Cost–benefit analysis of controlling rabies: placing economics at the heart of rabies control to focus political will

Stephanie A. Shwiff
USDA National Wildlife Research Center, stephanie.a.shwiff@aphis.usda.gov

J. L. Elser
USDA National Wildlife Research Center

K. H. Ernst
USDA National Wildlife Research Center

S. S. Shwiff
Texas A&M University

A. M. Anderson
USDA National Wildlife Research Center

Rev. Sci. Tech. Off. Int. Epiz., 2018, **37** (2), 681-689

Cost–benefit analysis of controlling rabies: placing economics at the heart of rabies control to focus political will

S.A. Shwiff [(1)]*, J.L. Elser [(1)], K.H. Ernst [(1)], S.S. Shwiff [(2)] & A.M. Anderson [(1)]

[(1)] National Wildlife Research Center, United States Department of Agriculture (USDA)/Animal and Plant Health Inspection Service (APHIS)/Wildlife Services, 4101 LaPorte Avenue, Fort Collins, CO 80521, United States of America
[(2)] Texas A&M University – Commerce, 2200 Campbell Street, Commerce, TX 75428, United States of America
*Corresponding author: stephanie.a.shwiff@aphis.usda.gov

Summary

Rabies is an economically important zoonosis. This paper describes the extent of the economic impacts of the disease and some of the types of economic analyses used to understand those impacts, as well as the trade-offs between efforts to manage rabies and efforts to eliminate it. In many cases, the elimination of rabies proves more cost-effective over time than the continual administration of post-exposure prophylaxis, animal testing and animal vaccination. Economic analyses are used to inform and drive policy decisions and focus political will, placing economics at the heart of rabies control.

Keywords

Cost–benefit analysis – Dog vaccination – Health economics – Post-exposure prophylaxis – Rabies – Zoonosis.

Introduction

Rabies is an economically unique zoonosis because most of its associated costs do not result from illness, but are the consequence of human deaths and efforts to prevent the disease in humans, livestock, wildlife and companion animals. This unique pattern of costs reflects two basic facts: the case fatality rate of rabies in humans is nearly 100%, and the disease is completely preventable through timely post-exposure prophylaxis (PEP) with rabies vaccine (1). As a result, many individuals who are at very low risk of developing the disease still seek post-exposure vaccination, even though this may not be the recommendation of health professionals (2).

Like all zoonotic diseases, rabies is maintained in an animal reservoir. Each rabies virus (RABV) variant has a unique geographical range and ecology, requiring different control and intervention strategies. In developed countries, where canine rabies has been eliminated, the virus may continue to circulate in wildlife, whereas in most developing countries, the principal reservoir is domestic dogs (*Canis lupus familiaris*). Human and livestock exposure is based on a multitude of risk factors (3, 4), and there are several pathways by which rabies causes economic damage. Although the close relationship between humans and dogs is the primary cause of RABV exposures for all variants, that relationship also provides many opportunities for mitigating its impact.

Rabies exposures in humans, companion animals or livestock result in economic impacts associated with vaccination or death. Because rabies patients die quickly, and there is no effective therapy, the cost of illness is relatively small, especially in the developing world. In contrast, the direct costs arising from factors such as PEP and livestock deaths are substantial, and they have been characterised in numerous studies (3, 5, 6, 7). Rabies also has indirect costs, including vaccination of livestock and companion animals and testing of animals suspected of rabies (4, 8). Other impacts of rabies on the broader economy can be captured by examining changes in different sectors that result from the direct and indirect impacts of the disease (9).

Of all the variants, canine RABV has been studied the most extensively. The global economic impact of canine rabies has been estimated by several studies and results highlight the fact that Asia disproportionately bears the burden of

doi: 10.20506/rst.37.2.2833

this zoonosis as a result of high levels of human deaths, high rates of PEP and low investment in preventative dog vaccination efforts. The total cost of canine rabies has been estimated to range from US$ 530 million in Latin America, Asia and Africa (10) to US$ 695 million in Asia and Africa (11). Hampson *et al.* (12) take into account the cost of human life lost by calculating disability-adjusted life years (DALYs) and estimate the overall global cost of canine rabies at US$ 8.6 billion. Anderson & Shwiff (13) account for the value of human life using a different methodology and arrive at an estimated global economic burden of canine rabies of US$ 124.2 billion annually. As a neglected disease, rabies disproportionately affects people in poor, rural areas, especially children (11, 14). These studies only consider costs incurred due to canine rabies and exclude costs arising from other RABV variants, implying that the real total cost of rabies presence worldwide is substantially higher.

