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Estimating human rabies mortality in the United Republic of Tanzania from dog bite injuries

Sarah Cleaveland,¹ Eric M. Fèvre,² Magai Kaare,³ & Paul G. Coleman⁴

Objective To make quantitative predictions about the magnitude of underreporting of human rabies deaths in the United Republic of Tanzania.

Methods Human rabies deaths were estimated by using a series of probability steps to calculate the likelihood of rabies developing after the bite of a suspected rabid dog, incorporating field data on the incidence of animal bite injuries, the accuracy of rabies recognition, the distribution of bite wounds, and post-exposure treatment.

Findings Predicted human rabies mortality was estimated to be (a) 1499 deaths per year (95% confidence interval 891–2238), equivalent to an annual incidence of 4.9 (2.9–7.2) deaths/100 000, when active surveillance data on bite incidence were used, and (b) 193 deaths per year (32–409), corresponding to an annual incidence of 0.62 (0.1–1.32) deaths/100 000, when national bite statistics were used. The annual mean number of rabies deaths officially recorded for the same period was 10.8 (7.7–14.0).

Conclusion In the United Republic of Tanzania, cases of rabies in humans have been greatly underreported. Dog bite injuries are an accessible source of epidemiological data that may be used to estimate the public health burden of rabies and to monitor epidemiological trends in developing countries.

Keywords Rabies/mortality/epidemiology; Dogs; Bites and stings/mortalité; Epidemiologic surveillance; Probability; Risk factors; United Republic of the United Republic of Tanzania (*source: MeSH, NLM*).

Mots clés Rage (Maladie)/mortalité/épidémiologie; Chien; Morsure et piqure/mortalité; Surveillance épidémiologique; Probabilité; Facteur risque; République-Unie de Tanzanie (*source: MeSH, INSERM*).

Palabras clave Rabia/mortalidad/epidemiología; Perros; Mordeduras y picaduras/mortalidad; Vigilancia epidemiológica; Probabilidad; Factores de riesgo; República Unida de Tanzania (*fuentes: DeCS, BIREME*).

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Voir page 309 le résumé en français. En la página 309 figura un resumen en español.

Introduction

Globally, rabies is considered to be a relatively insignificant human disease, accounting for only 1% of deaths attributable to infectious diseases (1). However, there is widespread recognition that the number of deaths officially reported in much of Africa does not reflect the true incidence of the disease. There have been many inconsistencies in the reported incidence of human rabies. For example, the 1996 World Survey of Rabies (2) recorded a global total of 33 212 cases, of which 238 were in Africa and 32 772 in Asia. In Ethiopia, 464 human cases were reported in Addis Ababa between 1992 and 1993 (3), whereas in the entire country only 26 and 35 cases were officially reported to the World Health Organization in 1992 (4) and 1993 (5) respectively.

Several explanations for underreporting have been proposed: patients with clinical rabies may stay at home or seek treatment from local healers; most cases do not receive laboratory confirmation; causes of death may be recorded locally but are not transmitted to the central authorities; a small

proportion of deaths attributable to rabies may not be recognized as such by medical staff (1, 6–9).

Many of these problems are clearly not unique to rabies. The poor quality of much public health information in sub-Saharan Africa has prompted several recent investigations into the distribution of major infectious diseases and the mortality and morbidity attributable to them. For example, climatological data together with models of acquired immunity have been used to estimate malaria mortality in sub-Saharan Africa (10). In countries with relatively poor data on tuberculosis, a consensus process has been used to provide plausible estimates of mortality caused by this disease (11). Other extrapolative work has been carried out in order to quantify the populations at risk from diseases such as meningitis and filariasis. This has involved the use of environmental and climatological surrogates from which the distribution and burden of disease have been inferred (12, 13).

Attempts to estimate the true scale of human mortality caused by rabies have been carried out only in India (2), Ethiopia (3) and a few other countries, and they are generally

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considered to have involved making well-informed guesses. We describe an approach to estimating human rabies mortality in the United Republic of Tanzania, using empirical data on the incidence and distribution of dog bite injuries, the accuracy of rabies recognition and the levels of post-exposure treatment, together with published data on the proportion of bite victims that develop clinical disease.

