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Progressive elimination of rabies in wildlife has been a general strategy in Canada and the United States; common campaign tactics are trap–vaccinate–release (TVR), point infection control (PIC), and oral rabies vaccination (ORV). TVR and PIC are labor intensive and the most expensive tactics per unit area (≈$616/km^2 [in 2008 Can$, converted from the reported $450/km^2 in 1991 Can$] and ≈$612/km^2 [$500/km^2 in 1999 Can$], respectively), but these tactics have proven crucial to elimination of raccoon rabies in Canada and to maintenance of ORV zones for preventing the spread of raccoon rabies in the United States. Economic assessments have shown that during rabies epizootics, costs of human postexposure prophylaxis, pet vaccination, public health, and animal control spike. Modeling studies, involving diverse assumptions, have shown that ORV programs can be cost-efficient and yield benefit:cost ratios >1.0.

Rabies continues to pose major public health concerns in Canada and the United States (*1–5*). Effective pet vaccination programs have controlled rabies in domestic dogs (*Canis familiaris*) in both countries, but rabies persists in wildlife reservoirs. In 2007, a total of 6,776 cases in wildlife were reported for the contiguous United States (*1*).

Oral rabies vaccination (ORV) is an evolving rabies control technology for use in wildlife (*6*). It involves distribution of baits containing orally immunogenic vaccines onto the landscape, thereby targeting wildlife to establish population immunity and prevent spread or eliminate specific rabies variants (*6*).

We reviewed the literature on ORV programs and economics in Canada and the United States. The first use of ORV sought to control rabies in red foxes (*Vulpes vulpes*) in Switzerland; subsequent programs were reported throughout much of western Europe (*7*,*8*). Switzerland, France, Belgium, and Luxembourg were deemed free of the red fox variant by 2001 (*8*).

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ORV in Ontario, Canada

Arctic Fox–Variant Rabies in Red Foxes

During 1989–1995, ORV was used in Ontario to progressively eliminate arctic fox (*Alopex lagopus*)–variant rabies that had spilled into (i.e., had been transmitted to another species) red foxes and spread southward (*9*). Each year ORV baits were distributed in southern Ontario (≈20 baits/km^2, from aircraft or by hand, over 8,850–29,590 km^2). The strategy was termed progressive elimination and resembled an expanding ORV wedge, which started near the center of the outbreak and expanded during successive years (Figure 1).

Within 5 years of program initiation, reported cases of rabid foxes declined from 203 cases/year to 4 cases/year in the baited areas (*9*,*10*). Spillover cases from red foxes to striped skunks (*Mephitis mephitis*) and livestock dropped from preepizootic (30-year) means of >36 and >42, respectively, to 0 by 1997 (*9*). Since 2003, only 13 cases of the variant in red foxes have been reported; these continue to be addressed by using focused control and enhanced surveillance (i.e., increased public health monitoring, examination of road-killed target animals, and rabies analyses of samples from trappers) (D. Donovan, Ontario Ministry of Natural Resources, pers. comm.).

Rabies in Raccoons and Skunks

During 1987–1991, to reduce spillover of rabies from red foxes to urban raccoons (*Procyon lotor*) and skunks, trap–vaccinate–release (TVR; capture live, vaccinate parenterally, and release on site) was integrated into ORV

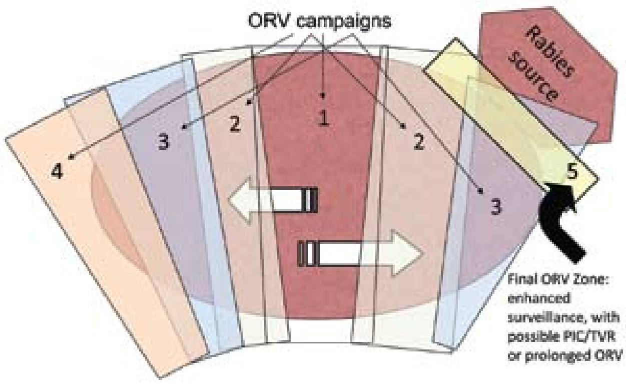

Figure 1. Expanding-wedge tactic with progressive elimination (*9*). Numbers represent successive oral rabies vaccination (ORV) zones. Potential savings are assumed for the area of progressive elimination, southern Ontario Province. The rectangle bordering the rabies source (i.e., 5) highlights an area of enhanced surveillance, possible point infection control (PIC) activities, trap–vaccinate–release (TVR) activities, or an ORV zone intended to deter future reemergence of the virus.

campaigns in the Toronto area (*10*). TVR was part of the red fox ORV program because Evelyn-Rokitnicki-Abelseth oral rabies vaccine is not immunogenic in skunks and raccoons (*6*,*9*). Live traps were set (20–75 traps/km^2) in a 60-km^2 portion of the city, and 66,168 ORV baits were distributed by hand in natural areas (20–40 baits/km^2). Of sampled foxes, 46%–80% had biomarkers from baits, and only 1 rabid fox was found during 1987–1992 (*10*). A recent update of ORV baiting in Toronto stated that 332,257 baits had been distributed during 1989–1999, and only 5 rabid foxes were found during 1990–2006 (*11*).

During 1999–2000, the raccoon variant of rabies was confirmed near Brockville, Ontario (*12*). To eliminate raccoon-variant rabies from the province, a point infection control (PIC) tactic, which integrated population reduction (PR; sometimes referred to as culling or depopulation), TVR, and ORV, was implemented (*12*). The initial PIC operation included concentric zones, each consisting of 1) an inner 5-km PR zone, 2) a middle 5-km TVR zone, and 3) an outer 8–15-km ORV zone (Figure 2). Additional PIC or modified PIC (no PR) operations were centered on newly discovered rabid raccoons (≈40).

Mean raccoon densities in PR zones dropped from 5.1–7.1/km^2 before to 0.6–1.1/km^2 after PIC operations. However, within 1 year, >37 more cases of raccoon-variant rabies occurred in the PIC regions (*12*). Intensive PIC was begun again and eliminated the variant from Ontario. Subsequently, to reduce the chances of raccoon-variant rabies recurring in southern Ontario, enhanced surveillance and annual ORV was conducted along the border of Ontario and New York (D. Donovan, pers. comm.). Elimination of raccoon rabies from Wolfe Island at the mouth of the St. Lawrence River using similar tactics was recently reported (*13*).

