⁻⁸ In contrast, some PBMs ignore the host-

pathogen relationship and indirectly predict the advance of an epidemic by utilizing the heterogeneity of geographical areas as explanatory varibales.^{9, 10}

In agent-based modeling (ABM) the population is treated as a collection of heterogeneous agents who autonomously make decisions, interact with their environment and each other, and ultimately give rise to macro phenomena. In ABM, agents are assigned a wide variety of characteristics drawn from realistic distributions of such attributes. Agent behavior also can be shaped by characteristics of the geographical areas to which agents are assigned. With recent advances in computer technology, available computational power allows physical and social scientists to model a large number of heterogeneous agents with complex behavior acting on a heterogeneous landscape.¹¹ In addition, characterizing the model's spatial units with real-world data from a geographic information system (GIS) database can greatly enhance the applicability of ABM models.¹²

In this paper, a hypothetical raccoon rabies epidemic is simulated within an ABM framework. The landscape in which the raccoon agents operate is divided into spatial units characterized by land use (see Model, below). In the style of Epstein and Axtell's "SugarScape" model, the raccoon agents are characterized by their gender, genotype (home range and metabolism), fat reserve (accumulated nutrient), and health (susceptiblity) (see Model).¹³ These raccoon agents migrate in and out of the model's space, search for nutrients, reproduce, transmit disease, and ultimately cause economic consequences. The rabies incidences in each simulation map out the economic damages

23
that the disease causes based on whether the disease is in its epidemic or endemic stage (see Models below).

METHODS

In addition to the Java programs which constitute the model (see Model, below), other public-use software programs are used that include model management activities such as scheduling, control of time, data collection, "garbage collection" (removal of unnecessary data from computer's memory), and visuals. The management activities are supported by a library of Java programs packaged in an interface called RePast provided by the Social Science Computing Research Center of the University of Chicago (version 2.0; distributed at http://repast.sourceforge.net/). The programs are compiled on an IBM personal computer with a Java compiler (Java 2 Platform, Standard Edition, version 1.4.2; distributed at

http://java.sun.com/j2se/1.4.2/download.html). The results of the model are used to verify if they conform with cited literature relating to raccoon ecology. Two different epidemic regimes (aggressive and non-aggressive) are simulated and compared (see Epidemic rule, below). The results of the simulations are compared in regards to the rate of movement of the epidemic front, and the relative intensity of raccoon rabies by geographical area.

MODELS

The models consist of a set of Java programs that specify the assignment of characteristics, and algorithms that describe the behaviors for each spatial unit $\{\bar{\mathbf{E}}\}$ and

raccoon agent $\{\bar{\mathbf{A}}\}$. The set of characteristics and behaviors $(\{\bar{\mathbf{E}}\}, \{\bar{\mathbf{A}}\})$, described in detail below, is based on abstract constructs and ecological and epidemiological parameters from available literature (see Appendix). The set ($\{\bar{E}\}, \{\bar{A}\}$) represents an artificial landscape where synthetic raccoon agents roam through time. The environmental characteristics in this model, EC (explained below), include the resolution of the space and the nutrient ranking of spatial units by land category. The environmental behavior consists of a nutrient grow back algorithm, G. Therefore, environmental characteristics and behavior can compactly be noted as $\mathbf{\bar{E}} = \{ \mathbf{EC}; \mathbf{G} \}$. Raccoon agent characteristics (AC) include gender, current age, death age, fat reserve, home range, and metabolism. Raccoon agent behavior includes movement (M), migration (Mi), reproduction (R), and epidemic transmission (E). The cost of raccoon rabies (C) encapsulates the set of behaviors of the raccoon agent. Therefore, the set of characteristics and behaviors which describe a raccoon agent is represented by $\bar{\mathbf{A}} =$ {AC; M, Mi, R, E, C}. Each time period in a simulation represents 1 week. Each simulation run consists of 2600 periods, which represents 50 years (each year is approximated to 52 weeks). Due to time constraint, only one run for each model is simulated with the exception of comparison of pre-epidemic population densities where two independent runs with the same specifications were compared.

Environmental characteristics, EC

Resolution and nutrient capacity

Resolution and type of environment serve as important variables in determination of raccoon population density (see Figure 2.1). The environment is comprised of a lattice

of two-dimensional square cells where each cell represents an area of 100 m² allowing a maximum density of 100 raccoons per km². Barring extreme population densities usually found in southern swamps,^{14, 15} there is a general consensus on the order of desirable habitat for the raccoon population (see Table 2.1). Raccoon densities of approximately 70/km² in a suburban area in Ohio, up to 50/km² in areas adjacent to bodies of water (marshes, swamps, and bottomlands) in eastern US, and up to 20/km² in farmlands in the eastern US have been reported.¹⁵ There have also been reports of approximately 15 raccoons/km² in a hollow in Virginia, and up to 5 raccoons/km² in prairies in North Dakota and Manitoba.^{15, 16}

Table 2.1 shows the ranking of categories of land use—based on reported upper limit values—in descending order where a higher ranking indirectly indicates more available nutrient for the raccoon agent. Hence, these rankings can serve as the nutrient capacity for the corresponding land use.

Environmental behavior

As a result of the raccoon agent's movement behavior (see Movement rule, below), the nutrient levels of occupied spaces fall below their capacity. The process of nutrient generation for different spatial units back to their capacity is not known and may be a complex function of other processes. Two different nutrient grow back (regeneration) rules are used to assess the sensitivity of the models to the environmental behavior. Differentiating the nutrient grow back algorithm allows us to test whether changing the algorithm from the Simple format to the Urban (see below) leads to different spatial

patterns and/or higher population densities. There is a myriad of other land use designation and nutrient grow back algorithms that could otherwise be used. For example, farmland may have different seasonal grow back rates or wetlands can have a relatively higher grow back rates. One may also use cardinal measures of nutrient availability for each land use.

Simple grow back rule, G₁

It is assumed that the value of nutrient for each spatial unit is increased at 1 unit per period up to its capacity level.

Urban grow back rule, G_1 , G_{∞}

It is postulated that in urban and suburban areas, where human garbage serves as the primary food source for raccoons, the nutrient source for raccoons is replenished weekly up to its capacity. For other areas, it is assumed that the value of nutrient is increased at 1 unit per period up to its capacity level.

Agent characteristics, AC

Kaufmann (1982) presents the most detailed description of the age distribution of raccoon population (see Appendix). He reports that although a raccoon can live in the wild for up to 16 years, most die within the first two years and only 1/100 live up to the age of 7 years.¹⁵ Major factors of morbidity are harsh weather for juveniles, road kills, hunting, and trapping.¹⁷ For example, in 1981 an estimated 846,000 raccoons were killed in Pennsylvania as a result of hunting activities.¹⁷ Assuming a 5% newborn

mortality, mortality rate of 60% of raccoons of up to a year old, 75% total mortality of a generation of raccoons within their first 2 years, and that 1/1000 raccoon reaches the age of 16, a hypothetical age distribution and its associated probabilities can be constructed for the raccoon population (see Figure 2.2 and Appendix).

When introduced to the simulation, each raccoon agent is randomly assigned a gender and a maximum age, and randomly drawn from the probability distribution described in Figure 2.2. In addition, first generation raccoons are randomly assigned a location in the environment, a proxy fat reserve (nutrient endowment) value drawn from a uniform distribution (minimum: 5, maximum 50) (U(5, 50)), and a proxy genotype: a home range level U(1, 7) and a metabolism level U(1, 5). Fat reserve, metabolism, and agent's successful movement in attaining more nutrients (see Movement rule, below) represent the competition the raccoon agents pose toward each other in search of nutrients. As a result, a morbidity factor of starvation may further reduce the maximum age of some raccoon agents.

Home range of a raccoon consists of the geographic area that it normally scouts for food. Merritt¹⁷ estimates a range of 0.05-50 km²/year for raccoons in Pennsylvania while Kaufmann¹⁵ reports typical estimates of 0.4-1 km² and up to 7.07 km² on a daily basis (also see Appendix). In this model, an agent with a home range level of 14 can have a weekly home range of up to 8.41 km² (see Figure 2.4, and Environmental characteristics, above). Although studies have been conducted on the extent of home range for raccoons, the home range distribution is not well known. Therefore, for each

model uniform distribution (U(1, 14)) is used for agent's home range, a counterpart model with normal distribution with mean of 7.5 km² and standard deviation of 2 km² (N(7.5, 2)) is used to assess the sensitivity of models' results to this variable (e.g., Model 1 uses uniform home range versus Model 3 which uses normal home range; see Table 2.2). Figure 2.5 shows the cumulative distribution function of the normal and uniform distributions. Genotypes of subsequent generations are assigned according to their parents' genotypes (see Reproduction rule, below). Agents are also characterized by their health: susceptible, infected, or incubating (see Epidemic rule, below).

Agent Behavior

Movement rule, M

Each agent moves once per period within its home range. Movements by agents are made sequentially and the order of movement by agents is randomly shuffled after every period. The movement rule is comprised of two different algorithms: one for the susceptible and incubating agents ($M_{S,Inc}$) and the other for the infected agents who move randomly (M_{Inf}).

Movement algorithm $M_{S,Inc}$

Within its home range, an agent moves to an unoccupied space with the highest level of nutrient and adds the amount of nutrient to its fat reserve. An amount equal to the agent's metabolism is then decreased from its fat reserve.

Movement algorithm M_{Inf}

The movement of infected agents is the same as above with the exception that the agent moves randomly within its home range and afflicts susceptible agents within its path to the new position and/or in the adjoining cells at its new position (see Algorithms E_A and E_N , below).

Migration rule, Mi

To resolve the interaction of the space and agent objects of the contiguous land area outside the model boundaries with those objects within the model's space, a migration rule is devised to facilitate migration of raccoon agents to and from the model's space. The raccoon agents are allowed to leave the boundary areas of the model's space if the population density within their home range exceeds a certain limit. Conversely, if the population density of agents along the borders of the model's space become sparse due to disease transmission, other susceptible raccoon agents migrate into the model's space.

Migration algorithm

If the raccoon population density exceeds a certain limit (90/km² used in models in this study) within the home range of a raccoon agent, and its home range range extends beyond the border of the model's space, the raccoon agent leaves the model's space. If the raccoon population density is $0/km^2$ and the average nutrient value of the space is at least 1 unit/km² around the border of the model's space, a susceptible raccoon agent with a random maximum age drawn from the probability distribution in Figure 2.2, metabolism (U(1, 5)), and home range (U(1, 14)) enters the model's space.

Reproduction rule, R

In order to reproduce, it must be mating season and the agents must be fertile. The start of the calendar year 0 is arbitrarily set to correspond with the week of August 21. Raccoon mating season extends from January to March; although, raccoon mating has been observed into the summer months.^{15-18, 20, 21} Two different mating season lengths are used in the simulations: 13-week (early January to early April), and 21-week (early January to early June). For example, Model 5 and Model 6 are differentiated only by their mating season length. Typically, male raccoons do not mate until the end of their second year while about 60% of female yearlings mate.^{15, 18-20} Hence, in the model, sixty percent of female yearlings are deemed fertile and male raccoon agents cannot reproduce until their second year. Female agents can mate only once per mating season. If there are no mates within home range of a fertile agent, the movement rule is followed (see above).

Reproduction algorithm

Within its home range, an agent selects the nearest susceptible neighbor of the opposite sex. If the neighbor is fertile *and* there is an adjacent empty space to the neighbor, the agent occupies the empty space and adds the amount of nutrient of that site to its strength. An amount equal to the agent's metabolism is then decreased from its strength. The female agent becomes pregnant. Raccoons have a gestation period of 60-73 days;^{15-19, 21} hence, a gestation period of 9 or 10 weeks is determined randomly from a uniform distribution. Raccoons have a litter of 1-7 offspring per birth, with a typical litter of

3-4.^{15-19, 21} Therefore, the number of offspring is determined randomly from a truncated normal distribution (N(3.5, 1)). After the gestation period is over, the offspring and their mother move together typically between 16 and 20 weeks and may live with the mother up to one year before the arrival of the next litter.^{15-18, 19} To simulate this time range, after a period of 18 weeks, half of the mothers wean their offspring, and the young are "born" in the mother's home range; the other half wean their offspring at 52 weeks. If there are not enough empty spaces within the mother's home range, the number of offspring is adjusted downward forcing the maximum limit of 100 raccoons/km². The home range and metabolism are assigned to each offspring randomly from a uniform distribution within the range of parent 1 is 3 and home range of parent 2 is 5, then home range of each offspring will be randomly drawn from a uniform distribution with a minimum of 0.49 km² and maximum of 1.21 km² (U(3, 5)) (see Figure 2.4 for further explanation).

Epidemic rule, E

Rabies incubation period in raccoons lasts 10-79 days; therefore, a newly infected agent in the model incubates for 1-11 week(s) and avoids contact with other agents.²² Following the incubation period, the agent acquires a large home range and metabolism and dies within 2 weeks of clinical disease.²² Infected agents cannot reproduce. Each model was run twice using two different algorithms for the disease transmission process: a "non-aggressive" regime (E_N) and an "aggressive" regime (E_A).

Epidemic algorithm E_N

An infected agent moves randomly to an unoccupied space within its home range and adds the amount of nutrient available at the new position to its fat reserve. An amount equal to the agent's metabolism is then decreased from its strength. The rabid agent afflicts all of its susceptible neighbors (up to 8 agents) with rabies. The newly infected agent(s) acquires high metabolism of 5 units, a large home range of 14 units (8.4 km² home range), and then enters its incubation period (U(1, 8) weeks). After the incubation period is over, the newly infected agent dies within U(1, 2) weeks.

Epidemic algorithm E_A

In addition to E_N , the agent also infects all susceptible agents within its shortest path to the new location (up to 20 agents including susceptible neighbors at new location).

RESULTS

The model's space, a hypothetical 20-kilometer square area, is comprised of a lattice of 100-m² grids (total of 40,000 spatial units). The composition of the landscape is designated as 20% urban, 20% wetland, 20% farmland, 15% forest, 15% prairie, 5% water and 5% other (see also Environmental characteristics, above). Figure 2.3 shows a spatial representation of the model's space with darker colors representing more nutritious spatial spaces. The model's space is further divided into 16 quadrants (see Figure 2.3) representing potential political divisions in a real life scenario. Initially 8,000 agents (20 agents/km²) are introduced to the space at period 0. At period 500, and every two weeks thereafter, a rabid agent breaches the southern border of the

model's space (quadrants 13-16, see Figure 2.3). Sixteen separate models differentiated with the type of epidemic process, nutrient growback rule, home range distribution and mating season length are simulated (see Table 2.2).

Pre-epidemic population densities

Table 2.3 presents the average population densities—based on one run for each model—by land use category for the 16 models. The average total population densities range from 8.76 (Model 1) to 14.57 raccoons/km² (Model 16) (average = 11.44, standard deviation = 1.74). Individually, the *t*-ratios of the average total population densities for the 16 models, on the basis of a two-tail *t* test, are all significant at 1% (see Table 2.3). In other words, total population densities for each quadrant did not significantly change from one period to another for the length of the simulation (2600 periods). For models with Simple nutrient grow back regime (Models 1-4 & 9-12), the average urban population densities range from 19.57 (Model 1) to 22.06 raccoons/km² (Model 4) (ave. = 20.70, s.d. = 0.82) while urban population densities of models with Urban nutrient grow back regime (Models 5-8 & 13-16) range from 47.67 (Model 5) to 63.07 raccoons/km² (Model 16) (ave. = 56.34, s.d. = 5.33). Individually, the *t*-ratios for all average urban population densities were significant at either 1% (5 cases) or 0.1% (11 cases) (see Table 2.3).

Wetland population densities for models with Simple nutrient grow back algorithm range from 16.15 (Model 1) to 21.03 raccoons/km² (Model 4) (ave. = 18.54, s.d. = 1.59), while the models with Urban nutrient grow back range from 3.10 (Model 5) to

5.47 raccoons/km² (Model 16) (ave. = 3.90, s.d. = 0.80). Individually, on a basis of a two tail test, four models have a significant *t*-ratio at the 0.1% level, four models are significant at 1%, and five models are significant at 20% (see Table 2.3). The remaining three wetland population density estimates are statistically insignificant. Farmland population densities range from 6.92 to 13.52 raccoon/km² in models with Simple nutrient grow back algorithm (ave. = 10.03, s.d. = 2.14), and range from 2.53 to 3.44 raccoons/km² in Urban models (ave. = 2.86, s.d. = 0.28). The *t*-ratios of six of the farmland population density estimates are significant at the 20% level, three are significant at 10%, and the remaining nine estimates are statistically insignificant.

Population density estimates for land use classes of forest, prairie, other, and inhabitable are all statistically insignificant. The lack of significance for these land uses may be partly explained by random placement of initial generation of the agents, random placement of migrants into the model, and congestion. Due to the insignificance of results of these land uses, discussion on effects of nutrient grow back algorithm, home range distribution, and length of mating season are focused on total, urban, wetland and farmland density estimates.

Cross-effect of nutrient grow back algorithm

Nutrient capacity based on land use designation and nutrient grow back algorithm make up the desirability of different spatial units to agents; hence, they are important factors in shaping the spatial distribution of the agents in the model. Nutrient capacity is designated with ordinal ranking of land use categories used in the model (see Table 2.1). Two different nutrient grow back algorithms are used in the model: Simple and Urban (see Environmental behavior, above).

Tables 2.4 and 2.5 present average densities for total, urban, wetland, and farmland populations. The remaining land uses are found to be statistically insignificant (see above). Average values in Tables 2.4 and 2.5 are based on the average of density estimates of each pair of identical models (before the onset of epidemic).

As expected, urban population density estimates of models with Urban nutrient grow back algorithm, on average, are larger (272%) than models with Simple nutrient grow back algorithm. On the other hand, population density estimates for wetland and farmland areas in the Simple nutrient grow back algorithm, on average, are 4.8 and 3.5 times larger than their Urban nutrient grow back counterparts. Different null and alternative hypotheses are considered for each group of population densities:

Total population densities:

- H_0^T : There is no difference between the total population density estimates and the two nutrient grow back algorithms.
- H_1^T : Urban nutrient grow back algorithm leads to <u>higher</u> total population densities.

Urban population densities:

- H_0^U : There is no difference between the urban population density estimates and the two nutrient grow back algorithms.
- H_1^U : Urban nutrient grow back algorithm leads to <u>higher</u> urban population densities.

Wetland population densities:

- H_0^{U} : There is no difference between the wetland population density estimates and the two nutrient grow back algorithms.
- H_1^U : Urban nutrient grow back algorithm leads to <u>lower</u> wetland population densities.

Farmland population densities:

- H_0^F : There is no difference between the farmland population density estimates and the two nutrient grow back algorithms.
- H_1^F : Urban nutrient grow back algorithm leads to <u>lower</u> farmland population densities.

