Transmission dynamics and economics of rabies control in dogs and humans in an African city

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Communicated by Burton H. Singer, Princeton University, Princeton, NJ, June 1, 2009 (received for review March 17, 2008)

Human rabies in developing countries can be prevented through interventions directed at dogs. Potential cost-savings for the public health sector of interventions aimed at animal-host reservoirs should be assessed. Available deterministic models of rabies transmission between dogs were extended to include dog-to-human rabies transmission. Model parameters were fitted to routine weekly rabid-dog and exposed-human cases reported in N'Djaména, the capital of Chad. The estimated transmission rates between dogs (β_d) were 0.0807 km²/(dogs·week) and between dogs and humans (β_{dh}) 0.0002 km²/(dogs·week). The effective reproductive ratio (R_e) at the onset of our observations was estimated at 1.01, indicating low-level endemic stability of rabies transmission. Human rabies incidence depended critically on dog-related transmission parameters. We simulated the effects of mass dog vaccination and the culling of a percentage of the dog population on human rabies incidence. A single parenteral dog rabies-mass vaccination campaign achieving a coverage of least 70% appears to be sufficient to interrupt transmission of rabies to humans for at least 6 years. The cost-effectiveness of mass dog vaccination was compared to postexposure prophylaxis (PEP), which is the current practice in Chad. PEP does not reduce future human exposure. Its cost-effectiveness is estimated at US $46 per disability adjusted life-years averted. Cost-effectiveness for PEP, together with a dog-vaccination campaign, breaks even with cost-effectiveness of PEP alone after almost 5 years. Beyond a time-frame of 7 years, it appears to be more cost-effective to combine parenteral dog-vaccination campaigns with human PEP compared to human PEP alone.

Most human deaths from rabies occur in tropical resource-limited countries (1). In Africa and Asia, an estimated 24,000 to 70,000 people die of rabies each year (2). The domestic dog is the main source of exposure and a primary vector for human rabies (3). Rabies in humans can be prevented by appropriate postexposure prophylaxis (PEP), a treatment not always available and affordable in resource-limited countries. Human rabies can also be prevented through vaccination of the animal vector. Recent work in Africa demonstrates that the intensity of rabies-control efforts seems to depend on the level of perceived prevalence. In the past decades, such efforts have not been able to interrupt cyclical epidemics showing significant synchrony between countries (4). However, evidence of successful and sustained vaccination programs to eliminate dog rabies from South America, Mexico, and the Caribbean provide hope for similar efforts in Africa (5). Unfortunately, human resources, diagnostic capacity, and financial resources of most sub-Saharan African countries are far away from those in South America. Bögel and Meslin show that in areas where the virus continually circulates in the dog population, over a period of 15 years, dog vaccination combined with PEP of dog-bite patients, is more cost-effective than PEP alone (6). In most countries however, little is known about the real cost of mass vaccination of dogs (7), and quantitative data are urgently needed to evaluate the cost-effectiveness of different rabies-control strategies. The objective of this article is to develop and validate a deterministic model of dog-human rabies transmission in an African urban center, using as an example N'Djaména, the capital of Chad. The model is used to quantify the dog-human transmission and as a tool for comparative cost-effectiveness assessment of different rabies-intervention strategies.

Results

Dog-to-Human Rabies Transmission. Routine weekly rabid-dog and exposed-human cases per square kilometer, collected by the Laboratoire de Recherches Vétérinaires et Zootechniques (LRVZ) is presented in Fig. 1. The corresponding model fits are depicted in these figures and illustrate a remarkably stable and low-level endemic transmission process. Weekly numbers of rabid-dog cases for the whole city vary between 0 and 3 (0.0043 per km^2), whereas weekly human exposure ranges between 0 and up to 12 (0.017 per km^2) cases. Table S1 [supporting information (SI)] presents all fitted parameters and values used in the model. The dog-to-dog transmission contact-rate (β_d) is 0.0807 km^2/(dogs·week), [95% confidence interval (CI): 0.0804, 0.0809 km^2/(dogs·week)] and dog-to-human transmission contact-rate (β_{dh}) of 0.0002 km^2/(dogs·week), [95% CI: 0.00017, 0.00024 km^2/(dogs·week)]. The number of exposed dogs (E_d) is 0.0061 (dogs/km^2) (95% CI: 0.006151, 0.006158 dogs/km^2). The effective reproductive ratio (R_e) at the onset of our observations is estimated at 1.01 and confirms the stable endemic dynamics of the disease.

