Re-evaluating the burden of rabies in Africa and Asia

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Objective To quantify the public health and economic burden of endemic canine rabies in Africa and Asia.
Methods Data from these regions were applied to a set of linked epidemiological and economic models. The human population at risk from endemic canine rabies was predicted using data on dog density, and human rabies deaths were estimated using a series of probability steps to determine the likelihood of clinical rabies developing in a person after being bitten by a dog suspected of having rabies. Model outputs on mortality and morbidity associated with rabies were used to calculate an improved disability-adjusted life year (DALY) score for the disease. The total societal cost incurred by the disease is presented.
Findings Human mortality from endemic canine rabies was estimated to be 55 000 deaths per year (90% confidence interval (CI) = 24 000–93 000). Deaths due to rabies are responsible for 1.74 million DALYs lost each year (90% CI = 0.75–2.93). An additional 0.04 million DALYs are lost through morbidity and mortality following side-effects of nerve-tissue vaccines. The estimated annual cost of rabies is US$ 583.5 million (90% CI = US$ 540.1–626.3 million). Patient-borne costs for post-exposure treatment form the bulk of expenditure, accounting for nearly half the total costs of rabies.
Conclusions Rabies remains an important yet neglected disease in Africa and Asia. Disparities in the affordability and accessibility of post-exposure treatment and risks of exposure to rabid dogs result in a skewed distribution of the disease burden across society, with the major impact falling on those living in poor rural communities, in particular children.

Keywords Rabies/mortality/economics; Dogs; Cost of illness; Disability evaluation; Health care costs; Probability; Models, Theoretical; Africa; Asia (*source: MeSH, NLM*).

Mots clés Rage (Maladie)/mortalité/économie; Chien; Coût maladie; Evaluation incapacité; Coût soins médicaux; Probabilité; Modèle théorique; Afrique; Asie (*source: MeSH, INSERM*).

Palabras clave Rabia/mortalidad/economía; Perros; Costo de la enfermedad; Evaluación de la incapacidad; Costos de la atención en salud; Probabilidad; Modelos teóricos; África; Asia (*fuente: DeCS, BIREME*).

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Introduction

More than 99% of all human deaths from rabies occur in the developing world (*1*), and although effective and economical control measures are available (*2*, *3*) , rabies remains a neglected disease throughout most of these countries (*4*, *5*). A major factor in the low level of political commitment to rabies control is a lack of accurate data on the true public health impact of the disease. It is widely recognized that the number of deaths officially reported greatly underestimates the true incidence of disease. Patients may not present to medical facilities for treatment of clinical disease; few cases receive laboratory confirmation; and clinical cases are often not reported by local authorities to central authorities (*1*, *6*, *7*).

These problems are not unique to rabies, and the recognized poor quality of much public health information from developing countries has prompted several investigations into the distribution of major infectious diseases and the mortality and morbidity attributable to them. Such studies are based on estimates of occurrence extrapolated from more readily quantifiable determinants of disease, such as vector distribution or host immunity (*8–10*). For rabies, a similar predictive approach has been used to estimate human deaths from rabies in the United Republic of Tanzania using a probability decision tree method to determine the likelihood of clinical rabies developing in a person bitten by a dog suspected to be rabid (*6*). Dog bites are reported proportionately more frequently than human

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cases of rabies and may provide an accessible data source from which human deaths from rabies can be inferred.

The objective of our study was to estimate the burden of rabies in Africa and Asia by applying data derived from these regions to this model and to thereby present a data-driven assessment of the human and economic costs of rabies in the developing world. We define Africa as all mainland countries on the continent plus Madagascar; Asia is defined as those countries falling under the WHO-defined South-East Asia Region and Western Pacific Region, including Pakistan. Only countries considered by WHO and the Office International des Epizooties as having endemic canine rabies were considered in this analysis. The list of all countries included in the study available from http://www.vet.ed.ac.uk/ctvm/Research/Appendices/appendices.html.

Methods

Human rabies deaths

Full details of the methods used in the dog-bite probability model have been published elsewhere (*6*). Briefly, the model recognizes that not all bites from rabid dogs result in infection and that not every infection leads to clinical signs and death. One of the principal factors influencing the outcome of a bite from a rabid dog is the location of the bite on the body (*11*, *12*). The model uses the distribution of injuries on the body together with the likelihood of the patient receiving successful treatment to predict the outcomes of bites from rabid dogs. The model thus allows the incidence of bites from suspected rabid dogs among the human population considered to be at risk to be used as a determinant of the number of human deaths from rabies.

