Economic Modeling of Oral Rabies Vaccination: Issues and Concepts

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ABSTRACT: This paper describes issues and concepts relevant to economic modeling of oral rabies vaccination (ORV) campaigns for managing wildlife rabies. Economic models of ORV are mathematical expressions used to predict and draw inferences about the costs and savings likely to be recouped by these rabies management efforts. Costs that are prevented due to ORV campaigns convert to savings. Comparison of campaign duration, bait cost, bait density, and bait distribution data for North American ORV campaigns showed that: 1) campaigns are lengthy, 2) those involving raccoons entail greater bait densities (i.e., related bait costs) and per unit area bait-distribution costs than those involving foxes and coyotes, and 3) all entail "enhanced" surveillance and establishment of maintenance barriers (i.e., deter translocation or reintroduction of new cases) upon completion. Key modeling issues were: model parameterization, ORV cost variables (i.e., bait costs, bait densities, and unit area distribution costs), time horizon, contingency costs, and ORV host specificity.

KEY WORDS: benefit-cost, disease, economics, model, oral rabies vaccination, wildlife

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INTRODUCTION

Rabies remains a significant mammalian disease worldwide (Niezgoda *et al*. 2002). Since the 1950s, total animal and pet cases of rabies have declined in the United States due mainly to domestic dog (*Canis familiaris*) vaccination programs, while wildlife cases have increased, attenuating this overall decline (Childs 2002). Data for 2004 showed that 94 (1.4%) domestic dog versus 6,836 (≈92%) wildlife cases were reported in the 49 states (excluding Hawaii) plus Puerto Rico (Krebs *et al*. 2005).

The development and use of oral rabies vaccination (ORV) for the control of rabies in wildlife has been in progress for over 25 years (Steck *et al*. 1982, Winkler and Bögel 1992). Essentially, baits containing a number of developed rabies virus vaccines are distributed onto the landscape at prescribed densities; target animals then forage on these baits and self-dose with the vaccine (Debbie *et al*. 1972, Linhart *et al*. 2002). The vaccination of wildlife populations via oral baits affords potential new ways of controlling rabies; however, the potential savings accrued from ORV campaigns are often complex and vague.

Modeling affords a relatively low-cost approach to studying economic parameters associated with ORV, and modeling provides important outputs for policy and decision making (Slate *et al*. 2002). The formulation of realistic mathematical expressions to characterize these projections rests upon modelers making sound assumptions and representations of monetary outlays associated with rabies management campaigns and recouped savings.

This paper reviews selected literature relevant to the economics and modeling of ORV programs. Several issues and concepts inherent to developing effective economic models for quantifying the benefits and costs of ORV campaigns are described.

RABIES ECONOMICS

Worldwide Statistics

Meltzer and Rupprecht (1998*a*,*b*) published comprehensive reviews of the global economics of human and animal rabies, concluding that this literature is replete with methodological shortcomings and poorly documented cost estimates. Impacts and costs of the disease differ greatly in various regions and countries– differences due mainly to whether or not domestic canine rabies has been controlled (Meltzer and Rupprecht 1998*b*). Many studies were reported that derived an estimate of medical post-exposure prophylaxis (PEP) costs as the sole index of rabies costs (Meltzer and Rupprecht 1998*a*). For the period 1991-1994, the order of mean (SE) case loads of human rabies (number/ million) for major continental areas where the disease is endemic was: 10.6 (4.7) Asia, 1.9 (0.6) Africa, and 0.7 (0.2) Americas, with Europe unreported (Meltzer and Rupprecht 1998*a*). The order of mean (SE) human PEPs administered was: 1,093.3 (331.9) Asia; 2,986.1 (2,419.8) Africa; 547.8 (109.3) Americas; and 127.2 (52.6) Europe (Meltzer and Rupprecht 1998*a*). For the Americas, the greater proportion of both case loads and PEPs occurred in Latin America– data reflective of the high incidence of rabies from domestic dogs and vampire bats (*Desmodus rotundus*) in this region.