The fear of developing rabies provides a powerful incentive for people to report animal bite injuries to hospitals, particularly when human post-exposure treatment is available (14, 15). Records of bite injuries from rabid animals may thus provide an accessible source of epidemiological data on rabies, which, in the United Republic of Tanzania, are routinely reported from district hospitals to the central authorities.

Not all bites from rabid dogs result in rabies. Not every bite results in infection and not every infection leads to 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. Bites on the head, face and neck, for example, carry a much higher risk than bites on a foot or leg (8, 16–20). We use the distribution of injuries to predict the outcomes of bites of rabid dogs.

Methods

The calculation of the predicted number of human rabies deaths in the United Republic of Tanzania is based on a series of probability steps, $P1$ to $P10$ (Fig. 1).

Step 1: Incidence of animal bite injuries

Incidence data for animal bite injuries were obtained from national statistics held by the Ministry of Agriculture and Cooperatives (1990–96) for the whole of the United Republic of Tanzania (21, 22) and from 24 villages within the Mara Region in

the north-west of the country where rabies awareness had been improved through community-based active surveillance and education programmes (15). For the same period, official data on human deaths were obtained from the Ministry of Health (23). In order to collect active surveillance data, community-based programmes were established in 24 villages selected at random from the midland zone of the Mara Region, a relatively homogeneous area of agropastoral land use, with a human population density of 40 inhabitants per square kilometre (15, 24, 25). Over a 14-month period in 1998–99 the number of bite injury cases in these villages was determined from records maintained at government district hospitals and veterinary offices. Whether or not the animals that inflicted bites were defined as suspected of being rabid was determined by the examining medical officers on the basis of the patients' history and/or reports from veterinary field officers.

Step 2 ($P1$): Rabies recognition probability

Data were collected from villages in the active surveillance studies on the proportion of suspect animal rabies cases that were subsequently confirmed by laboratory diagnosis. Whenever possible, brain stem samples of suspect rabid animals were obtained by livestock field officers using WHO collection kits (26). Rabies diagnosis was conducted at the Agence Française de Sécurité Sanitaire des Aliments, Nancy, France (a WHO rabies collaborating centre) and at the Onderstepoort Veterinary Institute, South Africa, using immunofluorescence diagnostic tests (27). An animal was classified as suspect if reported as such on submission of the sample. In the absence of this information a case was defined as suspect if the reported history included neurological signs and/or unprovoked aggression. We deliberately adopted a broad classification so that any biases would underestimate rather than overestimate the rabies recognition probability.

Step 3 ($P2$ – $P5$): Distribution of bite injuries

Bite injury data collected from three district hospitals in the Mara Region from 1993 to 1998 were classified according to the distribution of bite injuries on the body, the age of the victim, and the sex and status of the dog, whether or not it was suspected of being rabid. For patients bitten at multiple sites the bite wound was classified according to the site of highest risk (see Step 4).

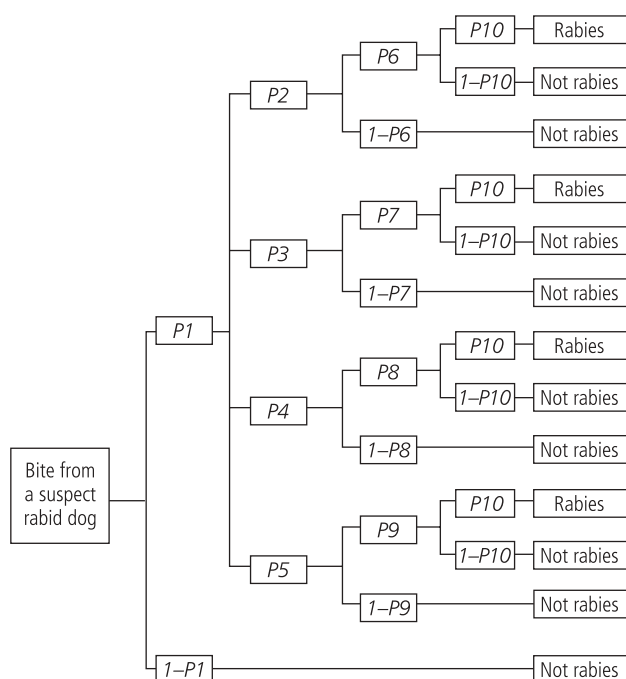
Step 4 ($P6$ – $P9$): Probability of developing rabies following the bite of a rabid dog

In order to estimate the likelihood of a person developing rabies following the bite of a rabid dog we were guided by data from the published literature describing the outcome of untreated bite injuries produced by dogs that had been confirmed as rabid (8, 16). These data indicated that, if left untreated, 30–60% of people bitten on the head, face or neck would develop rabies, whereas the expected mortality was 15–40% following bites on the hand and 0–10% following bites on the trunk and leg. Triangular distributions were assigned to these probabilities and the mode was taken as the midpoint between the minimum and maximum.