The human population at risk from canine rabies was taken as the number of people living in areas affected by canine rabies where the density of the dog population exceeds the threshold density at which canine rabies is capable of being maintained endemically. Dog-population densities were inferred from human densities derived from two regional population density datasets (*13*, *14*) with adjustments made to account for population growth (*15*). Associated dog-population numbers were calculated by dividing human figures by the regional average ratio of humans to dogs, based on values given in Table 1. The threshold density for rabies persistence was taken as 4.5 dogs/km², based on predictions produced from data on rabies transmission in rural Kenya (*16*); these data are consistent with empirical observations from elsewhere in Africa (*17–20*). This density falls within the range of estimates of rural dog-population densities (*21–23*), so the human population considered to be at risk was calculated using the regional rural ratios for humans to dogs. Implicit in this approach is the assumption that all human urban populations are at risk in rabies-affected areas.

Four basic scenarios were considered (Africa and Asia, both rural and urban); these reflect broad differences in factors that influence rabies epidemiology and the treatment of people exposed to the disease. Initial parameter estimates were derived following a review of the relevant literature, including publications from peer-reviewed journals and grey literature sources. Parameter estimates and confidence distributions were then fixed using a three-stage consensus approach (as described in reference *9*) within the WHO Burden of Rabies Working Group. First, a workshop was held during which parameter estimates were presented and discussed and preliminary predictions made using the model. Second, a comprehensive analysis using agreed upon estimates was conducted, and the model was validated against known data. Third, each participant was sent the results of this analysis, along with the data and assumptions. These were reviewed and adjusted as appropriate before final agreement was reached. The final model parameter estimates and distributions are presented in Table 2 (web version only, available at: http://www.who.int/bulletin).

For the analysis, Asia was subdivided into three units: China, India and Other Asia. Initial data sources and model validation indicated that parameter estimates for India and Other Asia were similar. However, preliminary model predictions for China overestimated the number of deaths by one order of magnitude when these same estimates were used compared with the 1000 deaths suggested by expert opinion. The discrepancy is possibly explained by the use of post-exposure treatment in China: the country accounts for two-thirds (5 million cases) of total post-exposure treatment (PET) used in Asia (*24*), and the locally-produced tissue-culture vaccine is safe and relatively inexpensive (*25*). These factors suggest that PET for rabies is more accessible and utilized more frequently in China than in the rest of Asia. To account for this in the model, the probability of a person bitten by a suspected rabid dog and receiving PET was assumed to be equally high in both urban and rural settings in China (minimum = 95%; most likely = 97%; maximum = 100%). In light of the paucity of data for China, the model's predictions for this country should be treated with caution.

The model was arrayed as a spreadsheet template (using Microsoft Excel 2000, Microsoft Inc., Redmond, WA). Uncertainty in parameter estimates, and inherent parameter variability due to between-country differences, were incorporated

Table 1. **Mean human:dog ratio for Africa and Asia** (determined from sources available from: http://www.vet.ed.ac.uk/ctvm/Research/Appendices/appendices.html)

Human:dog ratio	Region[a]					
	Africa		Asia		China	
	Urban	Rural	Urban	Rural	Urban	Rural
Mean ratio[b]	21.2 (12.5–37.1)	7.4 (5.7–9.7)	7.5 (4.8–10.1)	14.3(0–45.0)	NA[c]	NA
Mean ratio for region	12.3 (11.2–20.6)		9.5 (4.5–14.6)		48.3 (0–147.0)	

[a] Insufficient data were available to calculate a separate figure for India and for rural China versus urban China.
[b] Figures in parentheses are 95% confidence intervals.
[c] NA = not available.

Table 4. **Direct (medical) post-exposure treatment costing data and sources** (available from: http://www.vet.ed.ac.uk/ctvm/Research/Appendices/appendices.html)

Parameter	Estimate		Source
	Africa	Asia	
Patient numbers			
No. PET[a] cases per year	200 000	7 500 000	*11–14, 23–27*
No. (%) PET patients receiving tissue-culture vaccines	180 000 (90)	5 025 000 (67)	*11–14, 23–27*
No. (%) of patients receiving tissue-culture vaccine intramuscularly	180 000 (100)	4 874 250 (97)	*11–14, 23–27*
No. (%) of patients receiving tissue-culture vaccine intradermally	0 (0)	150 750 (3)	*11–14, 23–27*
No. (%) PET patients receiving nerve-tissue vaccines	20 000 (10)	2 475 000 (33)	*11–14, 23–27*
No. (%) PET patients receiving rabies immunoglobulin	2 000 (1)	450 000 (6)	*11–14, 23–27*
No. (%) PET patients receiving human rabies immunoglobulin	0 (0)	45 000 (10)	
No. (%) PET patients receiving equine rabies immunoglobulin	2 000 (100)	405 000 (90)	
Costs			
Common costs			
Material costs per injection (includes needles, syringes, swabs, etc.)	US$ 0.10		E. Miranda unpublished data, 2003
Overhead costs per PET visit (includes anti-rabies clinic staff salaries and administration costs)	US$ 0.50		*39*
Tissue-culture vaccine costs			
Intramuscular vaccination			
Vaccine cost per dose	US$ 10.00		WHO Procurement Services, personal communication, 2003
Visits per patient	3		*40*
Injections per patient	3		Assuming standard Essen regimen
Intradermal vaccination			
Vaccine cost per dose	US$ 2.50		WHO Procurement Services, personal communication, 2003
Visits per patient	3		E. Miranda unpublished data, 2003
Injections per patient	6		Assuming Thai Red Cross regimen
Nerve-tissue vaccine costs			
Vaccine cost per dose	US$ 0.40		*7*
Visits per patient	7		*33*
Injections per patient	7		Assuming standard regimen
Rabies immunoglobulin			
Human rabies immunoglobulin cost per dose	US$ 110.00		WHO Procurement Services, personal communication, 2003
Equine rabies immunoglobulin cost per dose	US$ 25.00		WHO Procurement Services, personal communication, 2003

