Comparison of vaccination strategies for the control of dog rabies in Machakos District, Kenya

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SUMMARY

Demographic and epidemiological field data were used in a deterministic model to describe dog rabies transmission in Machakos District, Kenya and to predict the impact of potential vaccination strategies for its control. The basic reproduction number ($R_0$) was estimated to be 2.44 (1.52–3.36, 95% confidence limits). There were three key model predictions. The first was that a threshold dog density ($K_T$) of 4.5 dogs km$^{-2}$ (3.8–5.2 dogs km$^{-2}$, 95% confidence limits) was required to maintain transmission. The second was that the estimated annual vaccination rate of 24% failed to decrease incidence and actually increased the stability of transmission and may be counter-productive. Thirdly, to control rabies, it was predicted that 59% (34%–70%, 95% confidence limits) of dogs should be vaccinated at any one time. This requires approximately 70% coverage for annual but only 60% coverage for semi-annual vaccination campaigns. Community-level vaccination trials are needed to test these predictions.

INTRODUCTION

In most parts of the developing world, rabies is prevalent in its most dangerous reservoir, dogs. Each year, approximately 4 million people in the developing countries of Asia, Africa, and South America receive post-exposure treatment and over 30000 die after being bitten by rabid dogs [1]. In more than 99% of all human rabies cases, the virus is transmitted from dogs, and over 90% of people who receive post-exposure treatment live in endemic areas for canine rabies [1].

In Kenya, the rabies problem has been greatest in Machakos District, where the disease has persisted, since the mid 1950s, even during periods when rabies was well controlled in the rest of the country [2]. In a one-year active surveillance for rabies carried out in the district during 1992–3, over 80% of the confirmed rabies cases were dogs and 97% of all human cases of bites by animals were due to dogs. The annual dog rabies incidence was estimated at 860 cases/1000 dogs [3], much higher than the range of annual incidence rates (per 100000 dogs) of dog rabies in African countries reported by passive surveillance (Natal, South Africa (11–8), Zimbabwe (11), Zambia (3–3), Malawi (12), Lesotho (1–5), Madagascar (4–7), Kenya (3–8), Tanzania (1–6), and Serengeti, Tanzania (8–16) [4]. The high incidence of rabies in Machakos has been attributed to a large, poorly controlled, and inadequately vaccinated dog population [5]. The current vaccination coverage of the Machakos dog population was estimated at 24% per annum [5].

In exploring the dynamic interactions between
rabies and dogs, the development of mathematical models can provide information on the relationships of key parameters, such as dog density and the proportion of susceptible dogs, important for rabies transmission. Models can be used to describe the temporal and spatial distribution and frequency of cases as well as predicting the impact of a variety of possible control measures [6–11]. In this study, the main objective was to compare the impact of different vaccination strategies on the transmission of rabies in the Machakos dog population. In assessing potential vaccination strategies, two key features of the dog population, density and turnover, were considered crucial from previous dog ecology studies [5]. A useful model for assessing the impact of vaccination on rabies transmission, incorporating population density, was developed by Anderson and others for European fox populations [12]. This model was adapted, incorporating dog population [5] and rabies incidence [3] data from the study region. In this paper, we investigate the relationship between dog density and rabies incidence using this empirical data. We then predict the impact of different vaccination frequency and coverage on rabies transmission. Model outputs were compared to observed patterns of rabies in Machakos District and other rural African sites.

**METHODS**

**Model framework**

The model framework included dividing the dog population into four rabies classes, susceptible (S), latent (L), infectious (I) and vaccinated (V) in a closed dog population. All classes were assumed to suffer a standard general mortality risk and rabies was considered invariably fatal. Susceptible dogs could either die for reasons other than rabies, become infected with rabies or be vaccinated. Rabies transmission from other host reservoir species to dogs and dog migration were assumed not to be important. To incorporate density effects on dog demographics [12] and rabies transmission, the density in each rabies class [12], rather than the number of individual dogs was modelled.