To test the above hypotheses, a *t*-statistic is calculated as follows:

$$t = \frac{\overline{X}_{1} - \overline{X}_{2}}{\sqrt{S_{p}^{2} \left(\frac{1}{n_{1}} + \frac{1}{n_{2}}\right)}}, \quad S_{p}^{2} = \frac{(n_{1} - 1)S_{1}^{2} + (n_{2} - 1)S_{2}^{2}}{n_{1} + n_{2} - 2}$$

Where \overline{X}_1 and \overline{X}_2 are the sample means, S_p^2 is pooled variance estimate, S_1^2 and S_2^2 are sample variances, and n_1 and n_2 are sample sizes.

Table 2.6 presents the calculated value for the t statistics for the above tests. For the total population density estimates, the t statistic indicates that, on the basis of a one-tail test, the null hypothesis is rejected at the 2.5% level of significance. The t statistics for the urban and wetland population density estimates indicate, on the basis of a one-tail test, that their respective null hypotheses are rejected at the 0.05% level of significance. Lastly, null hypothesis for the farmland population density estimates, based on a one-tail test, is rejected at 0.5% level of significance.

Overall, the Urban nutrient grow back algorithm causes the agents to intensively cluster in the urban areas and attract agents that otherwise would have stayed in the wetlands and farmlands. The fact that the total population density estimate is also significantly higher for the Urban nutrient grow back algorithm indicates that either there is more of a chance meeting between fertile mates during mating season and/or there are fewer deaths as caused by starvation of agents. The *t*-test results in Table 2.6 also indicate that the choice of nutrient grow back algorithm is significant regardless of the choice of home range distribution or mating season length.

Cross-effect of home range distribution

A sensitivity analysis of the home range distribution of the agents is conducted to test whether the home range distribution significantly affects the models' results. Similar to the analysis in Table 2.6, Table 2.7 presents a group of pair-wise comparisons between models with uniform and normal distribution. For example, observation 1 considers the averages of Models 1 & 9 (uniform distribution) versus averages of Models 3 & 11 (normal distribution). Constructing null hypotheses in the same fashion as above (Cross-effect of nutrient grow back), the *t* statistics indicate that, based on one-tail tests, the null hypotheses are not rejected at the 25% level with the exception of total population density (significant at 10% level). The insignificance of the results seem to be caused by the strong effect of the nutrient grow back algorithm. For this reason, a Z test is conducted between individual samples which are only differentiated by the home range distribution: Model 1 versus 3, Model 2 versus 4, Model 5 versus 7, Model 6 versus 8, Model 9 versus 11, Model 10 versus 12, Model 13 versus 15, and Model 14 versus 16. The Z statistic is calculated as follows:

$$Z = \frac{\overline{X}_{1} - \overline{X}_{2}}{\sqrt{\frac{S_{1}^{2}}{n_{1}} + \frac{S_{2}^{2}}{n_{2}}}}$$

Where \overline{X}_1 and \overline{X}_2 are the sample means, S_1^2 and S_2^2 are sample variances and n_1 and n_2 are sample sizes.

Table 2.8 presents summary description of each pair of model and the Z statistics for comparison of major categories of population density estimates. Each pair of model includes one model with uniform and one with normal home range distribution. The Z statistics indicate that population density estimates of models with normal home range distribution are consistently higher than those with uniform home range distribution (see also Table 2.3). Based on one-tail tests, out of the 32 Z statistics, 27 are significant at the 0.1% level. The remaining five estimates are significant at 0.5% (wetland, Models 5 & 7), 2.5% (wetland, Models 13 & 15), 5% (farmland, Models 6 & 8), 10% (farmland, Models 5 & 7), and the 25% level (farmland, Models 13 & 15) (see Table

2.8). Hence, overall, there is strong indication that normal home range among the agents leads to a higher population density estimate in each of the categories.

Cross-effect of mating season length

Although most of the raccoon mating occurs during a three-month period between late winter and early spring, some raccoons mate well into the summer season. Two different lengths of mating season (13 weeks and 21 weeks) are used in the model to assess the sensitivity of model results to this variable. Table 2.9 presents the Z statistics of pair-wise comparison of models which are differentiated by their mating season length. As expected, total population density and population density by every land use category increases (see Tables 2.3 and 2.9). Different null hypotheses (32 categories) are constructed for total, urban, wetland, and farmland population densities to test whether longer mating season leads to higher population estimates. The calculated Z statistics indicate that, based on a one-tail test, out of 32 categories, 20 categories are significant at the 0.1% level, three at the 0.5% level, five at the 1% level, one at the 2.5% level, one at the 10% level, and the remaining two at the 25% level (see Table 2.9). Even though our *a priori* expectation seems obvious in regards to increasing population densities that result from extended mating season, we would like to see the effect of population increase on the propagation of rabies epidemic (see Post-epidemic results, below).

Data consistency

Models 1 through 8 are identical to Models 9 through 16, respectively, until the rabies epidemic is introduced to the model's space at Period 500. For example, Model 2 and 10 both describe a model with Simple nutrient grow back rule, a uniform home range distribution and a 21-week mating season (see Table 2.2). For the 499 weeks of the pre-epidemic period, a pair-wise comparison was conducted to check whether fluctuations in the model, due to its random processes, significantly alter the spatial distribution of the agent population. Since the sample results are independent and large (499), a Z test was used to test whether there is a significant difference between the population density results from both models.

Means and standard deviations of total population density and of land use population density (7 categories) for each pair of similar models are presented in Tables 2.10-2.17. The null hypothesis is that the sample means of the agent population densities are not significantly different from each other. The Z statistics indicate that, with a level of significance of 0.01, two pairs of models have each one category (farmland density in Models 1 & 9, and wetland density in Models 2 & 10) that rejects the null hypothesis. The Z statistic of two pairs of models have each two categories (total and urban population densities for Models 5 & 13, and Modes 7 & 15) that reject the null hypothesis. The Z statistic of two pairs of models each had three categories (Models 6 & 14, and Models 8 & 16) that reject the null hypothesis. The Z statistic of the remaining two pairs of models (Models 3 & 11, and Models 4 & 12) each have four categories that reject the null hypothesis. Overall, 20 of 64 cases of population density estimates reject the null hypothesis.

Post-epidemic results

Each model's space is divided into 16 quadrants (see Figure 2.3) to keep track of the spatial front of the disease movement and the distribution of the intensity of the disease (number of new infections). From Period 500, and every two periods thereafter, an agent enters the model's space randomly within the 1 kilometer of the southern border of the model's space (Quadrants 13 – 16) (see Figure 2.3). The disease process ends on Period 2600 (approximately 40 years). Since the external initiation of disease is a random process and may result in spurious results within the border quadrants, focus of the spread and intensity of the epidemic is limited to the quadrants furthest away from the southern border, Quadrants 1-8 (see Figure 2.3). In the following subsections, cross effects of four variables—epidemic regime, nutrient grow back algorithm, home range distribution, and length of mating season—with respect to the speed of epidemic front and the intensity of the disease, is analyzed.

Cross effect of epidemic regime

Simulation results of eight pairs of models differentiated only by their epidemic regime (Models 1 & 9, 2 & 10, 3, & 11, 4 & 12, 5 & 13, 6 & 14, 7 & 15, and 8 & 16) are compared. These models, presented in Tables 2.18 and 2.19, are compared, in pairs, to assess the effect of epidemic regime on the intensity of the rabies epidemic and its rate of movement.

Speed of epidemic front

Tables 2.18 and 2.19 present the number of weeks lapsed from the onset of rabies in the model (Period 500) until rabies reaches quadrants 1 through 8. Models in Table 2.18 have Simple nutrient grow back algorithm, while models presented in Table 2.19 use the Urban method. Aggressive models are designated with E_A and non-aggressive models are designated as E_N .

Two hypotheses are constructed in regards to the speed of the epidemic:

- H_0^s : Infected agents in non-aggressive models, on average, reach Quadrants 1-8 with the same speed as those agents in the aggressive models.
- H_0^o : The order of infection by quadrant is the same for both the aggressive and non-aggressive models.

To test the first hypothesis, for each pair of models, a *t* test is constructed around the sample average of first week of infection by quadrants 1-8 (see Tables 2.18 and 2.19). The calculated *t* statistics indicate that the null hypothesis H_0^s is strongly rejected with the exception of Models 2 & 10 (see Tables 2.18 and 2.19). Simulation results from Models 2 & 10 indicate that, in the case where the models had a Simple nutrient grow back algorithm, normal home range, and 21-week mating season, in 7 out of 8 quadrants, the epidemic moved faster in the non-aggressive model (Model 10) (see Tables 2.18 and 2.19). This may be a spurious result and may be investigated further by

simulating multiple runs of the model and building a distribution for the first rabies occurrences.

For the second hypothesis, for each pair of models a non-parametric χ^2 test is constructed to test whether the order of infection by quadrant in models with different epidemic regime is the same. Tables 2.20 and 2.21 include the order of infection by quadrant and the pair-wise χ^2 statistic for each pair of models. Calculation of the χ^2 statistic is as follow:

$$\chi^{2} = \sum_{i=1}^{8} \frac{(O_{i} - E_{i})^{2}}{E_{i}}$$

Where E_i , the expected value, is assumed to be the ranking of first rabies cases of the aggressive model; and O_i , the observed value, is the corresponding first rabies case of the non-aggressive model.

The calculated χ^2 statistics indicate that out of the eight pairs of models, one pair (Models 1 and 9) reject the null hypothesis H_0^o with 0.5% level of significance. However, the remaining seven groups accept the null hypothesis between 10% and 99.5% level of significance (see Tables 2.20 and 2.21). It can be concluded that the cross effect of epidemic regime, on average, does not have a significant effect on the spatial pattern of rabies spread throughout the model's space. Hence, regardless of its speed, the epidemic front does not lose its shape. However, overall, the speed of rabies in models with aggressive epidemic regime is significantly higher than that of the nonaggressive models.

Intensity of infections

Tables 2.22 and 2.23 include the number of infections by quadrant throughout the approximately 40-year period of uninterrupted rabies epidemic in the model's space. With the exception of Model 14, all of the non-aggressive models, in total, produced more infections than their aggressive counterparts (see Tables 2.22 and 2.23). However, at the individual quadrant level, the disparity of number of infections between the two different epidemic regimes is mixed: 25 out of the 64 quadrants across the eight pairs of models had more infections in an aggressive epidemic regime.

The results of the models are compared, in pairs, to test the following hypothesis:

 H_0^o : The number of observations of infection by quadrant is the same for both the aggressive and non-aggressive models.

A χ^2 test is constructed with results of the aggressive model as the base scenario (expected), and results of the non-aggressive model as the observed. The χ^2 statistics in Tables 2.22 and 2.23 indicate the null hypothesis is rejected at a less than 0.5% level of significance.

Cross-effect of nutrient grow back algorithms

Simulation results of eight pairs of models differentiated only by their nutrient grow back algorithm (Models 1 & 5, 2 & 6, 3, & 7, 4 & 8, 9 & 13, 10 & 14, 11 & 15, and 12 & 16) are compared. These models, presented in Tables 2.24 and 2.25, are compared, in pairs, to assess the effect of nutrient grow back algorithm on the intensity of the rabies epidemic and its rate of movement.

Speed of epidemic front

Tables 2.24 and 2.25 present the number of weeks lapsed from the onset of rabies in the model until rabies reaches quadrants 1 through 8. Models in Table 2.24 use the aggressive epidemic regime, while models presented in Table 2.25 use the non-aggressive epidemic regime. Aggressive models are designated with E_A and non-aggressive models are designated as E_N .

Two hypotheses are constructed in regards to the speed of the epidemic:

- H_0^s : Infected agents in models with Urban nutrient grow back algorithm, on average, reach Quadrants 1-8 with the same speed as agents in models with Simple nutrient grow back algorithm.
- H_0^o : The order of infection by quadrant is the same for models with Simple or Urban nutrient grow back algorithm.

To test the first hypothesis, for each pair of models, a *t* test is constructed around the sample average of first week of infection by quadrants 1-8 (see Tables 2.24 and 2.25). Out of the eight pairs of models, the calculated *t* statistics indicate that the null hypothesis H_0^s is rejected at the 0.5% level of significance for two cases, 5% for three cases, 10% for two cases, and 25% for the remaining pair of models (see Tables 2.24 and 2.25). Hence, overall, the null hypothesis that the speed of epidemic is the same for models with Simple or Urban nutrient grow back algorithm is rejected.

For the second hypothesis, for each pair of models, a non-parametric χ^2 test is constructed to test whether the order of infection by quadrant in models with different nutrient grow back algorithm is the same. Tables 2.26 and 2.27 include the order of infection by quadrant and the pair-wise χ^2 statistic for each pair of models. Calculation of the χ^2 statistics indicate that one model pairing rejects the null hypothesis H_0^o at the 0.5% level of significance (Models 4 & 12). For the remaining 7 pairings, the null hypothesis is accepted between 50% and 99.5% level of significance. This suggests that the shape of the spatial epidemic is the same for models with Simple or Urban nutrient grow back algorithm.

Intensity of infections

Tables 2.28 and 2.29 include the number of infections by quadrant throughout the approximately 40-year period of uninterrupted rabies epidemic in the model's space. For all eight pairs of models, the models with Urban nutrient grow back algorithm, in

total, produced more infections than the models with Simple nutrient grow back algorithm (see Tables 2.28 and 2.29). Changing the nutrient grow back algorithm from Simple to Urban by far resulted in more infections than effect of any other variable in the model.

The results of the models are compared, in pairs, to test the following hypothesis:

 H_0^o : The number of observations of infection by quadrant is the same for both the Simple and Urban nutrient grow back algorithms.

A χ^2 test is constructed with results of the Simple nutrient grow back models as the base scenario (expected) and results of the Urban nutrient grow back models as the observed. The χ^2 statistics in Tables 2.28 and 2.29 indicate the null hypothesis is rejected at a less than 0.5% level of significance for each of the pairings.

Cross-effect of home range distribution

Simulation results of eight pairs of models differentiated by their home range distribution (Models 1 & 3, 2 & 4, 5 & 7, 6 & 8, 9 & 11, 10 & 12, 13 & 15, and 14 & 16) are compared. These models, presented in Tables 2.30 and 2.31, are compared, in pairs, to assess the effect of selection of home range distribution on the intensity of the rabies epidemic and its rate of movement.

Speed of epidemic front

Tables 2.30 and 2.31 present the number of weeks lapsed from the onset of rabies in the model until rabies reaches quadrants 1 through 8. Models in Table 2.30 use the aggressive epidemic regime, while models presented in Table 2.31 use the non-aggressive epidemic regime. Aggressive models are designated with E_A and non-aggressive models are designated as E_N .

Two hypotheses are constructed in regards to the speed of the epidemic:

- H_0^s : Infected agents in models with uniform home range distribution, on average, reach Quadrants 1-8 with the same speed as agents in models with normal home range distribution.
- H_0^o : The order of infection by quadrant is the same for models uniform and normal home range distribution.

To test the first hypothesis, for each pair of models, a *t* test is constructed around the sample average of first week of infection by quadrants 1-8 (see Tables 2.30 and 2.31).

Out of the eight pairs of models, the calculated *t* statistics indicate that the null hypothesis H_0^s is rejected at the 1% level of significance or less for all of the eight pairings (see Tables 2.30 and 2.31). Hence, overall, the null hypothesis that the speed of epidemic is the same for models with uniform and normal home range distribution is strongly rejected.

For the second hypothesis, for each pair of models, a non-parametric χ^2 test is constructed to test whether the order of infection by quadrant in models with uniform home range distribution is same as the models with normal home range distribution. Tables 2.32 and 2.33 include the order of infection by quadrant and the pair-wise χ^2 statistic for each pair of models. Calculation of the χ^2 statistics indicate that one model pairing rejects the null hypothesis H_0^o at the 10% level of significance (Models 2 & 4). For the remaining 7 pairings, the null hypothesis is accepted between 25% and above 99.5% level of significance. This suggests that the shape of the spatial epidemic is the same for models with uniform and normal home range distribution.

Intensity of infections

Tables 2.34 and 2.35 include the number of infections by quadrant throughout the approximately 40-year period of uninterrupted rabies epidemic in the model's space. For all eight pairs of models, the models with normal home range distribution, in total, produced more infections than the models with uniform home range distribution (see Tables 2.34 and 2.35).

The results of the models are compared, in pairs, to test the following hypothesis:

 H_0^o : The number of observations of infection by quadrant is the same for models with uniform home range distribution and models with normal home range distribution.

A χ^2 test is constructed with results of the models with uniform home range distribution as the base scenario (expected) and results of models with normal home range distribution as the observed. The χ^2 statistics in Tables 2.34 and 2.35 indicate the null hypothesis is rejected at a less than 0.5% level of significance for each of the pairings.

Cross-effect of mating season length

Simulation results of eight pairs of models differentiated by their home range distribution (Models 1 & 2, 3 & 4, 5 & 6, 7 & 8, 9 & 10, 11 & 12, 13 & 14, and 15 & 16) are compared. These models, presented in Tables 2.36 and 2.37, are compared, in pairs, to assess the effect of selection of home range distribution on the intensity of the rabies epidemic and its rate of movement.

Speed of epidemic front

Tables 2.36 and 2.37 present the number of weeks lapsed from the onset of rabies in the model until rabies reaches quadrants 1 through 8. Models in Table 2.36 use the aggressive epidemic regime, while models presented in Table 2.37 use the non-aggressive epidemic regime. Aggressive models are designated with E_A and non-aggressive models are designated as E_N .

51

Two hypotheses are constructed in regards to the speed of the epidemic:

- H_0^s : Infected agents in models with short mating season length, on average, reach Quadrants 1-8 with the same speed as agents in models with long mating season length.
- H_0^o : The order of infection by quadrant is the same for models short and long mating season.

To test the first hypothesis, for each pair of models, a *t* test is constructed around the sample average of first week of infection by quadrants 1-8 (see Tables 2.36 and 2.37). Out of the eight pairs of models, the calculated *t* statistics indicate that the null hypothesis H_0^s is rejected at the 1% level of significance or less for all of the eight pairings (see Tables 2.36 and 2.37). Hence, overall, the null hypothesis that the speed of epidemic is the same for models with uniform and normal home range distribution is strongly rejected.

For the second hypothesis, for each pair of models, a non-parametric χ^2 test is constructed to test whether the order of infection by quadrant in models with uniform home range distribution is same as the models with normal home range distribution. Tables 2.38 and 2.39 include the order of infection by quadrant, and the pair-wise χ^2 statistic for each pair of models. Calculation of the χ^2 statistics indicates that one model pairing rejects the null hypothesis H_0^o at the 10% level of significance (Models 5 & 6). For the remaining 7 pairings, the null hypothesis is accepted between 50% and above 95% level of significance. This suggests that the shape of the spatial epidemic is the same for models with uniform and normal home range distribution.