[a] PET = post-exposure treatment.

into the model by assigning confidence distributions to input parameters. Parameter distributions were sampled iteratively (until convergence at < 1.5%) using a Monte Carlo simulation procedure (@Risk Pro 4.5, Palisade Corp., Newfield, NY). Model predictions are reported using the means of the resulting probability distributions, with the 5th and 95th percentiles (90% confidence intervals) as the lower and upper bounds, respectively. A full account of the technical details of the model, including results of the sensitivity analysis, is available from: http://www.vet.ed.ac.uk/ctvm/Research/Appendices/appendices.html 3.

Disability-adjusted life year score

The disability-adjusted life year (DALY) score is a standardized, comparative measure of the burden of disease. The DALY score for a particular condition is a composite score of the years of life lost (YLL) due to premature mortality and the years of life lived with a disability (YLD) caused by the condition (*26*). To calculate a DALY score for rabies the following components were considered: a direct DALY score derived from mortality due to the disease and an indirect DALY score, taking into account morbidity and mortality following side-effects of nerve-tissue vaccines.

Direct DALY score

The output of the predictive model provided the estimated annual number of deaths due to rabies. Age-structures and sex-structures of rabies cases were obtained from seven reported studies (*27–33*). All parameter estimates and data sources related to the calculation of the rabies DALY score are given in Table 3 (web version only, available at: http://www.who.int/bulletin). Using these parameter estimates, a DALY score for rabies was determined using previously described methods (*26*, *34*). Parameter variability was again incorporated by assigning confidence distributions and using simulation software as described above. The 5th and 95th percentiles were used as the lower and upper bounds for the predicted scores.

Indirect DALY burden

Evidence suggests that non-rabies induced morbidity and mortality may constitute a sizeable proportion of the rabies burden in developing countries. Approximately one-third of all human rabies post-exposure treatments are carried out using crude nerve-tissue vaccines (*35*), despite the occurrence of severe and sometimes fatal allergic encephalomyelitic reactions (*36–38*). Nerve-tissue vaccines were classified into two groups based on differing incidence rates and clinicopathological signs of adverse reactions (*37*, *38*). These were the Semple type (made from phenol-treated sheep-brain or goat-brain tissue) and vaccines derived from suckling-mouse brain. For the purpose of this preliminary analysis, disability weights for post-vaccination neurological reactions, used in the calculation of the YLDs, were taken as those reported for similar conditions by Murray & Lopez (*39*) (Table 3). The use of equivalent disability weights represents an admittedly crude first attempt to determine a YLD component of the DALY score for rabies; future attempts would benefit from a formal disability weighting procedure.

The economic burden of rabies

The mortality rate and DALY score provide estimates of the burden of disease on human health. A second component of the impact of disease is the economic cost incurred by society as a result of the disease. The costs due to rabies were considered under the following categories:

- direct (medical) human costs from post-exposure treatment
- indirect (patient) costs from post-exposure treatment
- costs to control rabies among dogs
- livestock losses
- surveillance costs.

Table 4 and Table 5 give a breakdown of the costing data used in the economic analysis.

For this analysis, direct medical costs included the cost of biologicals (rabies vaccines and immunoglobulin) and the cost of their administration, including materials and staff salaries. Indirect costs included out-of-pocket expenses for patients, such as transport costs to and from rabies-treatment centres, and loss of income while receiving treatment (*40*). Costs associated with the treatment of dog bites and the administration of antibiotics and tetanus immunizations were not included. Due to the erratic frequency of reporting, national numbers of patients receiving post-exposure treatment annually were averaged over a period of 5 years (1996–2000). Countries for which no reports could be found for this period were considered not to have treated any patients. Post-exposure treatment was categorized by administration route (intramuscular or intradermal) on

Table 5. **Indirect (patient) costs of post-exposure treatment and other costs associated with rabies.** Data sources are available from: http://www.vet.ed.ac.uk/ctvm/Research/Appendices/appendices.html