Interventions. Our transmission model with the fitted transmission parameters (β_d) and (β_{dh}) provides a tool to assess different interventions. Although human prophylactic and postexposure vaccination prevents exposed persons developing clinical rabies, it has no effect on the transmission process and, therefore, does not prevent future human exposure. For interventions aimed at dogs, we assess the effects of scaling up mass-vaccination campaigns. Additionally, we assess the effect of culling roaming dogs, an intervention that is prescribed by Chadian legislation (Decree n°468 of 29 February 1961, Secretary of State of National Defense, N'Djaména, Chad), but has not actually been carried out.

Vaccination scenarios were simulated with coverage levels of 50% and 70%. A dog rabies mass-vaccination campaign with 70% coverage appears to be sufficient to interrupt the transmission of dog rabies (I_d tends to zero). As a result, human exposure (E_h) is also interrupted for the whole 6-year study period. (Fig. 2). A vaccination campaign with 50% coverage leads to a clearly visible breakdown of rabies transmission, but does not lead to complete elimination during the study period. Two annual shooting campaigns, each killing 5% and 10% of the

Author contributions: J.Z. and S.D. designed research; S.D., R.M., and S.N. performed research; J.H. contributed new reagents/analytic tools; J.Z., S.D., M.A.P., F.R., S.M.G., and J.H. analyzed data; and J.Z., S.D., M.A.P., F.R., S.M.G., and J.H. wrote the paper.

The authors declare no conflict of interest.

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This article contains supporting information online at www.pnas.org/cgi/content/full/0904740106/DCSupplemental.

www.pnas.org/cgi/doi/10.1073/pnas.0904740106

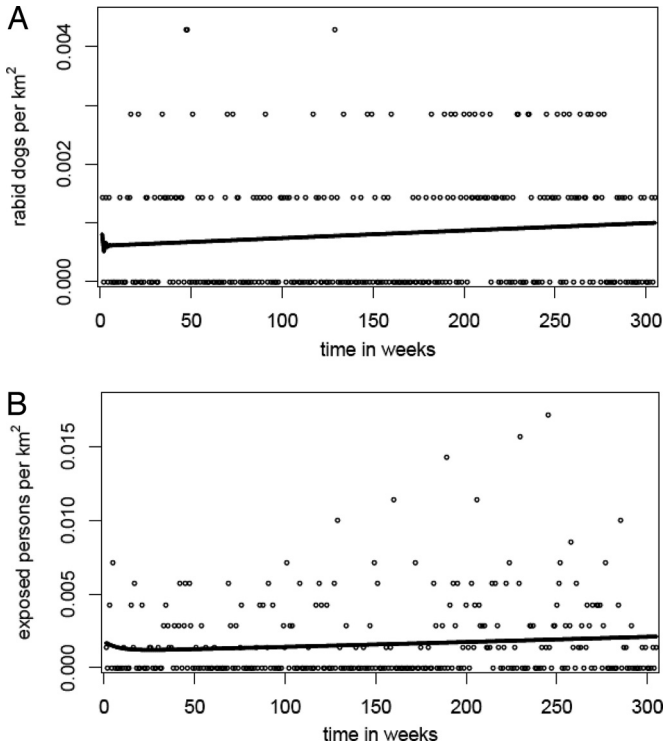

Fig. 1. Rabies transmission among dogs and from dogs to humans in N′Djaména (Chad). (*A*) Weekly incidence of rabid dogs per square kilometer. (*B*) Weekly incidence of exposed persons per square kilometer. Dots represent observed data points and the bold line their deterministic fit.