Intensity of infections

Tables 2.40 and 2.41 include the number of infections by quadrant throughout the approximately 40-year period of uninterrupted rabies epidemic in the model's space. For all eight pairs of models, the models with normal home range distribution, in total, produced more infections than the models with uniform home range distribution (see Tables 2.40 and 2.41).

The results of the models are compared, in pairs, to test the following hypothesis:

 H_0^o : The number of observations of infection by quadrant is the same for models with short (13 weeks) and long (21 weeks) mating seasons.

A χ^2 test is constructed with results of the models with uniform home range distribution as the base scenario (expected) and results of models with normal home range distribution as the observed. The χ^2 statistics in Tables 2.40 and 2.41 indicate the null hypothesis is rejected at a less than 0.5% level of significance for each of the pairings.

DISCUSSION

In this paper, I set out to develop a synthetic spatial environment and agents that mimic the major characteristics of raccoons and their relation to their natural habitat. Certain variables are altered to form different models to check the sensitivity of model results to the variables used as well as finding the best model that fit raccoon ecology. The preepidemic results indicate that while the order of population densities match the order of density estimates found in raccoon ecology literature, their magnitude does not (see Tables 2.1 and 2.3). Three explanations can be made regarding this difference: 1) The hypothetical environment does not represent reality well; hence, one can test a geo-referenced environment to see if the difference in the magnitude of population densities between simulation results and raccoon biology literature differ than those found in the present model,

2) The description of the environment may be too simplistic. Inclusion of other important variables such as roads that serve as paths of movement for raccoons may lead to different results,

3) Parameterization of characteristics and behavior of raccoons may need to be calibrated with the help of qualified raccoon biologists.

The pre-epidemic results also indicate that total population densities by land use category is sensitive to choice of nutrient grow back algorithm (27% increase with Urban grow back), home range distribution (13% increase with normal distribution), and length of mating season (11% increase with the longer mating season). This increase in total population densities eventually leads to higher incidences of raccoon

rabies once rabies is introduced to the model that may ultimately lead to higher economic cost.

For the post-epidemic results, four variables (epidemic regime, nutrient grow back, home range distribution, and length of mating season) are tested in regards to the rate of movement and the shape of the epidemic front, and the intensity of epidemic in terms of number of infections. Table 2.42 summarizes the effect of changes in variables on the simulation results.

Changing the epidemic regime from an aggressive to a non-aggressive epidemic regime (92% overall increase) had the most significant on the rate of movement of epidemic front (Table 2.42). In the aggressive models, the initial rapid movement of the disease serves as a culling instrument and consequently creates a barrier in form of low population density. This result is in agreement with literature on disease movement in that carrying capacity of susceptible population is the major factor in propagation of a disease. Overall, the rate of movement decreases when the nutrient grow back algorithm is changed from "Simple" to "Urban." This phenomenon is due to the clustering of raccoon agents in the Urban models. The agents become concentrated in the urban spatial units where nutrients are abundant and grow back to capacity each period after their nutrient is depleted. In contrast, in the Simple nutrient grow back models, agents are spread out and serve as conduits for spread of disease. Changing the variable from uniform to normal home range distribution, and from short to long mating season length did not have significant effect on the rate of disease movement. Overall,

55

the order of first infection observed by quadrant (shape of the epidemic front) was not affected by any variable changes. Hence, one can argue that the choice of environment variables used in these models in conjunction with the agent variables is robust when it comes to the shape of epidemic front. Overall, the intensity of disease epidemic in terms of new infections increased as the model variables were changed from aggressive to non-aggressive (32%), from Simple to Urban nutrient grow back algorithm (77%), from uniform to normal home range distribution (19%) and from short to long mating season length (23%). For home range distribution and mating season length, the majority of increase in the intensity of infections can be explained by the effect the change in these variables have on the increase of agent population in the pre-epidemic period (see Table 2.42). The most significant increase in intensity of infection was due to changing the nutrient grow back algorithm from Simple to Urban. Although this change in variable resulted in a slower movement front of the epidemic, it resulted in more new infections. As explained above, the clustering of agents to the more preferred urban spatial units provided less opportunity for the disease to move, but at the same time provided a cluster of susceptible agents for the infective agents. Hence, the disease lingered in the spatial units for a longer period in the urban areas and increased the likelihood of infection in these agent-concentrated areas.

Due to the time constraint, only one run of each model was simulated; hence, it should be noted that these results should be considered with caution. It is advised that multiple runs of each model be simulated and a confidence interval be constructed around the results.

REFERENCES: ARTICLE 2

- 1. Kermack WO, McKendrick AG. A contribution to the mathematical theory of epidemics. *Proc. R. Soc.* 1927; A115:700-721.
- Anderson RM, Jackson HC, May RM, et al. Population Dynamics of Fox Rabies in Europe. *Nature* 1981; 289:765-771.
- 3. Holmes EE, Lewis MA, Banks JE, et al. Partial differential equations in ecology: spatial interactions and population dynamics. *Ecology* 1994; 75(1):17-29.
- Smith ADM. A continuous time deterministic model of temporal rabies. In: Bacon, PJ ed. *Population dynamics of rabies in wildlife*. Orlando, Fla: Academic Press Inc, 1985; 131-145.
- Artois M, Langlais M, Suppo C. Simulation of rabies control within an increasing fox population. *Ecological Modelling* 1997; 23-34.
- Müller J. Optimal vaccination patterns in age-structured populations: endemic case. Mathematical and Computer Modelling 2000; 31:149-160.
- Iannelli M, Kim MY, Park EJ. Splitting methods for the numerical approximation of some models of age-structured population dynamics and epidemiology. *Applied Mathematics and Computation* 1997; 87:69-93.
- Garnerin P, Hazout S, Valleron AJ. Estimation of two epidemiological parameters of fox rabies: the length of incubation period and the dispersion distance of cubs. *Ecological Modelling* 1986; 33:123-135.
- Smith DL, Lucey B, Waller LA, et al. Predicting the spatial dynamics of rabies epidemics on heterogeneous landscapes. *Proc. Natl. Acad. Sci.* 2002; 99(6)3668:3672.

- Maasilta P. Forecasting the HIV epidemic in Finland by using functional small area units. *GeoJournal* 1997; 41.3:215-222.
- 11. Anderson J. Providing a broad spectrum of agents in spatially explicit simulation models: the Gensim approach. In: Gimblett HR ed. *Integrating geographic information systems and agent-based modeling techniques*. New York, NY: Oxford University Press, 2002; 21:58.
- 12. Gimblett HR. Integrating geographic information systems and agent-based technologies for modeling and simulating social and ecological phenomena. In: Gimblett HR ed. *Integrating geographic information systems and agent-based modeling techniques*. New York, NY: Oxford University Press, 2002; 1:20.
- Epstein JM, Axtell R. *Growing artificial societies*. Washington DC: Brookings Institution Press, 1996.
- 14. Lotze and Anderson (1979),
- Kaufmann JH. Raccoon and allies. In: Chapman JA, Feldhamer GA, eds. Wild mammals of North America. Baltimore: The Johns Hopkins University Press, 1982; 567-585.
- 16. Wilson DE, Ruff S. *The Smithsonian book of North American mammals*.Washington DC: Smithsonian Institution Press, 1999; 221-223.
- Merritt JF. *Guide to the mammals of Pennsylvania*. Matinko RA, ed. Pittsburgh,
 PA: University of Pittsburgh Press, 1987; 266-269.
- Whitaker JO, Hamilton WJ, eds. *Mammals of the eastern United States*. Third edition. Ithaca, NY: Comstock Publishing Associates, 1998; 427-433.

- Stuewer FE. Raccoons: their habits and management in Michigan. *Ecological Monographs*, 13(2):205-256.
- 20. Sanderson GC, Nalbandov AV. The reproductive cycle of the raccoon in Illinois. *Illinois Natural History Survey Bulletin* 1973. 31(2):29-84.
- Nowak RM. Walker's mammals of the world. Fifth Ed, Vol. II.. The Johns Hopkins University Press, 1991; 1100-1101.
- 22. Winkler WG, Jenkins SR. Raccoon rabies. In: Baer GM, ed. *The natural history of rabies*. 2nd ed. Boca Raton, Fla.: CRC Press Inc, 1991; 1991:325-340.
- 23. Uhaa IJ, Dato VM, Sorhage FE, et al. Benefits and costs of using an orally absorbed vaccine to control rabies in raccoons. *JAVMA*, 201(12):1873-1882, 1992.
- 24. Noah DL, Smith MG, Gotthardt JC, et al. Mass human exposure to rabies in New Hampshire: exposures, treatment, and cost.
- 25. Kreindel SM, McGuill M, Meltzer M, et al. The cost of rabies postexposure prophylaxis: one state's experience. *Public Health Reports*, 113:247-251, 1998.
- 26. Nelson RS, Cooper GH, Cartter ML, et al. Rabies postexposure prophylaxis Connecticut, 1990-1994. *MMWR*, 45(11):232-234, 1996.
- 27. Wyatt JD, Barker WH, Bennett NM, et al. Human rabies postexposure prophylaxis during a raccoon rabies epizootic in New York, 1993 and 1994. *Emerging Infectious Diseases* 1999, 5(3):415-423.
- 28. Kemere P, Liddel MK, Evangelou P, et al. Economic analysis of a large scale oral vaccination program to control raccoon rabies. *Unpublished Report*, 1999.


Figure 2.1—Factors relating to the raccoon population density



Figure 2.2—Probability distribution of age in wild raccoon population



Each quadrant is a 5 kilometer square (2500 spatial units) (Total of 40000 spatial units).
Seven different land uses, from darkest (most nutritious) to lightest (zero food value): urban, wetland, farmland, forest, prairie, other, inhabitable.

Figure 2.3—Representation of model's space with 7 different land use categories and 16 quadrants



Figure 2.4—Home range potential of a raccoon agent with home range of 7 units (2.25 km²) in a 100 m² cell lattice



- cdf := cumulative distribution function
- N(7.5, 2) := normal distribution with mean of 0.75 km and standard deviation of 0.2 km

- U(1, 14) := uniform distribution with minimum of 0.1 km and maximum of 1.4 km

Figure 2.5—Two possible home range distributions for the raccoon agents

Rank		Pop. Density (upper limit)
(nutrient capacity)	Land use	(raccoons/km ²)
6	Urban/suburban	70 ^a
5	Wetlands, marshes, swamps, bottomlands	50 ^a
4	Farmland/rural	20 ^a
3	Forest	15 ^b
2	Prairies	5 °
1	Above 2000 meter elevation, other	1
0	Water	0

a – Whitaker & Hamilton (1998)

b – Wilson & Ruff (1999)

c - Kaufmann (1982)

Table 2.1—Ranking of raccoon habitats

Epidemic	Model	Nutrient	Home range	Mating season
Regime		growback		(weeks)
Aggressive	1	Simple	U(1, 14)	13
	2	Simple	U(1, 14)	21
	3	Simple	N(7.5, 2)	13
	4	Simple	N(7.5, 2)	21
	5	Urban	U(1, 14)	13
	6	Urban	U(1, 14)	21
	7	Urban	N(7.5, 2)	13
	8	Urban	N(7.5, 2)	21
Non-Aggressive	9	Simple	U(1, 14)	13
	10	Simple	U(1, 14)	21
	11	Simple	N(7.5, 2)	13
	12	Simple	N(7.5, 2)	21
	13	Urban	U(1, 14)	13
	14	Urban	U(1, 14)	21
	15	Urban	N(7.5, 2)	13
	16	Urban	N(7.5, 2)	21

Notes:

- Each model is simulated once.

- The length of each model is 2600 periods with each period representing one week (total of 50 years @ 52 weeks/year).

- The size of model's space is comprised of a square lattice of 100m² cells representing 20 km on each side.

Table 2.2—Models: Article 2

Model	Total	Urban	Wetland	Farmland	Forest	Prairie	Other	Inhabitable
1	8.757 0	19.562=	16.148 0	6.912	1.654	0.535	0.183	0.235
	(3.355)	(3.349)	(6.064)	(7.364)	(2.729)	(0.513)	(0.192)	(0.229)
2	10.452 Θ	20.975=	18.792 Θ	10.944	2.322	0.616	0.205	0.261
	(3.908)	(3.842)	(5.888)	(9.315)	(3.160)	(0.531)	(0.232)	(0.260)
3	9.563O	20.209=	18.150=	8.492	1.591	0.467	0.186	0.203
	(3.397)	(3.405)	(5.174)	(8.355)	(2.961)	(0.417)	(0.198)	(0.215)
4	11.659 0	22.059=	21.026=	13.511 \$	2.840	0.459	0.206	0.245
	(4.015)	(4.019)	(4.883)	(10.088)	(4.307)	(0.434)	(0.227)	(0.269)
5	10.854 0	47.668Θ	3.094 �	2.658 †	1.316	0.606	0.289	0.267
	(3.762)	(14.862)	(2.303)	(1.700)	(1.267)	(0.591)	(0.339)	(0.306)
6	11.748Θ	51.920O	3.290 �	2.761>	1.297	0.653	0.302	0.319
	(4.102)	(16.627)	(2.597)	(1.595)	(1.234)	(0.603)	(0.358)	(0.306)
7	12.564 0	56.270=	3.491�	2.522 \$	1.155	0.607	0.279	0.267
	(4.032)	(16.422)	(2.468)	(1.536)	(1.248)	(0.552)	(0.399)	(0.328)
8	14.073 Θ	62.116 0	4.662	2.992 †	1.349	0.688	0.334	0.326
	(4.992)	(19.517)	(4.167)	(2.312)	(1.340)	(0.620)	(0.414)	(0.417)
9	9.242 0	19.911=	16.981 0	8.222	1.688	0.471	0.189	0.235
	(3.433)	(3.438)	(5.897)	(7.815)	(2.773)	(0.545)	(0.214)	(0.266)
10	9.962 0	20.578=	17.882 0	10.019	1.932	0.668	0.187	0.249
	(3.888)	(3.793)	(6.313)	(9.181)	(2.907)	(0.552)	(0.220)	(0.270)
11	10.2900	20.864=	19.272=	10.166	1.849	0.527	0.182	0.218
	(3.469)	(3.444)	(4.783)	(8.864)	(3.069)	(0.415)	(0.213)	(0.242)
12	10.939 0	21.395=	19.999=	11.942	2.312	0.453	0.204	0.238
	(3.842)	(3.819)	(5.052)	(9.718)	(3.615)	(0.418)	(0.212)	(0.253)
13	12.084 0	53.346=	3.413 ♥	2.862>	1.330	0.673	0.278	0.308
	(3.952)	(15.896)	(2.391)	(1.739)	(1.304)	(0.617)	(0.347)	(0.365)
14	12.733Θ	55.990Θ	3.990	2.878 \$	1.442	0.686	0.320	0.326
	(4.496)	(17.771)	(3.206)	(1.863)	(1.316)	(0.639)	(0.401)	(0.353)
15	13.505 0	60.306=	3.769 	2.774>	1.265	0.778	0.293	0.289
	(4.244)	(16.906)	(2.948)	(1.686)	(1.285)	(0.648)	(0.402)	(0.397)
16	14.568 0	63.070 0	5.461	3.434 \$	1.699	0.755	0.332	0.340
	(5.201)	(19.586)	(4.556)	(2.610)	(1.430)	(0.646)	(0.440)	(0.444)

- Models 1-4 and 9-12 utilize Simple grow back algorithm: each spatial unit with nutrient value below its capacity grows back nutrients 1 unit/period. Models 5-8 and 13-16 utilize Urban grow back algorithm: urban spatial units with nutrient value below its capacity grow back to capacity next period; remainder of spatial units follow simple grow back algorithm.

- Home range distribution of raccoon agents in Models 1, 2, 5, 6, 9, 10, 13, 14 are drawn from a uniform distribution while Models 3, 4, 7, 8, 15, 16 utilize normal home range distribution for raccoon agents.

- The length of mating season for Models 1, 3, 5, 7, 9, 11, 13, 15 is 13 weeks while length of mating season for even numbered models is 21 weeks.

- Standard deviations in parentheses.

- Number of observations = 499.

Table 2.3—Average pre-epidemic population densities by land use category

^{- =} *t*-ratio significant at 0.1% (2-tail), Θ *t*-ratio significant at 1% (2-tail), > *t*-ratio significant at 10% (2-tail), \clubsuit *t*-ratio significant at 20% (2-tail).

		Densities								
Models	Total	Urban	Wetland	Farmland						
1, 9	9.000	19.736	16.565	7.567						
	(0.343)	(0.247)	(0.590)	(0.926)						
2, 10	10.207	20.776	18.337	10.481						
	(0.347)	(0.280)	(0.643)	(0.654)						
3, 11	9.926	20.537	18.711	9.329						
	(0.514)	(0.463)	(0.794)	(1.184)						
4, 12	11.299	21.727	20.513	12.727						
	(0.509)	(0.469)	(0.726)	(1.110)						

- Averages and standard deviations are based on the average values of each model in a pair-grouping.

- Standard deviations are in parentheses.

Table 2.4—Major categories of average population densities for models with Simple nutrient grow back algorithm

	Densities								
Models	Total	Urban	Wetland	Farmland					
5, 13	11.469	50.507	3.253	2.760					
	(0.870)	(4.015)	(0.226)	(0.144)					
6, 14	12.241	53.955	3.640	2.820					
	(0.697)	(2.878)	(0.496)	(0.083)					
7, 15	13.035	58.288	3.630	2.648					
	(0.665)	(2.854)	(0.197)	(0.178)					
8, 16	14.320	62.593	5.061	3.213					
	(0.350)	(0.675)	(0.565)	(0.313)					

Notes:

- Averages and standard deviations are based on the average values of each model in a pair-grouping.

- Standard deviations are in parentheses.

Table 2.5—Major categories of average population densities for models with Urban nutrient grow back algorithm

		Nutrient grow back algorithm (Population density estimate)									
Observation	Simple Total	Urban Total	Simple Urban	Urban Urban	Simple Wetland	Urban Wetland	Simple Farmland	Urban Farmland			
1	9.000	11.469	19.736	50.507	16.565	3.253	7.567	2.760			
2	10.207	12.241	20.776	53.955	18.337	3.640	10.481	2.820			
3	9.926	13.035	20.537	58.288	18.711	3.630	9.329	2.648			
4	11.299	14.320	21.727	62.593	20.513	5.061	12.727	3.213			
Average	10.108	12.766	20.694	56.336	18.531	3.896	10.026	2.860			
s.d.	0.947	1.218	0.820	5.247	1.619	0.797	2.163	0.245			
t statistic	-3.4	470	-13.4	22★	16.219★		6.584 0				

- Observation 1 compares average of models with Simple nutrient grow back algorithm (Models 1 & 9) against average of models with Urban nutrient grow back algorithm (Models 5 & 13).