Parameter	Estimate		Source
	Africa	Asia	
Indirect PET[a] costs			
No. of PET patient visits	680 000	32 400 000	Calculated from Table 4
Proportion of visits accompanied by an adult	0.4	0.4	*2*, *16*
Total No. of visits (patients plus those accompanying them)	952 000	45 360 000	Calculated
Income loss			
No. of working days lost per person per PET visit	0.5	0.5	*15*
Daily per capita Gross National Income	US$ 1.87	US$ 3.50	*41*
Income loss per person per PET visit	US$ 0.94	US$ 1.75	Calculated
Transport costs			
Transport costs per person per visit	US$ 2.00	US$ 3.80	*40*, M. Kaare, personal communication, 2002
Dog rabies costs			
Vaccination costs			
No. dogs vaccinated annually	6 700 000	40 000 000	*11–14*, *23–27*
Cost per dog vaccinated	US$ 1.30	US$ 1.30	*42*
Population control costs			
No. dogs killed annually	200 000	5 000 000	*11–14*, *23–27*
Cost per dog killed	US$ 5.00	US$ 5.00	*43*
Livestock losses			
Total no. cattle	230 000 000	423 000 000	*44*
Rabies incidence rate/100 000 cattle	5	5	*11–14*, *23–27*
Annual no. of cattle deaths from rabies	11 500	21 150	Calculated
Cost per head of cattle	US$ 150.00	US$ 500.00	A. Shaw, unpublished data, 2002
Surveillance costs			
No. rabies diagnostic tests per year	5 300	16 500	*11–14*, *23–27*
Cost per test	US$ 5.68	US$ 5.68	*45*

[a] PET = post-exposure treatment.

Table 6. **Estimated human mortality caused by canine rabies in Africa and Asia**

Model output	Asia						Africa	
	India		China		Other Asia			
	Urban	Rural	Urban	Rural	Urban	Rural	Urban	Rural
Total population (millions)	284.7	732.2	459.1	816.1	295.7	525.4	294.2	498.1
Population at risk (millions)	284.7	710.4	459.1	498.3	295.7	409.1	294.2	340.1
No. bites from suspected rabid dogs (thousands)	409.4	893.4	660.1	626.7	425.2	514.5	374.3	427.8
No. of rabies deaths[a]	1 058	18 201	1 324	1 257	853	8 135	5 886	17 937
No. deaths/100 000 people	0.37	2.49	0.29	0.15	0.29	1.55	2.00	3.60
No. subregional deaths[b]	19 713 (4 192–39 733)		2336 (565–5 049)		9 489 (2 281–19 503)			
No. regional deaths	31 539 (8 149–61 425)						23 705 (6 903–45 932)	
Total no. deaths	55 270 (23 910–93 057)							
Overall no. deaths/100 000 people	1.38 (0.60–2.33)							
Predicted deaths in the absence of any post-exposure treatment	327 160 (166 904–525 427)							

[a] Rabies deaths are the means of output probability distributions calculated independently and may therefore not sum exactly.
[b] Figures in parentheses are the 5th and 95th percentiles of output probability distributions.

the basis that intradermal vaccination reduces costs by 60–80% compared to the standard intramuscular regimen (*41*, *42*). The total number of vaccine doses (i.e. injections) administered and the total number of visits made to rabies-treatment centres were derived from national estimates of the proportion of patients receiving treatment who were vaccinated with each schedule, after adjustment to account for patient drop-out during the course of treatment. Few published accounts dealing with treatment-seeking behaviour and compliance could be found so conservative estimates were made on the average number of visits per schedule: 3 instead of 5 for the Essen and Thai Red Cross regimens and 7 instead of 10–21 for the nerve-tissue vaccine schedules. The proportion of patients receiving the Zagreb schedule, based on available data, was negligible at the scale of this study. It was assumed that all children aged < 16 years were accompanied by an adult. Assessment of transport costs and income loss include costs to both patients and those accompanying them.

Annual dog vaccination figures could not be found for all countries so the average vaccination coverage of the estimated national dog population was calculated for those countries that submitted reports between 1996 and 2000 (10.3% in Africa and 9.7% in Asia); this figure was then applied to all countries in the region to predict the total number of dogs vaccinated. Cost predictions were based on the use of a central-point vaccination system. Vaccination costs per dog include all components of campaign organization, public awareness efforts, and biological and material costs. Indirect costs borne by dog owners were not included in the analysis.

Livestock losses to rabies can be significant; however, there are few published estimates of rabies incidence in livestock. Submission of cattle specimens to central veterinary laboratories reveals an annual incidence of 0.5–2 deaths/100 000 head of cattle; this is certain to be a gross underestimate. Assuming a rate of underreporting of 10, and using the lower end of the range of incidence rates to exclude transmission from wildlife reservoirs, an estimated incidence of 5 deaths/100 000 cattle is obtained.

Insufficient data were available to enable parameter variability to be explicitly incorporated into the economic analysis. An attempt was made to model the uncertainty surrounding parameter estimates by inputting estimates as triangular distributions (*43*), with the maxima and minima set as ± 10% of each parameter's values.