The dog population was assumed to grow. The growth rate was calculated as the difference between the estimated birth and death rates. Population growth was considered to be density-dependent, increasing towards an asymptotic threshold density [13]. Rabies transmission was also considered density-dependent, a linear function of the densities of susceptible and infectious dogs. Given the major difference in human and dog population densities in Machakos District [5], two scenarios were considered, peri-urban ( > 500 people km⁻¹) and rural (generally < 200 people km⁻³).

For modelling transitions between rabies classes, a set of four coupled, first-order, non-linear differential equations describing rabies dynamics were used:

\[
\begin{align*}
\frac{dS}{dt} &= a(S + V) - S(\beta I + b + \gamma N) \\
\frac{dL}{dt} &= \beta SI - (\sigma + b)L - \gamma NL \\
\frac{dI}{dt} &= \sigma L - (\alpha + b)I - \gamma NI \\
\frac{dV}{dt} &= \gamma NV - bV 
\end{align*}
\]

The basic reproduction number of rabies in the dog population could be estimated from the equation:

\[
R_0 = \frac{\beta S}{(\sigma + a)(\alpha + a)}. 
\]

The parameters in these equations included: (1) dog population parameters – general dog population mortality per year (b), dog birth rate per year (a) and a density-dependent mortality parameter (γ) that is a function of the dog population growth rate per year, r, and the maximum carrying capacity density of the dog population km⁻² (K) (γ = r/K) [12] and (2) rabies-specific parameters – contact rate between infectious and susceptible dogs per year (β), rabies-specific mortality rate per year (α), latent-to-infectious rate per year (σ) and vaccination rate per year (q). In this model, the host population density (N = S + L + I + V) is a dynamic variable affected by both the disease and density-dependent constraints (γ).

**Parameter estimation**

Dog population parameters were estimated in two field studies reported in more detail elsewhere [5]. Briefly, 6 sublocations of Machakos District were randomly selected and 25 dog-owning households randomly selected per sublocation. Schoolboys conducted a dog census by visiting all households in each study sublocation and dog densities km⁻² were estimated by dividing the number of dogs enumerated by the area of the sublocation. In addition, a cohort of dogs from the 150 sampled dog-owning households was identified and follow-up data (births, deaths, dog movements) on each dog initially sampled during a period of 1 year were collected. Annual rates for mortality (b), fecundity (a), and dog population growth rate (r) were calculated by combining the fecundity and survival data estimated from a one-year cohort study of dogs in 150 dog-owning households.
(25 from each of 6 sublocations) (see [5] for further details). For a defined population in a fixed area, the change in total dog population density (N) with respect to time was described by the equation:

$$\frac{dN}{dt} = rN(1 - \frac{N}{K})$$  \quad (6)

where $r$ is the intrinsic growth rate ignoring density effects and $K$ is the carrying capacity. Two estimates of $K$ were used, one for peri-urban and one for rural settings.

Rabies transmission parameters were largely estimated from one-year active surveillance study for rabies in the six sublocations (described in [3]). In each sublocation, a community rabies worker was recruited and trained. During the study period all potential rabies exposures were recorded on standard forms and, when possible, samples collected for rabies diagnosis.

Although there is some evidence that dogs are infective before signs develop [14], it was assumed that latent and incubation periods were equal. The latent ($1/\sigma$) and infective periods ($1/\alpha$) in years were obtained from data on natural infections [15].

The annual vaccination rate ($q$), achieved in Machakos, was estimated from both questionnaire and serological data collected during the follow-up study of household dogs [5]. Dogs, once vaccinated were assumed to be immune for life, given that life expectancy of dogs in Machakos (2–9 years) was slightly lower than the expected duration of immunity from the dog rabies vaccine used (Rabisin, Rhone-Merieux, Lyon, France) [16].