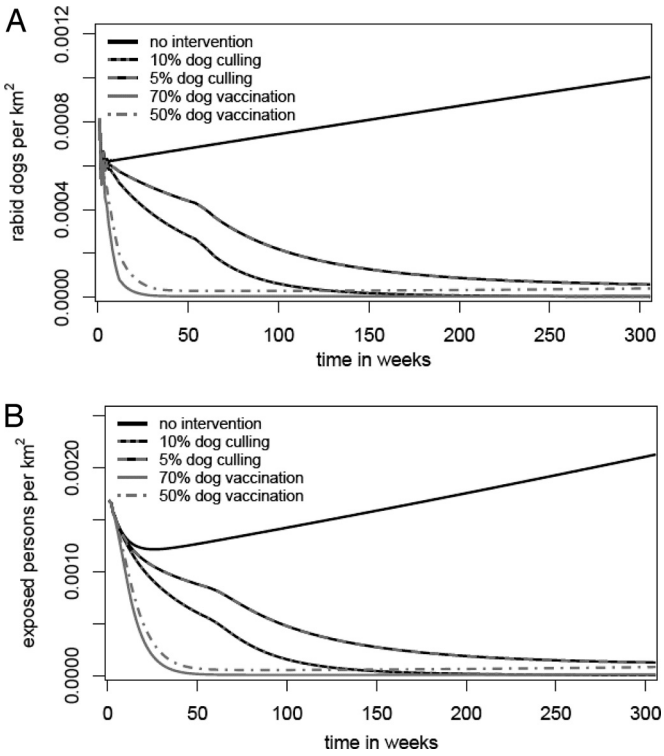

Fig. 2. Simulation of interventions aimed at animal host reservoirs on the transmission of rabies: single mass-vaccination campaigns of dogs with coverage of 70% and 50%, respectively and culling campaigns of 5% and 10% of the dog population, respectively, during 2 consecutive years, compared to no intervention. (*A*) Transmission among dogs, number of rabid dogs per square kilometer. (*B*) Transmission from dogs to humans, number of exposed persons per square kilometer.

dog population, reduce the number of rabid dogs but do not lead to complete elimination. The decrease of the number of rabid dogs is not as fast as that observed with vaccination campaigns. From a household survey on the vector population in N′Djaména, dog birth rate (b_d) was estimated at 0.013 per week (95% CI: 0.011, 0.015) and a mortality rate (m_d) at 0.0066 per week (95% CI: 0.0053, 0.0080).

Sensitivity Analysis of the Model. In a sampling-based sensitivity analysis, the model parameters were expressed as probability distributions (see Table S1). Fig. 3*A* shows 50% and 95% uncertainty limits (ULs) of the dynamics of rabid dogs without intervention and with 70% dog-vaccination coverage; Fig. 3*B* shows the same for exposed humans. In the vaccination scenario, ULs of rabid dogs and exposed humans are much narrower, falling together with central values. Further analysis to evaluate the impact of each parameter separately is presented in Fig. S1 (see also *SI Appendix*). Rabies transmission is very sensitive to the rabies-related mortality rate (μ_d), dog-to-dog transmission rate (β_d), and the probability of clinical outcome (r_d). The carrying capacity (K) and the initial number of dogs per square kilometer S_d (0) has a moderate impact. The model is very robust for changes in dog mortality rate (m_d), birth rate (b_d), the incubation period (i_d), and also in respect to the initial number of rabid I_d (0) or exposed dogs E_d (0). The model was not sensitive to any human parameter.

Cost-Effectiveness of Interventions. PEP alone, which is the current practice, results in an annual recurring cost of US $7,000 to US $8,000. A parenteral dog-vaccination campaign covering 70% of the estimated 23,500 dogs in N′Djaména costs approximately US $43,000 (7). The total cost of a single dog-vaccination campaign with human PEP reaches the break-even point with cumulated recurring costs for PEP alone after 5.9 years (95% UL: 4.6, 7.6 years, discount rate 5%) (Fig. 4). Cost-effectiveness of human PEP alone, which does not reduce human exposure, is estimated at US $46 per disability adjusted-life years (DALY) averted. Cost-effectiveness for dog vaccination with PEP, resulting in elimination of rabies for at least 6 years, reaches the break-even point with human PEP alone at close to 4.9 years (95% UL: 3.8, 6.3 years) (Fig. 5). It is more cost-effective to combine parenteral dog-vaccination campaigns and human PEP compared to human PEP alone beyond a time horizon of 7 years (see Fig. 5). Using cost per averted death as a unit of assessment, PEP alone costs US $876 per averted death. Dog mass vaccination reaches the break-even point with PEP alone at year 6 and is US $596 per averted death in year 10 (discount rate 5%).

The sensitivity analysis of the cost-effectiveness assessment was done by Monte Carlo simulation in @Risk (Palisade Inc.), with 58 variables expressed as probability distributions (Table S2). For the cost-effectiveness analysis, the most sensitive parameter for the 70% dog-vaccination scenario was the number of exposed persons [sensitivity (rank correlation coefficient) 0.54]; all other parameters had sensitivities of <0.1. The most sensitive parameters in the PEP-alone scenario were human postexposure-vaccine cost (0.35), loss of income per human case (0.16), and unit drug cost (0.12). The order of sensitivity of parameters in the cost-effectiveness analysis did not change across different discount rates (3, 5, and 10%) and varied only slightly in magnitude. For the cost-benefit analysis, the most sensitive parameter for the 70% dog-vaccination scenario was the public cost per vaccinated dog (0.94), human postexposure-vaccine cost (0.25), and loss of income per case (0.1). The most sensitive parameters in the PEP-alone scenario was the number of exposed persons (0.6); all other parameters had sensitivities