Rabies is a preventable disease in that vaccination exists for humans, companion animals, livestock and wildlife, and a number of countries have succeeded in eliminating canine rabies, resulting in long-term cost savings (15, 16, 17). For example, canine rabies was eliminated from the United States of America (USA), through the coordinated efforts of state and federal agencies. One of the factors in the success of elimination efforts was the implementation of an oral rabies vaccination (ORV) programme in wild and domestic canids in Texas, the impact of which has been evaluated by Shwiff *et al.* (16). Economic analyses such as this help to capture the impact of rabies to society. They inform resource allocation and disease management decisions. Understanding the economic trade-offs between suppression and treatment of rabies in humans versus treatment in animals is crucial to focusing political will to address the impacts caused by the disease. The tools exist to eliminate the disease; however, the economics determine whether or not elimination is feasible. This reality emphasises the importance of understanding the benefits and costs associated with rabies management in all potential reservoirs. This paper will describe the types of economic analyses used in rabies research, and discuss the status of economic research regarding rabies, which includes human treatment, control efforts in wildlife and potential strategies for eliminating rabies.

Types of economic analyses

A variety of types of analyses is available to economists. Benefit–cost analyses (BCAs) or cost–benefit analyses (CBAs) are useful for measuring and comparing the economic efficiency of policy options. For example, Anderson *et al.* (8) conducted a BCA to compare two options for controlling vampire bat rabies in Mexico, and Elser *et al.* (18) conducted a retrospective BCA on a raccoon rabies elimination programme in New York State, USA. A general BCA decision framework for mitigation of disease spread at the wildlife–livestock interface has also been developed to identify, assemble, and measure the components vital to the biological and economic efficiencies of animal disease mitigation efforts (19). Cost-effectiveness analysis is used to measure an outcome per unit of effort (which does not have to be monetary). Wera *et al.* (20) used this technique to determine the cost-effectiveness of mass dog vaccination campaigns on Flores Island, Indonesia, defining cost-effectiveness as public cost per averted canine rabies case. These tools, and others, allow researchers to determine optimal rabies management choices and provide methodology to reveal the magnitude of the economic impact of rabies on society.

Common metrics to measure the impact of rabies include: the direct and indirect impacts from medical treatment for dog bites; direct and indirect treatment for PEP; dog vaccination efforts; livestock losses; and DALYs. Typical results provided by economic analyses of rabies impacts include the overall impact of the disease burden, cost per dog vaccinated, cost per human life saved, cost of PEP, cost of dog vaccination programmes, and DALYs. In most cases, costs associated with human PEP make up the largest component of costs. Unfortunately, most studies do not have sufficient data to make these studies replicable in other locations, which makes the results regionally specific.

A new class of models is being developed that strikes a balance between biological sophistication and the ability to identify optimal rabies management strategies while recognising management resource constraints. These models are individual-based stochastic simulations that explicitly account for the links between effort, cost, and biological outcomes. Additionally, the objectives of these models are to construct a framework that *i)* accounts for population and disease dynamics; *ii)* allows removal, permanent sterilisation, temporary contraception and vaccination; *iii)* allows strategies to vary temporally, spatially and demographically; *iv)* allows mixed strategies; *v)* accommodates various levels of data availability; and *vi)* is flexible enough to allow parameterisation and functional forms for a variety of wildlife species and diseases. In the future, these models may provide a way to more appropriately integrate biological realities and economic considerations to provide rabies managers with the power and flexibility to clearly highlight the benefits and costs of different elimination strategies.

Human rabies treatment

Human rabies treatment is expensive and comprises a significant portion of the overall economic impact of rabies. Treatment usually consists of a series of four to five vaccinations over a span of several weeks, accompanied by a dose of rabies immunoglobulin (RIG). In the USA, medical costs for each suspected human rabies exposure, including PEP, are estimated to total US$ 3,000 (adjusted to 2017) and account for 70% of the cost of each rabies exposure event (5). In developing countries of Asia and Africa, PEP costs range from US$ 40 to US$ 64 (11, 21). However, many people seeking PEP are unable to receive the full course of treatment, so these costs reflect only partial treatment. Human or equine RIG is not available in many of these areas. In the Philippines and Tanzania, only about 1% of patients received RIG, while just 9% received RIG in South Africa (21). The cost of PEP is out of reach for many people in developing countries, where daily wages are often only US$ 1 or US$ 2 (22).

Rabies by variant

In terms of economic analysis, canine rabies has been the most extensively studied RABV variant. This is likely the case for several reasons. Firstly, humans are at greater risk of contracting this variant because of their close relationship with dogs (*C. lupus familiaris*), giving rise to related impacts and generating interest in studying these impacts. Secondly, even if the variant of rabies is commonly found in wildlife, the route to human exposure is still mainly through dogs as they interact with wildlife, thereby potentially exposing humans. This section examines the literature of economic analyses for each variant.

Raccoons

Raccoon (*Procyon lotor*) rabies is found primarily in the USA and Canada. It is enzootic in south-eastern Canada and in the north-eastern, mid-Atlantic and south-eastern regions of the USA (23, 24). Oral rabies vaccination has been used to prevent the spread of raccoon rabies westward, where abundant susceptible raccoon populations exist (25, 26). Between 2006 and 2010, approximately 38 million ORV baits were distributed along the Appalachian Ridge to form vaccination zones to strategically prevent the westward spread of raccoon rabies. These zones prevent the spread of the virus into other United States and Canadian territories, and so far, there has not been a breach of the ORV barrier (23, 27), indicating that this method of rabies management may be effective for the confinement and prevention of raccoon rabies and could be a component in potential strategies for eliminating the raccoon RABV variant (26).