Types of Costs and Savings

For benefit-cost purposes, costs that are prevented due to rabies management efforts become savings (see Kemere *et al*. 2002, Meltzer 1996, Sterner and Smith 2006). Costs vary by stage of the epizootic, geographical region, and thoroughness of measurement (Meltzer 1996). Direct (e.g., PEP, physician, veterinary, ORV baits, aircraft fuel), indirect (e.g., auxiliary transportation, lost wages, day care during PEP visits), and induced costs (e.g., rabies surveillance, specimen analysis) have been documented for rabies (Kreindel *et al*. 1998, Meltzer and Rupprecht 1998*a*, Shwiff *et al*. 2007, Sterner and Sun 2004, Uhaa *et al*. 1992). Still, these fail to include intangible costs associated with people or animals living in a rabies-endemic or epizootic area.

ORV

Data on the use of ORV to control rabies in wildlife can be gleaned from efforts to eliminate or prevent: 1) red fox (*Vulpes vulpes*) rabies in Europe (Stöhr and Meslin 1996, Zanoni *et al*. 2000); 2) arctic fox (*Alopex lagopus*) variant rabies in red fox vectors in Ontario Province Canada (MacInnes *et al*. 2001); 3) the introduction of raccoon (*Procyon lotor*) variant rabies into Ontario Province, Canada (Rosatte *et al*. 2001); 4) the northward spread of dog variant rabies in coyotes (*Canis latrans*) of south Texas (Fearneyhough *et al*. 1998, Sidwa *et al*. 2005); 5) the northward spread of gray fox (*Urocyon cinereoargenteus*) rabies in west Texas (Sidwa *et al*. 2005); and 6) the westward spread of raccoon variant rabies along the Appalachian Mountain Ridge in the eastern United States (Foroutan *et al*. 2002; Slate *et al*. 2002, 2005).

ECONOMIC MODELING OF ORV

Modeling

Economic models of ORV are schematic, mathematical, or statistical representations of the potential costs and savings to be derived from these rabies management campaigns (e.g., Kemere *et al*. 2002, Meltzer 1996, Sterner and Smith 2006). Modeling affords predictions and inferences about a phenomenon (i.e., benefits and costs of ORV) using low-cost, computerized manipulation of a set of parameters (Burnham and Anderson 2002). Numerous sub-types of models are recognized– compartment, least squares, input-output, linear regression, nonlinear regression, differential equation, etc. (see Burnham and Anderson 2002).

A key step in the development of models involves the selection of general characteristics of natural phenomena that determine or correlate with outputs (Burnham and Anderson 2002). Variables refer to specific values of parameters substituted into models for specific computations (e.g., 4.0 new infections/host, 75 baits/km^2, $100,000 reduction in human health costs/year).

A tradeoff exists in model parameterization. Because it is impossible to specify the myriad of parameters that determine a phenomenon, models afford relatively simplistic characterizations of "real-world" events (Burnham and Anderson 2002). Inclusion of more parameters ultimately allows greater prediction/inference, but more parameters also make computations more cumbersome and yield relatively less gain in prediction/inference per added parameter. Most models include from 2 to 5 parameters (Burnham and Anderson 2002).

The modeling of economic parameters associated with the use of ORV involves uncertainty (see Zerbe and Dively 1994). Uncertainty can be likened to a parameter of dispersion (variance) associated with a model's inputs and outputs (Sterner *et al*. 2004, Sterner and Smith 2006, Zerbe and Dively 1994). This variance results from the use of unknown, or poorly quantified, inputs (e.g., ORV bait acceptance by wildlife, effectiveness of rabies vaccination in wildlife population, human post-exposure treatment costs). Perhaps the simplest method of reducing uncertainty involves use of "worst- and best-case" scenarios; these scenarios provide estimates of minimum and maximum outputs of models that are expected using a set of assumptions– the limits of potential computations (Zerbe and Dively 1994). More sophisticated methods include sensitivity analysis (i.e., examining the effects exerted upon the dependent variable by iterative changes to one or more independent variables), Monte Carlo techniques (i.e., random samples of fixed size used to run iterative projections of a model), decision trees (i.e., probabilistic branching estimates for a set of possible outcomes involving fixed variables), and response surfaces (i.e., graphic plots of a set of iterative model outputs) (see Burnham and Anderson 2002, Sterner *et al*. 2004, Zerby and Dively 1994).