ORV in the United States

Canine-Variant Rabies in Coyotes in Southern Texas

During 1988–1994, a canine-variant of rabies described in Mexico was confirmed in 163 domestic dogs and 296 coyotes from 18 counties in southern Texas (*14*–*16*). In 1995, to prevent the northward spread of this variant, ORV baits (9–27 baits/km^2) were distributed in an arc-shaped band over a 24-county area (39,850 km^2) ≈200 km north of Laredo (*16*). During 1996–2003, annual baiting continued; ≈9.35 million baits were distributed onto ≈741,766 km^2 (*17*). Gradually, baits were distributed farther south, toward the Rio Grande River, in subsequent years, thereby collapsing the rabies-infected area (Figure 3). To protect livestock, coyotes were also removed from portions of the ORV zone during these years, but the effect of PR relative to ORV was not assessed (*18*,*19*). PR is considered an important component of many rabies-control models (*20*).

After 1 year of baiting, the mean rate of canine-variant cases at the leading edge of the epizootic area was 2.8/10,000 km^2. This rate was similar to that of the preepizootic period and suggestive that the northward spread of the epizootic had ceased (*16*). Subsequent surveillance showed a gradual decline in cases from 122 in 1995 to 0 in 2004 (*17*). Currently, to maintain an immune buffer and prevent canine rabies from reemerging in southern Texas, this program baits an ORV zone 30–65 km wide along the international border each year (E. Oertli, Texas Department of State Health Services, pers. comm.).

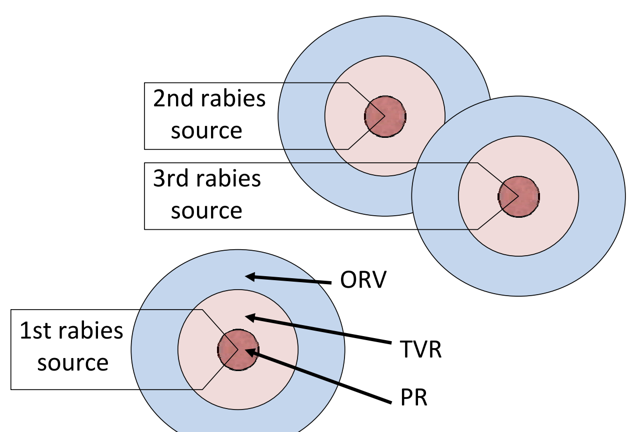

Figure 2. Point infection control (PIC) tactic. Concentric rings around the location of a rabid animal represent vector population reduction (PR), trap–vaccinate–release (TVR), and ORV zones (*12*). Each new source leads to repeated, overlapping ORV, TVR, and PR rings. Potential savings are assumed within the zones and for assumed distances beyond the zones.

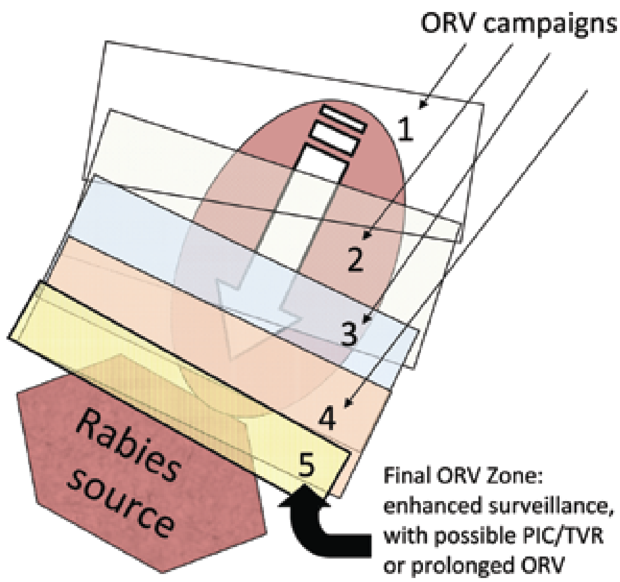

Figure 3. Collapsed-bands tactic with progressive elimination (*17*). Numbers represent successive oral rabies vaccination (ORV) zones that attempt to collapse the baited area, exclude virus incursion outside, and lead to a maintenance zone that prevents reintroduction of the disease after the current population matures and vaccination effects are lost. Potential savings are assumed to occur within the ORV areas and for assumed distances beyond the zone. The rectangle bordering the rabies source (i.e., 5) high-lights an area of enhanced surveillance, possible point infection control (PIC) activities, trap–vaccinate–release (TVR) activities, or an ORV zone intended to deter future reemergence of the virus.

Gray Fox–Variant Rabies in West-Central Texas

During 1988–1994, a total of 283 gray foxes (*Urocyon cinereoargenteus*) and 241 other domestic and wild animals in west-central Texas were confirmed positive for a unique rabies variant typically found in gray foxes (*17*). This outbreak was spatially distinct from the outbreak of canine rabies in southern Texas. To control this epizootic, during 1995–2009 (and ongoing), ORV (29–39 baits/km^2) was conducted annually by encircling the epizootic area using ≈32-km–wide ORV strips; an added 16- to 24-km vaccination buffer of ORV baits was created along the northern and eastern edges of the rabies-variant area; this tactic has been referred to as a purse string–like tactic (i.e., encircle and shrink) (*17*; Figure 4). An area of ≈350,000 km^2 was baited annually. Evidence of bait biomarkers and positive rabies virus neutralizing antibody titers was found for 39% and 62% of foxes, respectively, sampled from the ORV zone, confirming that numerous foxes had been vaccinated.

In 2007, new cases of gray fox rabies occurred northwestward along the Pecos River and in west-central Texas. To prevent further spread of this variant, ORV was used (E. Oertli, pers. comm.). The rabies-control goal has not changed from one of containment and elimination of the gray fox variant from Texas. However, in light of recent surveillance, the anticipated strategy of establishing and maintaining an ORV zone along the Rio Grande River to prevent potential reemergence from Mexico has been delayed and is being refined to include prolonged enhanced surveillance as a key factor in allocating resources and gauging success (E. Oertli, pers. comm.).

Raccoon-Variant Rabies in the Eastern United States

The National Rabies Management Program began in 1997 and coordinates ORV and related wildlife rabies–control activities in the United States (*21*,*22*). One of its priorities is to prevent the spread of raccoon-variant rabies into uninfected areas, particularly west of its current distribution along the Appalachian Ridge (*22*). The Program integrates natural terrain features (e.g., rivers, lakes, and poor habitat along mountain ridges) with ORV zones (baited at 50–75 baits/km^2) to create a 40–50 km zone of vaccinated raccoons to help prevent the spread of the virus (Figure 5).

