

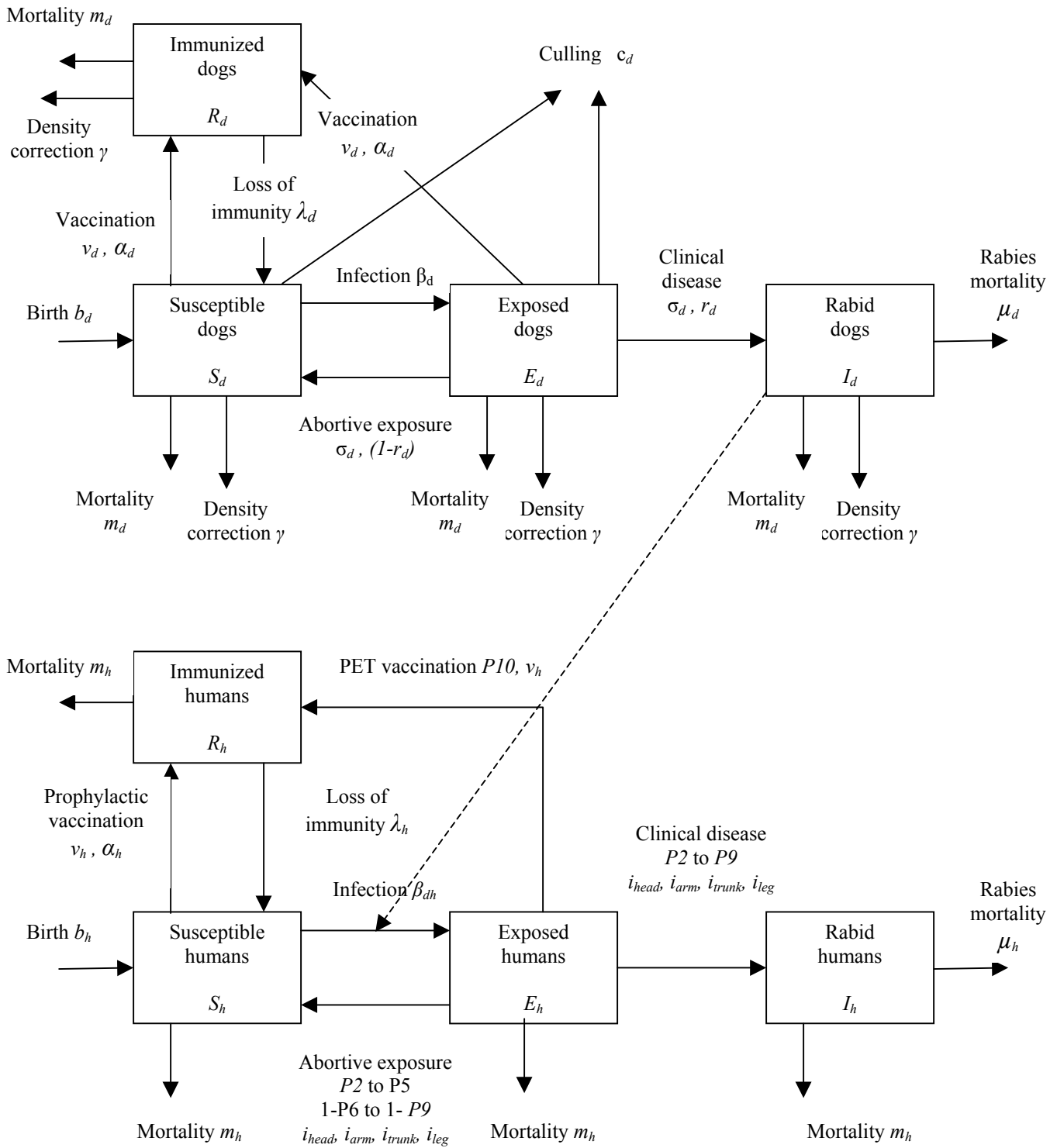
SI Appendix

Model Flow Chart of Dog-Human Rabies Transmission

Area dependent densities of the dog and human populations were assumed and initial values calculated by using a surface for the study area of N'Djaména of 700 km². The initial number of exposed dogs (E_d) was unknown and fitted in the model. The initial condition for the number of rabid dogs (I_d) per km² was estimated using the average number of the recorded rabid dogs over the study period. The initial number of immunized dogs (R_d) was set to zero. We considered a density dependent death rate, γN_d , for all compartments of the dog population (susceptible, exposed, rabid and immunized dogs), where (N_d) is the total dog population and γ is given by the difference between the dog birth rate (b_d) and mortality rate (m_d), divided by the carrying capacity (κ) (equation 5, appendix 2). The carrying capacity of the dogs, (κ), per km² is assumed to be 33.6 dogs/km² (estimated from the initial dog population and the study area). Exposed dogs that do not develop clinical rabies are considered as abortively exposed ($\sigma_d (1-r_d)E_d$). ($1/\sigma_d$) weeks is the incubation period of the disease and (r_d) is the risk of clinical outcome in dogs (K. Hampson, personal communication). Loss of dog vaccination immunity (λ_d) is based on (15) and assumes a 80% protective immunity at 6 months and 7% protective immunity at 12 months post vaccination.