- Observation 2 compares average of Models 2 & 10 against average of Models 6 & 14.

- Observation 3 compares average of Models 3 & 11 against average of Models 7 & 15.

- Observation 4 compares average of Models 4 & 12 against average of Models 8 & 16.

- \star *t* statistic significant at 0.05% (1-tail), Θ *t* statistic significant at 0.5% (1-tail), \Box *t* statistic significant at 2.5% (1-tail).

Table 2.6—Comparison of major categories of population densities for models with Simple versus Urban nutrient grow back algorithm

		Home range distribution (Population density estimate)								
Observation	Uniform Total	Normal Total	Uniform Urban	Normal Urban	Uniform Wetland	Normal Wetland	Uniform Farmland	Normal Farmland		
1	9.000	9.926	19.736	20.537	16.565	18.711	7.567	9.329		
2	10.207	11.299	20.776	21.727	18.337	20.513	10.481	12.727		
3	11.469	13.035	50.507	58.288	3.253	3.630	2.760	2.648		
4	12.241	14.320	53.955	62.593	3.640	5.061	2.820	3.213		
Average	10.729	12.145	36.244	40.786	10.449	11.979	5.907	6.979		
s.d.	1.425	1.929	18.519	22.768	8.119	8.864	3.791	4.882		
t statistic	-1.1	81ቱ	-0.3	-0.255		-0	.347			

Notes:

- Observation 1 compares average of models with uniform home range distribution (Models 1 & 9) against average of models with normal home range distribution (Models 3 & 11).

- Observation 2 compares average of Models 2 & 10 against average of Models 4 & 12.

- Observation 3 compares average of Models 5 & 13 against average of Models 7 & 15.

- Observation 4 compares average of Models 6 & 14 against average of Models 8 & 16.

- 🕆 *t* statistic significant at 10% (1-tail).

Table 2.7—Comparison of major categories of population densities for models with Uniform versus Normal home range distribution: t statistics

		Models							
	1, 3	9, 11	2, 4	10, 12	5,7	13, 15	6, 8	14, 16	
Nutrient grow back	Simple	Simple	Simple	Simple	Urban	Urban	Urban	Urban	
algorithm \rightarrow									
Mating season \rightarrow	13 weeks	13 weeks	21 weeks	21 weeks	13 weeks	13 weeks	21 weeks	21 weeks	
Land use category									
Total	-3.769★	-4.793★	-4.811★	-3.994★	-6.930★	-5.475★	-8.038★	-5.961★	
Urban	-3.029★	-4.374★	-4.355★	-3.388★	-8.676★	-6.700★	-8.883★	-5.980★	
Wetland	-5.611★	-6.739★	-6.523★	-5.850★	-2.628Θ	-2.094>	-6.243★	-5.895★	
Farmland	-3.169★	-3.675★	-4.177★	-3.214★	1.325□	0.808Φ	-1.834♥	-3.870★	

- Each pair of model includes one model with uniform home range distribution and another with normal home range distribution. *See* Table 2.2 for key.

★ Z statistic significant at 0.1% (1-tail), Θ Z statistic significant at 0.5% (1-tail), > Z statistic significant at 2.5% (1-tail), ♥ Z statistic significant at 5% (1-tail), □ Z statistic significant at 10% (1-tail), Φ Z statistic significant at 25% (1-tail).

Table 2.8—Comparison of major categories of population densities for pairs of models with uniform versus normal home range distribution: Z statistics

		Models								
	1, 3	9, 11	2, 4	10, 12	5, 7	13, 15	6, 8	14, 16		
Nutrient grow back algorithm \rightarrow	Simple	Simple	Simple	Simple	Urban	Urban	Urban	Urban		
Home range \rightarrow	Uniform	Uniform	Normal	Normal	Uniform	Uniform	Normal	Normal		
Land use category	_	_		_		_				
Total	-7.350★	-3.098★	-8.901★	-2.802Θ	-3.589★	-2.424�	-5.251★	-3.537★		
Urban	-6.193★	-2.912Θ	-7.842★	-2.305>	-4.259★	-2.477�	-5.119★	-2.386�		
Wetland	-6.990★	-2.329♦	-9.030★	-2.335�	-1.260Ф	-3.224★	-5.401★	-6.964★		
Farmland	-7.584★	-3.329★	-8.560★	-3.017 0	-0.985 Φ	-0.142□	-3.777★	-4.740★		

Notes:

- Each pair of model includes one model with a short mating season (13 weeks) and another with long mating season (21 weeks). *See* Table 2.2 for key.

- \star Z statistic significant at 0.1% (1-tail), Θ Z statistic significant at 0.5% (1-tail), \Diamond Z statistic significant at 1% (1-tail), > Z statistic significant at 2.5% (1-tail), \Box Z statistic significant at 10% (1-tail), Φ Z statistic significant at 25% (1-tail).

Table 2.9—Comparison of major categories of population densities for pairs of models with 13-week versus 21-week mating season: Z statistics

	Mod	el 1	Model 9			Accept null
Densities	average	s.d.	average	s.d.	Z	hypothesis, $\alpha = 0.01$
Total	8.757	3.355	9.242	3.433	2.259	Yes
Urban	19.562	3.349	19.911	3.438	-1.627	Yes
Wetland	16.148	6.064	16.981	5.897	2.203	Yes
Farmland	6.912	7.364	8.222	7.815	2.724	No
Forest	1.654	2.729	1.688	2.773	0.192	Yes
Prairie	0.535	0.513	0.471	0.545	-1.903	Yes
Other	0.183	0.192	0.189	0.214	0.405	Yes
Water	0.235	0.229	0.235	0.266	0.013	Yes

- Null hypothesis: sample means of models are not significantly different from each other.

Table 2.10—Consistency of models with Simple nutrient grow back algorithm, uniform home range distribution and 13-week mating season: Z statistics

	Mod	Model 2		10		Accept null
Densities	average	s.d.	average	s.d.	Z	hypothesis, $\alpha = 0.01$
Total	10.452	3.908	9.962	3.888	1.986	Yes
Urban	20.975	3.842	20.578	3.793	1.639	Yes
Wetland	18.792	5.888	17.882	6.313	2.355	No
Farmland	10.944	9.315	10.019	9.181	1.580	Yes
Forest	2.322	3.160	1.932	2.907	2.031	Yes
Prairie	0.616	0.531	0.668	0.552	-1.518	Yes
Other	0.205	0.232	0.187	0.220	1.211	Yes
Water	0.261	0.260	0.249	0.270	0.734	Yes

Note:

- Null hypothesis: sample means of models are not significantly different from each other.

Table 2.11—Consistency of models with Simple nutrient grow back algorithm, uniform home range distribution and 21-week mating season: Z statistics

	Mod	el 3	Model 11			Accept null
Densities	average	s.d.	average	s.d.	Z	hypothesis, $\alpha = 0.01$
Total	9.563	3.397	10.290	3.469	-3.344	No
Urban	20.209	3.405	20.864	3.444	-3.020	No
Wetland	18.150	5.174	19.272	4.783	-3.558	No
Farmland	8.492	8.355	10.166	8.864	-3.070	No
Forest	1.591	2.961	1.849	3.069	-1.354	Yes
Prairie	0.467	0.417	0.527	0.415	-2.299	Yes
Other	0.186	0.198	0.182	0.213	0.362	Yes
Water	0.203	0.215	0.218	0.242	-1.032	Yes

- Null hypothesis: sample means of models are not significantly different from each other.

Table 2.12—Consistency of models with Simple nutrient grow back algorithm,normal home range distribution and 13-week mating season: Zstatistics

	Mod	Model 4		12		Accept null
Densities	average	s.d.	average	s.d.	Z	hypothesis, $\alpha = 0.01$
Total	11.659	4.015	10.939	3.842	2.893	No
Urban	22.059	4.019	21.395	3.819	2.674	No
Wetland	21.026	4.883	19.999	5.052	3.263	No
Farmland	13.511	10.088	11.942	9.718	2.502	No
Forest	2.840	4.307	2.312	3.615	2.098	Yes
Prairie	0.459	0.434	0.453	0.418	0.242	Yes
Other	0.206	0.227	0.204	0.212	0.101	Yes
Water	0.245	0.269	0.238	0.253	0.376	Yes

Note:

- Null hypothesis: sample means of models are not significantly different from each other.

Table 2.13—Consistency of models with Simple nutrient grow back algorithm,normal home range distribution and 21-week mating season: Zstatistics

	Model 5		Model	13		Accept null
Densities	average	s.d.	average	s.d.	Z	hypothesis, $\alpha = 0.01$
Total	10.854	3.762	12.084	3.952	-5.037	No
Urban	47.668	14.862	53.346	15.896	-5.828	No
Wetland	3.094	2.303	3.413	2.391	-2.149	Yes
Farmland	2.658	1.700	2.862	1.739	-1.874	Yes
Forest	1.316	1.267	1.330	1.304	-0.165	Yes
Prairie	0.606	0.591	0.673	0.617	-1.757	Yes
Other	0.289	0.339	0.278	0.347	0.489	Yes
Water	0.267	0.306	0.308	0.365	-1.921	Yes

- Null hypothesis: sample means of models are not significantly different from each other.

Table 2.14—Consistency of models with Urban nutrient grow back algorithm, uniform home range distribution and 13-week mating season: Z statistics

	Mod	el 6	Model	14		Accept null
Densities	average	s.d.	average	s.d.	Z	hypothesis, $\alpha = 0.01$
Total	11.748	4.102	12.733	4.496	-3.617	No
Urban	51.920	16.627	55.990	17.771	-3.736	No
Wetland	3.290	2.597	3.990	3.206	-3.794	No
Farmland	2.761	1.595	2.878	1.863	-1.069	Yes
Forest	1.297	1.234	1.442	1.316	-1.803	Yes
Prairie	0.653	0.603	0.686	0.639	-0.831	Yes
Other	0.302	0.358	0.320	0.401	-0.758	Yes
Water	0.319	0.306	0.326	0.353	-0.326	Yes

Note:

- Null hypothesis: sample means of models are not significantly different from each other.

Table 2.15—Consistency of models with Urban nutrient grow back algorithm, uniform home range distribution and 21-week mating season: Z statistics

	Mod	el 7	Model	Model 15		Accept null
Densities	average	s.d.	average	s.d.	Z	hypothesis, $\alpha = 0.01$
Total	12.564	4.032	13.505	4.244	-3.590	No
Urban	56.270	16.422	60.306	16.906	-3.825	No
Wetland	3.491	2.468	3.769	2.948	-1.616	Yes
Farmland	2.522	1.536	2.774	1.686	-2.470	Yes
Forest	1.155	1.248	1.265	1.285	-1.367	Yes
Prairie	0.607	0.552	0.778	0.648	-4.487	Yes
Other	0.279	0.399	0.293	0.402	-0.585	Yes
Water	0.267	0.328	0.289	0.397	-0.969	Yes

- Null hypothesis: sample means of models are not significantly different from each other.

Table 2.16—Consistency of models with Urban nutrient grow back algorithm, normal home range distribution and 13-week mating season: Z statistics

	Mod	Model 8		16		Accept null
Densities	average	s.d.	average	s.d.	Z	hypothesis, $\alpha = 0.01$
Total	14.073	4.992	14.568	5.201	-1.534	Yes
Urban	62.116	19.517	63.070	19.586	-0.771	Yes
Wetland	4.662	4.167	5.461	4.556	-2.890	No
Farmland	2.992	2.312	3.434	2.610	-2.833	No
Forest	1.349	1.340	1.699	1.430	-3.987	No
Prairie	0.688	0.620	0.755	0.646	-1.658	Yes
Other	0.334	0.414	0.332	0.440	0.078	Yes
Water	0.326	0.417	0.340	0.444	-0.525	Yes

Note:

- Null hypothesis: sample means of models are not significantly different from each other.

Table 2.17—Consistency of models with Urban nutrient grow back algorithm, normal home range distribution and 21-week mating season: Z statistics

				Mode	ls			
	1	9	2	10	3	11	4	12
Nutrient grow back algorithm \rightarrow	Simple	Simple	Simple	Simple	Simple	Simple	Simple	Simple
Epidemic regime \rightarrow	E _A	E_N	E _A	E_N	E _A	E _N	EA	E_N
Quadrant								
1	55	79	67	60	82	97	52	127
2	42	81	63	49	68	111	53	123
3	42	105	64	63	56	112	56	135
4	50	155	89	80	44	190	85	147
5	44	57	47	34	32	78	38	69
6	30	79	45	33	36	71	39	65
7	28	93	46	44	30	77	37	86
8	40	108	58	70	38	111	35	113
average	41.375	94.625	59.875	54.125	48.250	105.875	49.375	108.125
s.d.	9.086	29.335	14.682	16.966	18.745	37.934	16.604	30.972
t	-4.9	904	0.7	25	-3.8	352	-4.	729
Rejection level of H_0^s	0.1	%	25	%	0.5	%	0.:	5%

- Null hypothesis: infected agents in non-aggressive models, on average, reach quadrants 1-8 with the same speed as those agents in the aggressive models.

Note: Each group of models contains two independent samples.7 degrees of freedom rejection level.

Table 2.18— Number of weeks lapsed after onset of rabies until its appearance by quadrant (1 through 8) in models with Simple nutrient grow back algorithm: aggressive vs. non-aggressive epidemic regimes

				Mode	ls		_	
	5	13	6	14	7	15	8	16
Nutrient grow back algorithm \rightarrow	Urban	Urban	Urban	Urban	Urban	Urban	Urban	Urban
Epidemic regime \rightarrow	E _A	E_N	E _A	E_N	E _A	E _N	E _A	E_N
Quadrant								
1	63	191	88	89	66	146	60	97
2	59	188	85	90	74	154	53	92
3	57	203	93	108	85	158	58	92
4	56	198	93	135	82	170	70	99
5	43	93	58	58	48	104	47	62
6	39	139	57	61	51	104	46	61
7	35	167	64	103	56	122	52	68
8	44	196	58	121	59	154	59	89
average	49.500	171.875	74.500	95.625	65.125	139.000	55.625	82.500
s.d.	10.447	38.144	16.639	26.971	14.004	25.523	7.836	16.027
t	-8.	752	-1.8	385	-7.1	77	-4.	261
Rejection level of H_0^s	0.1	%	10	%	0.1	%	0.:	5%

- Null hypothesis: infected agents in non-aggressive models, on average, reach quadrants 1-8 with the same speed as those agents in the aggressive models.

- Note: Each group of models contains two independent samples.

- 7 degrees of freedom rejection level.

Table 2.19— Number of weeks lapsed after onset of rabies until its appearance by
quadrant (1 through 8) in models with Urban nutrient grow back
algorithm: aggressive vs. non-aggressive epidemic regimes

				Mode	ls			
	1	9	2	10	3	11	4	12
Nutrient grow back								
algorithm \rightarrow	Simple	Simple	Simple	Simple	Simple	Simple	Simple	Simple
Epidemic regime \rightarrow	E _A	E_N	E _A	E_N	EA	E _N	EA	E_N
Quadrant								
1	8	2	7	5	8	4	5	6
2	4	4	5	4	7	5	6	5
3	5	6	6	6	6	7	7	7
4	7	8	8	8	5	8	8	8
5	6	1	3	2	2	3	3	2
6	2	3	1	1	3	1	4	1
7	1	5	2	3	1	2	2	3
8	3	7	4	7	4	6	1	4
χ^2	30.3	843	3.8	355	8.3	71	12.	450
Rejection level of H_0^o	0.5	5%	90	1%	50	%	10)%

- Null hypothesis: the order of infection by quadrant is the same for both the aggressive and nonaggressive models.

Note: Each group of models contains two independent samples.
7 degrees of freedom rejection level.

- Measurement level of data is ordinal.

Table 2.20— Order of infection by quadrant (1 through 8) in models with Simple nutrient grow back algorithm: aggressive vs. non-aggressive epidemic regimes

		Models						
	5	13	6	14	7	15	8	16
Nutrient grow back algorithm \rightarrow	Urban							
Epidemic regime \rightarrow	E _A	E _N						
Quadrant								
1	8	5	6	3	5	4	7	7
2	7	4	5	4	6	5	4	5
3	6	8	7	6	8	7	5	6
4	5	7	8	8	7	8	8	8
5	3	1	2	1	1	1	2	2
6	2	2	1	2	2	2	1	1
7	1	3	4	5	3	3	3	3
8	4	6	3	7	4	6	6	4
χ^2	10.2	211	8.9	26	1.6	35	1.1	117
Rejection level of H_0^o	25	%	50	1%	99	%	99.	.5%

- Null hypothesis: the order of infection by quadrant is the same for both the aggressive and nonaggressive models.

- Note: Each group of models contains two independent samples.

7 degrees of freedom rejection level.Measurement level of data is ordinal.

Table 2.21—Order of infection by quadrant (1 through 8) in models with Urban nutrient grow back algorithm: aggressive vs. non-aggressive epidemic regimes

		Models						
	1	9	2	10	3	11	4	12
Nutrient grow back algorithm \rightarrow	Simple	Simple	Simple	Simple	Simple	Simple	Simple	Simple
Epidemic regime \rightarrow	E _A	E_N	E _A	E_N	E _A	E_N	EA	E_N
Quadrant								
1	849	724	878	1104	1025	2447	1144	1151
2	395	312	749	740	368	1033	608	549
3	687	232	1239	1349	816	497	956	368
4	245	53	114	328	434	59	10	7
5	1319	1508	1604	2114	1863	3104	2196	2596
6	1133	1679	2440	2185	1598	2622	1558	2182
7	618	1083	1065	2340	987	1817	1389	1986
8	68	89	146	196	202	147	227	133
Totals	5,314	8,235	7,293	8,088	9,777	12,424	12,598	15,270
χ^2	1134	.22	220	2.10	5818	8.99	98	5.62
Rejection level of H_0^o	<0.5	%	<0.	5%	<0.:	5%	<0	.5%

- Null hypothesis: the number of infection by quadrant is the same for both the aggressive and non-aggressive models.

- Note: Each group of models contains two independent samples.

- Critical value for the non-parametric chi-square test is 24.32 for $\alpha = 0.001$ (d.f. = 7).