During 1997–2007, the ORV zone was expanded from parts of Ohio to encompass parts of 8 states (i.e., Ohio, Pennsylvania, West Virginia, Virginia, Tennessee, North Carolina, Georgia, and Alabama) along the Appalachian Ridge. A total of 58 bait distributions (usually 1/year) total-

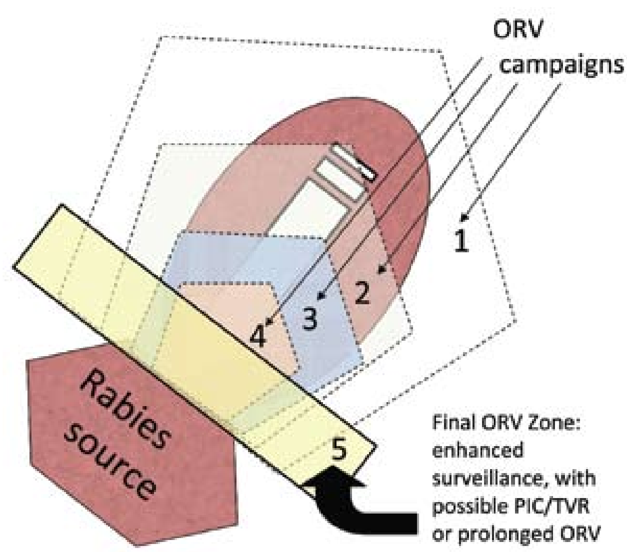

Figure 4. Purse string–like tactic with progressive elimination (*17*). Numbers represent successive oral rabies vaccination (ORV) zones that attempt to roughly encircle and shrink the baited area, exclude virus incursion from outside, and lead to a maintenance zone that prevents reintroduction of the disease after the current population matures and vaccination effects are lost. Potential savings are assumed to occur within the ORV areas and for assumed distances beyond the outer zone. The rectangle bordering the rabies source (i.e., 5) highlights an area of enhanced surveillance, possible point infection control (PIC)/trap–vaccinate–release (TVR) activities, or an ORV zone intended to deter future reemergence of the virus.

ing ≈41,018,800 baits and covering ≈530,825 km² (range of 28,660 km² to 84,225 km²/distribution) have characterized this effort as of 2007 (R. Hale, US Department of Agriculture, pers. comm.). On the basis of rates of spread of 30–60 km/year in the Mid-Atlantic states before 1997 (*22–24*), ORV is viewed as having slowed movement of the virus and, with contingency actions to eliminate some dispersed cases, prevented westward spread of rabies among raccoons. Relatively low and variable vaccination rates have been found, despite the use of relatively high bait densities (50–100/km²). Estimated raccoon vaccination rates, based solely on the index of rabies virus neutralizing antibody response, range from 10% to 55% (*22*). The need to vaccinate annually is dictated mainly by high death rates for juveniles and a relatively young age structure for raccoons in North America; juveniles often account for 50% of raccoon populations (*22*). Still, enhanced and public health surveillance indicate that areas west of the Appalachian Ridge remain free of raccoon-variant rabies (*1*,*22*,*23*).

To maintain the integrity of the Appalachian Ridge ORV zone, contingency actions have been needed. In 2004, emergency ORV baiting and TVR were used in northeast Ohio between the established ORV zone and the eastern suburbs of Cleveland (*25*). TVR of >300 raccoons and multiple ORV distributions occurred in this contingency action. This ORV zone had been widened earlier because of encroachment of rabid raccoons from Pennsylvania (*26*).

Other contingency actions unrelated to the westward spread of raccoon rabies have also been implemented. In 2004, an ORV zone created near the Cape Cod Canal to prevent spread of raccoon-variant rabies onto Cape Cod, Massachusetts, was breached, and raccoon-variant rabies spread rapidly throughout the peninsula (T. Algeo, US Department of Agriculture, pers. comm.). Currently, ORV is used twice a year (spring and fall) in the eastern half of the Cape, and baiting is moved gradually westward until an ORV zone can be reestablished along the Cape Cod Canal (J.C. Martin, Tufts Cummings School of Veterinary Medicine, pers. comm.). Additionally, to prevent raccoon rabies from reemerging in southern Ontario, ORV baiting for raccoon-variant rabies continues in northern New York. Confirmed positive raccoon-variant cases in southern Quebec have led to extensive PIC and ORV campaigns to prevent the disease from reaching Montreal. Together, these events and contingency actions illustrate the challenges posed by raccoon rabies, the importance of enhanced surveillance, plus the need to anticipate unexpected contingency actions and their related costs as a component of ORV campaigns.

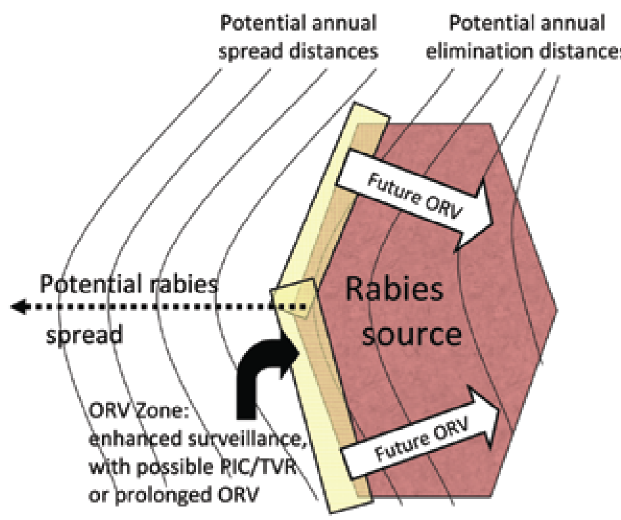

Figure 5. Oral rabies vaccination (ORV) preventive spread or elimination tactic with eventual progressive elimination (*22*). The ORV zone of vaccinated animals is intended to prevent spread of the disease beyond the ORV zone; potential elimination is assumed to result from successive baiting campaigns into the infected area. Potential savings are assumed beyond the ORV zone (or within the zone, if elimination is possible); disease spread rates, final distances of infectious impacts, and durations of ORV bait distributions ultimately determine the magnitude of potential savings. PIC, point infection control activities; TVR, trap–vaccinate–release activities.