Published ORV Economic Models

Meltzer (1996) described a hypothetical cost-benefit model to examine a 30-year time horizon for ORV use in reducing rabies-caused expenses. Key input variables included: 3% annual discount rate, 97 baits/km^2 19 raccoons/km^2, 5 baits/raccoon, $1.50 bait price, $38/km^2 bait application cost, $1.52/person/year ORV induced savings during epizootic, $0.30/person/year ORV induced savings post-epizootic, 40 people/km^2, and $16/pet vaccination. Two ORV scenarios were examined. Scenario 1 involved expanding concentric rings starting with 37 km radius (3,256 km^2) with successive 9.25 km-wide "donuts" baited 2 years each for 20 years, and a final 9.25 km-wide "donut" baited for the last 10 years. Scenario 2 entailed the hypothetical baiting of the maximum area described for Scenario 1 for an initial 2 years, then adding a 9.25 km-wide "donut" zone around the area and baiting it for 28 years. Pet vaccination and PEP treatment were the two main factors gleaned from sensitivity analyses that justified ORV. Scenario 1 yielded >$2 million in recouped savings relative to ORV expenses; this occurred even at a 5% discount rate for inflation when an increase in pet vaccinations (20%) was included. No other Scenario 1 or 2 analyses yielded positive returns on invested ORV funds.

Kemere *et al*. (2002) published a detailed economic model of ORV and deterrence of the spread of raccoon-variant rabies westward along the Appalachian Ridge. Main input variables were: 7% discount rate, area baited of 102,650 km^2, bait density of 75/km^2, bait price $1.30, aerial distribution $8.62/km^2, and ORV evaluation $15.00/km^2. Eight scenarios were set up: (Scenarios 1 and 2) 42 km annual westward movement of raccoon rabies with and without a 20% increase in pet vaccination costs (45 to 65%) included in potential savings; (Scenarios 3 and 4) 125 km annual westward movement of the disease with and without a 20% increase in pet vaccination costs (45 to 65%) included in potential savings; (Scenarios 4 and 5) the same as Scenarios 1 and 2, but with a 5-year period of fixed baiting then decreasing to 40% of the bait costs for 15 years; and (Scenarios 7 and 8) the same as Scenarios 3 and 4, but with a 20-year period of fixed baiting costs. Savings of medical and non-medical outlays were to be recouped westward of the ORV zone by areas staying "raccoon-variant free" over a 20-year period; empirical costs were based upon data collected for a raccoon rabies epizootic in New Jersey (Uhaa *et al*. 1992). Results showed that 1) all scenarios, except the 42 km-per-year movement rate with 20-year fixed baiting costs (benefit-cost ratio = 0.5), exceeded 1.1 benefit-cost ratios, 2) total estimated net present values for Scenarios 1 to 4 ranged between $109 million and $496 million ($95.7 million in discounted program costs), and 3) returns for Scenarios 5 to 8 ranged between $48 million and 422 million ($157.3 million in discounted program costs).

ORV AND ECONOMIC MODELING ISSUES

Economic Parameterization

The ORV strategy used to control rabies determines parameter selection in economic models. Four strategies have been described for ORV campaigns in North America (Table 1):

1) progressive wide-area baiting with final establishment of a barrier (MacInnes *et al*. 2001)
2) point infection control (PIC– use of culling, trap vaccinate and release and ORV in successive zones around a detected rabies case; Rosatte *et al*. 2001)
3) purse string (i.e., using ORV to encircle and shrink the zone of infected animals; Sidwa *et al*. 2005)
4) barrier (i.e., deterring the spread of rabies to non-endemic areas via a zone of vaccinated animals; Slate *et al*. 2002, 2005).