Table 2.22—Number of infections by quadrant in models with Simple nutrient grow back algorithm: aggressive versus non-aggressive epidemic regimes

				Mode	ls			
	5	13	6	14	7	15	8	16
Nutrient grow back algorithm \rightarrow	Urban	Urban	Urban	Urban	Urban	Urban	Urban	Urban
Epidemic regime \rightarrow	E _A	E _N	E _A	E_N	E _A	E _N	EA	E_N
Quadrant								
1	1253	1514	1356	1796	1754	1750	1713	2055
2	1136	965	1364	1217	1519	932	1614	1494
3	1825	2363	2095	3142	2400	2690	2474	3059
4	1322	963	1596	1459	1514	1502	1849	1762
5	1996	2687	2561	3265	2288	3066	3136	3384
6	742	3008	1135	3827	1409	3035	1887	4002
7	892	1430	1477	2289	1103	1852	1617	2677
8	611	436	840	814	611	829	980	812
Totals	5,680	10,356	11,726	8,972	13,366	17,809	15,656	19,245
χ^2	7870	.18	771	9.26	2989	9.35	333	3.45
Rejection level of H_0^o	<0.5	%	<0.	5%	<0.5	5%	<0.	.5%

- Null hypothesis: the number of infection by quadrant is the same for both the aggressive and non-aggressive models.

- Note: Each group of models contains two independent samples.

- Critical value for the non-parametric chi-square test is 24.32 for $\alpha = 0.001$ (d.f. = 7).

Table 2.23—Number of infections by quadrant in models with Urban nutrient grow back algorithm: aggressive versus non-aggressive epidemic regimes

				Mode	ls			
	1	5	2	6	3	7	4	8
Epidemic regime \rightarrow	E _A	E _A	E _A	E _A	EA	E _A	E _A	E _A
Nutrient grow back								
algorithm \rightarrow	Simple	Urban	Simple	Urban	Simple	Urban	Simple	Urban
Quadrant								
1	55	63	67	88	82	66	52	60
2	42	59	63	85	68	74	53	53
3	42	57	64	93	56	85	56	58
4	50	56	89	93	44	82	85	70
5	44	43	47	58	32	48	38	47
6	30	39	45	57	36	51	39	46
7	28	35	46	64	30	56	37	52
8	40	44	58	58	38	59	35	59
average	41.375	49.500	59.875	74.500	48.250	65.125	49.375	55.625
s.d.	9.086	10.447	14.682	16.639	18.745	14.004	16.604	7.836
t	-1.6	60	-1.8	364	-2.	040	-0.9	63
Rejection level of H_0^s	109	6	10	1%	5	%	25	%

- Null hypothesis: infected agents in models with Urban nutrient grow back algorithm, on average, reach quadrants 1-8 with the same speed as infected agents in models with Simple nutrient grow back algorithm.

Note: Each group of models contains two independent samples.7 degrees of freedom rejection level.

Table 2.24— Number of weeks lapsed after onset of rabies until its appearance by quadrant (1 through 8) in models with aggressive epidemic regime: Simple versus Urban nutrient grow back

				Mode	ls				
	9	13	10	14	11	15	12	16	
Epidemic regime \rightarrow	E _N	E _N	E _N	E_N	E _N	E_N	E _N	E _N	
Nutrient grow back									
algorithm \rightarrow	Simple	Urban	Simple	Urban	Simple	Urban	Simple	Urban	
Quadrant									
1	79	191	60	89	97	146	127	97	
2	81	188	49	90	111	154	123	92	
3	105	203	63	108	112	158	135	92	
4	155	198	80	135	190	170	147	99	
5	57	93	34	58	78	104	69	62	
6	79	139	33	61	71	104	65	61	
7	93	167	44	103	77	122	86	68	
8	108	196	70	121	111	154	113	89	
average	94.625	171.875	54.125	95.625	105.875	139.000	108.125	82.500	
s.d.	29.335	38.144	16.966	26.971	37.934	25.523	30.972	16.027	
Т	-4.541		-3.0	584	-2.	049	2.0	78	
Rejection level of H_0^s	0.5	%	0.5	5%	5	%	5%	5%	

- Null hypothesis: infected agents in models with Urban nutrient grow back algorithm, on average, reach quadrants 1-8 with the same speed as infected agents in models with Simple nutrient grow back algorithm.

- Note: Each group of models contains two independent samples.

- 7 degrees of freedom rejection level.

Table 2.25— Number of weeks lapsed after onset of rabies until its appearance by quadrant (1 through 8) in models with non-aggressive epidemic regime: Simple versus Urban nutrient grow back

				Mode	S			
	1	5	2	6	3	7	4	8
Epidemic regime \rightarrow	E _A	E _A	E _A	E _A	E _A	E _A	E _A	E _A
Nutrient grow back								
algorithm \rightarrow	Simple	Urban	Simple	Urban	Simple	Urban	Simple	Urban
Quadrant								
1	8	8	7	6	8	5	5	7
2	4	7	5	5	7	6	6	4
3	5	6	6	7	6	8	7	5
4	7	5	8	8	5	7	8	8
5	6	3	3	2	2	1	3	2
6	2	2	1	1	3	2	4	1
7	1	1	2	4	1	3	2	3
8	3	4	4	3	4	4	1	6
χ^2	4.855 2.893 7.568		68	30.121				
Rejection level of H_0^O	75%	6	90	%	50	%	0.5	5%

- Null hypothesis: the order of infection by quadrant is the same for models with Simple or Urban nutrient grow back algorithm.

- Note: Each group of models contains two independent samples.

- 7 degrees of freedom rejection level.

Table 2.26— Order of infection by quadrant (1 through 8) in models with
aggressive epidemic regime: Simple versus Urban nutrient grow
back algorithm

				Model	S			
	9	13	10	14	11	15	12	16
Epidemic regime \rightarrow	E _N							
Nutrient grow back								
algorithm \rightarrow	Simple	Urban	Simple	Urban	Simple	Urban	Simple	Urban
Quadrant								
1	2	5	5	3	4	4	6	7
2	4	4	4	4	5	5	5	5
3	6	8	6	6	7	7	7	6
4	8	7	8	8	8	8	8	8
5	1	1	2	1	3	1	2	2
6	3	2	1	2	1	2	1	1
7	5	3	3	5	2	3	3	3
8	7	6	7	7	6	6	4	4
χ^2	6.568		3.6	3.633 2.833 (0.3	10
Rejection level of H_0^o	50%	6	90	1%	90	%	99.	5%

- Null hypothesis: the order of infection by quadrant is the same for models with Simple or Urban nutrient grow back algorithm.

Note: Each group of models contains two independent samples.7 degrees of freedom rejection level.

Table 2.27—Order of infection by quadrant (1 through 8) in models with nonaggressive epidemic regime: Simple versus Urban nutrient grow back algorithm

				Mode	ls			
	1	5	2	6	3	7	4	8
Epidemic regime \rightarrow	E _A							
Nutrient grow back	Simple	Urban	Simple	Urban	Simple	Urban	Simple	Urban
algorithm \rightarrow	Simple	Orbaii	Shipe	Ofball	Shipe	Ofball	Shipe	Orban
Quadrant								
1	849	1253	878	1356	1025	1754	1144	1713
2	395	1136	749	1364	368	1519	608	1614
3	687	1825	1239	2095	816	2400	956	2474
4	245	1322	114	1596	434	1514	10	1849
5	1319	1996	1604	2561	1863	2288	2196	3136
6	1133	742	2440	1135	1598	1409	1558	1887
7	618	892	1065	1477	987	1103	1389	1617
8	68	611	146	840	202	611	227	980
Totals	5,314	9,777	8,235	12,424	7,293	12,598	8,088	15,270
X	13141.71		2534	49.80	1084	41.93	3455	57.13
Rejection level of H_0^o	<0.5%		<0	.5%	<0	.5%	<0.	5%

- Null hypothesis: the number of infection by quadrant is the same for both the aggressive and non-aggressive models.

- Note: Each group of models contains two independent samples.

- Critical value for the non-parametric chi-square test is 24.32 for $\alpha = 0.001$ (d.f. = 7).

Table 2.28—Number of infections by quadrant in models with aggressive epidemic regime: Simple versus Urban nutrient grow back algorithm

				Mode	ls			
	9	13	10	14	11	15	12	16
Epidemic regime \rightarrow	E _N							
Nutrient grow back algorithm \rightarrow	Simple	Urban	Simple	Urban	Simple	Urban	Simple	Urban
Quadrant								
1	724	1514	1104	1796	2447	1750	1151	2055
2	312	965	740	1217	1033	932	549	1494
3	232	2363	1349	3142	497	2690	368	3059
4	53	963	328	1459	59	1502	7	1762
5	1508	2687	2114	3265	3104	3066	2596	3384
6	1679	3008	2185	3827	2622	3035	2182	4002
7	1083	1430	2340	2289	1817	1852	1986	2677
8	89	436	196	814	147	829	133	812
Totals	5,680	13,366	10,356	17,809	11,726	15,656	8,972	19,245
χ^2	40865.04		108.	10834.57		07.62	4674	82.30
Rejection level of H_0^o	<0.	5%	<0	.5%	<0	.5%	<0.	5%

Note: Critical values for the non-parametric chi-square test are 18.48 for $\alpha = 0.01$, and 24.32 for $\alpha = 0.001$ (d.f. = 7).

Table 2.29— Number of infections by quadrant in models with non-aggressiveepidemic regime: Simple versus Urban nutrient grow back algorithm

				Mode	ls			
	1	3	2	4	5	7	6	8
Epidemic regime \rightarrow	E _A							
Nutrient grow back								
algorithm \rightarrow	Simple	Simple	Simple	Simple	Urban	Urban	Urban	Urban
Quadrant								
1	55	82	67	52	63	66	88	60
2	42	68	63	53	59	74	85	53
3	42	56	64	56	57	85	93	58
4	50	44	89	85	56	82	93	70
5	44	32	47	38	43	48	58	47
6	30	36	45	39	39	51	57	46
7	28	30	46	37	35	56	64	52
8	40	38	58	35	44	59	58	59
χ^2	39.45		19	.53	51.	77	46	.29
Rejection level of H_0^o	<0.	5%	1	%	<0.	5%	<0	.5%

- Null hypothesis: infected agents in models with uniform home range distribution, on average, reach quadrants 1-8 with the same speed as infected agents in models with normal home range distribution.

- Each group of models contains two independent samples.

- 7 degrees of freedom rejection level.

Table 2.30—Speed of epidemic front in models with aggressive epidemic regime: uniform versus normal home range distribution

				Mode	el			
	9	11	10	12	13	15	14	16
Epidemic regime \rightarrow	E _N	E_N						
Nutrient grow back								
algorithm \rightarrow	Simple	Simple	Simple	Simple	Urban	Urban	Urban	Urban
Quadrant								
1	79	97	60	127	191	146	89	97
2	81	111	49	123	188	154	90	92
3	105	112	63	135	203	158	108	92
4	155	190	80	147	198	170	135	99
5	57	78	34	69	93	104	58	62
6	79	71	33	65	139	104	61	61
7	93	77	44	86	167	122	103	68
8	108	111	70	113	196	154	121	89
χ^2	34.97		458	3.53	61.	93	33	.37
Rejection level of H_0^o	<0.	5%	<0.	5%	<0.:	5%	<0	.5%

- Null hypothesis: infected agents in models with uniform home range distribution, on average, reach quadrants 1-8 with the same speed as infected agents in models with normal home range distribution.

Note: Each group of models contains two independent samples.7 degrees of freedom rejection level.

Table 2.31—Speed of epidemic front in models with non-aggressive epidemic regime: uniform versus normal home range distribution

				Mode	ls			
	1	3	2	4	5	7	6	8
Epidemic regime \rightarrow	E _A							
Nutrient grow back	Simple	Simple	Simple	Simple	Urbon	Urbon	Urban	Urbon
algorithm \rightarrow	Simple	Simple	Simple	Simple	UIDall	UIDall	UIDall	UIDall
Quadrant								
1	8	8	7	5	8	5	6	7
2	4	7	5	6	7	6	5	4
3	5	6	6	7	6	8	7	5
4	7	5	8	8	5	7	8	8
5	6	2	3	3	3	1	2	2
6	2	3	1	4	2	2	1	1
7	1	1	2	2	1	3	4	3
8	3	4	4	1	4	4	3	6
χ^2	10.836		12.	360	8.3	71	3.0)26
Rejection level of H_0^o	25	%	10)%	50	%	90)%

- Null hypothesis: the order of infection by quadrant is the same for models with uniform home range distribution and those with normal home range distribution.

- Note: Each group of models contains two independent samples.

- 7 degrees of freedom rejection level.

- Measurement level of data is ordinal.

Table 2.32— Order of infection by quadrant (1 through 8) in models withaggressive epidemic regime: uniform versus normal home rangedistribution

				Mode	ls			_		
	9	11	10	12	13	15	14	16		
Epidemic regime \rightarrow	E _N	E_N	E _N	E_N	E _N	E _N	E _N	E _N		
Nutrient grow back	Simple	Simple	Simple	Simple	Urbon	Urban	Urban	Urbon		
algorithm \rightarrow	Simple	Simple	Simple	Simple	UIDall	UIDall	UIDall	UIDall		
Quadrant										
1	2	4	5	6	5	4	3	7		
2	4	5	4	5	4	5	4	5		
3	6	7	6	7	8	7	6	6		
4	8	8	8	8	7	8	8	8		
5	1	3	2	2	1	1	1	2		
6	3	1	1	1	2	2	2	1		
7	5	2	3	3	3	3	5	3		
8	7	6	7	4	6	6	7	4		
χ^2	11.343		11.343		2.760		0.7	18	7.569	
Rejection level of H_0^o	25	%	95	%	>99.	.5%	50)%		

- Null hypothesis: the order of infection by quadrant is the same for models with uniform home range distribution and those with normal home range distribution.

- Note: Each group of models contains two independent samples.

7 degrees of freedom rejection level.Measurement level of data is ordinal.

Table 2.33—Order of infection by quadrant (1 through 8) in models with nonaggressive epidemic regime: uniform versus normal home range distribution

				Mode	l			
	1	3	2	4	5	7	6	8
Epidemic regime \rightarrow	E _A	E _A	EA	E _A	E _A	E _A	EA	E _A
Nutrient grow back	Simple	Simple	Simple	Simple	Urban	Urban	Urban	Urban
algorithm \rightarrow	Shipe	Shipe	Simple	Simple	UIUali	Olbali	Orban	UIUali
Quadrant								
1	849	1025	878	1144	1253	1754	1356	1713
2	395	368	749	608	1136	1519	1364	1614
3	687	816	1239	956	1825	2400	2095	2474
4	245	434	114	10	1322	1514	1596	1849
5	1319	1863	1604	2196	1996	2288	2561	3136
6	1133	1598	2440	1558	742	1409	1135	1887
7	618	987	1065	1389	892	1103	1477	1617
8	68	202	146	227	611	611	840	980
Totals	5,314	9,777	7,293	12,598	5,680	13,366	11,726	15,656
χ^2	1107.94		947	.47	1230).71	912	2.42
Rejection level of H_0^o	<0.	5%	<0.	5%	<0.5	5%	<0.	.5%

- Null hypothesis: the number of infection by quadrant is the same for models with uniform home range distribution and those with normal home range distribution.

- Note: Each group of models contains two independent samples.

- Critical value for the non-parametric chi-square test is 24.32 for $\alpha = 0.001$ (d.f. = 7).

Table 2.34— Number of infections in models with aggressive epidemic regime: uniform versus normal home range distribution

				Mode	el			
	9	11	10	12	13	15	14	16
Epidemic regime \rightarrow	E _N	E_N	E _N					
Nutrient grow back	Simple	Simple	Simple	Simple	Urban	Urban	Urban	Urbon
algorithm \rightarrow	Simple	Shiple	Simple	Simple	UIUali	Olball	UIUali	UIUali
Quadrant								
1	724	2447	1104	1151	1514	1750	1796	2055
2	312	1033	740	549	965	932	1217	1494
3	232	497	1349	368	2363	2690	3142	3059
4	53	59	328	7	963	1502	1459	1762
5	1508	3104	2114	2596	2687	3066	3265	3384
6	1679	2622	2185	2182	3008	3035	3827	4002
7	1083	1817	2340	1986	1430	1852	2289	2677
8	89	147	196	133	436	829	814	812
Totals	8,235	12,424	8,088	15,270	10,356	17,809	8,972	19,245
χ^2	3337.520		1758	6.062	595.	723	206.436	
Rejection level of H_0^o	<0.	5%	<0.	5%	<0.:	5%	<0	.5%

- Null hypothesis: the number of infection by quadrant is the same for models with uniform home range distribution and those with normal home range distribution.

- Note: Each group of models contains two independent samples.

- Critical value for the non-parametric chi-square test is 24.32 for $\alpha = 0.001$ (d.f. = 7).

Table 2.35— Number of infections in models with non-aggressive epidemic regime: uniform versus normal home range distribution

				Mode	s			
	1	2	3	4	5	6	7	8
Epidemic regime \rightarrow	E _A							
Nutrient grow back	Simple	Simple	Simple	Simple	Urbon	Urban	Urban	Urbon
algorithm \rightarrow	Simple	Simple	Simple	Simple	UIDall	UIDall	UIDall	UIDall
Quadrant								
1	55	67	82	52	63	88	66	60
2	42	63	68	53	59	85	74	53
3	42	64	56	56	57	93	85	58
4	50	89	44	85	56	93	82	70
5	44	47	32	38	43	58	48	47
6	30	45	36	39	39	57	51	46
7	28	46	30	37	35	64	56	52
8	40	58	38	35	44	58	59	59
χ^2	82.44		55	.73	110	.58	17	.63
Rejection level of H_0^o	<0.	5%	<0.	5%	<0.	5%	1	%

- Null hypothesis: Infected agents in models with short mating season length, on average, reach Quadrants 1-8 with the same speed as agents in models with long mating season length.

Each group of models contains two independent samples.7 degrees of freedom rejection level.

Table 2.36— Speed of epidemic front in models with aggressive epidemic regime: comparison of models with 13-week versus 21-week mating season

	Models							
	9	10	11	12	13	14	15	16
Epidemic regime \rightarrow	E _N							
Nutrient grow back algorithm \rightarrow	Simple	Simple	Simple	Simple	Urban	Urban	Urban	Urban
Quadrant						•		
1	79	60	97	127	191	89	146	97
2	81	49	111	123	188	90	154	92
3	105	63	112	135	203	108	158	92
4	155	80	190	147	198	135	170	99
5	57	34	78	69	93	58	104	62
6	79	33	71	65	139	61	104	61
7	93	44	77	86	167	103	122	68
8	108	70	111	113	196	121	154	89
χ^2	145.56		27.66		280.23		184.71	
Rejection level of H_0^o	<0.5%		<0.5%		<0.5%		<0.5%	

- Null hypothesis: Infected agents in models with short mating season length, on average, reach Quadrants 1-8 with the same speed as agents in models with long mating season length.

- Each group of models contains two independent samples.

- 7 degrees of freedom rejection level.