Assuming raccoon rabies would continue to move westward in the absence of these zones, the ORV programme, coupled with natural barriers (such as the Appalachian Mountains and various river systems), proves to be economically efficient. The cost of establishing and maintaining the ORV zones is estimated to be between US$ 58 million and US$ 148 million (27). The cost estimates of ORV in Ohio between 1997 and 2000 were US$ 102,261 per km^2, and the mean baseline cost of blanket rabies prevention techniques for the state is estimated to be US$ 397,728 per year (28). Foroutan *et al.* (29) concluded that ground distribution of ORV costs less than air distribution, and the cost of the baits themselves accounts for 85% of total costs.

Although there are very few human deaths attributable to the raccoon RABV variant in the USA, rabid raccoons pose a significant threat to humans and pets, due to the species being well adapted to life in urban and suburban areas (23). Humans are at risk of rabies through direct exposure, and exposure to pets that have been exposed to a rabid raccoon. Though there may not be a large number of human fatalities related to raccoon rabies, the presence of rabid raccoons does increase the number of livestock and pets annually tested for rabies, as well as the amount of PEP administered in that area (27).

In March 2008, three cattle died in Hampshire County, West Virginia, after being exposed to a rabid raccoon. The remaining 85 cattle were euthanised once the dead cattle tested positive for rabies, in order to prevent the spread of the virus. In addition, ten people were evaluated for possible exposure to rabies following the event, and all ten received rabies PEP, resulting in an estimated total cost of US$ 103,985 for this single event (30). In a separate event in Guernsey, Ohio, another 64 calves were euthanised following a confirmed death from raccoon rabies in the herd, and six humans received PEP following the incident. The total cost of this event was US$ 44,974 (30). These cases highlight an important component of raccoon rabies: while direct contact with a rabid raccoon may occur, it is often the case that exposure is indirect through a raccoon interacting with dogs and cats (*Felis catus*) as well as livestock, resulting in potential human exposure.

Skunks and bats

Skunk rabies cases comprise about 26% of all wild animal rabies cases in North America, and the three skunk RABV variants collectively have the broadest geographical distribution in the USA, occurring in 22 north and south-central states and California (24). While there is no ORV bait available for skunks or bats, several baits are in development and research has highlighted the economic necessity for this development (31). In California specifically, rabies is enzootic, with striped skunks (*Mephitis mephitis*) and bats (Chiroptera) acting as the main wildlife reservoirs. Seventy percent of California rabies cases are linked to terrestrial species that most often include striped skunks, spotted skunks (*Spilogale putorius*), and grey foxes (*Urocyon cinereoargenteus*), and 30% of cases involve bats (31).

Bats also comprise approximately 26% of all reported rabies cases in the USA, and are the second-most reported rabid animal (24). Since 2000, vampire bats (*Desmodus rotundus*) have been the leading cause of human rabies in Latin America and the Caribbean (32), and vampire bat rabies is a major public health concern in tropical and subtropical areas of Latin America (8). Vampire bats transmit RABV to livestock and humans through their haematophagous behaviour, and are often the species most responsible for the transmission of RABV to livestock (8). In cattle, bat rabies can result in hide damage, weight loss, decreased milk production and death. Rabies virus transmitted to humans by bats results in death if PEP is not administered (8).

The vampire bat can be found in Mexico as far north as the states of Sonora and Tamaulipas, and could potentially extend into south Texas in the next few decades as a result of climate change (33). Between 1997 and 2006, the average annual number of PEP treatments administered in Mexico was 955, costing 1,500 Mexican pesos (US$ 77) per person (8). If vampire bat rabies were to spread to southern Texas, the total economic impact is estimated to be between US$ 7 million and US$ 9.2 million (33). Vaccination of bat populations through ORV and available vaccine strategies is not feasible (8). Primary means of vampire bat rabies mitigation are bat control and livestock vaccination. Livestock vaccination has been found to be economically efficient while bat control has not (8).

Dogs

Rabies in canids causes the greatest economic impact of all the variants, in that 99% of all global human rabies cases are caused by domestic dogs (24). As a result, the canine variant has received the most research attention and most published evidence about the impact of rabies is about this variant. However, there is still a substantial lack of information regarding the overall economic impact of canine rabies and the value of dog vaccination programmes, as well as a lack of data that can be extrapolated to other canine rabies-endemic regions (25, 34). A few studies provide overall estimates of the global impact of canine rabies; however, the majority of the studies that address the economics of canine rabies deal with a specific region or dog vaccination programme evaluation and are unsuited for replication in other regions.