$R_o$ was estimated in two ways. The first was by counting all confirmed secondary cases exposed by confirmed primary case during the active surveillance study. The second was to estimate $R_o$ from outbreak data [11] using the expression:

$$R_o = 1 + \alpha(v/\alpha + g)$$  \quad (7)

The standard error $R_o$ was calculated using the method in [17]. The outbreak data method assumes that the incidence of rabies cases grows exponentially during the early stages of an outbreak such that the number of cases during time $t$, $y(t) = ke^{vt}$, where, $v$ is the exponential growth rate parameter of the outbreak and $k$ is a constant. In equation 7, $1/\sigma$ is the average latent period, $1/\alpha$ is the life expectancy of a rabid dog, and $g$, the generation time of the rabies virus. Data used were from an outbreak that occurred in Sultan Hamud Sublocation during the one-year active surveillance study. The parameter $\beta$ was estimated by inversion of equation 5.

### Model predictions

#### Current situation

The deterministic model developed was run in a Corel Quattro Pro for Windows (Corel Corporation Limited, version 6.0) spreadsheet. Both the peri-urban and rural transmission scenarios were considered. As an initial assessment, transmission parameters estimated from field studies ([3] and [5]) were input in the model. The predicted incidence of rabies and $R_o$ were then compared to empirical field data.

#### Dog density

A key interest was to estimate the effect of dog density on rabies transmission. The threshold density of dogs required for transmission was estimated by the method of [12] using the equation:

$$K_T = (a + \sigma)(a + \alpha)/\beta\sigma$$  \quad (8)

For densities above $K_T$, the dog density ($K$) for rural and peri-urban areas was used as a variable to assess how alternative vaccination strategies performed under different dog densities.

#### Dog vaccination

The critical question with respect to rabies control by dog vaccination was what proportion ($p$) of the dog population at a given density must be vaccinated to prevent rabies transmission. This proportion was estimated [18] by:

$$p > 1 - 1/R_o$$  \quad (9)

where $R_o$ is the basic reproduction number as defined in equation (5).

Two vaccination regimes, an annual and a biannual “pulse” vaccination were assessed. For each, the vaccination period lasted 4 weeks and only susceptible dogs that had entered the population through births since the previous vaccination were vaccinated. As stated above, dogs were vaccinated only once as the immunity induced was assumed to be lifelong. The effects of vaccination were modelled at a weekly interval over a 2-year period and the outcome measure for the effectiveness of vaccination was the mean rabies prevalence over the 2 years.

### RESULTS

#### Parameter estimates

Five of the six sublocations were largely rural with dog densities ranging from 6–21 dogs km$^{-2}$ (mean 11 dogs km$^{-2}$). However, one sublocation (Kikambuani)
was markedly different from the others with an average of dog densities 10 times that of the other sublocations. This sublocation has the highest agricultural potential and is nearest to the capital city (Nairobi).

A cohort of 305 dogs of known ages was identified from the 150 households surveyed (182 males and 123 females). Half of the dogs were young, a year old or less and there were more males than females in all age classes. This was reflected by the uniformly lower survival rates for females compared to males. The life expectancy for dogs was estimated to be 2-9 years. During the year, 97 dogs died and 30 were withdrawn from the study for an annual estimated mortality rate of 0.33 (97/(305-30)/2).

Most (54%) female dogs had a litter during the year with a mean litter size of 4.7 puppies. Fecundity rates averaged 1.3 per year [5]. By combining the fecundity and survival data, a population growth rate (\( r \)) of 9% (4-14%, 95% confidence limits) was estimated.

The dog demography data and other epidemiological parameters used to explore the dynamics of the dog rabies model are displayed in Table 1. It was not possible to calculate the variance of the infective period (\( \alpha \)) since the data in [15] gives only the mean (0.814 weeks) and range (0.29–1.71 weeks) and so the estimate of S.E. (\( R_0 \)) excludes this source of error. The estimated mean population density of susceptible (S) dogs for the five mostly rural sublocations was 11 dogs km\(^{-2}\) and the highest recorded population density of 21 dogs km\(^{-2}\) was adapted as the carrying capacity (\( K \)) for the rural settings (Table 1). The dog population density of 110 dogs km\(^{-2}\) was used as the carrying capacity for peri-urban areas (Table 1).