For the initial number of the weekly exposed humans per km² (E_h), the average over the whole observation period was used. The density of clinically rabid humans (I_h) was assumed to be zero at the beginning of the simulation. The parameters $P2$ to $P5$ represent the probabilities of bite injury at different body locations (9), and parameters $P6$ to $P9$ are the probabilities of developing rabies following the bite of a rabid dog (9). The rate of human clinical rabies development, given exposure, was given by the sum of the product of bite probabilities at particular parts of the body times the probability of developing rabies after this bite divided by the respective incubation period ($I_h = P2*P6/i_{head} + P3*P7/i_{arm} + P4*P8/i_{trunk} + P5*P9/i_{leg}$), where i_{head} , i_{arm} , i_{trunk} , and i_{leg} are the median incubation periods of rabies after a bite at different body locations (9). Abortive exposure in humans was represented by $(P2*(1-P6)/i_{head} + P3*(1-P7)/i_{arm} + P4*(1-P8)/i_{trunk} + P5*(1-P9)/i_{leg})$. The human clinical rabies mortality rate, (m_{rh}) was assumed to be 1 per week (9).

Immunized humans (R_h) (initial value 0) represent either persons with post-exposure treatment (PEP) or prophylactic vaccination. PEP vaccination coverage was represented by $P10$, using an analogous notation to Cleaveland (9). Prophylactic vaccination of humans (v_h) is rarely performed in N'Djaména but is recommended by WHO under particular circumstances (35). Although the human vaccination rate (α_h) and post exposure treatment rate (P 10) have not been made use of in this current work, they have been included in the model for completeness and to allow the model to be used in any future assessment of treatments and/or vaccine interventions directed at humans. Loss of human vaccination immunity (λ_h) was not used in our intervention assessments but might be used in studies on human prophylactic vaccination.



Equations: Differential Equations of the Dog-Human Rabies Transmission Model.

Dogs

$$\frac{dS_d}{dt} = b_d N_d + v \lambda_d R_d + (\sigma_d (1 - r_d) E_d) - m_d S_d - \beta_d S_d I_d - \gamma N_d S_d - v_d \alpha_d S_d - c_d S_d \quad (1)$$

$$\frac{dE_d}{dt} = \beta_d S_d I_d - m_d E_d - \gamma N_d E_d - (\sigma_d (1 - r_d) E_d) - v_d \alpha_d E_d - \sigma_d r_d E_d - c_d E_d \quad (2)$$

$$\frac{dI_d}{dt} = \sigma_d r_d E_d - m_d I_d - \gamma N_d I_d - \mu_d I_d \quad (3)$$

$$\frac{dR_d}{dt} = (v_d \alpha_d (S_d + E_d)) - m_d R_d - \gamma N_d R_d - \lambda_d R_d \quad (4)$$

$$\gamma = \left(\frac{(b_d - m_d)}{K N_d} \right) \quad (5)$$

$$N_d = S_d + E_d + I_d + R_d \quad (6)$$

Humans

$$\frac{dS_h}{dt} = (b_h (S_h + E_h + R_h)) + \lambda_h R_h + \left(E_h \left(\frac{P2(1-P6)}{i_{head}} + \frac{P3(1-P7)}{i_{arm}} + \frac{P4(1-P8)}{i_{trunc}} + \frac{P5(1-P9)}{i_{leg}} \right) \right) - m_h S_h - v_h \alpha_h S_h - \beta_{dh} S_h I_d \quad (7)$$

$$\frac{dE_h}{dt} = \beta_{dh} S_h I_d - m_h E_h - P10 v_h E_h - \left(E_h \left(\frac{P2P6}{i_{head}} + \frac{P3P7}{i_{arm}} + \frac{P4P8}{i_{trunc}} + \frac{P5P9}{i_{leg}} \right) \right) - \left(E_h \left(\frac{P2(1-P6)}{i_{head}} + \frac{P3(1-P7)}{i_{arm}} + \frac{P4(1-P8)}{i_{trunc}} + \frac{P5(1-P9)}{i_{leg}} \right) \right) \quad (8)$$

$$\frac{dI_h}{dt} = \left(E_h \left(\frac{P2P6}{i_{head}} + \frac{P3P7}{i_{arm}} + \frac{P4P8}{i_{trunc}} + \frac{P5P9}{i_{leg}} \right) \right) - m_h I_h - \mu_h I_h \quad (9)$$

$$\frac{dR_h}{dt} = P10v_{eh}E_h + v_{eh}v_{ch}S_h - m_hR_h - v_{lh}R_h \quad (10)$$

Effective Reproductive Number R_e at the Beginning of the Observation Period $t=0$

$$R_e = \frac{\sigma_d r_d \beta_d S_0}{(b_d + \sigma_d)(m_{rd} + b_d)} \quad (11)$$

Cost-Benefit and Cost-Effectiveness Assessment with @Risk Functions.

Break down of social and private cost:

Dog Vaccination (7)

Public cost = Marginal dog vaccination cost
+ Equipment of Vaccination Costs
+ Staff per diem
+ Transportation
+ Information;

Private cost = Lost worktime

Human Post Exposure Treatment

Public cost = Negligible compared to private cost
Private cost = Marginal human vaccination cost
+ Transportation
+ Laboratory fee for dog examination
+ Drug cost
+ Outpatient cost
+ Income loss

Societal cost = Public cost + Private cost.

Equations for the Cost-Effectiveness Calculations

$$CE_{PET \text{ alone}} = \frac{\text{annual cost of PET}}{\text{annual DALYs}} \tag{12}$$

cost of dog vaccination campaign + annual cost of PET

$$CE_{\text{dog vaccination and PET}} = \frac{\text{annual DALYs}_{\text{PET alone}} - \text{annual DALYs}_{\text{dog vaccination and PET}}}{\text{annual DALYs}_{\text{PET alone}}}$$

(13)

(Datafile: cost_effectiveness_rabies_control.xls)