An estimated 7.5 million people receive PEP each year as a result of potential exposure to canine RABV, and the total cost of canine rabies has been estimated to range from US$ 530 million to US$ 124 billion, depending on the regions being considered and the cost components included (10, 11, 12, 13). The cost for an individual PEP treatment ranges between US$ 30 and US$ 40 across all regions (10), and it has been estimated that 83% of the total rabies control budget in both Asia and Africa is put towards PEP (35).

Canine rabies causes an estimated 59,000 human deaths per year, although estimates can go as high as 69,000, and is responsible for the loss of 3.7 million DALYs annually (10, 12). The majority of those deaths occur in Africa (36.4%) and Asia (59.6%), with only 0.05% of deaths occurring in the Americas, 70% of which occur in Haiti (12). India alone accounts for 35% of human deaths from canine rabies, but the estimated death rate was highest in the poorest countries in sub-Saharan Africa (12). The role of rabies prevention can be clearly seen when we look at the figures for PEP and dog vaccination in the different regions: for each human death attributed to canine rabies, Latin America performs 41,000 PEP treatments and vaccinates 2.8 million dogs, Asia performs 200 PEP treatments and about 1,000 dog vaccinations, and Africa performs eight PEP treatments and vaccinates eight dogs (10).

Several dog vaccination campaigns have been undertaken to address endemic canine rabies in developing countries. The World Health Organization (WHO), with funding support from the Bill and Melinda Gates Foundation, addressed canine rabies in three sites: South-eastern Tanzania; Cebu Province in the Philippines; and KwaZulu-Natal Province in South Africa (21). A study of the economic costs of these projects found that the cost per dog vaccinated varied (range: US$ 1.18 to US$ 6.61) and appeared to be influenced by human and dog density (costs were lower where densities were higher), as well as overall vaccination coverage. Transportation costs were insignificant in urban areas but they were an important cost driver in rural areas, where house-to-house campaigns were required to reach dispersed populations. The vaccine itself accounted for a very small portion of the total cost of dog vaccination. In contrast, the cost of the average human PEP course ranged from US$ 44.91 to US$ 64.38 across the three sites. It is important to note that many bite victims did not receive the full course of treatment, and very few received RIG (range: 1% to 9%). Others did not seek treatment at all, so the PEP costs reported here were lower than would be required if every bite victim received a complete course of PEP. This study demonstrated that the cost and success of a dog vaccination campaign will be highly site specific, varying according to the presence or absence of an existing rabies management programme, knowledge of the local dog population, and support from external donors. Léchenne *et al.* (36) reported that a mass dog vaccination campaign in N'Djamena, Chad, achieved more than 70% coverage and resulted in a 90% decrease in reported dog rabies cases within one year, illustrating the profound impact dog vaccination programmes can have on rabies prevalence.

Haiti remains one of the few rabies-endemic countries in the Western Hemisphere. It is estimated that only 31% of people exposed to rabies seek treatment, resulting in 130 deaths each year (37). A survey conducted in Haiti revealed that 3.2% of respondents had experienced a dog bite in the previous year, which is problematic in a country where the dog vaccination rate does not reach the 70% threshold recommended for herd immunity (38). Haiti represents a country where increased dog vaccination could significantly reduce the prevalence of rabies, but further knowledge of dog ecology and increased access to vaccines are necessary.

In 1987, a canine rabies outbreak took place in Hermosillo, Mexico, resulting in 2.5% of city residents being bitten by a dog, 60% of whom were administered PEP. The PEP cost of this single outbreak was an estimated US$ 682,500 per 100,000 citizens (39). In 1988 in the USA, an epizootic of canine rabies began in South Texas. It continued for six years, during which time 216 domestic dogs and 270 coyotes (*Canis latrans*) were confirmed rabid. Over these six years, aerial baiting was used to dispense vaccine-laden baits throughout the infected area, costing a total of over US$ 26 million (16). The integration of ORV was a major contributing factor that led to freeing the USA of canine rabies (26). Mass dog vaccination campaigns in Tanzania and Bali Island, Indonesia, have been successful in decreasing cases of rabies in dogs and humans (35).

Flores Island, Indonesia, is populated by more than 1.8 million humans and 236,500 dogs, and there have been 19 reported cases of human fatalities attributed to canine rabies (35). Between 2001 and 2011, the average annual cost of rabies and rabies control on Flores Island was approximately US$ 1.12 million. Costs associated with rabies and rabies control on Flores Island included the culling of dogs, PEP administration, mass vaccination, pre-exposure treatment, dog bite investigation, testing of dogs suspected of being rabid, and the quarantine of imported dogs (35). Of those costs, dog culling is the most expensive, accounting for 39% of the total cost, followed by PEP treatments (35%) and mass vaccination of canines (24%). The total cost of rabies control measures in humans on Flores Island is estimated to be US$ 4.82 million. In Indonesia, 150 to 300 fatal rabies cases in humans are reported annually (35).