Step 5 ($P10$): Probability of receiving post-exposure treatment

Vaccine availability was determined from Mara Region hospital records for 1993–97. Data from 1998 and 1999 were excluded

Fig. 1. Decision tree for determining probability of rabies death following the bite of a suspect rabid dog (probabilities $P1$ – $P10$ are defined in Table 1)



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because additional human vaccine was provided by research projects and was thus not representative of the situation in the United Republic of Tanzania as a whole. To be conservative in our estimate of human deaths we assumed that any patient receiving post-exposure treatment would not develop rabies, regardless of the number of vaccine doses received or the interval between the bite injury and the start of treatment.

Population at risk

Population projections based on 1988 government census data were used to estimate the population at risk when calculating incidence figures from both national bite statistics and from data obtained in villages in the active surveillance study (24).

Predicting human rabies deaths

We calculated the probability of dying of rabies following a bite from a suspected rabid dog, P_{Death} , from the probability tree (Fig. 1) as:

$$P_{\text{Death}} = P1 \times [(P2 \times P6) + (P3 \times P7) + (P4 \times P8) + (P5 \times P9)] \times (1 - P10).$$

If the incidence of suspected rabid dog bites per 100 000 per year is i and the population at risk is Q , then the total number of deaths caused by rabies per year is given by $(i \times Q \times P_{\text{Death}})/100\,000$.

The total number of rabies deaths per year was calculated using projected 1998 population figures (i.e. $Q = 30.9$ million). We estimated confidence limits for the total number of deaths attributable to rabies by attaching probability distributions to the input parameters (i and $P1 - P10$, Table 1) and running Monte Carlo simulations using Palisade @RISK software (Windows version 1.0, Palisade 1997) for 3000 iterations. At each iteration the value of each input parameter was chosen at random from within the defined probability distribution. The mean and range within which 95% of the total rabies mortality estimates fell were recorded using the suspected rabid dog bite incidence values from both the national statistics and the active surveillance study.

Results

Incidence of dog bite injuries

National statistics

Between 1990 and 1996 a total of 23 709 bite injuries were reported from suspect rabid animals in the United Republic of Tanzania, giving a mean of 3387 (1779–4994) cases per year. The mean annual bite incidence was 12.5 (6.7–18.3) cases per 100 000.

Mara Region

In the Mara Region the vast majority of bites reported to district hospitals were inflicted by dogs (96.6%, $n = 964$). Where the status of the dog was recorded, 685/914 dogs (74.9%) were classified as suspect rabies cases. The age distribution of bite victims differed significantly from that of the general population of the Mara Region ($\chi^2 = 103.4$, degrees of freedom = 14, $P < 0.001$): an elevated proportion of children in the age range 5–15 years was bitten by suspect rabid dogs (Fig. 2). Within the active surveillance area, which covered a total human population of 81 725, an average of 84.9 (41.0–128.9) suspected rabid dog bites per year were recorded, corresponding to an annual incidence of 103.9 (50.1–157.7) bite injuries/100 000.