### Table 1. Dog population and rabies parameters estimated for Machakos District, Kenya, 1992–3

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Variable</th>
<th>Estimate used</th>
<th>Standard error</th>
</tr>
</thead>
<tbody>
<tr>
<td>( b )</td>
<td>Per capita death rate</td>
<td>0.33 year(^{-1} )</td>
<td>0.027</td>
</tr>
<tr>
<td>( r )</td>
<td>Per capital population growth rate</td>
<td>0.09 year(^{-1} )</td>
<td>0.026</td>
</tr>
<tr>
<td>( a )</td>
<td>Per capita birth rate, ( r + b )</td>
<td>0.42 year(^{-1} )</td>
<td>0.287</td>
</tr>
<tr>
<td>( K )</td>
<td>Mean habitat carrying capacity</td>
<td>Rural (( K = 21 \text{ dogs km}^{-2} ))</td>
<td>11.55</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peri-urban (( K = 110 \text{ dogs km}^{-2} ))</td>
<td>6.66</td>
</tr>
<tr>
<td>( \beta )</td>
<td>Transmission coefficient</td>
<td>14.68 km(^2) year(^{-1} )</td>
<td>11.55</td>
</tr>
<tr>
<td>( \sigma )</td>
<td>1/( \sigma ) is the average latent period</td>
<td>12.44 year(^{-1} )</td>
<td>6.66</td>
</tr>
<tr>
<td>( \alpha )</td>
<td>Death rate of rabid dogs</td>
<td>63.88 year(^{-1} )</td>
<td></td>
</tr>
<tr>
<td>( q )</td>
<td>Proportion vaccinated</td>
<td>0.24</td>
<td>0.024</td>
</tr>
</tbody>
</table>

During the course of the one-year surveillance for rabies in Machakos, the number of confirmed secondary cases exposed to a confirmed primary case and the basic reproduction number (\( R_0 \)) per sublocation are shown in Table 2. There was no association between dog densities per sublocation and \( R_0 \). The sublocation with the lowest dog density of six dogs km\(^{-2}\) (Sultan Hamud) had the highest \( R_0 \) (Table 2). Overall, 30 confirmed secondary cases were exposed by 14 primary cases for an \( R_0 \) value of 2.14 (1.4–2.88, 95% confidence limits).

The local rabies outbreak used for the other estimation of \( R_0 \) is shown in Figure 1. The exponential growth (\( e \)) of the epidemic peaked after 14 weeks and it comprised of 24 confirmed rabid dogs. The estimated \( e \) of the epidemic was 0.15 with a S.E. of 0.056 and \( R_0 \) was 1.85 with a S.E. of 0.47. Since the outbreak occurred in a population of partially vaccinated dogs (24% vaccination cover), \( R_0 \) was

### Table 2. THE NUMBER OF CONFIRMED SECONDARY CASES/PRIMARY CASE AND BASIC REPRODUCTION NUMBER (\( R_0 \)) BY SUBLOCATION IN MACHAKOS DISTRICT, KENYA, 1992–3