Table 7. **Estimated disability-adjusted life year (DALY) score for rabies in Africa and Asia**

Component	DALY score[a]		
	Africa	Asia	Total
Rabies deaths[b]	747 558 (217 690–1 448 514)	994 607 (257 275–1 939 125)	1 743 015 (754 019–2 934 656)
Nerve-tissue vaccine reactions	360 (142–586)	44 525 (17 585–72 575)	44 885 (17 727–73 162)
Total	747 918 (217 954–1 449 014)	1 039 119 (302 324–1 983 646)	1 787 886 (799 615–2 984 109)
Total (assuming no post-exposure treatment)			9 504 237 (4 848 684–15 264 050)

[a] DALY scores are the means of output probability distributions calculated independently and may therefore not sum exactly.
[b] Figures in parentheses are the 5th and 95th percentiles of output probability distributions.

Results

Model outputs

The results of the predicted human mortality, disability-adjusted life year score and economic burden of rabies are presented in Table 6, Table 7 and Table 8, respectively. The predicted number of human deaths remained within the reported confidence limits when the threshold dog density was doubled to 9 dogs/km² (46 000; 90% confidence interval (CI) = 19 000–79 000). Setting the threshold density to 0 (i.e. assuming that all people are at risk within areas where canine rabies is endemic) also had little effect on the model: in such a scenario the predicted number of deaths was 67 000 (90% CI = 30 000–110 000).

Discussion

This paper provides the results of the first attempt at a quantitative prediction of the burden of rabies in Africa and Asia. Although we attempted to incorporate the entire range of parameter variability, the final result is still likely to be an underestimate of total mortality and morbidity caused by rabies in these regions. Only deaths due to canine rabies were assessed, omitting that fraction of human cases resulting from exposure to rabid wild animals (*35*). In determining the number of humans at risk, only populations in areas where canine rabies is endemic were included. This ignores the possibility of sporadic outbreaks in areas of low dog density or the introduction of the virus into a previously rabies-free population, as happened on the Indonesian island of Flores in 1997 (*44*).

The results of the modelling are consistent with those of other studies that have estimated the true incidence of rabies at a national level. The recent national survey by the Association for the Prevention and Control of Rabies in India (*45*) estimated a total of 18 500 human deaths from rabies in the country each year, which is close to the predicted figure of 19 700 in this report. The model also estimated the annual number of patients receiving post-exposure treatment in India as 1.07 million, which again is in good agreement with the reported national estimate of 1.1 million (*46*). The model's predictions for China are less consistent: the predicted number of patients receiving post-exposure treatment is 1.25 million which is four times lower than national estimates of 5 million; the predicted number of deaths remains more than double that estimated by expert opinion. However, recent figures communicated by the Chinese authorities are more in line with the model's predictions (Personal communication, 2004): more than 2000 cases of rabies in humans were reported in 2003, with an 80% increase in the first quarter of 2004 (compared to the same period in 2003). Given the gross underreporting associated with rabies deaths, this suggests that the model may in fact be an underestimate of the true number, and the original prediction of approximately 10 000 deaths may prove more realistic. Detailed studies on dog ecology and rabies epidemiology and treatment in China are necessary to resolve this.

WHO's 1999 *World survey of rabies* (*35*) reported 1722 human rabies deaths from the study regions: 147 in Africa and 1575 in Asia. The predicted figure of 55 000 deaths suggests that only 3% of human rabies deaths are recorded by central health authorities, a rate of underreporting of between 20 times (Asia) and 160 times (Africa). This is in agreement with findings from other studies using active surveillance methods that found the incidence of human rabies is up to 100 times greater than what is officially recorded (*6*, *47*).

The burden of rabies is not evenly distributed across all sectors of society but is influenced by age-related and socioeconomic factors. The total cost (direct medical costs and indirect patient costs, excluding those of any accompanying people) of an average post-exposure treatment course as determined in this study is US$ 39.57 in Africa and US$ 49.41 in Asia. This amounts to a substantial fraction of annual per capita gross national income (GNI): 5.80% for the average person living in Africa and 3.87% for someone living in Asia. Even if medical costs are fully subsidized by the government, out-of-pocket patient expenses still comprise 1.5–2% of per capita GNI. Often government subsidies extend only to the provision of cheaper nerve-tissue vaccines, with tissue-culture vaccines being provided only to those patients able to pay for them. There is therefore an income-related risk factor in exposure to the side-effects of nerve-tissue vaccines. This is compounded by occupational