In most cultures, dogs provide companionship and are woven into the social fabric of everyday life, which provides the pathway to impacts but also the means by which elimination is possible. Vaccination of dogs is the key to prevention and elimination of RABV in dogs and humans, while PEP only prevents rabies in humans but does not have any potential to eliminate the disease (40). In addition, in developing countries, PEP is relatively expensive (costs may exceed two to three months of wages) and often difficult to obtain (3, 41, 42). Bögel and Meslin (40) determined that, after 15 years, a canine rabies control programme consisting of a combination of PEP and canine vaccination becomes more cost effective than PEP alone. In one African city, the costs of a combined programme of PEP and canine rabies vaccination achieved parity with the costs of PEP alone after six years (3). The economic analyses of canine rabies highlighted in this paper commonly point to several reoccurring themes, such as the fact that rabies is preventable and elimination is possible but requires extensive dog vaccinations that can be costly. Canine rabies can cause substantial economic loss, but it is completely preventable and its prevention is economically efficient. Elimination is possible if political will generates enough support for successful mass dog vaccination campaigns.

Conclusions

Not all losses from zoonotic diseases are preventable (4, 43). In some cases, effective vaccines do not exist for all of the main vectors and, in the case of highly contagious zoonoses, large outbreaks can happen rapidly and involve thousands of people simultaneously. In addition, for those zoonotic diseases that have high morbidity implications, illness can persist for a long time, causing economic impacts for many years. Rabies, however, is unique, in that the economic impact of the disease is not a result of morbidity and is only associated with mortality to a limited extent; rather, it is mainly the result of management of the disease and treatment to prevent human death. This zoonosis is unique in that a vaccine exists for almost all of the reservoir species and certainly the most important, namely dogs, and this means elimination is feasible. The result of all of these factors is that economic gains can be made by the successful elimination of the disease.

A consistent finding across most studies of the economic impact of rabies is that vaccinating reservoir species is key to reducing impacts. In terms of canine rabies, the evidence is clear and consistent: vaccination of dogs reduces human impacts in terms of human death and causes a decrease in the number of PEP treatments carried out. Those countries or regions most impacted by rabies are those that choose to invest less in dog vaccination efforts and more in PEP. This is best exemplified by Asia, which experiences over half of all human and cattle deaths while performing more than 90% of PEP vaccinations and about half of dog vaccine administrations. Asia invests the least in PEP and dog vaccination per human death. Latin America invests heavily in human death prevention in that, for every human death, it has administered over 40,000 PEP treatments and vaccinated 2.8 million dogs. Asia, however, only performs eight PEP treatments and eight dog vaccinations per human death. This conclusively determines why there is minimal loss of human life in Latin America due to rabies and substantial loss of life to rabies in Asia.

Enough economic analysis has been conducted globally to prove that canine rabies elimination can be economically efficient and provide a positive return on investment. Future economic analysis will likely be able to illustrate the trade-offs between different management goals and budget constraints. Managers will be able to clearly illustrate the value of mass dog vaccination campaigns in reducing the need for PEP and saving human lives. Ultimately, this should generate the political support needed to meet the goal of eliminating canine rabies worldwide by 2030.

■

Analyse du rapport coûts-bénéfices de la lutte contre la rage : placer l'économie au cœur de la lutte contre la rage pour mobiliser la volonté politique

S.A. Shwiff, J.L. Elser, K.H. Ernst, S.S. Shwiff & A.M. Anderson

Résumé

La rage est une zoonose importante au plan économique. Les auteurs décrivent la portée de l'impact économique de la rage et présentent quelques modèles d'analyse économique utilisés pour comprendre ces effets ; ils analysent également les compromis à trouver entre les efforts consacrés à la gestion de la rage et ceux dédiés à son élimination. Dans bien des cas, il est plus rentable sur le long terme d'éliminer la rage que de procéder à la gestion continue de la prophylaxie post-exposition chez l'homme et au dépistage et à la vaccination des animaux. Les analyses économiques servent à documenter et à orienter les décisions concernant les mesures à prendre afin de mobiliser la volonté politique nécessaire, en plaçant l'économie au cœur de la lutte contre la rage.

Mots-clés

Analyse du rapport coûts-bénéfices – Économie de la santé – Prophylaxie post-exposition – Rage – Vaccination des chiens – Zoonose.

■

Análisis de la relación costo-beneficio del control de la rabia, o cómo hacer de la economía el eje de la lucha antirrábica para aglutinar la voluntad política

S.A. Shwiff, J.L. Elser, K.H. Ernst, S.S. Shwiff & A.M. Anderson

Resumen

La rabia es una zoonosis que reviste importancia económica. Los autores exponen la magnitud del impacto económico de la enfermedad y algunas de las modalidades de análisis económico utilizadas para aprehender esas consecuencias, así como el juego de equilibrios entre las medidas de gestión de la rabia y las actividades destinadas a eliminarla. En muchos casos, la eliminación de la enfermedad ofrece a la larga mayor eficacia, en relación con el costo, que la continua labor de administración de profilaxis tras exposición, realización de pruebas en animales y vacunación de estos. Los análisis económicos sirven para fundamentar y encauzar las decisiones de planificación y para aglutinar la voluntad política, haciendo de los aspectos económicos un eje de la lucha contra la rabia.