Table 2.37— Speed of epidemic front in models with non-aggressive epidemic regime: comparison of models with 13-week versus 21-week mating season

	Models							
	1	2	3	4	5	6	7	8
Epidemic regime \rightarrow	E _A							
Nutrient grow back	Simple	Simple	Simple	Simple	Urbon	Urban	Urban	Urbon
algorithm \rightarrow	Simple	Simple	Simple	Simple	UIDall	Ulban	Urban	UIDali
Quadrant								
1	8	7	8	5	8	6	5	7
2	4	5	7	6	7	5	6	4
3	5	6	6	7	6	7	8	5
4	7	8	5	8	5	8	7	8
5	6	3	2	3	3	2	1	2
6	2	1	3	4	2	1	2	1
7	1	2	1	2	1	4	3	3
8	3	4	4	1	4	3	4	6
χ^2	4.051		7.318		13.121		5.235	
Rejection level of H_0^o	90%		50%		10%		75%	

- Null hypothesis: the order of infection by quadrant is the same for models with short and long mating season length.

Note: Each group of models contains two independent samples.
7 degrees of freedom rejection level.

- Measurement level of data is ordinal.

Table 2.38— Order of infection by quadrant (1 through 8) in models with aggressive epidemic regime: 13-week versus 21-week mating season

	Models							
	9	10	11	12	13	14	15	16
Epidemic regime \rightarrow	E _A							
Nutrient grow back	Simple	Simple	Simple	Simple	Urban	Urban	Urban	Urbon
algorithm \rightarrow	Simple	Simple	Simple	Simple	Urban	Urban	Urban	Urban
Quadrant								
1	2	5	4	6	5	3	4	7
2	4	4	5	5	4	4	5	5
3	6	6	7	7	8	6	7	6
4	8	8	8	8	7	8	8	8
5	1	2	3	2	1	1	1	2
6	3	1	1	1	2	2	2	1
7	5	3	2	3	3	5	3	3
8	7	7	6	4	6	7	6	4
χ^2	7.633		2.500		2.943		4.560	
Rejection level of H_0^o	50%		95%		90%		75%	

- Null hypothesis: the order of infection by quadrant is the same for models with short and long mating season length.

Note: Each group of models contains two independent samples.
7 degrees of freedom rejection level.

- Measurement level of data is ordinal.

Table 2.39—Order of infection by quadrant (1 through 8) in models with nonaggressive epidemic regime: 13-week versus 21-week mating season

	Model							
	1	2	3	4	5	6	7	8
Epidemic regime \rightarrow	E _A	E _A	EA	E _A				
Nutrient grow back	Simple	Simple	Simple	Simple	Urbon	Urbon	Urban	Urbon
algorithm \rightarrow	Simple	Simple	Simple	Simple	Ulban	Ulban	Ulban	UIDall
Quadrant								
1	849	878	1025	1144	1253	1356	1754	1713
2	395	749	368	608	1136	1364	1519	1614
3	687	1239	816	956	1825	2095	2400	2474
4	245	114	434	10	1322	1596	1514	1849
5	1319	1604	1863	2196	1996	2561	2288	3136
6	1133	2440	1598	1558	742	1135	1409	1887
7	618	1065	987	1389	892	1477	1103	1617
8	68	146	202	227	611	840	611	980
Totals	5,314	8,235	7,293	8,088	9,777	12,424	12,598	15,270
χ^2	2813.908		835.937		988.535		1022.135	
Rejection level of H_0^o	<0.5%		<0.5%		<0.5%		<0.5%	

- Null hypothesis: The number of observations of infection by quadrant is the same for models with short (13 weeks) and long (21 weeks) mating seasons.

- Note: Each group of models contains two independent samples.

- Critical value for the non-parametric chi-square test is 24.32 for $\alpha = 0.001$ (d.f. = 7).

Table 2.40— Number of infections in models with aggressive epidemic regime: 13weeks versus 21 weeks mating season
		Model							
	9	10	11	12	13	14	15	16	
Epidemic regime \rightarrow	E _N								
Nutrient grow back	Simple	Simple	Simple	Simple	Urbon	Urbon	Urban	Urbon	
algorithm \rightarrow	Simple	Simple	Simple	Shiple	UIUali	UIUali	UIUali	UIUali	
Quadrant									
1	724	1104	2447	1151	1514	1796	1750	2055	
2	312	740	1033	549	965	1217	932	1494	
3	232	1349	497	368	2363	3142	2690	3059	
4	53	328	59	7	963	1459	1502	1762	
5	1508	2114	3104	2596	2687	3265	3066	3384	
6	1679	2185	2622	2182	3008	3827	3035	4002	
7	1083	2340	1817	1986	1430	2289	1852	2677	
8	89	196	147	133	436	814	829	812	
Totals	724	1104	2447	1151	1514	1796	1750	2055	
χ^2	5,680		10,356		11,726		8,972		
Rejection level of H_0^o	<0.	5%	<0.	5%	<0.5	5%	<0.5%		

Notes:

- Null hypothesis: The number of observations of infection by quadrant is the same for models with short (13 weeks) and long (21 weeks) mating seasons.

- Note: Each group of models contains two independent samples.

- Critical value for the non-parametric chi-square test is 24.32 for $\alpha = 0.001$ (d.f. = 7).

Table 2.41— Number of infections in models with non-aggressive epidemic regime:13 weeks versus 21 weeks mating season

Change of Variable	Speed	Order	Intensity	Pre-epidemic pop. densities
Epidemic regime $(E_A \rightarrow E_N)$	↑ 92%	\leftrightarrow	↑ 32%	N/A
Nutrient grow back algorithm $(S \rightarrow U)$	↓ 33%	\leftrightarrow	↑ 77%	↑ 27%
Home range distribution $(U \rightarrow N)$	\leftrightarrow	\leftrightarrow	↑ 19%	↑ 13%
Mating season $(13 \rightarrow 21)$	\leftrightarrow	\leftrightarrow	↑ 2 3%	↑ <u>1</u> 1%

Notes:

- Epidemic regime: $E_A := aggressive$, $E_N := non-aggressive$.

- Nutrient grow back algorithm: S := simple, U := urban.

- Home range distribution: U := uniform, N := normal.

- Mating season length: 13 := 13-week period, 21 := 21-week period.

Table 2.42—Summary of effects of model variables with respect to speed and shape of epidemic front

ARTICLE 3

Economic Analysis of a Raccoon Rabies Abatement Program: An Agent-Based Modeling Approach

OBJECTIVE

Develop a dynamic model that simulates the spread of raccoon rabies, and assess the cost-effectiveness of orally administered rabies vaccine (ORV) as an intervention method to abate raccoon rabies epidemic and its spread.

INTRODUCTION

In spite of the extensive research in modeling of outbreaks of terrestrial rabies, and advances in vaccine development and methodologies for eradication of rabies from its natural reservoirs, there are scant reports on systematic analysis of economic consequences of rabies and its intervention.¹ In this paper, I present results of agent-based models that represent two different scenarios: one that simulates a raccoon rabies epidemic outbreak and its potential economic cost in a hypothetical area where it has previously been unaffected by raccoon rabies; the other that simulates the economic cost of an effective ORV barrier that includes portions of the epidemic front and its

adjacent "rabies-free" area. The economic costs of these two scenarios, for different ORV strategies, are compared to assess the economic viability of an ORV program.

METHODS

The technical specifications of the model are the same as those described in Article 2 with the exception of the ORV and rabies cost rules which are described below. Results of the models are used to assess the cost-effectiveness of different ORV abatement strategies compared to an uninterrupted raccoon rabies epidemic.

MODELS

The models in this paper are a continuation of the models described in Article 2 which consist of characterization of geographical areas by land use and its associated nutrient growback rule ({ $\bar{\mathbf{E}}$ }), and agents by their genotype and behaviors ({ $\bar{\mathbf{A}}$ }) (see Article 2). Results of simulations of two uninterrupted raccoon rabies epidemic scenarios (aggressive epidemic: ({EC; G}, {AC; M, Mi, R, E_A}) and non-aggressive epidemic: ({EC; G}, {AC; M, Mi, R, E_A}) and non-aggressive epidemic: ({EC; G}, {AC; M, Mi, R, E_N})) in a previously rabies-free area is compared to alternative rabies abatement strategies (see Article 2). The alternative scenarios include the enhancement of the environment with an ORV program (see below); hence, { $\bar{\mathbf{E}}$ } is modified to {EC; G, V}. Therefore, the characteristics and behavior of the model that includes an ORV abatement strategy in compact form are denoted as ({ $\bar{\mathbf{E}}$ }, { $\bar{\mathbf{A}}$ }) = ({EC; G, V}, {AC; M, Mi, R, E, C}).

Space

The model's space, a hypothetical 20-kilometer square space, is comprised of a lattice of 100-m² grids (total of 40,000 spatial units). The composition of the landscape is designated as 20% urban, 20% wetland, 20% farmland, 15% forest, 15% prairie, 5% water and 5% other (see Article 2). The model's space is further divided into 16 quadrants (see Figure 3.1). Since the external initiation of disease is a random process and may result in spurious results within the border quadrants, focus of the spread and intensity of the epidemic is limited to the quadrants furthest away from the southern border, Quadrants 1-8 (see Figure 3.1).

Agents

Initially, 8,000 agents are introduced to the model (20 agents/km²). For a duration of 500 periods, the agents move around in the model's space, reproduce, die, and give rise to their spatial distribution according to the land use categories (see Article 2). In addition, agents move in and out of the model's space through the migration rule (see Article 2). At period 500 and every two periods thereafter, a rabid agent enters the model's space through its southern boundary. The point of entry for the rabid animal is selected randomly, and each rabid animal can live up to a maximum of two weeks. Each rabid agent that enters the model's space lives for two periods. Rabid agents move randomly within their home range (see Movement rule, Article 2) and infect susceptible neighbors at their new position (non-aggressive epidemic regime). In the aggressive epidemic regime, the rabid agent also infects all susceptible agents in its shortest path to the new location (also see Epidemic rule, Article 2).

ORV rule, V

One method used to control and limit the spread of rabies is to vaccinate wildlife hosts with ORV.^{2, 3} ORV is encased in baits and distributed over a designated area so that the healthy susceptible portions of the population that serve as hosts will consume the vaccine and bait and become protected against rabies infection. An effective ORV area would stop the spread of rabies into geographical areas where raccoon rabies has not been detected before. In the models presented here, the rate of bait placement serves as a policy variable. The size of ORV barrier can also serve as a policy variable; however, since the size of the model space in this paper is relatively small, this variable is not tested. Other essential variables that determine the effectiveness of an ORV program are the uptake of the vaccine baits by the target population and its effectiveness (seroconversion rate). A sensitivity analyses is conducted around variables that are not deemed certain: bait distribution and vaccine uptake (see Results), effectiveness of the ORV, nutrient grow back algorithm of spatial units (see Article 2), and epidemic regime (aggressive versus non-aggressive, see Article 2, and Table 3.1).

Vaccine uptake

Roscoe et al⁴ estimate that an ORV baiting (at a rate of 64 baits/km²) in a 552-km² area in New Jersey resulted in seroconversion of 61% of the sampled raccoons. Traces of the vaccine were observed in 73% of raccoons in another sample in the same area. If we assume that the proportion of vaccinated raccoons is a concave function of amount of baits distributed per square kilometer, the range of this function would be from 0% of raccoons vaccinated at zero amount of effort to nearly 100% at very high rate of bait distribution. In this paper, a concave function of distribution rates is assumed with 70, and 175 baits/km² corresponding to vaccination rates of 65%, and 99%, respectively. The simulations are conducted using different values of vaccination rates (see Figure 3.2). Accordingly, the additional cost of the increase in baits used is reflected in the abatement cost.

Effectiveness

Rupprecht et al⁵ estimate that raccoons that ingested a form of ORV were protected from rabies from 30 to 205 days from the time of ingestion. One of the vaccine effectiveness regimes that is used in this paper is that when an agent becomes vaccinated, it is protected against rabies between 5 and 30 weeks (U(5, 30)). Most studies relating to the efficacy of ORV in raccoons have been conducted in laboratory settings and may be much different in the field where variables such as herd immunity also play a role in protection of the susceptible raccoons from rabies infection. Therefore, a different range of rabies protection (U(30, 45)) is used in some of the models to assess the sensitivity of results to the effectiveness of ORV. Figure 3.3 shows the proportion of vaccinated susceptible agents through a duration of two years (four ORV bait distributions at periods 500, 526, 552 and 578) with two different ORV regimes. In one regime, the vaccination uptake by the susceptible animals is 65% and the ORV effectiveness is distributed from a uniform distribution with a rnge of 5 to 30 weeks. The other regime, represents a superior ORV technology with is effectiveness distributed from a uniform distribution with a range of 30 to 45 weeks and the ORV

effort results in successful vaccination of 99% of the susceptible agents within the ORV barrier.

Figure 3.3 illustrates the implications of different assumptions on vaccine uptake and effectiveness distribution. Hence, for an ORV strategy with 65% vaccine uptake and an effectiveness distribution of U(5, 30), an average of 41.7% (minimum 8%) of the susceptible agents in the ORV barrier are vaccinated during the two years depicted in Figure 3.3. While the 99% vaccine uptake (effectiveness: U(30, 45)) strategy has an average vaccination rate of 86% (minimum 61%).

ORV algorithm

ORV is typically distributed in an immune barrier that includes geographical areas that cover portions of the raccoon rabies epidemic front and its adjacent "rabies-free" area. Different rates of bait distribution (70, 100, 175 baits/km²), and effectiveness distributions for a 10-kilometer wide ORV barrier is used to measure their cost-effectiveness. The 10-kilometer ORV barrier includes quadrants 5-12 in the model's space (see Figure 3.4). At period 500, and every 26 periods thereafter, the ORV is placed in the designated barrier. ORV baits are distributed at a cost of \$23.23/km² and \$1.47/bait (average of eight ORV distribution events in Ohio, see Article 1). Total cost of ORV areas (V) and raccoon rabies cost (C) that spill into the ORV areas are then computed for each period. The simulation ends at period 2600 (total of 50 years at 52 periods per year).

Rabies cost rule

Epidemic is defined as a period of time where there is a rapid increase in the level of infection in an area. The epidemic period for raccoon rabies, in a medium-sized state, typically lasts 3-4 years. The infection level eventually decreases as the number of susceptible animals decreases whereby the infection enters the endemic stage. Due to the frequency of rabies incidences, rabies cost in a region depends on whether rabies is in its pre-epidemic (rabies free), epidemic, or endemic stage. A possible way of mapping simulated rabies incidences to actual increase in rabies cost is to classify whether a geographical entity, say a county, is in its pre-epidemic, epidemic or endemic stage. The increase in raccoon rabies costs for epidemic and endemic areas, compared to a base cost of a pre-epidemic year, is estimated in the form of \$/km² based on other cost estimates for such areas cited from available literature (see below).

There has been sparse reporting on the cost of raccoon rabies. The most complete set of cost estimates of raccoon rabies, presented by Uhaa et al (1992), indicates the cost of an uninterrupted raccoon rabies epidemic in two counties in New Jersey (area: 2,137 km²) in 1990 to be \$1,011,844 (\$474/km²).²³ This estimate is based on the increase in expenditure of human and animal health care, animal control, laboratory costs, rabies education and research, and additional vaccination of pet animals from a pre-epizootic year (1988) to an epizootic year (1990). Uhaa's rabies cost estimate does not include many elements such as value of avoided pain and suffering, or the public's willingness to pay to avoid the disease. Excluding the pet animal vaccinations, which are

mandatory by law, the raccoon rabies cost estimate for this period is reduced to \$523,400 (\$245/km²) (see Table 3.1).

Most other studies relating to the cost of raccoon rabies focus on the overuse of preexposure prophylaxis and post-exposure prophylaxis (PEP). Pre-exposure prophylaxis is a medical treatment to prevent persons from potential exposure to rabies and typically includes a visit to a clinic and administration of a set of biologics. PEP is a medical treatment for persons suspected of having been exposed to rabies and typically includes an initial visit to the clinic and administration of a set of biologics and four return visits for administration of booster shots. Noah (1996) claims that unwarranted overuse of PEP administration resulted in 665 persons receiving PEP due to a single positive case of rabies in a pet store in New Hampshire.²⁴ The biologics cost alone for the New Hampshire case was estimated at \$1.1 million.²⁴ Through a survey of hospitals in Massachusetts, Kreindel et al (1998) estimated the cost of pre-exposure prophylaxis (\$924) and PEP administration (\$2,376) (see Table 3.2).²⁵ As a result of raccoon rabies epidemic, the use of PEP in Massachusetts (area: 20,300 km²) increased from 105 cases in a pre-epidemic year (1991) to 2,680 cases in an epidemic year (1995). Hence, the annual incremental cost of PEP and its administration to the state of Massachusetts in an epidemic year was estimated between \$488,800 (\$24/km²) in 1992 and \$6.1 million (\$301/km²) in 1995 (see Table 3.3).

Nelson (1996) estimated that in Connecticut (Area: 12,549 km²) where the first raccoon rabies epizootic was identified in March 1991, the number of PEP increased from an

estimated 41 persons in 1990 to 887 in 1994 (see Table 3.4).²⁶ Using Nelson's average cost of biologics (\$1,352) charged by the hospitals to the patients, Connecticut incurred an additional annual cost of \$351,520 (24/km²) in 1991 to \$1.2 million (\$91/km²) in 1994 (see Table 3.4). In a study area of four counties in NY (area: 7,090 km²), Wyatt et al (1999) estimated that the use of PEP increased from less than 15 in a pre-epidemic year (1992) to 699 cases in an epidemic year.²⁷ Incremental PEP biologics cost alone, estimated at \$1,500 per patient, rose from \$22,500 in a pre-epidemic year (1992) to more than \$1 million in an epidemic year (1994) (see Table 3.5).

A summary of incremental rabies cost of an epidemic year compared to a pre-epidemic year presented in Tables 3.1-3.5 is tabulated in Table 3.6 below. Uhaa et al's proportion of costs of PEP-related costs (38%) versus other rabies-related costs (62%) was used to extrapolate "Other costs" of raccoon rabies epidemic for the remainder of the studies (see Table 3.6). Similarly, Kriendel et al's proportion of PEP biologics (73%) versus PEP administration (27%) was used to determine the PEP administration costs for the Connecticut and New York studies (see Table 3.6). From these data we can obtain an estimate of a range of potential economic cost per square kilometer of \$200-\$500 for raccoon rabies in an epidemic year. For the purpose of this study, we assess three different scenarios of low rabies cost (\$200/km²), medium rabies cost (\$350/km²), and high rabies cost (\$500/km²) to estimate the range and midpoint of potential raccoon rabies cost in epidemic periods (see Table 3.7).