Table 8. **Estimated annual expenditure due to rabies**

	Cost[a]		
Category	**Africa**	**Asia**	**Total**
PET costs[b, c]	9.1 (8.2–10.0)	475.9 (435.0–520.5)	485.0 (443.4–530.1)
Direct (medical)	5.9 (5.2–6.6)	190.3 (171.4–210.5)	196.2 (176.9–216.7)
Indirect (patient)	3.2 (2.9–3.5)	285.6 (259.2–312.1)	288.7 (262.2–315.4)
Income loss	1.3 (1.2–1.4)	113.5 (104.4–122.9)	114.7 (105.7–124.1)
Transport costs	1.9 (1.7–2.1)	172.1 (154.1–190.5)	174.0 (155.9–192.5)
Dog rabies control costs	9.7 (8.8–10.6)	77.0 (71.5–82.3)	86.7 (80.7–92.8)
Vaccination costs	8.7 (7.8–9.6)	52.0 (47.1–57.0)	60.7 (55.4–66.3)
Population control costs	1.0 (0.9–1.1)	25.0 (22.5–27.5)	26.0 (23.4–28.6)
Livestock losses	1.7 (1.5–1.9)	10.5 (9.4–11.8)	12.3 (11.0–13.7)
Surveillance costs	0.03 (0.026–0.032)	0.09 (0.08–0.10)	0.12 (0.11–0.13)
Total	20.5 (19.3–21.8)	563.0 (520.0–605.8)	583.5 (540.1–626.3)

[a] Costs are in millions of US$.
[b] PET = post-exposure treatment.
[c] Figures in parentheses are the 5th and 95th percentiles of output probability distributions.

and socioeconomic risk factors in the initial exposure to infection, further skewing the burden of rabies towards those sectors of society least able to bear it (*45*, *48*). The results of our study predict that there will be five times more rabies deaths in rural areas than in urban areas. Children in particular are at a higher risk of exposure to rabid dogs. Typically, 30–50% of those receiving post-exposure treatment are children aged < 16 years (*6*, *49*). Children are also more likely to suffer multiple bites and bites to the face and head, both of which carry a higher risk of contracting rabies (*31*, *50*).

Rabies continues to impact human health despite the existence of proven cost-effective control measures. Vaccinating domestic dogs against rabies results in a significant reduction in the incidence of bites among the human population from dogs suspected to be rabid, and this control strategy has been shown to be the most cost-effective in the medium–long term (*4*); costs are typically recouped within 5–10 years, mainly through decreased expenditure on human post-exposure treatment. ■

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Résumé

Réévaluation de la charge que représente la rage en Afrique et en Asie

Objectif Quantifier le fardeau économique et la charge pour la santé publique que représente la rage canine endémique en Afrique et en Asie.

Méthodes Les données provenant de ces régions ont été appliquées à un ensemble de modèles épidémiologiques et économiques associés. On a estimé le nombre de personnes qui seraient exposées à la rage canine endémique à partir des données de la densité canine et le nombre des décès humains dus à la rage au moyen d'un modèle de probabilité pas à pas utilisé pour déterminer la probabilité qu'une personne mordue par un chien présumé enragé présente la maladie. La mortalité et la morbidité liées à la rage fournies par les modèles ont été utilisées pour affiner le calcul des années de vie ajustées sur l'incapacité (DALY) pour la maladie. Le coût social total de la maladie est présenté.

Résultats On a estimé à 55 000 [intervalle de confiance (IC) à 90% = 24 000-93 000] le nombre annuel des décès humains dus à la rage canine endémique. Les décès dus à la rage sont responsables de 1,74 million d'années de vie ajustées sur l'incapacité perdues chaque année (IC à 90% = 0,75-2,93). Quelque 0,04 million d'années de vie ajustées sur l'incapacité supplémentaires sont en outre perdues du fait de la morbidité et de la mortalité dues aux effets secondaires des vaccins préparés sur tissu nerveux. Le coût annuel estimatif de la rage est de US$ 583,5 millions (IC à 90% = US$ 540,1 – 626,3 millions). Le coût des traitements post-exposition supporté par les malades constitue l'essentiel des dépenses, soit près de la moitié du coût total de la rage.

Conclusion La rage reste une maladie importante mais négligée en Afrique et en Asie. Les écarts aux plans de l'accessibilité financière et physique du traitement post-exposition et du risque d'exposition aux chiens enragés rendent inégale la distribution de la charge de morbidité dans la société, les personnes les plus touchées étant les habitants des communautés rurales défavorisées, et en particulier les enfants.

Resumen

Reevaluación de la carga de rabia en África y Asia

Objetivo Cuantificar la carga que supone la rabia canina endémica en África y Asia en términos económicos y de salud pública.

Métodos Se aplicaron datos de esas regiones a un conjunto de modelos epidemiológicos y económicos relacionados. La población humana expuesta al riesgo de sufrir rabia canina endémica se predijo a partir de los datos disponibles sobre la densidad de perros, y las defunciones por rabia humana se estimaron usando una serie de pasos probabilísticos para determinar el riesgo de aparición de rabia clínica en una persona que hubiera sido mordida por un perro sospechoso de albergar rabia. Los resultados modelizados sobre la mortalidad y la morbilidad asociadas a la rabia se usaron para obtener un valor mejorado de los años de vida ajustados en función de la discapacidad (AVAD) para la enfermedad. Se presenta el costo social total asociado a esta dolencia.