Table 1. Probability distributions of parameters used in Monte Carlo simulations

Variable	Estimate
A. Suspected rabid dog bite incidence	
National incidence of suspected rabid dog bites per 100 000 per year	Triangular: minimum = 6.7, mode = 12.5, maximum = 18.3
Number of bites injuries per year in active surveillance areas, (N)	Poisson: mean = 84.9
Average population at risk in active surveillance areas, R(R)	Point estimate: 81 725
The annual incidence per 100 000 of suspected rabid dog bites in the active surveillance area is calculated as $100\,000 \times N/R$	
B. Probability tree parameters (P1–P10)	
P1 Suspected rabid dog being rabid	Binomial: $p = 0.680$, $n = 25$
P2 Bite injury to the head	Point estimate: 0.070 (22/315)
P3 Bite injury to the arms	Point estimate: 0.384 (121/315)
P4 Bite injury to the trunk	Point estimate: 0.060 (19/315)
P5 Bite injury to the legs	Point estimate: 0.486 (153/315)
P6 Development of rabies following bite injury to the head	Triangular: minimum = 0.03, mode = 0.45, maximum = 0.6
P7 Development of rabies following bite injury to the arms	Triangular: minimum = 0.275, mode = 0.15, maximum = 0.4
P8 Development of rabies following bite injury to the trunk	Triangular: minimum = 0.05, mode = 0.0, maximum = 0.1
P9 Development of rabies following bite injury to the leg	Triangular: minimum = 0.05, mode = 0.0, maximum = 0.1
P10 Probability of receiving post-exposure treatment if bitten by a suspected rabid dog	Binomial: $p = 0.563$, $n = 487$

Rabies recognition probability (P1)

Within the active surveillance areas, 25 samples taken from dogs defined as suspect rabies cases were submitted for laboratory diagnosis. Of these, 17 (68.0%) were confirmed positive by immunofluorescence.

Distribution of bite injuries (P2–P5)

Bite injuries were reported more frequently on the head and hands, and less frequently on the legs, of people bitten by suspect rabid dogs than of people bitten by non-suspect rabid dogs ($\chi^2 = 32.7$, degrees of freedom = 3, $P < .001$). We therefore used the distribution of bite injuries from suspect rabid dogs only (Table 1).

Post-exposure treatment (P10)

At least one dose of post-exposure rabies vaccine was given to 274/487 (56.3%) patients reporting bites from suspect rabid dogs. The interval between bite injury and presentation for treatment ranged from 0 to 171 days (median = 3 days).

Human rabies deaths

From 1990 to 1996 the mean number of officially reported rabies deaths was 10.8 (7.7–14.0) per year, corresponding to an average incidence of 0.041 (0.028–0.053) deaths/100 000 per year.

Table 2. Age distribution of the annual incidence of rabies deaths predicted on basis of active surveillance data and on the national bite incidence data from official records

Age class	Rabies mortality predicted on basis of active surveillance data Deaths/100 000/year	Rabies mortality predicted on basis of national bite incidence data Deaths/100 000/year
0–4 years	3.23 (2.01–4.73)	0.42 (0.07–0.87)
5–9 years	7.23 (4.44–10.63)	0.93 (0.16–1.97)
10–14 years	7.36 (4.24–11.34)	0.95 (0.16–2.05)
> 15 years	3.92 (2.30–5.98)	0.50 (0.08–1.08)
ALL	4.85 (2.88–7.24)	0.62 (0.10–1.32)

Predicted human rabies deaths

On the basis of extrapolating bite incidence data from active surveillance areas to the whole of the United Republic of Tanzania, 1499 (891–2238) human rabies deaths were predicted per year, equivalent to an annual incidence of 4.9 (2.88–7.24) deaths/100 000. The value of $P1$ for which the estimated number of deaths was equal to the official number recorded was 0.006 (0.003–0.010) (Fig. 3). The distribution of predicted deaths by age class is shown in Table 2. Predicted rabies deaths were highest in the age range 5–15 years.

On the basis of the national statistics on bites the annual number of deaths caused by rabies was estimated as 193 (32–409). This was equivalent to an annual incidence of 0.62 (0.1–1.32) deaths/100 000. The value of $P1$ for which the estimated number of deaths was equal to the mean official number recorded was 0.119 (0.019–0.26) (Fig. 3).

Discussion

Rabies clearly emerges as a significant public health problem in the United Republic of Tanzania. The incidence of human rabies predicted on the basis of active surveillance data on bite incidence (4.9 deaths/100 000) was up to 100 times greater than that officially recorded. Furthermore, dog bite records provide an accessible and valuable source of epidemiological data that have generally been underexploited.

Although much higher than incidence figures derived from government data, our estimate is similar to the annual incidence of 2.5 human rabies deaths/100 000 reported during active surveillance studies in Kenya's Machakos District (14).