Palabras clave

Análisis de la relación costo-beneficio – Economía de la salud – Profilaxis tras exposición – Rabia – Vacunación canina – Zoonosis.

■

References

1. Blanton J.D., Palmer D. & Rupprecht C.E. (2010). – Rabies surveillance in the United States during 2009. *JAVMA*, **237** (6), 646–657. doi:10.2460/javma.237.6.646.

2. Moran G.J., Talan D.A., Mower W., Newdow M., Ong S., Nakase J.Y., Pinner R.W. & Childs J.E. for the Emergency ID Net Study Group (2000). – Appropriateness of rabies postexposure prophylaxis treatment for animal exposures. *JAMA*, **284** (8), 1001–1007. doi:10.1001/jama.284.8.1001.

3. Zinsstag J., Dürr S., Penny M.A., Mindekem R., Roth F., Gonzalez S.M., Naissengar S. & Hattendorf J. (2009). – Transmission dynamics and economics of rabies control in dogs and humans in an African city. *Proc. Natl. Acad. Sci. USA*, **106** (35), 14996–15001. doi:10.1073/pnas.0904740106.

4. Narrod C., Zinsstag J. & Tiongco M. (2012). – A One Health framework for estimating the economic costs of zoonotic diseases on society. *EcoHealth*, **9** (2), 150–162. doi:10.1007/s10393-012-0747-9.

5. Shwiff S.A., Sterner R.T., Jay M.T., Parikh S., Bellomy A., Meltzer M.I., Rupprecht C.E. & Slate D. (2007). – Direct and indirect costs of rabies exposure: a retrospective study in Southern California (1998–2002). *J. Wildl. Dis.*, **43** (2), 251–257. doi:10.7589/0090-3558-43.2.251.

6. Shwiff S., Aenishaenslin C., Ludwig A., Berthiaume P., Bigras-Poulin M., Kirkpatrick K., Lambert L. & Bélanger D. (2013). – Bioeconomic modelling of raccoon rabies spread management impacts in Quebec, Canada. *Transbound. Emerg. Dis.*, **60** (4), 330–337. doi:10.1111/j.1865-1682.2012.01351.x.

7. Sterner R.T., Meltzer M.I., Shwiff S.A. & Slate D. (2009). – Tactics and economics of wildlife oral rabies vaccination, Canada and the United States. *Emerg. Infect. Dis.*, **15** (8), 1176–1184. doi:10.3201/eid1508.081061.

8. Anderson A., Shwiff S., Gebhardt K., Ramirez A.J., Shwiff S., Kohler D. & Lecuona L. (2014). – Economic evaluation of vampire bat (*Desmodus rotundus*) rabies prevention in Mexico. *Transbound. Emerg. Dis.*, **61** (2), 140–146. doi:10.1111/tbed.12007.

9. Diao X., Alpuerto V. & Nwafor M. (2009). – Economywide impact of avian flu in Nigeria: a dynamic CGE model analysis. HPAI Research Brief No. **15**. Department for International Development, London, United Kingdom, 8 pp. Available at: www.gov.uk/dfid-research-outputs/economywide-impact-of-avian-flu-in-nigeria-a-dynamic-cge-model-analysis (accessed on 17 August 2018).

10. Shwiff S., Hampson K. & Anderson A. (2013). – Potential economic benefits of eliminating canine rabies. *Antiviral Res.*, **98** (2), 352–356. doi:10.1016/j.antiviral.2013.03.004.

11. Knobel D.L., Cleaveland S., Coleman P.G., Fèvre E.M., Meltzer M.I., Miranda M.E.G., Shaw A., Zinsstag J. & Meslin F.-X. (2005). – Re-evaluating the burden of rabies in Africa and Asia. *Bull. WHO*, **83** (5), 360–368. Available at: www.ncbi.nlm.nih.gov/pmc/articles/PMC2626230/ (accessed on 22 June 2018).

12. Hampson K., Coudeville L. […] & Dushoff J. on behalf of the Global Alliance for Rabies Control Partners for Rabies Prevention (2015). – Estimating the global burden of endemic canine rabies. *PLoS Negl. Trop. Dis.*, **9** (4), e0003709. doi:10.1371/journal.pntd.0003709.

13. Anderson A. & Shwiff S.A. (2015). – The cost of canine rabies on four continents. *Transbound. Emerg. Dis.*, **62** (4), 446–452. doi:10.1111/tbed.12168.

14. Taylor L.H. & Nel L. (2015). – Global epidemiology of canine rabies: past, present, and future prospects. *Vet. Med. Res. Rep.*, **6**, 361–371. doi:10.2147/VMRR.S51147.

15. Schneider M.C., Belotto A., Adé M.P., Hendrickx S., Leanes L.F., Rodrigues M.J.de F., Medina G. & Correa E. (2007). – Current status of human rabies transmitted by dogs in Latin America. *Cad. Saúde Pública*, **23** (9), 2049–2063. doi:10.1590/S0102-311X2007000900013.