Rabies-related Costs

Several studies have documented the costs associated with wildlife-rabies epizootics (*27–31*; see online Technical Appendix 1, available from www.cdc.gov/EID/content/15/8/1176-Techapp1.pdf). Costs have been adjusted for inflation to 2008 US$ or Can$. A raccoon-variant rabies epizootic in the early 1990s in Hunterdon and Warren Counties, New Jersey, more than doubled rabies-related control costs from $6.67/county resident at $591/km² ($4.05/county resident and $359/km², US$ in 1990) to $16.13/county resident at $1,503/km² ($9.79/county resident at $913/km², US$ in 1990) (*27*).

In Massachusetts, a multiyear study found that the median cost of postexposure prophylaxis (PEP) was $3,356/patient ($2,376/patient; range $1,038–$4,447, US$ in 1995); 69% of the cost was for biologics (*28*). Numbers of PEP administrations increased 26-fold, from 1.7/100,000 residents in 1991 to 45/100,000 residents in 1995 (*28*). Estimates for Connecticut were similar (*29*).

A raccoon-variant epizootic in New York State began in 1991, and the resultant rate of PEP administrations ranged from the equivalent of 24 to 34/100,000 residents (no preepizootic estimates of PEP given) (*30*). During 1998–1999, the mean PEP cost was $1,501/person treated ($1,136/person, US$ in 1998; biologics and administration), equivalent to between $36,024 and $51,034/100,000 residents ($27,264 and $38,624/100,000, US$ in 1998); New York City's population is excluded from these estimates. This lower cost compared with that for Massachusetts (*28*) and Connecticut (*29*) may be the result of local

public health department coordination of PEP administrations in New York State (*30*).

Recently (1998–2002), rabies exposure costs were estimated at $4,066/patient ($3,688/patient, US$ in 2005) in southern California (*31*). Average direct (biologics, medical costs) and indirect costs (travel to physicians, day care for medical appointments) were estimated at $2,827/patient and $1,239/patient, respectively ($2,564/patient and $1,124/patient, US$ in 2005).

ORV Program Costs

Bait costs and detailed descriptions of the areas baited, which allowed computations of unit area expenses, are available in Table 1 and online Technical Appendix 2 (available from www.cdc.gov/EID/content/15/8/1176-Techapp2.pdf). ORV programs in Canada and the United States have lasted from >1 for some to >11 years for others and have often required integration of contingency actions (Table 1). The most expensive tactics have been labor-intensive PIC and TVR, but their effectiveness is crucial to maintaining the overall integrity of certain ORV campaigns (*10–13*,*22*,*25*). PIC programs have been reported to cost $612/km^2 ($500/km^2, Can$ in 1999); costs reported for 3 PIC operations for raccoons totaled $469,247 ($363,100, Can$ in 1999; *12*). TVR costs have ranged from $616/km^2 to $1,573/km^2 ($450/km^2 to $1,150/km^2, Can$ in 1991; Table 1).

The target species of ORV greatly affects costs, mainly because of species-specific, bait-density requirements. Bait densities for foxes and coyotes have been less than half those for raccoons (Table 1). Thus, gray fox and coyote ORV programs in Texas averaged $48/km^2 ($42/km^2, US$ in 2004; Table 1), and raccoon programs in the eastern United States averaged between $111/km^2 ($108/km^2, US$ in 2007) and $198/km^2 ($153/km^2, US$ in 1999). Cumulative cost of the Appalachian Ridge ORV program has totaled ≈$57 million since its inception in 1997; baits accounted for 72% of the funds expended (Tables 1, 2).

Annual costs vary as changes in ORV zones occur, as contingency actions occur, and as ORV programs shift from preventing spread to eliminating variants in given geographic areas. Individual bait prices in the United States range from $1.00 to $1.25 (US$ in 2008, depending on bait type). Because of improved production efficiency, bait prices have decreased slightly during the past 5 years.

Table 1. Major oral rabies vaccination campaigns, Canada and the United States*

Country and reference	Strategy or tactic	Duration, y	Target species	Unit bait cost	Target bait density, no./km^2	ORV, TVR, or PIC area, km^2/y†	Cost/km^2‡
Canada							
(*9*)	ORV progressive elimination	>7§	Red fox	Not reported	18–20	8,850–31,460	No estimate
(*10*)	TVR	5§	Skunk, raccoon, red fox	>$2.00 (Can$ 1991)	20/den fox only	60	$450–$1,150 (Can$ in 1991)
(*12*)	PIC	>1§	Raccoon	>$2.00 (Can$)	70	225 PR, 485 TVR, 1,200 ORV	$500 (Can$ in 1999)
United States§							
D. Slate, unpub. data (2007)	ORV zone (Appalachian Ridge)	>1§	Raccoon	$1.22 (US$)	50–75	28,659–84,225	$108 (US$ in 2007)
(*26*)	ORV zone (Ohio–Pennsylvania border)	4§	Raccoon	$1.37–$1.52 (US$)	75	3,872–6,497	$153; range $102–$262 (US$ in 1999)¶
(*17*)	ORV progressive elimination	>9§	Coyote	Not reported	19–27	38,850	$42 (US$ in 2004)#
(*17*)	ORV progressive elimination	>8§	Gray fox	Not reported	27–39	56,202	$42 (US$ in 2004)#

*Unless otherwise noted, costs are in Can$ or US$. No discounting for inflation was used; this article and online Technical Appendix 2 (www.cdc.gov/EID/content/15/8/1176-Techapp2.pdf) provide inflation-corrected costs in 2008 Can$ or US$.
†Components of reported areas differ according to tactic and strategy. Oral rabies vaccination (ORV) entails topographic areas at which baits are distributed at target densities over landscape. Trap–vaccinate–release (TVR) involves relatively limited topographic areas of intense live trapping and parenteral vaccination of captured animals. Point infection control (PIC) involves successive concentric rings of population reduction, TVR and ORV; the concentric rings become distorted if subsequent rabid animals are caught within these rings. New concentric rings are now formed according to these occurrences. Additionally, depending on habitat or location of urban centers, ORV may be used in a larger strip to create an added ORV preventive zone.
‡Most cost estimates include purchase of baits, aircraft, fuel, and equipment but often omit accurate labor charges.
§Surveillance, TVR, PIC, or ORV bait distributions continue at present; therefore, current duration and areas baited differ from those reported. According to Foroutan et al. (*26*), ORV baitings continue as part of the National ORV Program (Slate et al. [*22*]).
¶According to Foroutan et al. (*26*), areas were baited twice each year. In 1997, the first baiting was conducted over a smaller area (1,780 km^2), and in May 1997 (initial) and June 1999, 2 smaller emergency baitings (in response to a breach in the ORV zone) were conducted, covering $\leq$1,701 km^2. Average costs include a baiting in April 1999, when several tests of bait densities (high) were conducted.
#According to Sidwa et al. (*17*), the area baited had shrunk over time because of progressive coyote-variant rabies elimination, but the purse string (gray fox) tactic and ORV-baited area were expanded in 2007 as the gray fox variant spread north along the Pecos River and into southern Texas. The area cost estimate was derived as the quotient of a reported $3.8 million/year program cost and average annual 33,669 km^2 (dog and coyote) and 56,202 km^2 (gray fox) bait zones (sum 89,871 km^2) cited in online Technical Appendix 2.