The validity of these indirect estimates of human rabies mortality depends on two key assumptions. The first, which applies to both of our estimates, is that the proportion of untreated people dying in the United Republic of Tanzania following a bite on the head, hand, trunk and limbs is similar to that reported in Europe and Asia in the 20th century (8, 16). The second, which applies only to estimates based on active surveillance studies, is that data from the Mara Region are representative of the United Republic of Tanzania as a whole.

Fig. 2. Age distribution of patients bitten by suspect rabid dogs ($n = 615$) in relation to the Mara Region population as a whole ($n = 970\ 942$)

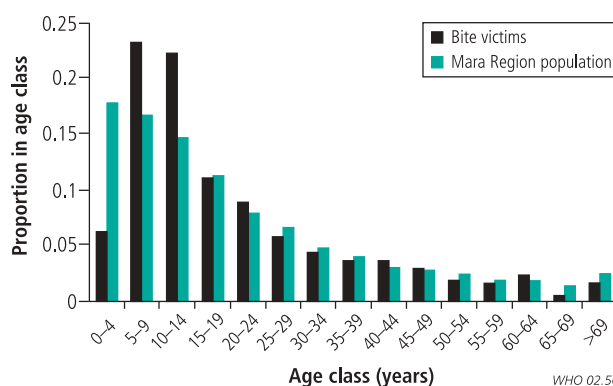
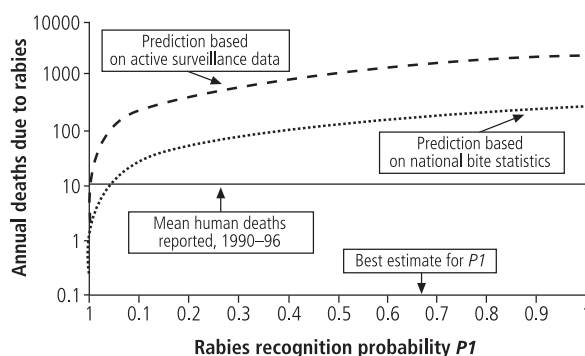


Fig. 3. Predicted annual human rabies deaths in the United Republic of Tanzania in relation to rabies recognition probability $P1$ and the number of deaths officially recorded



Regarding the development of clinical rabies, factors such as wound severity, the proportion of rabid dogs excreting virus, and viral pathogenicity could influence the outcome of exposure (8). As hospital records in this study provided insufficient data on the severity of wounds, we assumed that all reported bites involved penetration of the skin and were not superficial scratches or licks, which would carry a lower risk. We considered this a reasonable assumption since the difficulty and expense of travelling in rural areas of the United Republic of Tanzania made it unlikely that people who had sustained only minor scratches would travel to hospital.

Field data on the excretion of virus in saliva are very limited. However, samples of salivary glands collected from four rabid dogs in this study were all antigen-positive on immunofluorescence. It is not possible to determine if differences between strains of virus influence the proportion of humans who develop rabies after exposure but there is currently no evidence that the Africa-1b canid strain of rabies isolated from Tanzanian dogs (28) is less pathogenic than other isolates obtained from dogs.

Wherever the likely direction of bias in parameter estimates could be anticipated, e.g. in the administration of post-exposure treatment, we have tried to be conservative in our calculations. For some of the parameters, such as the rabies recognition probability ($P1$), multiple sources of variation in both the clinical signs and the likelihood of killing and sampling

suspected rabid dogs make it difficult to predict whether our value overestimates or underestimates the true probability. Nonetheless, by assigning probability distributions to each parameter in the Monte Carlo simulation we have been able to set limits on the uncertainties at each step of the process and produce robust confidence intervals for the final estimate of mortality. A number of approaches could be adopted in order to validate these estimates in the field, including trace-back studies to determine the survival of untreated bite victims and the collection of verbal autopsy data from household surveys. However, both approaches are likely to be more time-consuming and costly than that of obtaining data on bite wounds. Particular care would be needed when interpreting verbal autopsy data, as many cases of human rabies in rural Africa are perceived as being caused by sorcery rather than disease (29).