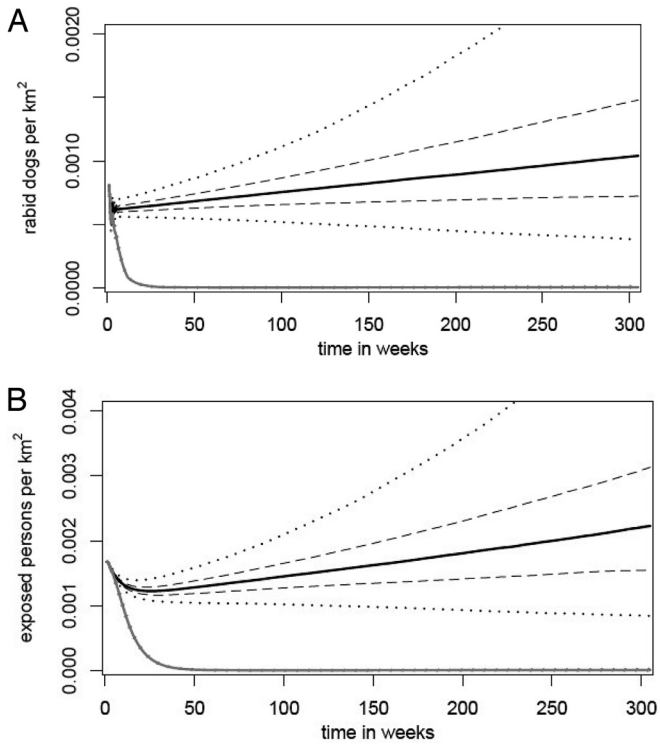

Fig. 3. Sensitivity of the rabies transmission dynamic model to uncertain parameters (probability distributions are shown in Table S1). (*A*) Rabid dogs per square kilometer and (*B*) exposed persons per square kilometer with their respective 50% (*gray dashed line*) and 95% (*gray dotted line*) Monte Carlo uncertainty intervals of the sensitivity analysis for no intervention and 70% dog vaccination.

<0.1. The order of sensitivity of parameters in the cost-benefit analysis did not change across different discount rates (3, 5, and 10%) and varied only slightly in magnitude. Manual sensitivity analysis of discount rates (3, 5, and 10%) showed that the average break-even of both cost-benefit (see Fig. 4) and cost-effectiveness analyses (see Fig. 5) shifted to the right with increased discount rates, and ranged between 5.7 and 6.5 years for cost-benefit analysis and between 4.7 and 5.4 years for cost-effectiveness analysis. From a policy-oriented perspective, public funding of dog vaccinations will be central in achieving

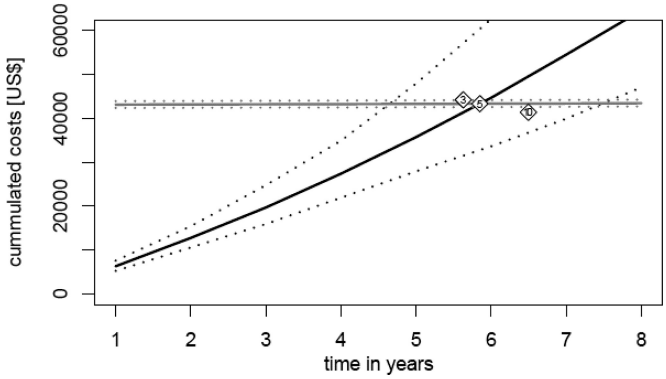

Fig. 4. Cumulated and discounted costs of human PEP alone, with 95% uncertainty interval (*black line with black dotted limits*), and human PEP with dog vaccination with 95% uncertainty interval (*gray line with gray dotted limits*). Break-even points are numbered diamonds for sensitivity analysis with 3%, 5%, and 10% discount rates.