Resultados La mortalidad humana por rabia canina endémica se estimó en 55 000 defunciones anuales (intervalo de confianza (IC) del 90% = 24 000-93 000). Las defunciones por rabia causan unas pérdidas de 1,74 millones de AVAD cada año (IC90% = 0,75-2,93). Otros 40 000 AVAD se pierden como consecuencia de la morbilidad y mortalidad asociadas a los efectos colaterales de las vacunas obtenidas con tejido nervioso. El costo anual estimado de la rabia asciende a US$ 583,5 millones (IC90% = US$ 540,1 - 626,3 millones). Los costos del tratamiento postexposición asumidos por los pacientes constituyen el grueso del gasto correspondiente, pues suponen casi la mitad del costo total de la rabia.

Conclusión La rabia sigue siendo una importante y sin embargo descuidada enfermedad en África y Asia. Las disparidades en la asequibilidad y accesibilidad del tratamiento postexposición y en el riesgo de exposición a perros rabiosos se traducen en una distribución asimétrica de la carga de morbilidad en la sociedad, de tal manera que el impacto principal de la enfermedad recae en los habitantes de las comunidades rurales pobres, sobre todo en los niños.

ملخص

إعادة تقييم عبء داء الكَلَب في أفريقيا وآسيا

الهدف: عملنا على تحديد كمية العبء الملقى على عاتق الصحة العمومية والعبء الاقتصادي الذي يسببه داء الكَلَب المنقول بالكلبيات في كل من آسيا وأفريقيا.

الطريقة: لقد أخضعت المعطيات التي تم جمعها من الأقاليم المدروسة لمجموعة مترابطة من النماذج الوبائية (الإبيديميولوجية) والاقتصادية. وقد وضعت تقديرات لتعداد السكان المعرَّضين لخطر الإصابة بداء الكَلَب المتوطن المنقول بالكلبيات بالانتفاع من المعطيات حول كثافة الكلاب، والوفيات الناجمة عن إصابة الناس بداء الكَلَب، وذلك باستخدام سلاسل من الخطوات في الاحتمالات لتعيين المقدار التقريبي لحالات الكَلَب السريرية (الإكلينيكية) التي تظهر بين من يتعرض للعض من كلب يشتبه بإصابته بداء الكَلَب. وقد استخدمت نتائج النماذج الخاصة بالوفيات ومعدلات المراضة المرافقة للإصابة بالكَلَب لحساب أحراز محسَّنة لسنوات العمر المصححة باحتساب مدد العجز (دالي) الناجمة عن داء الكلب. ثم عرضت التكاليف الاجتماعية الإجمالية الناجمة عن داء الكلب.

الموجودات: لقد قدرت عدد حالات الوفيات الناجمة عن داء الكلب المتوطن المنقول بالكلبيات بحوالي 55 000 وفاة كل عام وبفاصله ثقة 90% وتتراوح بين 24 000 و 93 000 وفاة وقد أدت الوفيات الناجمة عن الكلب إلى خسارة 1.74 مليون سنة من سنوات العمر المصححة باحتساب مدد العجز (دالي) كل عام، وبفاصلة ثقة 90% وتتراوح بين 0.75 و2.93 مليون سنة؛ كما حدثت خسارة مقدارها 0.04 مليون سنة من سنوات العمر المصححة باحتساب مدد العجز (دالي) كل عام وذلك بسبب المراضة والوفيات التي تنجم عن التأثيرات الجانبية للقاحات المشتقة من النسج العصبية. وقد قدر أن التكاليف السنوية لداء الكَلَب 583.5 مليون دولار أمريكي، بفاصلة ثقة 90% وتتراوح بين 540.1 و626.3 مليون دولار أمريكي. ويتحمل المرضى ما يقرب من نصف مجمل النفقات في الفترة التالية للتعرُّض والمعالجة بعد الإصابة بداء الكلب.

الاستنتاج: لايزال داء الكَلَب من الأمراض الهامة والمهملة في أفريقيا وآسيا. وقد أدى التباين بين الاستطاعة على تحمل التكاليف وإتاحة خدمات المعالجة التالية للتعرُّض إلى جانب أخطار التعرُّض للكلاب المصابة بداء الكلب إلى توزع متجانف لعبء المرض في المجتمع، مع إلقاء العبء الكبير على عاتق السكان في المجتمعات الريفية والفقيرة ولاسيَّما الأطفال منهن.