Kemere et al (1999) estimates on the economic impact of raccoon rabies were based on population of affected geographic areas (\$/100,000 population).²⁸ Excluding the pet animal vaccination costs, these estimates were distinguished by incremental cost (compared to pre-epidemic year) of epidemic year (\$87,800/100,000) and endemic year (\$51,700/100,000). Although one cannot readily compare these hypothetical cost figures (\$/population) with those in Tables 3.1-3.6 (\$/km²), it can be said that rabies cost for endemic years, according to Kemere et al, is roughly 60% of an epidemic year (see Table 3.7).

The proxy costs presented in Table 3.7 is used to map the level of rabies activity in a specified area (based on quadrants in models in this paper) to its cost.

RESULTS

To demonstrate the methodology of systematically calculating cost of an uninterrupted raccoon rabies event and the cost of potential alternative ORV distribution strategies, three models are selected from Article 2: Models 1, 5 and 16 (see Table 3.8). Results from Article 2 indicate that Model 1 has the fastest moving epidemic front with rabies reaching Quadrants 1-8 in an average of 42 weeks (see Table 3.9 and also Article 2). The amounts of time it takes for the rabies epidemic to reach Quadrants 1-8 in Models 5 and 16, on average, are 50 and 83 weeks, respectively. Article 2 also indicates that, in an uninterrupted rabies epidemic event, in Quadrants 1-8, Model 16 results in the largest number if infections (19,245) (see Table 3.10). In contrast, between the 16 models simulated in Article 2, in Quadrants 1-8, Model 1 produced the least number of infections (5,314) while Model 5 produced 9,777 infections (see Table 3.10). For each

model, four different ORV strategies are used representing different combinations of ORV uptake (65% and 99%) and effectiveness (U(5, 30) and U(30, 45)) (see Table 3.8). Vaccine uptake is assumed to be associated with different levels of bait distribution effort (see Vaccine uptake, above); hence, the cost of increased effort for a higher uptake level is reflected in the ORV costs (see also ORV algorithm and cost, above). Table 3.8 also presents the major model components that differentiate the three models from each other.

Speed of the epidemic front

Table 3.9 shows the amount of time it takes the epidemic to reach each Quadrants 1-8 after the introduction of rabies for each model. For Model 1, strategies ORV 1 and ORV 2 do not stop the rabies from reaching Quadrants 1-8; however, they do slow it down between 80% and 90%. Strategy ORV 3 stops the rabies from reaching the northernmost quadrants (1-4) while ORV 4 stops rabies within seven of Quadrants 1-8 (see Table 3.9).

Strategy ORV plans for Model 5—which is differentiated from Model 1 by its nutrient grow back algorithm (Urban in Model 5, Simple in Model 1; see Article 2) significantly reduces the speed of the epidemic front with strategies ORV 9 (49%), ORV 10 (220%), and ORV 11 (170%). ORV 12 manages to stop the rabies from reaching five of the eight northern quadrants. None of the ORV strategies used to abate the rabies epidemic in Model 16 is effective with rabies spreading throughout the entire model space with each one of the strategies. However, there is significant reduction in the speed of the epidemic within the four ORV strategies (15% - 614%).

Number of Infections

For Quadrants 1-8, total number of infections was higher for one ORV strategy used for Model 1 than its uninterrupted rabies event. The number of infections was also higher for three of the four ORV strategies used for Model 5; while reducing the number of infections drastically to 41 cases with ORV 12. All ORV strategies produced higher infections than the uninterrupted rabies event of Model 16.

Epidemic and ORV costs

Table 3.11 includes the net present value of the economic cost of the three uninterrupted rabies epidemic events and 12 ORV distribution strategies. Although the total cost of each uninterrupted rabies event (aggressive and non-aggressive) is less than their ORV distribution strategy counterparts, it is not necessarily true that an ORV distribution strategy is not warranted in face of a rabies epidemic. Given an effective ORV distribution nbarrier, the benefits of keeping the space beyond the model's space rabies free may outweigh the cost of ORV strategy. It is also worthwhile to note that most of the costs of the ORV strategies are for the purchase of bait: 82% of 70 baits/km² strategy, and 92% for 175 baits/km².

DISCUSSION

In this paper, three models that represent three separate simulation of raccoon rabies epidemic in a hypothetical area are selected from Article 2. For each model, four different ORV strategies are implemented in separate simulations to compare the effect of each ORV strategy on the speed of epidemic and number of infections with that of the uninterrupted counterpart model. The four different ORV strategies consist of different combination of ORV distribution effort, and assumed effectiveness of the ORVs. Not all ORV strategies proved to be effective in that the disease still moved across the ORV barrier in to the area that was supposed to be protected by it; however, overall, the rate of movement was greatly diminished. For three ORV distribution strategies, where effectiveness of the ORV was assumed to last between 30 and 45 days, the ORV barrier proved to be effective. One of these scenarios assumed ORV uptake of 65% by the susceptible population in the ORV barrier, while the other two scenarios assumed 99% uptake. These results underscore the need for improvement in ORV technology.

There were mixed results on the number of infections in each model before and after implementation of an ORV distribution strategy. In Model 1, the number of infections increased under an ORV distribution strategy in one of four cases, while in Models 5 and 16 in three and four out of four cases, respectively, the number of infections rose after implementation of an ORV distribution strategy. Although it seems counterintuitive that implementation of an ORV distribution strategy would actually increase the number of rabies cases, it seems that this peculiar result is a byproduct of the relatively small model space and the edge effect created by the influx of susceptible migrant agents into the model. In the uninterrupted rabies simulations, after the epidemic front sweeps throughout the model, the model's space initially gets populated around the edges and eventually agents move to the middle of model's space. Under the ORV strategies, the vaccinated agents in the middle portion of the model's space continue to reproduce and therefore extend a larger susceptible and unprotected agent population than an uninterrupted rabies event. It is also possible that the reproduction rule and/or spatial characteristics and grow back rule (see Article 2) are not realistic and results in the overpopulation of the model's space.

The benefit cost ratios indicate that given the coverage of the model's space (400 km²), implementation of an ORV distribution strategy is not economically justifiable. However, the benefits derived from an effective ORV distribution strategy by far extends beyond the adjacent areas of the ORV barrier. For example, in a westward movement of raccoon rabies, an effective ORV distribution strategy in the state of Ohio would benefit all states west of Ohio. These benefits would be realized in the form foregone medical costs and epidemic outbreak program costs borne by the local, state and federal agencies. Moreover, this analysis does not take into account potential loss of wildlife, pet animals, livestock, psychological trauma to humans or their willingness to pay for abatement of raccoon rabies spread. Rabies in wildlife is typically a regional and persistent health problem; therefore, the economic costs and benefits of an ORV program should be considered over a broad region and over a long period. Collaboration among different regions could result in several economies of scale, such as reduced price of ORV from the purchase of large quantities of baits. Regional cooperation could also lead to economies of scale by hiring new personnel and purchasing new equipment and material; in existing ORV programs, both are currently contracted out to external agencies (eg, fixed-wing aircraft, pilots, etc.). Hence, in order to assess the economic viability of an ORV strategy in face of raccoon rabies epidemic, different policies in regards to the procurement of materials and personnel need to be considered.

The information presented here can be refined with additional knowledge on raccoon ecology and epidemiologic characteristics of rabies in raccoons to predict future spread of rabies as well as the economic impact of using ORV. Several scenarios may need to be evaluated, and they will be important in determining the feasibility of regional and national efforts and in designing future interventions to control this public health problem.

REFERENCES: ARTICLE 3

- 1. Meltzer MI, Rupprecht CE. A review of the economics of the prevention and control of rabies," *Pharmacoeconomics* 1998; 14:365-383.
- Winkler WG, Jenkins SR. Raccoon rabies. In: Baer GM, ed. *The natural history of rabies*. 2nd ed. Boca Raton, Fla.: CRC Press Inc, 1991; 1991:325-340.
- Rupprecht CE, Wiktor TJ, Johnston DH, et al. Oral immunization and protection of raccoons (*Procyon lotor*) with a vaccinia-rabies glycoprotein recombinant virus vaccine. *Proc Natl Acad Sci U S A* 1986; 83:7947-7950.
- Roscoe DE, Holste WC, Sorhage FE, Campbell C et al. Efficacy of an oral vacciniarabies glycoprotein recombinant vaccine in controlling epidemic raccoon rabies in New Jersey. J Wildl Dis. 1998 Oct; 34(4):752-63.
- Rupprecht CE, Hamir AN, Johnston DH, Koprowski H. Efficacy of a vacciniarabies glycoprotein recombinant virus vaccine in raccoons (Procyon lotor). *Rev Infect Dis.* 1988 Nov-Dec; 10 Suppl 4:S803-9.



Notes: Each quadrant is a 5 kilometer square (2500 spatial units) (Total of 40000 spatial units). Seven different land uses, from darkest (most nutritious) to lightest (zero food value): urban, wetland, farmland, forest, prairie, other, inhabitable.

Figure 3.1—Representation of model's space with 7 different land use categories and 16 quadrants



Figure 3.2—Assumed relationship of vaccine uptake and intensity of ORV bait distribution



Figure 3.3—Proportion of susceptibles vaccinated in ORV barrier with different baiting strategies and effectiveness distribution



Figure 3.4—Designation of quadrants and ORV barrier in the model's space

Cost item	1988 (pre-epidemic) total cost adjusted ^b (\$/km ²)	1990 (epidemic) total cost (\$/km ²)	Unit incremental cost (\$/km ²) ^c	
Veterinarian	6.08	9.26	3.18	
Advertising	2.81	3.39	0.57	
Bite investigations	2.97	8.80	5.83	
Confinements	0	16.25	16.25	
Other rabies control activities	46.27	116.23	69.96	
Specimen preparation	1.17	16.39	15.23	
Specimen testing	3.14	21.98	18.84	
Education/training/consultation	2.77	22.78	20.02	
Epidemiology/research	0.47	0.54	0.08	
Clerical/administrative	3.51	5.19	1.68	
Pre-exposure prophylaxis	1.07	25.27	24.20	
Post-exposure prophylaxis	0.64	69.73	69.09	
Total	\$70.88	\$315.80	\$244.92	

a – Uhaa et al (1992)

b - Cost values adjusted to 1990 dollar.

c – Unit incremental cost is difference of pre-epidemic year (1988) and epidemic year (1990) divided by the area of the two counties in NJ (2,137 km²).

Table 3.1—Estimated incremental raccoon rabies cost of an epidemic year in two counties in NJ in 1990^a

Cost item	pre-exposure prophylaxis	PEP
Biologics	762	1,646
First emergency room visit	87	87
Physician emergency treatment	75	75
4 emergency room return visit	NA	284
4 physician follow-up visits	NA	284
Total cost per patient	\$924	\$2,376

a - Kriendel et al (1998)

Table 3.2—Estimated cost of administration of pre-exposure prophylaxis and PEP in Massachusetts ^a

Year	Estimated #	PEP admi cost	inistration s (\$)	Incremental unit PEP administration cost from a pre-epizootic year (\$/km ²) ^d		
	of patients	Lower limit ^c	Upper limit ^c	Lower limit	Upper limit	
1991 ^b	105	97,020	249,480			
1992	634	585,816	1,506,384	24.08	61.92	
1993	1141	1,054,284	2,711,016	47.16	121.26	
1994	2172	2,006,928	5,160,672	94.08	241.93	
1995	2680	2,476,320	6,367,680	117.21	301.39	

a – Kriendel et al (1998)

b – Pre-epidemic year

c – Lower limit and upper limit values based on all patients receiving pre-exposure or PEP treatment, respectively (see Table 3.2).

d – Incremental unit PEP administration cost for each epidemic year is based on [(est. # of patients – 105 patients in pre-epidemic year) * (cost value from Table 3.2 (\$/patient))]/ 20,300 km².

Table 3.3—Estimated number of rabies prophylaxis patients and its incremental unit cost per km² in epidemic years in Massachusetts: 1991-1995 ^a

Year	Estimated number of patients	PEP biologics cost (\$)	Incremental unit biologics cost from a pre-epizootic year (\$/km ²) ^c
1990 ^b	41	55,432	
1991	260	351,520	23.59
1992	672	908,544	67.98
1993	837	1,131,624	85.76
1994	887	1,199,224	91.14

a - Nelson (1996)

 $b- \ Pre-epidemic \ year$

 c – Incremental unit biologics cost for each year is based on [(est. # of patients – 41 patients in a preepidemic year) * (\$1,352/patient)]/12,549 km²

Table 3.4—Estimated number of rabies patients, PEP biologics cost, and additional unit cost per km² in epidemic years in Connecticut: 1990-1994^a

Year	Estimated number of patients	PEP biologics cost (\$)	Incremental unit biologics cost from a pre-epidemic year (\$/km ²) ^c
1992 ^b	< 15	22,500	
1993	474	711,000	97.11
1994	699	1,048,500	144.71

a – Wyatt et al (1999)

b – Pre-epidemic year

 c – Incremental unit biologics cost for each year is based on [(est. # of patients – 15 patients in a preepidemic year) * (\$1,500/patient)]/7,090 km²

Table 3.5—Estimated number of rabies patients, PEP biologics cost, and additional unit cost per km² in epidemic years in four counties in NY: 1992-1994^a

Study Area	PEP biologics	PEP administration	Other costs	Total
State of MA (20,300 km ²)	92 ^a	34 ^a	206 ^b	\$332
State of CT (12, 974 km ²)	65 [°]	24 ^d	145 ^b	\$234
Four counties in NY (7,090 km ²)	121 ^e	45 ^d	271 ^b	\$437
Two counties in NJ $(2,137 \text{ km}^2)$		93 ^f	152 ^f	\$245

Notes: All values in \$/km². Italic values are estimated.

a – Kriendel et al (1998). PEP biologics and administration costs are based on average of 4 epidemic years (1992-1995).

b - Other cost is based on proportion of costs in Uhaa et al's study: 62% of total cost.

c - Nelson (1996). PEP biologics cost is based on average of 4 epidemic years (1991-1994).

d – PEP study is based on Kriendel et al's study: 27% of total PEP cost.

e - Wyatt et al (1999). PEP biologics cost is based on average of 2 epidemic years (1993-1994).

f – Uhaa et al (1992). PEP biologics and administration cost based on one epidemic year (1990).

Table 3.6—Estimated incremental raccoon rabies unit cost estimates in epidemic years

Year	Low	Medium	High
Epidemic	200	350	500
Endemic	120	210	300

Note: All values in \$/km².

Table 3.7—A possible raccoon rabies cost schedule in epidemic and endemic years

	ORV	strategy	I	Major model comp	onents	
Model	Uptake	Effectiveness	Epidemic regime	Nutrient grow back algorithm	Mating season length	
1	N/A	N/A	EA	Simple	13 weeks	
ORV 1	65%	U(5, 30)				
ORV 2	99%	U(5, 30)				
ORV 3	65%	U(30, 45)				
ORV 4	99%	U(30, 45)				
5	N/A	N/A	EA	Urban	13 weeks	
ORV 9	65%	U(5, 30)				
ORV 10	99%	U(5, 30)				
ORV 11	65%	U(30, 45)				
ORV 12	99%	U(30, 45)				
16	N/A	N/A	E _N	Urban	21 weeks	
ORV 5	65%	U(5, 30)				
ORV 6	99%	U(5, 30)				
ORV 7	65%	U(30, 45)]			
ORV 8	99%	U(30, 45)				

Notes: $E_A = Aggressive regime, E_N = Non-aggressive regime.$ N/A = Not Applicable, no ORV strategy used.

Barrier size is 20 km in length and 10 km in width (Quadrants 5-12, see Figure 3.4).

Table 3.8—Models: Article 3

	Quadrant								
Model	1	2	3	4	5	6	7	8	
1	55	42	42	50	44	30	28	40	
ORV 1	75	81	83	115	56	49	55	83	
ORV 2	88	79	82	121	42	44	58	112	
ORV 3	RF	RF	RF	RF	35	30	44	48	
ORV 4	RF	RF	RF	RF	RF	449	RF	RF	
5	63	59	57	56	43	39	35	44	
ORV 9	80	88	100	101	57	68	45	51	
ORV 10	200	188	192	208	103	82	89	208	
ORV 11	126	141	158	175	69	89	145	191	
ORV 12	RF	RF	RF	RF	263	262	366	RF	
16	97	92	92	99	62	61	68	89	
ORV 5	96	99	121	148	46	53	59	143	
ORV 6	127	139	157	168	100	65	108	109	
ORV 7	154	153	189	199	56	53	53	83	
ORV 8	785	797	817	826	108	107	409	205	

Notes: RF = Rabies Free

Table 3.9—Number of weeks lapsed after onset of rabies until its appearance by quadrant (1-8)

	Quadrant								
Model	1	2	3	4	5	6	7	8	Total
1	849	395	687	245	1319	1133	618	68	5,314
ORV 1	969	410	243	63	1394	705	260	45	4,089
ORV 2	903	930	2177	583	583	286	164	40	5,666
ORV 3	0	0	0	0	26	44	7	1	78
ORV 4	0	0	0	0	0	1	0	0	1
5	1253	1136	1825	1322	1996	742	892	611	9,777
ORV 9	1226	906	1590	1329	1952	1478	1131	596	10,208
ORV 10	1510	1558	1981	1444	2016	1916	952	313	11,690
ORV 11	2315	1623	2627	1870	2937	2334	1357	427	15,490
ORV 12	0	0	0	0	15	24	2	0	41
16	2055	1494	3059	1762	3384	4002	2677	812	19,245
ORV 5	3229	2681	4547	2254	4383	3344	1496	536	22,470
ORV 6	8864	4168	8849	2861	4174	1721	998	351	31,986
ORV 7	5957	3363	7766	2354	3851	1952	1021	304	26,568
ORV 8	4589	3731	11638	2987	1288	657	594	185	25,669

 Table 3.10—Number of infections by quadrant (1-8)

Model	ORV	Epidemic	Total	Range (\$Millions)	B/C Ratio	
1	0	1,761,969	1,761,969	1.01-2.52	N/A	
ORV 1	865,710	1,727,739	2,593,449	1.85-3.33	0.679	
ORV 2	1,925,112	1,806,947	3,732,060	2.96-4.51	0.472	
ORV 3	865,710	1,351,874	2,217,584	1.64-2.80	0.795	
ORV 4	1,925,112	996,931	2,922,044	2.49-3.35	0.603	
5	0	1,687,122	1,687,122	0.97-2.41	N/A	
ORV 9	865,710	1,715,286	2,580,997	1.85-3.32	0.683	
ORV 10	1,925,112	1,640,306	3,565,418	2.86-4.27	0.494	
ORV 11	865,710	1,686,020	2,551,730	1.83-3.27	0.690	
ORV 12	1,925,112	1,272,575	3,197,687	2.65-3.74	0.551	
16	0	1,791,269	1,791,269	1.02-2.56	N/A	
ORV 5	865,710	1,679,624	2,545,334	1.83-3.27	0.692	
ORV 6	1,925,112	1,787,981	3,713,093	2.95-4.48	0.475	
ORV 7	865,710	1,776,023	26,41,733	1.88-3.40	0.667	
ORV 8	1,925,112	1,559,990	3,485,102	2.82-4.15	0.506	

Notes:

- Net present value calculated at an interest rate of 5%.