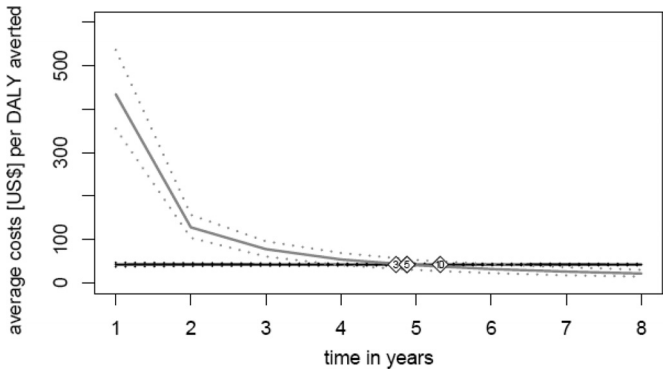

Fig. 5. Average and discounted cost-effectiveness of human PEP alone with 95% uncertainty interval (*black line with black dotted limits*), and human PEP with dog vaccination with 95% uncertainty interval (*gray line with gray dotted limits*). Break-even points are numbered diamonds for sensitivity analysis with 3%, 5%, and 10% discount rates.

effective control, as this cannot be borne by private dog owners (8).

Discussion

The presented passive-canine rabies-surveillance data were obtained from routine operations at the rabies laboratory in N′Djaména, the capital of Chad. We expect under-reporting in these numbers, but at present we are unable to estimate its level. A dog-bite study similar to ref. 9 is ongoing. The upper 95% UL of the number of rabid dogs in Fig. 3*A* reflects the probable range with the given data, but the true level may actually be even higher because of lack of funds to pay for transport and laboratory cost and lack of awareness (9). The reported data may have been affected by a pilot vaccination campaign in 2002, which resulted in the vaccination of 3,000 dogs (about one-tenth of the entire dog population) (10) and periods of civil unrest in April-May and November, 2006. The reliability of the diagnostic laboratory tests has been confirmed earlier (11, 12).

The surveillance data reflects only the rabies cases and situation of N′Djaména; very little is known about the rabies situation in other urban or rural areas of Chad. In most African countries, rabies diagnosis is possible only in capitals and major cities. We therefore question whether the data provided by Hampson et al. (4) really represents the situation across whole countries, and not merely the capitals of the respective countries. In this work, we omit reactive intervention when fitting the model (4). In contrast to Hampson et al. (4), we did not observe oscillating patterns in the numbers of rabid dogs or exposed people, but only a very slow, steady increase of dog rabies incidence.

The dispersal and external introduction of rabid dogs are essential elements of spatial spread of the disease. We have no information concerning the rate of introduction of latently infected or rabid dogs into N′Djaména. However, we can assume that during our observation period, an unknown number of latently infected dogs entered the city area and their contribution to the transmission is considered by the observed data. The spatial distribution of the dog population is not homogeneous in the city area, because of uneven spatial distribution of the human population and differing preferences for dog ownership; however, this has not been considered in the model. Dog density and carrying capacity are sensitive parameters in the model and better empirical data on their levels and variability is warranted.

Dog-Human Transmission. To our knowledge, our model is unique in presenting a deterministic dog-human rabies-transmission model. This model provides a tool to assess cost-benefit and

cost-effectiveness of different interventions in humans and animal hosts (13). The occurrence of rabies in short time intervals appears as a series of random events for which deterministic models are not always appropriate (4). ULs of exposed humans are wide, reflecting those of rabid dogs. Subsequently to dog vaccination, the number of exposed humans decreases sharply and within very narrow ULs (see Fig. 3). Human-rabies incidence is significantly influenced by variability of the dog-to-dog transmission rate (β_d), the probability of clinical outcome in dogs (r_d), and rabies-related mortality rate in dogs (μ_d) (see Fig. S1). These parameters depend largely on the contact rate between dogs, biological properties of the rabies virus, and the pathophysiology of rabies in dogs. The rabies-related mortality rate in dogs (μ_d) is also determined by socio-cultural factors, as aggressive dogs are often killed by humans, thus preventing further exposure. Rabies is therefore a prime example of close linkage of human and animal health, expressed as "one medicine," a term coined by C. Schwabe (14).

Interventions. As the transmission dynamics are very robust to changes in dog-mortality rate (m_d) (see Fig. S1), a culling policy is less likely to interrupt transmission (particularly for owned dogs) as compared to a mass-vaccination strategy, and socially not acceptable. A much higher transmission rate, as suggested above, would affect the threshold coverage of vaccination. Among the compared intervention strategies, mass vaccination of 70% of the dog population is the most profitable and cost-effective intervention, sufficient to interrupt rabies virus transmission for at least 6 years.