Although creative modelers will conceive of many useful economic parameters related to ORV savings, a basic set of parameters for the aforementioned strategies will entail the following five parameters: 1) mean rate of rabies spread (km/year); 2) mean rabies-caused expenditures ($/year or $/epizootic); 3) mean ORV distribution costs [$/area; this parameter represents a composite of the unit bait price ($/bait), bait application rate (baits/km^2), area of application (km^2), and ground or air mode of ORV distribution costs ($/km^2)]; 4) mean ORV effectiveness (% animals vaccinated); and 5) mean time for recouping savings (years).

ORV Cost Variables

Table 1 presents selected ORV data derived from the major North American rabies campaigns. Examination of these data show that ORV involving raccoons, versus foxes and coyotes, entail a doubling of bait densities (i.e., related bait costs) and roughly a 4-fold increase (>$111.00) in per unit area distribution costs. In retrospect, the $1.50 bait price and $38/km^2 bait application costs used in Meltzer's (1996) hypothetical models appear to be high and low, respectively– model outputs probably suspect. These cost differences suggest that the inclusion of more comprehensive rabies-caused cost impacts will probably be needed in economic modeling efforts with raccoon-variant campaigns than with campaigns involving canids.

While most modelers recognize that potential increased PEP and pet vaccination costs (i.e., 20% increased pet vaccinations occurred in a New Jersey epizootic of raccoon rabies) typically account for most costs during epizootics (Meltzer 1996, Uhaa *et al*. 1992), many modelers have cited pre-exposure prophylaxis, public health case investigation, animal control, animal quarantine, livestock vaccination, livestock replacement, and educational costs as other rabies-related impacts (Kemere *et al*. 2002, Meltzer 1996, Sterner *et al*. 2004, Sterner and Sun 2004, Uhaa *et al*. 1992). Studies to collect empirical estimates of these variables are needed.

Time Horizon

Four of the 5 cited campaigns have involved ≥7 years of major baiting activity to secure the ORV strategies (e.g., MacInnes *et al*. 2001, Sidwa *et al*. 2005, Slate *et al*. 2005; Table 1). Additionally, all of the campaigns will require entailed prolonged "enhanced" surveillance (i.e., increased public health monitoring, rabies analyses of road-killed target animals, and rabies analyses of trapping samplings of target animals) and set up of "maintenance" barriers (i.e., zones to detect potential reintroduced rabies from traditional foci or translocation sources) to allow PIC of new cases (see Rosatte *et al*. 2001, Sidwa *et al*.

Table 1. Selected ORV application variables reported for North American wildlife rabies campaigns[a].

Study	Length	Host Species	Bait Cost ($US)[b]	Target Bait Density (#/ km^2)	Area Baited (km/year)[c]	Cost/Area ($/km^2)[b]
Canada						
MacInnes *et al.* (2001)	7 years[c]	Red fox	no estimate	18 - 20	8,850 - 31,460	no estimate
Rosatte *et al.* (2001)	1 year[c]	Raccoon	$2.16	70	1,200	$180
United States						
Sidwa *et al.* (2005)	11 years[c]	Coyote	$1.30[e]	19 - 27	36,669[d]	$42[d]
Sidwa *et al.* (2005)	>11 years[c]	Gray fox	$1.30[e]	27 - 39	56,202[d]	$42[d]
Slate *et al.* (2005)	>8 years[c]	Raccoon	$1.30[e]	75	110,659[e]	$153[e]

[a] Whenever possible, data were those reported by authors of studies. No adjustment for net present value was performed on these data because in many cases bait prices, fuel costs, etc. have fluctuated greatly as ORV efforts have expanded (i.e., bait price has declined, plane fuel has varied dramatically, etc.). In a few cases, estimates were derived from other relevant information or related papers by key authors of the cited studies.

[b] Canadian dollar conversion rate = $0.90 U.S.

[c] Surveillance, TVR, culling, or ORV bait distributions continue at present.

[d] Area cost estimate based on $3.8 million/year cost, with 33,669 km^2 and 56,202 km^2 values (total area of 89,871 km^2) provided in Sidwa *et al.* (2005) for coyote and gray fox campaigns, respectively.