- Duration of the net present value is 40 years.

- Median estimate of the epidemic cost is used for total cost.

- B/C ratio is the ratio of benefits of total foregone costs of uninterrupted model (Models 1, 5, and 16) and total cost of an ORV model (e.g., B/C ratio for ORV8 = \$1,791,269/\$3,485,102)

Table 3.11—Net present value of alternative ORV strategies versus an uninterrupted rabies epidemic

BIBLIOGRAPHY

- 1. Uhaa LJ, Dato VM, Sorhage FE, et al. Benefits and costs of using an orally absorbed vaccine to control rabies in raccoons. *J Am Vet Med Assoc* 1992; 201:1873-1882.
- 2. Kreindel SM, McGuill M, Meltzer M, et al. The cost of rabies postexposure prophylaxis: One state's experience. *Public Health Rep* 1998; 13:247-251.
- 3. Robbins AH, Borden MD, Windmiller BS, et al. Prevention of the spread of rabies to wildlife by oral rabies vaccination of raccoons in Massachusetts. *J Am Vet Med Assoc* 1998; 213:1407-1412.
- 4. Winkler WG, Jenkins SR. Raccoon rabies. In: Baer GM, ed. *The natural history of rabies*. 2nd ed. Boca Raton, FL: CRC Press Inc.; 1991:325-340.
- 5. Fischman HR, Grigor JK, Horman JT, et al. Epizootic of rabies in raccoons in Maryland from 1981 to 1987. *J Am Vet Med Assoc* 1992; 201:1883-1886.
- 6. Torrence ME, Jenkins SR, Glickman LT. Epidemology of raccoon rabies in Virginia, 1984 to 1989. *J Wildl Dis* 1992; 28:369-376.
- 7. Krebs JW, Rupprecht CE, Childs JE. Rabies surveillance in the United States during 1999. *J Am Vet Med Assoc* 2000; 217:1799-1811.
- 8. Smith KA. Update on rabies in Ohio. Ohio Vet Med Assoc Newslett 1998; 29:5.
- 9. Wandeler A, Rosatte RC, Williams D, et al. Update: Raccoon rabies epizootic -United States and Canada, 1999. *MMWR Morb Mortal Wkly Rep* 2000; 49:31-35.
- 10. Aubert, MFA. Costs and benefits of rabies control in wildlife in France. *Rev sci tech* 1999; 18:533-543.

- 11. Nelson RS, Cooper GH, Cartter ML, et al. Rabies postexposure prohylaxis— Connecticut, 1990-1994. *MMWR Morb Mortal Wkly Rep* 1996; 45:232-234.
- Rupprecht CE, Wiktor TJ, Johnston DH, et al. Oral immunization and protection of raccoons (*Procyon lotor*) with a vaccinia-rabies glycoprotein recombinant virus vaccine. *Proc Natl Acad Sci U S A* 1986; 83:7947-7950.
- 13. Anderson RM, Jackson HC, May RM, et al. Population dynamics of fox rabies in Europe. *Nature* 1981; 289:765-771.
- 14. Wandeler AI. Oral immunization of wildlife. In: Baer GM, ed. *The natural history* of rabies. 2nd ed. Boca Raton, FL: CRC Press Inc., 1991; 485-503.
- 15. Fearneyhough MG, Wilson PJ, Clark KA, et al. Results of an oral rabies vaccination program for coyotes. *J Am Vet Med Assoc* 1998; 212:498-502.
- 16. Meltzer MI, Rupprecht CE. A review of the economics of the prevention and control of rabies," *Pharmacoeconomics* 1998; 14:365-383.
- 17. Meltzer, MI. Assessing the costs and benefits of an oral vaccine for raccoon rabies: a possible model. *Emerg Infect Dis* 1996; 2:336-342.
- 18. Kermack WO, McKendrick AG. A contribution to the mathematical theory of epidemics. *Proc. R. Soc.* 1927; A115:700-721.
- 19. Anderson RM, Jackson HC, May RM, et al. Population Dynamics of Fox Rabies in Europe. *Nature* 1981; 289:765-771.
- 20. Holmes EE, Lewis MA, Banks JE, et al. Partial differential equations in ecology: spatial interactions and population dynamics. *Ecology* 1994; 75(1):17-29.
- Smith ADM. A continuous time deterministic model of temporal rabies. In: Bacon, PJ ed. *Population dynamics of rabies in wildlife*. Orlando, Fla: Academic Press Inc, 1985; 131-145.

- 22. Artois M, Langlais M, Suppo C. Simulation of rabies control within an increasing fox population. *Ecological Modelling* 1997; 23-34.
- 23. Müller J. Optimal vaccination patterns in age-structured populations: endemic case. *Mathematical and Computer Modelling* 2000; 31:149-160.
- 24. Iannelli M, Kim MY, Park EJ. Splitting methods for the numerical approximation of some models of age-structured population dynamics and epidemiology. *Applied Mathematics and Computation* 1997; 87:69-93.
- 25. Garnerin P, Hazout S, Valleron AJ. Estimation of two epidemiological parameters of fox rabies: the length of incubation period and the dispersion distance of cubs. *Ecological Modelling* 1986; 33:123-135.
- Smith DL, Lucey B, Waller LA, et al. Predicting the spatial dynamics of rabies epidemics on heterogeneous landscapes. *Proc. Natl. Acad. Sci.* 2002; 99(6)3668:3672.
- 27. Maasilta P. Forecasting the HIV epidemic in Finland by using functional small area units. *GeoJournal* 1997; 41.3:215-222.
- 28. Anderson J. Providing a broad spectrum of agents in spatially explicit simulation models: the Gensim approach. In: Gimblett HR ed. *Integrating geographic information systems and agent-based modeling techniques*. New York, NY: Oxford University Press, 2002; 21:58.
- 29. Gimblett HR. Integrating geographic information systems and agent-based technologies for modeling and simulating social and ecological phenomena. In: Gimblett HR ed. *Integrating geographic information systems and agent-based modeling techniques*. New York, NY: Oxford University Press, 2002; 1:20.
- 30. Epstein JM, Axtell R. *Growing artificial societies*. Washington DC: Brookings Institution Press, 1996.

- 31. Lotze AH. In: Chapman JA, Feldhamer GA, eds. *Wild mammals of North America*. Baltimore: The Johns Hopkins University Press, 1982; 586-597.
- 32. Kaufmann JH. Raccoon and allies. In: Chapman JA, Feldhamer GA, eds. *Wild mammals of North America*. Baltimore: The Johns Hopkins University Press, 1982; 567-585.
- 33. Wilson DE, Ruff S. *The Smithsonian book of North American mammals*. Washington DC: Smithsonian Institution Press, 1999; 221-223.
- 34. Merritt JF. *Guide to the mammals of Pennsylvania*. Matinko RA, ed. Pittsburgh, PA: University of Pittsburgh Press, 1987; 266-269.
- 35. Whitaker JO, Hamilton WJ, eds. *Mammals of the eastern United States*. Third edition. Ithaca, NY: Comstock Publishing Associates, 1998; 427-433.
- 36. Stuewer FE. Raccoons: their habits and management in Michigan. *Ecological Monographs*, 13(2):205-256.
- 37. Sanderson GC, Nalbandov AV. The reproductive cycle of the raccoon in Illinois. *Illinois Natural History Survey Bulletin* 1973. 31(2):29-84.
- 38. Nowak RM. *Walker's mammals of the world*. Fifth Ed, Vol. II.. The Johns Hopkins University Press, 1991; 1100-1101.
- 39. Winkler WG, Jenkins SR. Raccoon rabies. In: Baer GM, ed. *The natural history of rabies*. 2nd ed. Boca Raton, Fla.: CRC Press Inc, 1991; 1991:325-340.
- 40. Uhaa IJ, Dato VM, Sorhage FE, et al. Benefits and costs of using an orally absorbed vaccine to control rabies in raccoons. *JAVMA*, 201(12):1873-1882, 1992.
- 41. Noah DL, Smith MG, Gotthardt JC, et al. Mass human exposure to rabies in New Hampshire: exposures, treatment, and cost.

- 42. Kreindel SM, McGuill M, Meltzer M, et al. The cost of rabies postexposure prophylaxis: one state's experience. *Public Health Reports*, 113:247-251, 1998.
- 43. Nelson RS, Cooper GH, Cartter ML, et al. Rabies postexposure prophylaxis Connecticut, 1990-1994. *MMWR*, 45(11):232-234, 1996.
- 44. Wyatt JD, Barker WH, Bennett NM, et al. Human rabies postexposure prophylaxis during a raccoon rabies epizootic in New York, 1993 and 1994. *Emerging Infectious Diseases* 1999, 5(3):415-423.
- 45. Kemere P, Liddel MK, Evangelou P, et al. Economic analysis of a large scale oral vaccination program to control raccoon rabies. *Unpublished Report*, 1999.
- 46. Meltzer MI, Rupprecht CE. A review of the economics of the prevention and control of rabies," *Pharmacoeconomics* 1998; 14:365-383.
- 47. Winkler WG, Jenkins SR. Raccoon rabies. In: Baer GM, ed. *The natural history of rabies*. 2nd ed. Boca Raton, Fla.: CRC Press Inc, 1991; 1991:325-340.
- 48. Rupprecht CE, Wiktor TJ, Johnston DH, et al. Oral immunization and protection of raccoons (*Procyon lotor*) with a vaccinia-rabies glycoprotein recombinant virus vaccine. *Proc Natl Acad Sci U S A* 1986; 83:7947-7950.
- Roscoe DE, Holste WC, Sorhage FE, Campbell C et al. Efficacy of an oral vacciniarabies glycoprotein recombinant vaccine in controlling epidemic raccoon rabies in New Jersey. J Wildl Dis. 1998 Oct; 34(4):752-63.
- 50. Rupprecht CE, Hamir AN, Johnston DH, Koprowski H. Efficacy of a vacciniarabies glycoprotein recombinant virus vaccine in raccoons (Procyon lotor). *Rev Infect Dis.* 1988 Nov-Dec; 10 Suppl 4:S803-9.

Parameter	Value	Source				
Environment characteristic						
Nutrient capacity	Urban/suburban: 6	Assumed				
	Wetlands: 5					
	Rural, agricultural: 4					
	Forest: 3					
	Prairie: 2					
	High elevation, other: 1					
	Water: 0					
Raccoon density	Swamps, mangroves, flood plain forests,	Wilson & Ruff (1999) ⁱ				
	and marshes: up to 50/km ²					
	Farmland: up to 20/km ²					
	VA forest: $7.4 / \text{km}^2$ during epizootic,					
	14.8/km ² without epizootic					
	Typical: $0.4 - 1/\text{km}^2$	Whitaker & Hamilton				
	Up to: $50/\text{km}^2$	(1998) ⁱⁱ				
	Rural: up to $20/\text{km}^2$					
	Average: 2.3-20/km ²	Nowak (1991) ⁱⁱⁱ				
	Record: $407/\text{km}^2$					
	Range: $2 - 20/\text{km}^2$	Merritt (1987) ^{iv}				
	Prairies of ND: $0.5 - 1/\text{km}^2$	Kaufmann (1982) ^v				
	Prairies of Manitoba: $1.5 - 3.2/\text{km}^2$					
	Bottomlands and marshes in midwestern					
	and eastern US: up to $20/\text{km}^2$					
	Swamp in AL: $49/km^2$					
	Suburb in OH: $68.7/\text{km}^2$					
	Marsh in MO: 400/km ²					
Environment behavior		-				
Nutrient grow back rule	Up to capacity in suburban and urban	Abstract construct				
6	1 unit/week in agriculture and forest					
Agent characteristics						
Death age	Few live more than 5 years	Whitaker & Hamilton				
		(1998)				
	Few live more than 5 years	Nowak (1991)				
	Reports of 13 – 16 year old wild raccoons					
	4 - 6 years in wild, up to 17 years in	Merritt (1987)				
	captivity					
	Average in MO: 1.8 years	Kaufmann (1982)				
	Average in AL: 3 years					
	Most die during first 2 years					
	1/100 reach 7 years					
	Up to: 16 years in wild					
	Juvenile mortality rate: up to 60%/annum					
	Total population mortality rate: up to					
	50%/annum					

Appendix – Basis for the values of ecological and epidemiological parameters of the model

Parameter	Value	Source
Agent characteristic	s continued	
Fat reserve	Varies. Random endowment +	Assumed
	accumulated food/period –	
	metabolism/period	
Metabolism	1-5 units	Assumed
	$0.32 \operatorname{cc} O_2/g \operatorname{hr}$	Kaufmann (1982)
Agent behavior: mo	vement rule	
Movement	Travel 0.75-2.5 km/night	Wilson & Ruff (1999)
	Juvenile: moved 264 km	Whitaker & Hamilton (1998)
	Maximum: 11.2 km/night	Kaufmann (1982)
	MN juvenile: 1.7 km/week in 156 weeks	
	Manitoba juvenile: 10.8/week in 23 weeks	
Home range	Males: 0.65 km ²	Nowak (1991)
	Females: 0.39 km^2	
	Range: 0.002-49.6 km ²	
	Typical: 8 km ² /year	Macdonald (1989) ^{vi}
	Range: $0.5 - 50 \text{ km}^2/\text{year}$	
	Range: $0.05 - 50 \text{ km}^2/\text{year}$	Merritt (1987)
	Maximum: $0.79 \text{ km}^2 - 7.07 \text{ km}^2$	Kaufmann (1982)
	Suburban: $0.07 \text{ km}^2 - 0.38 \text{ km}^2$	
	Prairies in ND: : 78.54 km^2	
	Typical: $0.4 - 1 \text{ km}^2$	
Agent behavior: mig	ration rule	
Migration	52% of raccoons immigrated to previously	Wilson & Ruff (1999)
	epizootic area	
Agent behavior: rep	roduction rule	
Mating season	Feb-Jun, Peak: Mar	Wilson & Ruff (1999)
	Dec-Aug, Peaks: Feb-Mar	Nowak (1991)
	Late Jan – early Feb	Macdonald (1989)
	Can also mate into summer	
	Typical: Jan – Feb	Merritt (1987)
	Northern limit: Feb-Jun, Peak: March	Kaufmann (1982)
	Entire North America: Jan-Mar Peak: Feb	
	GA, LA, SC: most in Mar	
	AL: Mar – Jun, Peak: Apr	
	FL: year-round, most in Dec – Aug	
	Feb-Mar	Stuewer (1943) ^{vii}

Appendix continued

Agent behavior: reprod	uction rule continued	
Birth season	Typical: Apr – May in North	Whitaker & Hamilton (1998)
	Few in late summer	
	Apr-Jun	Nowak (1991)
	Typical: late Mar – Apr	Merritt (1987)
	Northern limit: May – Sep (most in	Kaufmann (1982)
	May)	Ň,
	Entire North America: typically Apr	
	AL: most in Jun	
	AL, FL, SC: may be year round	
	GA, LA, SC: most in May	
	Mar-Jun	Sanderson & Nalbandov (1973) ^{viii}
Female fertility	Up to 60% of yearlings	Kaufmann (1982)
	19 out of 35 yearlings	Sanderson & Nalbandov (1973)
	50% of yearlings	Stuewer (1943)
Male fertility	Typically do not breed until second	Whitaker & Hamilton (1998)
	season	Kaufmann (1982)
		Stuewer (1943)
Litter size	Average: 4, Range: 3 – 7	Wilson & Ruff (1999)
	Typical: 3 – 7, Range: 1 – 8	Whitaker & Hamilton (1998)
	Average: 3 – 4, Range: 1 – 7	Nowak (1991)
	Average: 4, Range: 3 – 6	Merritt (1987)
	Typical: 2 – 5, Range: 1 – 8	Kaufmann (1982)
	Average: 4, Range: 2 – 6	Goldman (1950) ^{ix}
	Average: 4, Range: 3 – 7	Stuewer (1943)
Gestation period	63 – 65 days	Wilson & Ruff (1999)
-	63 days	Whitaker & Hamilton (1998)
		Merritt (1987)
		Stuewer (1943)
	60 – 73 days	Nowak (1991)
	Range: 54 – 70 days, Typical: 63 - 65	Kaufmann (1982)
	days	
	63 - 70 days	Goldman (1950)
Separation of young	20 weeks after birth	Wilson & Ruff (1999)
	North: after arrival of new litter	Whitaker (1998)
	South: as early as Fall after birth	
	North: 1 year after birth	Macdonald (1989)
	South: Fall after birth	
	16 – 20 weeks	Stuewer (1943)
	Typical: by 16th week	Kaufmann (1982)
	Up to 1 year	
Agent behavior: epidem	nic rule	-
Incubation period	10 - 107 days	Various sources as reported by
		Winkler & Jenkins (1991) ^x
Morbidity rate	<1 – 13 days	Various sources as reported by
		Winkler & Jenkins (1991)

Appendix continued

ⁱ Wilson DE, Ruff S. *The Smithsonian book of North American mammals*. Washington DC: Smithsonian Institution Press, 1999; 221-223.

ⁱⁱ Whitaker JO, Hamilton WJ, eds. *Mammals of the eastern United States*. Third edition. Ithaca, NY: Comstock Publishing Associates, 1998; 427-433.

ⁱⁱⁱ Nowak, RM. *Walker's mammals of the world*. 5th ed., vol. II. Baltimore: The Johns Hopkins University Press, 1991; 1100-1101.

^{iv} Merritt JF. *Guide to the mammals of Pennsylvania*. Matinko RA, ed. Pittsburgh, PA: University of Pittsburgh Press, 1987; 266-269.

^v Kaufmann JH. Raccoon and allies. In: Chapman JA, Feldhamer GA, eds. *Wild mammals of North America*. Baltimore: The Johns Hopkins University Press, 1982; 567-585.

^{vi} Macdonald D, ed. *The encyclopaedia of mammals*. London: Unwin Hyman Limited, 1989; 100-101. ^{vii} Stuewer FE. Raccoons: their habits and management in Michigan. *Ecological Monographs*, 13(2):205-256.

^{viii} Sanderson GC, Nalbandov AV. The reproductive cycle of the raccoon in Illinois. *Illinois Natural History Survey Bulletin* 1973. 31(2):29-84.

^{ix} Goldman EA. *Raccoons of north and middle America. United States Department of Interior, Fish and Wildlife Service, North American Fauna 60.* Washington DC: United States Government Printing Office, 1950.

^x Winkler WG, Jenkins SR. Raccoon rabies. In: Baer GM, ed. *The natural history of rabies*. 2nd ed. Boca Raton, Fla.: CRC Press Inc, 1991; 325-340.