16. Shwiff S.A., Kirkpatrick K.N. & Sterner R.T. (2008). – Economic evaluation of an oral rabies vaccination program for control of a domestic dog–coyote rabies epizootic: 1995–2006. *JAVMA*, **233** (11), 1736–1741. doi:10.2460/javma.233.11.1736.

17. Rupprecht C.E., Barrett J., Briggs D., Cliquet F., Fooks A.R., Lumlertdacha B., Meslin F.-X., Müller T., Nel L.H., Schneider C., Tordo N. & Wandeler A.I. (2008). – Can rabies be eradicated? *Dev. Biol. (Basel)*, **131**, 95–121.

18. Elser J.L., Bigler L.L., Anderson A.M., Maki J.L., Lein D.H. & Shwiff S.A. (2016). – The economics of a successful raccoon rabies elimination program on Long Island, New York. *PLoS Negl. Trop. Dis.*, **10** (12), e0005062. doi:10.1371/journal.pntd.0005062.

19. Shwiff S.A., Sweeney S.J., Elser J.L., Miller R.S., Farnsworth M.L., Nol P., Shwiff S.S. & Anderson A.M. (2016). – A benefit–cost analysis decision framework for mitigation of disease transmission at the wildlife–livestock interface. *Hum. Wildl. Interact.*, **10** (1), Article 12. Available at: https://digitalcommons.usu.edu/hwi/vol10/iss1/12 (accessed on 22 June 2018).

20. Wera E., Mourits M.C., Siko M.M. & Hogeveen H. (2016). – Cost-effectiveness of mass dog vaccination campaigns against rabies in Flores Island, Indonesia. *Transbound. Emerg. Dis.*, **64** (6), 1918–1928. doi:10.1111/tbed.12590.

21. Elser J.L., Hatch B.G., Taylor L.H., Nel L.H. & Shwiff S.A. (2017). – Towards canine rabies elimination: economic comparisons of three project sites. *Transbound. Emerg. Dis.*, **65** (1), 135–145. doi:10.1111/tbed.12637.

22. Fields G.S. (2011). – Poverty and low earnings in the developing world. Cornell University, Industrial and Labor Relations (ILR) School, Ithaca, New York, 30 pp. Available at: http://digitalcommons.ilr.cornell.edu/workingpapers/152 (accessed on 22 June 2018).

23. Anderson A., Shwiff S.A. […] & Slate D. (2014). – Forecasting the spread of raccoon rabies using a purpose-specific group decision-making process. *Hum. Wildl. Interact.*, **8** (1), Article 14. Available at: https://digitalcommons.usu.edu/hwi/vol8/iss1/14 (accessed on 22 June 2018).

24. Vercauteren K.C., Ellis C., Chipman R., DeLiberto T.J., Shwiff S.A. & Slate D. (2012). – Rabies in North America: a model of the One Health approach. *In* Proc. 14th Wildlife Damage Management (WDM) Conference (S.N. Frey, ed.), 18–21 April, Nebraska City, Nebraska, United States of America. WDM Working Group, the Wildlife Society, Bethesda, Maryland, United States of America, 56–63. Available at: https://digitalcommons.unl.edu/icwdm_usdanwrc/1202 (accessed on 22 June 2018).

25. Meltzer M.I. & Rupprecht C.E. (1998). – A review of the economics of the prevention and control of rabies. *PharmacoEconomics*, **14** (4), 365–383. doi:10.2165/00019053-199814040-00004.

26. Slate D., Algeo T.P., Nelson K.M., Chipman R.B., Donovan D., Blanton J.D., Niezgoda M. & Rupprecht C.E. (2009). – Oral rabies vaccination in North America: opportunities, complexities, and challenges. *PLoS Negl. Trop. Dis.*, **3** (12), e549. doi:10.1371/journal.pntd.0000549.

27. Kemere P., Liddel M.K., Evangelou P., Slate D. & Osmek S. (2000). – Economic analysis of a large scale oral vaccination program to control raccoon rabies. *In* Proc. 3rd National Wildlife Research Center (NWRC) special symposium on human conflicts with wildlife: economic considerations (L. Clark, ed.), 1–3 August, Fort Collins, Colorado, United States of America. United States Department of Agriculture, Fort Collins, Colorado, United States of America, 109–116. Available at: www.aphis.usda.gov/wildlife_damage/nwrc/symposia/economics_symposium/kemereHR.pdf (accessed on 22 June 2018).

28. Gordon E.R., Krebs J.W., Rupprecht C.R., Real L.A. & Childs J.E. (2005). – Persistence of elevated rabies prevention costs following post-epizootic declines in rates of rabies among raccoons (*Procyon lotor*). *Prev. Vet. Med.*, **68** (2–4), 195–222. doi:10.1016/j.prevetmed.2004.12.007.

29. Foroutan P., Meltzer M.I. & Smith K.A. (2002). – Cost of distributing oral raccoon-variant rabies vaccine in Ohio: 1997–2000. *JAVMA*, **220** (1), 27–32. doi:10.2460/javma.2002.220.27.