<table>
<thead>
<tr>
<th>Sublocation</th>
<th>Number of secondary/primary cases</th>
<th>Basic reproduction number (( R_0 ))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kikambuani</td>
<td>2/1</td>
<td>2.00</td>
</tr>
<tr>
<td>Sultan Hamud</td>
<td>19/6</td>
<td>3.17</td>
</tr>
<tr>
<td>Ngoni</td>
<td>3/3</td>
<td>1.00</td>
</tr>
<tr>
<td>Muvau</td>
<td>2/1</td>
<td>2.00</td>
</tr>
<tr>
<td>Ikombe</td>
<td>4/3</td>
<td>1.33</td>
</tr>
<tr>
<td>Total or average</td>
<td>30/14</td>
<td>2.14</td>
</tr>
</tbody>
</table>
corrected upwards by dividing by the proportion of dogs that was unvaccinated (76%) prior to the outbreak giving a point estimate of 2–44 (1.52–3.36, 95% confidence limits). Since the two methods for the estimation of $R_0$ gave comparable values (2.14 and 2.44), the $R_0$ value obtained using the latter method was adopted because it is largest and so gives most conservative estimates of $p$.

**Model predictions**

**Current situation**

The model predicted that, using the parameter values listed in Table 1, annual vaccination rates of 24%, the estimate for Machakos District [5], applied over a long time increased the stability of the association between rabies and dogs leading to the endemic establishment of rabies characterized by only minor fluctuations in prevalence levels and dog density. This is displayed in Figure 2 where a comparison of rabies prevalence and dog density in a rural setting is made with and without vaccination. Thus, the model predicts that low levels of vaccination will greatly reduce the amplitude of oscillations in incidence of rabies, as well as reduce the period of the cycles.

**Dog density**

Since the estimated $R_0$ value for both the rural areas and the peri-urban area were comparable (Table 2), the $R_0$ value of 2.44 was adapted for both scenarios. Under these settings, the model predicted that there is a threshold density ($K_T$) below which rabies will not persist in the population. This threshold density is given by equation 8. The parameter values listed in Table 1 gave a $K_T$ value of 4.5 dogs km$^{-2}$ (3.8–5.2, 95% confidence limits). Thus, the model predicted that rabies would not persist where the carrying capacity ($K$) of the environment was below 4.5 dogs km$^{-2}$.

**Dog vaccination**

For the effective control of rabies, two different vaccination scenarios were tested, an annual vaccination campaign and a bi-annual vaccination programme. The model predicted that low vaccination rates for both scenarios had no impact at all in reducing the mean rabies prevalence in 2 years (Fig. 3). For an annual vaccination campaign, the current programme in Machakos District, the model predicted that vaccination coverage of approximately 70% would be required for the effective protection of dogs against rabies with 95% confidence ($p$ of 59% with 95% confidence limits of 34–70%) (Fig. 3). However, when the vaccination frequency was increased to twice per year, a vaccination rate of approximately 60% was adequate for the same purpose ($p$ of 45% with 95% confidence limits of 14–60%). The model did not have a stochastic component and so the prob-
Predicted rabies prevalence, current vaccination coverage versus no vaccination

Predicted dog density, current vaccination coverage versus no vaccination

Fig. 2. A comparison of the effect of low annual vaccination rates and no vaccination on rabies prevalence and dog density.

Fig. 3. A comparison of mean dog rabies prevalence over 2 years under yearly and twice yearly vaccination coverage in rural and peri-urban areas.

ability of rabies extinction during the periods of very low prevalence could not be estimated.

DISCUSSION

The relatively simple model framework used in this study provided predictions which were consistent with field observations both for the Machakos District dog population and for other rural African sites.

The two estimates of the basic reproduction number ($R_0$), 2.14 and 2.44, were consistent with estimates obtained from four rabies outbreaks across a range of rural and urban settings (1.63–2.33) [11]. While one might expect that $R_0$ estimates should vary with dog density and/or population size [19], with larger values of $R_0$ for larger and denser dog populations, published estimates (summarized in [11]) do not clearly exhibit this trend for populations with rabies. This is a topic requiring further study, so that vaccination coverages for different sizes and densities of dog populations can be appropriately planned.