Table 2. Approximate, undiscounted total costs of largest oral rabies vaccine programs, North America, 1989–2004*

Location, target species	Years	Total undiscounted costs, million $	Average undiscounted annual costs, million US$	Reference
Ontario, red foxes	1989–2000	Can$43†	3.5	S.A. Shwiff, unpub. data*
Texas, coyotes and gray foxes	1995–2003	US$34	3.8	(*17*)‡
Appalachian Ridge, raccoons	1997–2007	US$57	5.2	D. Slate, unpub. data§

*Costs are estimates in Can$ or US$ as reported in original publication or as cited by unpublished source.
†S.A. Shwiff et al. (unpub. data) based their calculations on certain data presented in *9,32*.
‡Sidwa et al. (*17*) stated that (for both programs combined) average annual costs were $3.8 million. We computed this value as follows: 9 years × $3.8 million = $34 million total (i.e., Sidwa et al. did not clarify what was included in their cost estimate).
§D. Slate (2007, unpub. data) provided air, bait, fuel, and staff costs, although some staff hours and fuel costs were omitted for initial campaigns during 1997–2001; a total of 9,394 staff hours, $5,868,262 aircraft costs, $923,481 fuel costs, and $50,187,380 bait costs were reported for 58 campaigns involving the dispensing of 41,018,811 baits over 530,825 km^2. The software used to determine bait distribution costs was prepared by staff of the United States Department of Agriculture, Animal and Plant Health Inspection Service, Wildlife Services, National Rabies Management Program. After deselecting the bait zones, flight lines were drawn by using the topography (e.g., avoiding water and residential areas) to determine the flight lines and transects. After that had been established, the bait zones were populated with the lines and measured to determine the total length (km). Flight lines determine total flight hours: ([km × 0.539958 nautical miles]/flight speed [knots] = flight hours). Fuel usage is computed as follows: (flight hours × consumption rate [91 gallons/h] × fuel price/gallon = total fuel cost). Costs were also influenced by air transect width, distance to airports for refueling, and end-of-transect turning distance.

Potential ORV-Induced Savings

One ex post study (actual returns, after the fact) provided detailed estimates of PEP administrations in Ontario during 1956–2000 (*32*). Annual PEP administrations increased from ≈1,000/year during the 1960s and 1970s to >2,000/year during 1982–1993, then decreased to ≈1,000/year again after large-scale ORV campaigns targeting red foxes began in 1989 (*9*,*10*,*32*). Many factors could account for these changes, including revisions of PEP administration guidelines. The initial increase in PEP administrations possibly occurred as a result of fewer adverse effects from use of the new human diploid cell vaccine and stability in numbers of rabies cases (*32*). The latter decrease in PEP administrations was coincident with ORV-caused elimination of arctic fox–variant rabies from southern Ontario (*9*).

Modeling the Benefits and Costs of ORV

Measured costs of an epizootic of raccoon rabies in New Jersey were used to model the costs and benefits of a hypothetical ORV program (*27*). The model projected net savings for ORV (Table 3) based on the assumptions that the ORV program would require a 2-year campaign and that expenditures to protect human health would remain constant. The model did not allow for reintroduction of rabies or for the potential reemergence of rabies. Benefit:cost ratios (BCRs) related to this hypothetical use of ORV were reported as ≥2.2 (*27*; online Technical Appendix 3, available from www.cdc.gov/EID/content/15/8/1176-Techapp3.pdf) summarizes key principles of benefit:cost modeling).

Use of ORV to eliminate raccoon rabies from a hypothetical area of 34,447 km^2 was modeled under 2 scenarios (*33*). Scenario 1 assumed that concentric ORV zones (rings) would expand outward from a center over a 20-year period and that the ORV zone would be maintained for 10 more years to prevent reintroduction. Scenario 2 assumed that the entire area would be baited in the first 2 years and that a ring-shaped ORV zone would be maintained for 28 more years. In the first scenario, inclusion of an expected 20% increase in pet vaccinations (*27*) as a benefit resulted in $3.1 million net savings from ORV; removing pet vaccinations as a savings yielded a net cost of $7.7 million ($6.2 million, US$ in 2000; Table 3). The second scenario yielded no net savings unless the cost of maintaining a containment zone was removed from the model (*33*).

The economics of a large-scale ORV program to prevent the westward spread of raccoon-variant rabies in the eastern United States was modeled and used in planning the current Appalachian Ridge program (*34*). Scenarios assumed that a raccoon-variant rabies epizootic would advance in 40 or 127 km/year (fixed rates) bands to the west of the current leading edge of raccoon-variant rabies along the Appalachian Ridge (*22*). Input variables were as follows: 7% discount rate, 102,650 km^2 ORV zone, 75 baits/km^2, $1.63/bait ($1.30/bait, US$ in 2005), $10.78/$km^2$ ($8.62/$km^2$, US$ in 2000) aerial distribution, and $18.75/$km^2$ ($15.00/$km^2$, US$ in 2000) post-ORV evaluation. The effect of an epizootic was calculated in terms of unit human population within bands. Results showed that all 8 scenarios, except the 40 km/year spread rate with 20-year fixed baiting costs, yielded BCRs ≥1.1 and that total estimated net present values of the program were $48–496 million with >$96 million in discounted program costs (*34*). Because of natural geographic features, raccoon population dynamics, and other factors that affect the spatial and temporal spread of rabies, an assumed variable spread of the virus westward would have been more realistic (*25*,*26*). As in previous models (*27*,*33*), estimates of net savings (>50%) for scenarios were enhanced by inclusion of potential pet vaccination costs.