[e] Data for 2003 used as representative (see Slate *et al.* 2005), with bait cost from Kemere *et al.* 2002 and cost/area value gleaned from Foroutan *et al.* (2002).

2005). Although these PIC activities are likely to involve restricted areas, fewer bait distributions, but possibly increased per unit area costs (see Table 1) than wide-area campaign activities, these costs still should be included in ORV economic evaluations. Economic time horizons of >20 years for the recovery of ORV campaign costs appear warranted (Meltzer 1996, Kemere *et al*. 2002). In fact, current data suggest that modeled time horizons need to be increased, especially for raccoon-variant ORV campaigns.

Contingency Costs

As discussed for time horizons, the need to include costs for enhanced surveillance and eventual maintenance barriers into economic models of ORV seems necessary. Unforeseen contingencies often arise in ORV campaigns that can add sizable costs to campaigns. For example, Russell *et al*. (2005) discussed a 2004 "breach" of the Appalachian Ridge ORV barrier, which had raccoon-variant positive animals detected in Lake County, Ohio. Extensive emergency efforts and funds were expended to re-establish the original barrier, with ≈300 raccoon specimens submitted for rabies determinations. Although no cost estimate of this extensive trap vaccinate and release, added ORV, plus diagnostic effort is published, estimated contingency costs need to be expected and estimated in future economic models of ORV.

ORV Host Specificity

The use of ORV is rabies-variant (host-species) specific (Johnston and Tinline 2002). Containment or elimination of rabies epizootics using a vaccine for a specific variant of the virus in terrestrial species neither prevents epizootics involving other variants nor "spillover" infections (i.e., transfer of rabies from reservoir species to mammals that do not sustain the virus for long periods). In most geographic areas, especially within the United States, overlapping distributions of reservoir species and rabies variants occur (Childs 2002). The simultaneous occurrence of 2 or more variants of the virus and multiple reservoir species [e.g., red fox, raccoon, skunks (*Mephitis mephitis*, *Spilogale putoris*) plus bats] in an area complicates modeling ORV effectiveness and ORV economics.

A recent study of rabies incidence and costs in New York showed that bats (*Chiroptera* spp.) accounted for only 4.6% of tested rabid animals, but 26% of the administered PEPs– a result attributed to the high proportion of individuals who were uncertain of the extent of contact with bats (Chang *et al*. 2002). Variants of bat rabies occur throughout the distributional range of terrestrial host species, and no ORV for bats exists. Economic computations of ORV savings from campaigns with terrestrial species must be adjusted for these other, "confounding" rabies cases and costs (Figure 1; see Slate *et al*. 2005).

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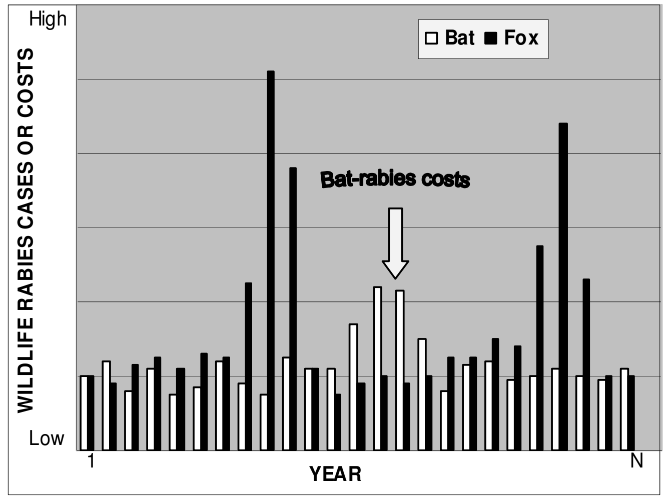

Figure 1. Plot of theoretical yearly costs of wildlife rabies epizootics (bat and fox cases); the potential cost savings from ORV for fox rabies must be adjusted because baseline bat rabies cases and sporadic epizootic costs (bat rabies) will continue to occur during and after the fox ORV campaign– not all rabies-caused costs can be attributed as savings from fox ORV.

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