The model predicted threshold dog density below which rabies would not persist in the Machakos dog population. The predicted $K_T$ in this study was in
broad agreement with field observations in Machakos and other areas of sub Saharan Africa. In the Serengeti District in Tanzania, rabies appears to be endemic in dog populations which exceed 5 dogs km$^{-2}$ but not in others having approximately 1 dog km$^{-2}$ [10]. In Zimbabwe, dog rabies has persisted in communal lands with mean densities of six dogs km$^{-2}$ [15, 20] but not in commercial farming areas of lower dog densities. Similarly, dog rabies in South Africa occurs in higher dog density areas and does not persist in adjacent areas with dog densities of 1–4 dogs km$^{-2}$ [21]. The threshold density for rabies persistence and the relationship between density and transmission noted, implies that, if all other conditions are equal, rabies control efforts should be focussed on areas of higher dog density.

In addition, the estimated proportion ($p$) (59%; 34–70%, 95% confidence limits) of dogs in Machakos requiring vaccination was consistent with empirical [22, 23] and model based [11] estimates for the control of rabies in different dog populations. Most estimates of required vaccination coverage, as in this study, are based on small sample sizes. At an annual vaccination rate of 24%, a vaccination coverage estimated for the Machakos dog population for the year 1992 [5], the model predicted that rabies would level to an endemic equilibrium with only slight fluctuations in prevalence (Fig. 2). Thus, low vaccination rates reduce the amplitude of oscillations in incidence of rabies as well as reducing the period of the cycles. Both these effects of vaccination will tend to increase stability and decrease the likelihood of stochastic “fadeout” of the disease [6]. This prediction is in broad agreement with what has been observed in Machakos since rabies was first reported there in 1956 [2]. Historical data from a 10-year period (1981–90) [3] suggest only minor fluctuations in rabies incidence with cycles of 3–4 years. Similar low amplitude 3–5 year cycles in partially vaccinated dog populations have been observed in South Africa [21] and Tunisia [24].

Theoretically, increasing vaccination rates is expected to lower rabies prevalence. This effect is illustrated in Figure 3 where the prevalence of rabies decreased almost linearly with increased annual and bi-annual vaccination rates. Although the model predicts that for the effective control of rabies 70% of the dogs have to be protected by vaccination at any one time (to exceed the upper 95% confidence limit of proportion vaccinated), herd immunity would wane in the period between vaccination campaigns, mainly due to susceptible dogs entering the population by birth. Increasing vaccination frequency to twice per year decreases the vaccination coverage to approximately 60% using the same criteria. This difference in vaccination coverage associated with increasing vaccination frequency reflects the young age and very high turnover of the susceptible dog population [5]. In Machakos, only 50% of dogs survive to one year of age.

The effectiveness of high vaccination rates in the reduction of rabies incidence, as predicted by the model, has been demonstrated in Tunisia [24], Brazil [25], and Peru [26] where one-time mass dog vaccination campaigns achieving vaccination coverages of 78–88% led to near zero incidences of rabies in both humans and animals. However, experiences from these mass vaccination campaigns indicate that achieving such high proportions of the dog population were a tremendous challenge, logistically and financially, even as a single exercise. Operational research is required to compare, using field trials, the feasibility and sustainability of annual vaccination campaigns requiring high vaccination coverage versus bi-annual vaccination requiring lower coverage.

In conclusion, the predictions of the deterministic rabies transmission model developed were very consistent with field observations of the threshold density for rabies persistence, the incidence of rabies in Machakos, the cyclic behaviour in rabies incidence in partially vaccinated dog populations, and the probable vaccination coverage required to prevent rabies transmission. The fact that the model predicts well these important features of rabies epidemiology implies that it is worthy of further study and elaboration. A few priority aspects to be considered in future include: the role of rabies introduction from outside the District by dogs or wildlife, the differences in vaccination coverage required for the range of dog density situations found in Machakos (from 6–110 dogs km$^{-2}$) and the impact of increasing vaccination frequency. The latter two issues need to be assessed by community-level rabies control trials to see if these predictions hold true or whether a more detailed transmission framework needs to be adopted.

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