Concerning vaccination immunity, Akakpo et al. assume a fast immunity loss (15). This seems realistic, given that dogs in Sahelian cities often suffer from malnutrition and multiparasitism, which affects their immune response. In Peru however, 93% of all dogs are still protected 1 year after vaccination (16), while in a Tanzanian study above 80% are still protected after 6 months and 73% after 1 year (17). The latter conditions are similar to those in N′Djaména (18), but to be more conservative, we use the levels of immunity loss provided by Akakpo et al. (15).

PEP in N′Djamena is restricted to wound treatment and active immunization, as anti-rabies Ig is not available. If vaccines are not available, patients often have to find treatment in neighboring Cameroon, which increases vaccine costs even more. The estimated human vaccine cost in our study is therefore rather conservative. In the context of N′Djaména, which is comparable to many African cities, the cost-effectiveness of combining dog mass vaccination with PEP is within the most cost-effective interventions in public health after 8 years, comparable to combined micronutrient and measles immunization (19).

Conclusion

We observe a low level, endemic, stable rabies transmission among dogs, and from dogs to humans, in the city of N′Djamena, Chad. The effective reproductive ratio estimated from the model was close to 1, indicating that interventions directed at dogs would be feasible and effective in reducing transmission. Among the intervention strategies compared, mass vaccination of 70% of the dog population is the most profitable and cost-effective intervention. As effective transmission may occur at a much higher rate than observed, mass vaccination should aim for coverage as high as possible. The addition of transmission from dogs to humans in the deterministic model revealed a critical dependence of human-rabies incidence on the contact rate between dogs, the biological properties of the rabies virus, the pathophysiology of rabies in dogs, and sociocultural determinants of human-dog interaction. The model allows comparison of the cost-benefits and cost-effectiveness of different interventions, in particular the trade-off between interventions in humans alone or in combination with interventions in the animal host. Under the current conditions of endemic stability, and assuming a discount rate of 5%, a single parenteral mass dog-vaccination campaign reaching 70% coverage is, on average, profitable after 6 years, and more cost-effective over a period of longer than 7 years when compared to PEP for exposed humans alone. In the case of urban rabies in N′Djaména, which may apply to many other African cities, rabies can be effectively controlled by publicly funded (8) dog mass vaccination. Human health benefits are higher from combined dog vaccination and PEP than from PEP alone.

Methods

The presented work took place within a research framework requested by the Chadian veterinary authorities. This work is unique in establishing the capacity for rabies diagnosis by immunofluorescence-antibody test (IFAT) at the central veterinary laboratory (Laboratoire de Recherches Vétérinaires et Zootechniques) in January 2001 (11). After an introductory period of 15 months, the rabies laboratory at LRVZ continued to perform rabies diagnosis by IFAT and recorded dog-rabies diagnoses and human exposure as a routine service. In the year 2001, the city of N′Djaména had an extrapolated human population of 775,020 inhabitants (18) and covered a surface area of ≈700 km^2. The owned-dog population in 2001, as estimated by a representative household survey, was ≈23,560 dogs (95% CI: 14,570, 37,898) (18). Assuming that 10% of the dogs were ownerless, the average dog density was estimated as 37 dogs per km^2 (10).

Rabies Surveillance and Diagnosis. Data concerning the number of confirmed dog-rabies cases was collected during the period of January 2001 to November 2006 (305 weeks) from routine passive surveillance at LRVZ. This dataset (see Table S3) was used to fit the model parameters. In the first few weeks of the observation period, the population was informed extensively about the clinical signs of dog rabies, diagnosis, and prevention. For each animal brought to the laboratory for examination, data on age, sex, origin, and the ownership status of the animal were gathered routinely via questionnaire. For exposed persons, age, sex, origin of the patient, and her or his relation to the animal owners were recorded routinely. Interviews were in French with questions translated into Arab, Sara, or Ngambai, as needed.

All exposed persons were referred to a medical service for postexposure treatment at their own charge. For ethical reasons, and to ensure postexposure treatment for all people exposed to a confirmed rabid animal, a stock of human antirabies vaccine (Lyssavac by Berna and SII Rabivax by Serum Institute of India Ltd.) was kept at the LRVZ during the study. This vaccine was used in times of shortages, but otherwise was not promoted to guarantee continuation of supply in pharmacies. Vaccines were given free of charge to people who could not afford to purchase them. Diagnosis of rabies was made using the direct IFAT at LRVZ. This test, described in ref. 20, is the standard diagnostic tool for rabies and the method most widely used to diagnose rabies in humans and animals (21).