Another model examined specific costs of baiting campaigns for raccoon rabies along the Ohio–Pennsylvania border (*26*). This model incorporated movement and life-cycle data for rabid and nonrabid raccoons. An area of 400 km^2 with a 10-km ORV zone was assumed to be baited. Benefits were predicted to accrue mainly in a 5-km strip on the west side of the ORV zone. Assumptions about rac-

coon carrying capacity and percentage ORV vaccination efficiency influenced the rate of rabies spread. This model predicted a net cost for ORV; however, a simple extrapolation implied that net savings would have occurred if the benefits were projected for a 100-km strip west of the ORV zone (*26*).

Ex post modeling was conducted for the ORV campaigns that eliminated red fox–vectored rabies in Ontario. Estimated ORV benefits (PEP + animal rabies tests + livestock indemnity) ranged from \$35.4 million to \$99.3 million (\$35 million to \$98 million, Can\$ in 2007; total program costs were \$78.0 million (\$77 million, Can\$ in 2007) (S.A. Shwiff, unpub. data). BCRs ranged from 0.49 to 1.36, and outputs implied a lag effect for savings; BCRs were <1.0 during 1990–1992 and ≥1.0 during 1993–2000.

Recently, an ex post modeling analysis was performed for the 1995–2006 ORV program that eliminated canine-variant rabies from southern Texas (*16*,*17*,*35*). Total expen-

Table 3. Comparison of selected modeling studies that examined the economics of oral rabies vaccination programs*

Reference	Locale, tactics, target species	Type of study, model	Duration modeled, y	Cost and density of vaccine baits; distribution costs†	Results	Comments
(*27*)	2 counties in New Jersey, ORV, raccoon	Benefit:cost, cost data collected from field with hypothetical baiting program	5	\$1–\$2/bait; 62–200 baits/km^2; distribution \$100/km^2	Net savings \$13.34–\$20.78/ county resident (1990 US\$); \$1,244/km^2 – \$1,939/km^2	Probably unrealistic: assumed only 2 baitings; no contingency costs; main economic benefit = reduced pet vaccinations
(*33*)‡	Hypothetical 34,447 km^2-area, expanding circle then maintained barrier zone, raccoon	Benefit:cost of hypothetical baiting program, extensive sensitivity analyses	30	\$1.50/ bait; 100 baits/km^2 (range 40–115); distribution \$39/km^2 (maximim \$100/ km^2)	Net savings of \$3.1 million if reduced pet vaccinations included as benefit. Net cost (\$6.2 million) if pet vaccinations excluded.	Lack of data required many assumptions; bait density, cost/ bait, and value of pet vaccinations were the most critical elements
(*34*)§¶	Appalachian Ridge area, ORV, raccoon	Benefit:cost model of program to deter westward spread of raccoon rabies	20	\$1.30/bait, 75 baits/km^2 ; aerial distribution \$8.62/ km^2; evaluation \$15/km^2	Net savings \$100–\$500 million (2000 US\$)	Assumed that without ORV, rabies would move 42 or 125 km/y west; distribution costs are low; animal vaccinations are critical component
(*26*)#	Ohio–Pennsylvania, ORV zone (400 km^2), raccoon	Simulation of individual raccoons + benefit:cost model to prevent westward spread of raccoon rabies	40	\$1.47/bait; 3 scenarios of 70, 100, 175 baits/km^2. Distribution \$23.23/km^2	Net costs (1999 US\$; savings recouped 5 km band west of zone)	Complex model showing importance of many biological factors determining potential for success and net savings
(*35*)	Texas, progressive elimination, collapsed bands, coyote	Retrospective benefit:cost model; projected population-based PEP and animal test costs for 20 southern to 232-county expansion area	12	\$26.3 million total cost (2006 US\$; Texas Department of State Health Services accumulated value)	Net savings \$98–\$354 million; BCRs of 3.7–13.4; range of savings for 100%, 50% and 25% of PEP and rabies tests in epizootic area.	Simple model showing wide-area expansion. ORV proved cost-efficient if projections were reduced to 7% of the PEP and tests for epizootic counties
S.A. Shwiff, unpub. data	Ontario, progressive elimination, expanded wedge, arctic-fox variant, red fox	Benefit:cost measured costs but had to model savings	12	\$77.4 million (2006 Can\$) for total ORV	Net savings in 3 of 4 scenarios: reductions in animal rabies testing accounted for most net savings.	Assumed multiple estimates of future rabies-related costs

*No inflation corrections used. ORV, oral rabies vaccination; PEP, postexposure prophylaxis; BCRs, benefit:cost ratios.
†Distribution costs exclude cost of bait purchases. US\$ except as indicated.
‡For example, Meltzer (*33*) posited a baseline assumption with a distribution cost of \$39/km^2.
§Kemere et al. (*34*) assumed that the "… effectiveness of vaccination programs would be validated through surveillance and testing of raccoon populations in the ORV zones … [evaluation cost] also includes educational, promotional, and overhead expenses."
¶Although Kemere et al. (*34*) did not explicitly allow for contingency costs (to allow for breaches of ORV zones, etc.), they did sensitivity analyses assuming "… the full program costs are used for the entire period instead of dropping to 40% after 5 years."
#Foroutan et al. (*26*) only considered benefits extending up to 5 km west of the ORV zone. A simple extrapolation would suggest that net savings would occur if the calculated benefits were to extend some 100–150 km west of the ORV zone.

ditures for the ORV program were compared with benefits accrued from likely PEP administrations and animal rabies tests estimated for the 20-county epizootic area and projected to an area involving most of the state. Estimated benefits ranged from $95 million to $369 million ($89 million to $346 million, US$ in 2006); total ORV program costs were reported as $28 million ($26,358,221 US$ in 1995–2006). BCRs ranged from 3.4 to 13.1, depending on assumed incidence of PEP administrations and animal tests (*35*). This study confirmed that 56/100,000 residents received PEP during the epizootic, a high rate for the sparsely populated area of southern Texas where the disease occurred (*35*).

Conclusions

ORV of wildlife has had positive public health effects. Multiyear campaigns have led to progressive elimination of arctic fox–variant and canine-variant rabies in Ontario and Texas, respectively. PIC, TVR, and ORV zones have prevented raccoon-variant rabies from becoming established in Ontario. Campaigns to contain and eliminate rabies in gray foxes of west-central Texas continue, and spillover of gray fox–variant rabies into coyotes may pose new challenges for preventing the spread of this variant. The ORV zones and contingency actions along the Appalachian Ridge have, thus far, prevented westward spread of raccoon rabies. Habitat alterations to reduce potential carrying capacities of raccoons through local no-feeding regulations and improved refuse management would aid rabies control efforts, but these measures are difficult to implement and enforce. Improved bait-vaccine technology, potentially integrating reproductive inhibitors into TVR campaigns for specific urban raccoon and skunk populations, may improve wildlife rabies elimination.