30. Chipman R.B., Cozzens T., Shwiff S.A., Biswas R., Plumley J., O'Quinn J., Algeo T.P., Rupprecht C.E. & Slate D. (2013). – Costs of raccoon rabies incidents in cattle herds in Hampshire County, West Virginia, and Guernsey County, Ohio. *JAVMA*, **243** (11), 1561–1567. doi:10.2460/javma.243.11.1561.

31. Shwiff S.A., Sterner R.T., Hale R., Jay M.T., Sun B. & Slate D. (2009). – Benefit cost scenarios of potential oral rabies vaccination for skunks in California. *J. Wildl. Dis.*, **45** (1), 227–233. doi:10.7589/0090-3558-45.1.227.

32. Vigilato M.A., Cosivi O., Knöbl T., Clavijo A. & Silva H.M. (2013). – Rabies update for Latin America and the Caribbean. *Emerg. Infect. Dis.*, **19** (4), 678. doi:10.3201/eid1904.121482.

33. Anderson A., Shwiff S.S. & Shwiff S.A. (2014). – Economic impact of the potential spread of vampire bats into south Texas. *In* Proc. 26th Vertebrate Pest Conference (R.M. Timm & J.M. O'Brien, eds), 3–6 March, Waikoloa, Hawaii, United States of America. University of California, Davis, California, United States of America, 305–309. Available at: www.aphis.usda.gov/wildlife_damage/nwrc/publications/14pubs/14-143%20anderson.pdf (accessed on 22 June 2018).

34. World Health Organization (WHO) (2013). – WHO Expert Consultation on Rabies: second report. WHO Technical Report Series No. **982**. WHO, Geneva, Switzerland, 150 pp. Available at: http://apps.who.int/iris/bitstream/10665/85346/1/9789240690943_eng.pdf (accessed on 23 April 2018).

35. Wera E., Velthuis A.G., Geong M. & Hogeveen H. (2013). – Costs of rabies control: an economic calculation method applied to Flores Island. *PLoS One*, **8** (12), e83654. doi:10.1371/journal.pone.0083654.

36. Léchenne M., Oussiguere A., Naissengar K., Mindekem R., Mosimann L., Rives G., Hattendorf J., Moto D.D., Alfaroukh I.O. & Zinsstag J. (2016). – Operational performance and analysis of two rabies vaccination campaigns in N'Djamena, Chad. *Vaccine*, **34** (4), 571–577. doi:10.1016/j.vaccine.2015.11.033.

37. Wallace R.M., Reses H., Franka R., Dilius P., Fenelon N., Orciari L., Etheart M., Destine A., Crowdis K. & Blanton J.D. (2015). – Establishment of a canine rabies burden in Haiti through the implementation of a novel surveillance program. *PLoS Negl. Trop. Dis.*, **9** (11), e0004245. doi:10.1371/journal.pntd.0004245.

38. Schildecker S., Millien M., Blanton J., Boone J., Emery A., Ludder F., Fenelon N., Crowdis K., Destine A. & Etheart M. (2016). – Dog ecology and barriers to canine rabies control in the Republic of Haiti, 2014–2015. *Transbound. Emerg. Dis.*, **64** (5), 1433–1442. doi:10.1111/tbed.12531.

39. Eng T.R., Fishbein D.B., Talamante H.E., Hall D.B., Chavez G.F., Dobbins J.G., Muro F.J., Bustos J.L., de los Angeles Ricardy M. & Munguia A. (1993). – Urban epizootic of rabies in Mexico: epidemiology and impact of animal bite injuries. *Bull. WHO*, **71** (5), 615–624. Available at: www.ncbi.nlm.nih.gov/pmc/articles/PMC2393488/ (accessed on 17 August 2018).

40. Bögel K. & Meslin F. (1990). – Economics of human and canine rabies elimination: guidelines for programme orientation. *Bull. WHO*, **68** (3), 281–291. Available at: www.ncbi.nlm.nih.gov/pmc/articles/PMC2393068/ (accessed on 22 June 2018).

41. Frey J., Mindekem R., Kessely H., Doumagoum Moto D., Naïssengar S., Zinsstag J. & Schelling E. (2013). – Survey of animal bite injuries and their management for an estimate of human rabies deaths in N'Djaména, Chad. *Trop. Med. Int. Hlth*, **18** (12), 1555–1562. doi:10.1111/tmi.12202.

42. Hampson K., Dobson A., Kaare M., Dushoff J., Magoto M., Sindoya E. & Cleaveland S. (2008). – Rabies exposures, post-exposure prophylaxis and deaths in a region of endemic canine rabies. *PLoS Negl. Trop. Dis.*, **2** (11), e339. doi:10.1371/journal.pntd.0000339.

43. Zinsstag J., Schelling E., Roth F., Bonfoh B., De Savigny D. & Tanner M. (2007). – Human benefits of animal interventions for zoonosis control. *Emerg. Infect. Dis.*, **13** (4), 527–531. doi:10.3201/eid1304.060381.