Demographic Parameters of Dogs and Humans. Demographic parameters for the dog population of N′Djaména were assessed by a household survey. A dog demographic survey was carried out in 343 households. The number of dogs, the sex and birth date of each dog, and the number of litters of each female dog were recorded. Every household was visited monthly from December 2005 to July 2006, and all canine births, deaths, acquisitions, and exits were recorded. In April and May 2006, no data could be collected because of civil unrest in N′Djaména. We calculated the birth rates (b_d) as the total number of live births during the observation period divided by the size of the study population (assessed as number of dogs at baseline). Mortality rates (m_d) were assessed by the Kaplan Meyer estimate (SAS SAS Institute Inc. Lifetest procedure). Human birth (b_h) and mortality rates (m_h) of the local human population were estimated from data provided by the Chadian Division of Health Information (22).

Transmission Model and Data Fitting. We extended existing deterministic models of rabies transmission between dogs (4, 23, 24) to include dog-to-human rabies transmission. For dogs and humans, we considered 4 compartments each, representing their respective infection or immunity status: "S" for susceptible, "E" for exposed, "I" for infectious (i.e., rabid), and "R" for immune individuals, using a subscript "d" for dogs and "h" for humans. A flow diagram and the equations are given in *SI Appendix* (equations 1–11). The model parameters, and their respective sources, are summarized in Table S1. Briefly, two underlying processes are considered for dogs and humans: First,

we consider dog and human populations of the city of N'Djaména with respective birth rates (b_d) and (b_h) and mortality rates (m_d) and (m_h), considering the mortality of rabid dogs (μ_d) and rabid humans (μ_h) separately. Second, rabies transmission between dogs is considered as the flow of susceptible dogs (S_d) to exposed dogs (E_d), fitted by the dog-to-dog transmission constant (β_d). Exposed dogs (E_d) become clinically rabid dogs (I_d) depending on the inverse of the incubation period (σ_d) and the probability of developing clinical rabies (r_d). Vaccination of dogs was simulated by moving a proportion of susceptible dogs to the immunized dogs (R_d) compartment, depending on vaccine efficacy (v_d) and dog-vaccination rate (α_d). Transmission from dogs to humans, indicated by a dashed arrow in the model sketch, reflects the flow of susceptible humans (S_h) to exposed humans (E_h) fitted by the dog-to-human transmission constant (β_{dh}). Exposed humans (E_h) develop clinical human rabies (I_h), depending on probability of the bite localization (*P2–P5*), the probability of developing rabies after exposure (*P6–P9*) (see Table S1), divided by respective incubation periods, for example, (i_{head}). The postexposure vaccination (PEP) of humans is simulated by the flow from exposed humans (E_h) to immunized humans (R_h); similarly, prophylactic human vaccination is sketched as flow from susceptible humans (S_h) to immunized humans (R_h). The model is a coupled system of differential equations and was implemented in Vensim (Ventana Systems Inc.) software, with steps of 1 week (t), and validated in Matlab (The MathWorks).

Dog-to-dog (β_d) and dog-to-human transmission rates (β_{dh}), and the initial number of exposed dogs (E_d), were fitted to the weekly data series of rabies-positive dogs and exposed people to rabies-positive dogs (see *SI Text Passive Surveillance of Dog Rabies Cases and Human Exposure in N'Djaména, Chad from January 2001 to November 2006*). The 2 transmission rates were fitted simultaneously using a Powell nonlinear maximum-likelihood optimization algorithm in Vensim. The transmission rates and the initial number of exposed dogs were additionally fitted with Matlab, using nonlinear regression assuming both Normal- and Poisson-distributed errors. Because there was not a new outbreak of rabies but ongoing endemic transmission, no estimate for the basic reproductive ratio R_0 was derived. The effective reproductive ratio was estimated as 1.01, indicating stable transmission. The formula is given in *SI Appendix* (Eq. 11) and was derived in a similar fashion to ref. 25.