Rabies campaigns have been relatively expensive. We estimate that ≥$130 million (combined Can$ and US$) has been spent on ORV programs in North America during the past 10 years. Programs have proved lengthy (typically >5 years), have required enhanced surveillance, and have often required contingency actions to ensure rabies elimination without reintroduction.

Most economic assessments and modeling studies indicate that ORV programs can yield cost savings (*32–35*). Regional increases in PEP administrations (and associated public health costs) from 2–4/100,000 before to 24/100,000 (*30*), 45/100,000 (*28*), or 66/100,000 (*27*) residents during or after have been documented for nonbat rabies epizootics. Reduced PEP, epizootic-related pet vaccinations, animal diagnostic tests, public education activities, and other factors represent costs avoided by ORV programs. Direct estimates of wild mammal populations and the relationship of these to numbers of PEP administrations are difficult to obtain; this topic was beyond the scope of our review but needs research.

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etymologia

Lyssavirus

[lis′ə-vi″rəs]

From the Greek *lyssa* (frenzy or madness) and Latin *virus* (poison). In Greek mythology, Lyssa was the goddess of rage, fury, and rabies, known for driving mad the dogs of the hunter Acteon and causing them to kill their master. Aristotle (4th century BCE) said, "Dogs suffer from the madness. This causes them to become irritable and all animals they bite to become diseased." The disease in humans was characterized by hydrophobia, in which the sick person was simultaneously tormented with thirst and with fear of water. Hippocrates is believed to refer to rabies when he said that persons in a frenzy drink very little, are disturbed and frightened, tremble at the least noise, or are seized with convulsions.

Lyssavirus is a genus of the family Rhabdoviridae, which includes rabies virus and other related viruses that infect mammals and arthropods (e.g., Australian bat lyssavirus, Duvenhage virus, European bat lyssaviruses 1 and 2, Lagos bat virus).

Source: Steele JH, Fernandez PJ. History of rabies and global aspects. In: Baer GM. The natural history of rabies, 2nd ed. New York; CRC Press; 1991. Philadelphia: Saunders; 2007; Mahy B. The dictionary of virology, 4th edition. London: Academic Press; 2009. Dorland's illustrated medical dictionary, 31st edition.

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Technical Appendix 1

Wildlife Rabies-related Costs (Details of Published Studies; No Inflation Corrections Used)

A cost-comparison study examined expenditures for controlling rabies before (1988) and during (1990) a raccoon-variant rabies epizootic in Hunterdon and Warren counties, New Jersey, USA (*1*). This study examined perhaps the most diverse set of costs thus far reported, but these entailed relatively short-term, small-area estimates. The epizootic more than doubled rabies-related control costs, from \$4.05 (\$359/km^2) to \$9.79/county resident (\$913/km^2, 1990 US\$). Both before and during the epizootic, pet vaccinations were the largest single cost component of rabies expenses; the costs for vaccinations of domestic animals were \$337,998/100,000 residents in 1988 and \$640,552/100,000 residents in 1990. The next largest category was "other rabies control activities" (e.g., public health, public education) accounting for 11% of costs in 1988 and 13% in 1990. The number of persons receiving postexposure prophylaxis (PEP) increased from 2 in 1988 (1/100,000 residents) to 131 in 1990 (66/100,000 residents). Although the average cost was \$555/person treated in 1988 and \$1,138/person in 1990, PEPs only accounted for 8% of the rabies-related costs at the peak of the epizootic in New Jersey in 1999.

In Massachusetts, a multiyear study focused on the increased use and cost of PEP during 1991 (1 year before a rabies epizootic) and from 1992 through 1995 of a raccoon rabies epizootic in the state (*2*). The median cost of PEP was \$2,376/person (range: \$1,038–\$4,447; 1995 US\$); 69% of the cost was due to biologics. Estimates were similar for Connecticut (*3*). Numbers of PEP administrations increased from 1.7/100,000 residents in 1991 to 45/100,000 residents in 1995 (26-fold increase). Thus, this rabies epizootic increased PEP-related costs by \$102,880/100,000 residents.

During the 1990s, New York State reported an epizootic of raccoon-variant rabies (*4*). The number of PEPs given in the state during the epizootic ranged from 2,422 in 1995 to a high of 3,373 in 1997 (no preepizootic numbers reported; New York City (NYC) is excluded from this statewide public health study). These are roughly equivalent to 24 and 34 PEPS per 100,000 residents (calculated using 2000 census count of 10 million state residents, excluding NYC). The mean PEP cost was $1,136/person treated (1998 US$, biologics and administration), equivalent to between $27,264/100,000 and $38,624/100,000 residents. This amount is notably lower than the amount recorded in Massachusetts (*2*), but New York coordinates aspects of PEP (*4*).

Recently (1998–2002), when a skunk rabies epizootic spread from San Luis Obispo to Santa Barbara County, the direct and indirect costs due to rabies exposure in southern California were documented, (*5*). County records documented the medical and public health activities required of 134 patients (equivalent to 4.1/100,000 county resident-years, using 2002 population estimates for 5 years). The public health costs included case investigations and animal control expenses. Telephone interviews of 55 patients who were given PEP provided indirect patient-related expenses related to receiving PEP (e.g., alternative medicine, daycare, travel, time lost from work). The mean total cost of a suspected human rabies exposure was $3,688/patient; average direct (biologics, medical costs) and indirect costs were $2,564/patient and $1,124/patient, respectively (2005 US$).

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Technical Appendix 2

Correction for Inflation of Selected Costs in Original Publications

This Technical Appendix provides selected oral rabies vaccination (ORV), point infection control (PIC), trap–vaccinate–release (TVR), and postexposure propylaxis (PEP) costs for studies cited in the article; published costs are corrected for inflation. The annual Consumer Price Index (CPI %) between 1990 and 2007 for "all goods and services (urban consumers)" was used to derive 2008 values. Bank of Canada (http://www.bankofcanada.ca/en/rates/inflation_calc.html) and the United States Bureau of Labor Statistics (http://www.bls.gov/CPI/#overview) were sources of CPI rates.