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Table 2. **Parameter estimates, probability distributions and data sources used in the prediction of human deaths from rabies from injury data on dog bites** (data sources available from: http://www.vet.ed.ac.uk/ctvm/Research/Appendices/appendices.html)

Parameter	Description	Probability distribution	Parameter estimates				Source of data
			Africa		Asia		
			Urban	Rural	Urban	Rural	
	Annual incidence of suspect bites from rabid dogs per 100 000 humans	Trigen:[a] Practical minimum Most likely Practical maximum Bottom and top percentiles	 6 100 227 0%; 95%	 6 100 227 0%; 95%	 50 120 250 5%; 95%	 15 100 250 5%; 95%	*1–6*
P10	Probability of an individual bitten by a dog suspected to be rabid receiving successful post-exposure treatment	Trigen: Practical minimum Most likely Practical maximum Bottom and top percentiles	 0.80 0.85 0.90 5%; 95%	 0.55 0.60 0.60 5%; 95%	 0.95 .097 1.00 10%; 100%	 0.70 0.75 0.80 10%; 90%	*2, 7*
P1	Probability of a suspected rabid dog being confirmed rabid on laboratory diagnosis	Beta:[b] No. of suspect dogs examined No. confirmed rabid P1	 9 285 5 291 0.64		India 5 863 2 906 0.50	Other Asia 59 588 22 923 0.38	*2, 3, 8–15*
P2	Probability of a bite to the head or neck	Point probability	0.07				*2, 16, 17,* E. Miranda unpublished data, 2003
P3	Probability of a bite to the upper extremity (arm or hand)	Point probability	0.38				*2, 16, 17,* E. Miranda unpublished data, 2003
P4	Probability of a bite injury to the trunk of the body	Point probability	0.06				*2, 16, 17,* E. Miranda unpublished data 2003
P5	Probability of a bite to the lower extremity (leg or foot)	Point probability	0.49				*2, 16, 17,* E. Miranda unpublished data, 2003
P6	Probability of developing rabies following a bite to the head by a rabid dog	Triangular: Minimum Most likely Maximum	 0.30 0.45 0.60				*18–21*
P7	Probability of developing rabies following a bite to an upper extremity by a rabid dog	Triangular: Minimum Most likely Maximum	 0.15 0.28 0.40				*18–21*
P8	Probability of developing rabies following a bite to the trunk by a rabid dog	Triangular: Minimum Most likely Maximum	 0 0.05 0.10				*18–21*
P9	Probability of developing rabies following a bite to a lower extremity by a rabid dog	Triangular: Minimum Most likely Maximum	 0 0.05 0.10				*18–21*

[a] The Trigen distribution avoids the use of absolute maxima and minima by allowing the specification of a likely range for the parameter together with an estimation of the probability that the parameter will fall outside this range (top and bottom percentiles).

[b] The Beta distribution is a binomial process allowing estimation of the probability of success p, given s successes from n trials. Assuming a non-informative Uniform (0, 1) prior, the Beta distribution takes the form $p = \text{Beta}(s + 1, n - s + 1)$. See reference *22* for a discussion of commonly used probability distributions.

Table 3. **Parameter estimates and data sources used to calculate the disability-adjusted life year (DALY) score for rabies** (data sources available from: http://www.vet.ed.ac.uk/ctvm/Research/Appendices/appendices.html)

Parameter	Estimate		Source
	Africa	Asia	
No. human rabies deaths per year[a]	23 788 (7 280–44 112)	30 942 (6 017–61 657)	Model output (Table 3)
No. PET[b] cases per year	200 000	7 500 000	*12–14, 23–27*
No. (%) of PET patients receiving nerve-tissue vaccines	20 000 (10)	2 475 000 (33)	*12–14, 23–27*
No. (%) of NTV[c] patients receiving Semple-type nerve-tissue vaccine	16 000 (80)	1 980 000 (80)	*12–14, 23–27*
No. (%) of NTV patients receiving suckling-mouse brain nerve tissue vaccine	4 000 (20)	495 000 (20)	*12–14, 23–27*
Rate of neurological complications per 100 patients receiving Semple vaccine	Triangular: Minimum = 0.035; Most likely = 0.40; Maximum = 0.83		*16, 28–31*
Case–fatality rate for cases of Semple neurological complications	0.17		*30, 32, 33*
Disability weight for Semple neurological complications	0.613		*34* (disability weight for an episode of bacterial meningitis)
Disability duration for Semple neurological complications	Triangular: Minimum = 1 day; Most likely = 8 days; Maximum = 1 year		*35*
Rate of neurological complications per 100 patients receiving suckling-mouse brain vaccine	Triangular: Minimum = 0.013; Most likely = 0.03; Maximum = 0.08		*29, 31, 35, 36*
Case–fatality rate for cases of neurological complications from suckling-mouse brain vaccine	0.22		*29*
Disability weight for suckling-mouse brain neurological complications	0.725		*34* (disability weight for an injured spinal cord)
Disability duration for suckling-mouse brain neurological complications	200 days		*37*
DALY formula parameters			
Discount rate *r*	0.03		*38*
Age-weighting correction constant *C*	0.1658		*38*
Age-weighting function constant	0.04		*38*

[a] Values in parentheses are 90% confidence intervals.
[b] PET = post-exposure treatment.
[c] NTV = nerve-tissue vaccine.