Interventions. In a pilot parenteral dog-rabies mass-vaccination campaign in N'Djaména in 2002 we could demonstrate that a vaccination coverage of 70% of the dogs can be achieved (10), as recommended by the World Health Organization (21) and Coleman and Dye (26). A transmission model was used to estimate the time and cost to achieve effective control for the whole city of N'Djaména. Such estimates contribute to inform policy planning in a context of severe resource constraint. We assumed a dog vaccine efficacy (v_d) of 94% (27), and by considering 2 vaccination coverage rates (α_d) of 70% and, more pessimistically, of 50%. We assume that susceptible and exposed asymptomatic dogs are vaccinated over a period of 10 continuous weeks (campaign duration). To achieve 70% vaccination, we expressed (α_d) as an exponential decay function, valid for 10 weeks, with a decay parameter of −0.12 per week. To achieve 50% vaccination coverage, the decay parameter is set to approximately −0.069 per week. Culling was simulated assuming the elimination of 10% and 5% of the total dog populations. To represent this culling in the model, we introduced an additional parameter (c_d) −0.0105 week^{-1} (10% elimination) and (c_d) −0.00513 week^{-1} (5% elimination), essentially representing an exponential decay of the culling intervention over a period of 10 weeks. Culling was assumed to occur once a year for 2 consecutive years. As part of a pilot mass-vaccination campaign against rabies in N'Djaména, we assessed vaccination coverage and cost, and estimated the cost per dog vaccinated for the public sector and for society (7). If all 23,560 dogs in N'Djaména were vaccinated, the average cost would be US $2.61 to society € 1 = US $1.35 [www.oanda.com (accessed August 23, 2007).] (7). The range of cost of human postexposure treatment was collected at different hospitals and health centers in N'Djaména and is given in Table S2. Briefly, local transport cost included the expenses of transport to a pharmacy or health center. The unit laboratory fee for dog examination included the cost of rabies diagnosis for a suspected dog and transport to the laboratory. Human vaccine unit cost covered the 5 postexposure human antirabies vaccinations and 1 additional vaccination after 6 months. The drug unit cost covered the cost of disinfection and wound dressing. The outpatient unit cost is the fee incurred for health care at a health center. Loss of income is the opportunity cost of labor lost by the patient or by the dog owner to vaccinate his or her dog.

The age distribution of exposed humans was based on ref. 11. Age groups were 0 to 5 years, 5 to 15 years, and >15 years, the proportions of exposed persons being 19%, 36%, and 45%, respectively, which is in line with Coleman et al. (24). For estimation of DALY averted, we assumed that 16% of the exposed persons would develop clinical rabies without timely administered PEP (9). Because of the short duration of clinical disease, we did not consider years of life lost with a disability, but estimated only years of life lost (24) using the standard DALY formula by Murray (28) and Family Model West, Level 26 lifetables (see *SI Text*). The discount rate was varied between 3, 5 and 10%. A high discount rate, such as 10%, gives very little value to costs and benefits occurring in the longer term. With this we reflect the urgent need of a developing country such as Chad with poor economic performance and high population growth to invest in projects providing returns sooner rather than later. It is more common in assessing the economics of potential projects in developing countries to use a lower discount rate, such as 3%. However, this does not consider the urgency seen in developing countries for return and development. The age-weighting function (b) was 0.04 and the age-weighting constant (C) was 0.1658. The disability weight (D) and the age-weighting modulation factor are set to 1. Cost-effectiveness of human PEP alone is calculated as discounted cumulated cost of annual PEP divided by the discounted cumulative number of annual DALYs averted. Cost-effectiveness of dog vaccination plus human PEP is calculated as discounted total cost of a parenteral dog-vaccination campaign in year 1 and concurrent cumulated annual cost of human PEP divided by the difference of cumulative number of annual DALYs averted with PEP alone and cumulative number of annual DALYs averted with parenteral dog vaccinations and human PEP (see *SI Text*).

Sensitivity Analysis. Extensive multivariate sensitivity analysis was done at the level of the model and at the level of the economic analyses. Uni- and multivariate sensitivity analyses of the model parameters were implemented in *R* (29). To perform 1 multivariate test, the distribution for each parameter specified is sampled, and the resulting values used in a simulation (2,000 replications). All simulations then are summarized by calculating median values and 95% uncertainty limits (see Fig. 3). The uncertainty of numbers of exposed humans derived from the transmission model, variability of cost of human postexposure treatment, and dog vaccination were expressed as probability distributions using @Risk (Palisade) analogous to ref. 30 (see Table S2). Discount rates were varied manually between 3, 5, and 10%.

ACKNOWLEDGMENTS. We thank all international institutions, collaborators, and campaign workers for their successful teamwork. We thank the Swiss Rabies Centre for diagnostic support; the reviewers for their critical remarks, which helped to improve the manuscript; and Kate Snedeker for her editing support. We also thank the sponsors of this study: The Swiss Federal Veterinary Office, the Wolfermann-Nägeli Foundation, the Commission for Research Partnership with Developing Countries, and the Emilia Guggenheim-Schnurr Foundation. The National Center of Competence Research North-South provided cofunding (to J.Z.).

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