Table 1. Annual Consumer Price Index inflation (% change between years)*

Year	Canada	United States
1990	4.8	5.4
1991	5.6	4.2
1992	1.4	3.0
1993	1.9	3.0
1994	0.1	2.6
1995	2.2	2.8
1996	1.5	2.9
1997	1.7	2.3
1998	1.0	1.6
1999	1.8	2.2
2000	2.7	3.4
2001	2.5	2.8
2002	2.2	1.6
2003	2.8	2.3
2004	1.8	2.7
2005	2.2	3.4
2006	2.0	3.2
2007	2.2	2.8
2008	2.3	3.8

*Briefly, costs cited in the original publications were compounded for years subsequent to the originally specified oral rabies vaccination, trap–vaccinate–release, point infection control, and postexposure prophylaxis cost estimates. If no monetary year was provided in the original article, we arbitrarily specified a likely year for the authors' calculations based on 1–2-year publication lags. As of June 25, 2008, currency conversion was as follows: 0.98 Can$ = 1.00 US$; whereas, as of May 5, 2009 1.00 Can$ = 1.19 US$.

Table 2. List of originally cited studies and inflated cost estimates for ORV, TVR, PIC, or PEP variables in 2008 Can$ or US$*

Study and reference	Year or assumed year of original monetary estimate	Current cost (Can$ or US$ in 2008)
ORV/TVR/PIC†		
(*1*)	No estimate	No estimate
(*2*)	1990	TVR $616/km^2 Can$
(*3*)	1999	PIC $605/km^2 Can$
		ORV only $245/km^2 Can$
Slate (prior unpub. data)		ORV $111/km^2 US$
(*4*)	1999	ORV $198/km^2 US$
(*5*)	2004	ORV $48/km^2 US$
PEP‡		
(*6*)	1990	$1,874/patient US$
(*7*)	1995	$3,356/patient US$
(*8*)	1995	1,501/patient US$
(*9*)	2005	$4,066/patient US$

*ORV, oral rabies vaccination; TVR, trap–vaccinate–release; PIC, point infection control; PEP, postexposure prophylaxis.
†Rosatte et al. (2001), Slate (prior unpublished data), and Foroutan et al. (2002) report ORV costs for raccoons (i.e., bait densities of 50–75/km^2; Sidwa et al. (2004) report ORV for coyote and gray fox (i.e., bait densities of 19-39/km^2).
‡Chang et al. (2002) report PEP for New York (i.e., biologics are paid by state); Shwiff et al. (2007) report both direct and indirect costs of PEP.

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Technical Appendix 3

Principles of an Economic Analysis of Oral Rabies Vaccination Programs

Rabies, Oral Rabies Vaccination and Use of Benefit:cost Analyses

There are often no human rabies cases directly related to an epizootic of terrestrial rabies. Thus, it is often impossible to conduct a cost-effectiveness analysis—an often-recommended method for public health economics studies, in which the analytic output would be cost per averted case of human rabies (*1*). Thus, published studies have used benefit:cost methods, in which researchers attempt to evaluate all of the benefits and costs from ORV programs in dollar values (*1,2*). The general benefit:cost equation below illustrates the basic concept:

Net savings (costs) = value of reduced rabies-related costs –
costs of oral rabies vaccination (ORV) program.

Where: Value of reduced rabies–related costs = (some portion of) costs of rabies epizootic = additional pet vaccinations + additional livestock vaccinations + pet replacements + livestock replacements + additional human preexposure rabies prophylaxis + additional human postexposure prophylaxis (PEP) + costs of treating adverse side effects of additional PEPs + costs of case investigations by public health units + additional laboratory tests + quarantine of suspected rabid animals + public educational materials + potential loss of endangered mammals in areas near epizootics (*3*).

To date, prevention of costs of additional pet vaccinations and PEP have been the main economic impacts of rabies epizootics used to evaluate benefits of ORV programs (*4–7*). It is controversial to consider additional pet vaccinations as a cost of rabies epizootic (typically, before a rabies epizootic, vaccination rates in dogs in the United States are between 20% and 50% (*8*). Experience has shown that ORV programs cannot guarantee elimination of all rabies

risks to pets (e.g., ORV zones have been breached, bat rabies is not controlled by current ORV programs). It has been argued that it is potentially a benefit, and not a cost, if pet rabies vaccination rates increase, regardless of cause (S.A. Shwiff, unpub. data). Also, pet replacement costs have never, to our knowledge, actually been measured, and there has yet to be a valuation of a loss of endangered species due to a rabies epizootic.

ORV-Related Program Cost

Costs of an ORV program (often multiyear) can be defined as follows (*3–5*):

Costs of an ORV program per year = (area covered in 1 year × vaccine-bait density per unit area × price of individual vaccine-baits) + distribution costs + costs of injuries/accidents + costs of contingency plans

Vaccine-baits have, to date, been distributed by fixed-wing aircraft, helicopters, and ground (i.e., personnel either walking or driving). Although accidents and injuries associated with ORV operations have been rare, the potential for these costs remain and must be considered in any economic assessment of ORV. Injuries to employees performing baiting operations are typically covered by some form of preexisting insurance (i.e., costs are prepaid and thus not usually included), but potential public injury or death due to various events remains a possibility. To date, in the United States, only 1 accident involving a citizen's exposure to the live vaccine in ORV baits has occurred. The citizen sued the public health agency responsible for distributing the baits. The court, however, ruled in favor of the public health department, incurring zero cost to the public (*9*).

Analytic Timeline

Rabies epizootics usually last ≥2 years and may exhibit cyclic patterns (i.e., number of rabid animals increase and decrease as the animal population changes). The costs of controlling rabies can be considered as having 3 different time periods: preepizootic, during epizootic, and postepizootic. It is possible that during the postepizootic period rabies control costs will not subside to preepizootic levels (*1*). Similarly, an ORV program will typically last ≥5 years. Thus, an economic study of ORV programs must incorporate the multiyear aspects of benefits and costs.

Perspective and Discounting

Because a substantial part of the costs of a rabies epizootic and an ORV program are borne by public health entities, it is appropriate that any analyses of an ORV program take a societal perspective as the principal perspective. Furthermore, because rabies epizootics and ORV programs may each take several years, benefits and costs must be appropriately discounted (*1,2,6*).

Units of Analysis

The economics of ORV are determined by human population density (i.e., increased human population results in increased probability and numbers of PEPs, pet vaccinations, etc.). It has been shown that human population density can impact the number of animals tested for rabies (*10*). Thus, it is recommended that both benefits and costs of ORV programs be calculated in terms of $/unit area (S.A. Shwiff, unpub.data). This allows for ready comparison within a program over time (as populations change), comparison between programs (with possible differences by targeted species and locale), and consideration of targeting and prioritization (by economic criteria).

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