Caution clearly has to be exercised in extrapolating data on the incidence of animal bites in the Mara Region to the whole of the United Republic of Tanzania. Although rabies is reported throughout the country, patterns of infection are likely to vary between regions. In north-western United Republic of Tanzania, for example, dog rabies is endemic in the Mara Region but only sporadic in the adjacent Ngorongoro District (30). Cultural and religious factors may influence patterns of dog ownership and knowledge of rabies, which may in turn affect patterns of disease, recognition of rabies in local communities, and the probability of seeking post-exposure treatment in hospitals. Nonetheless, patterns of land use and human population densities throughout rural United Republic of Tanzania are relatively homogeneous as a result of the *Ujamaa* process of village development that followed independence, and the characteristics of the Mara Region are broadly typical of rural United Republic of Tanzania, where more than 81% of the population live (24). Furthermore, the annual figures for the incidence of animal bites in the Mara Region are comparable to those reported in similar areas of rural Kenya (234 bites/100 000) (14). In order to provide a preliminary estimate of human rabies mortality for the United Republic of Tanzania as a whole, we therefore consider it reasonable to extrapolate from the Mara Region data, given the caveats outlined above.

Even without extrapolating across regions, i.e. when using national statistics on bite injuries, the predicted incidence of human rabies (0.62 deaths/100 000) was 10 times higher than that officially reported. The number of official cases would only exceed the predicted number of human deaths if fewer than 12% of suspect rabid dogs were truly rabid (17), a level well below that recorded here (68%) and in studies in Kenya (51–58%) (14, 31), Swaziland (50%) (32) and Zimbabwe (36%) (33).

Our prediction that rabies mortality is highest in children is consistent with the age distributions of cases reported in the Philippines (34), Ethiopia (35, 36) and the USA in the mid-20th century (37). A high proportion of childhood deaths increases the number of disability-adjusted life years lost and therefore

the public health burden of a disease (38). Although rabies was not included in the first global burden of disease survey (39), recent global estimates of disability-adjusted life years lost for rabies place the disease in eighty-sixth position with respect to public health burden (40). This is undoubtedly a low estimate as it is based on the incidence of officially reported cases only.

The public health burden of rabies is not limited to mortality or disability-adjusted life years lost to disease. There are additional arguments in favour of increasing the resources available for rabies control (9). The high cost of human post-exposure treatment is a major economic burden on public health budgets (1, 41, 42) and fear of the disease causes considerable psychological trauma in communities. Human rabies is entirely preventable through appropriate post-exposure treatment or vaccination of reservoir hosts. However, no successful national rabies control programmes have been implemented in Africa over the past two decades. The reasons for this are manifold (43). A lack of awareness of the magnitude of the rabies problem and a lack of data on epidemiological trends serve only to exacerbate the difficulties, hampering the development of disease control initiatives.

This study demonstrates that data on bite injuries provide a useful and accessible source of epidemiological information that could be used effectively to enhance rabies surveillance in human and animal populations, detect trends in disease incidence, improve the allocation of medical and veterinary resources, and assess the impacts of rabies control measures. ■

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Conflicts of interest: none declared.

Résumé

Estimation de la mortalité par rage humaine consécutive à une morsure de chien en République-Unie de Tanzanie

Objectif Etablir des prévisions chiffrées sur l'ampleur de la sous-notification des décès par rage humaine en République-Unie de Tanzanie.

Méthodes Les décès par rage humaine ont été estimés selon une série d'étapes de calcul permettant de déterminer la probabilité de contracter la rage après morsure d'un chien suspect, compte tenu des données de terrain sur l'incidence des lésions par morsure d'animal, de l'exactitude du diagnostic de rage, de la distribution des lésions par morsure et du traitement après exposition.

Résultats La mortalité prévue par rage humaine a été estimée à 1499 décès par an (intervalle de confiance à 95 % : 891-2238), soit une incidence annuelle de 4,9 (2,9-7,2) décès/100 000 ha-

bitants lorsqu'on utilisait les données de la surveillance active de l'incidence des morsures, et à 193 (32-409) décès par an, soit une incidence annuelle de 0,62 (0,1-1,32) décès/100 000 habitants lorsqu'on utilisait les statistiques nationales concernant les morsures. La moyenne annuelle officielle pour la même période était de 10,8 (7,7-14,0) décès par rage.

Conclusion En République-Unie de Tanzanie, les cas de rage humaine sont très largement sous-notifiés. Les lésions par morsure de chien sont une source accessible de données épidémiologiques qui peuvent être utilisées pour estimer le poids de la rage en santé publique et surveiller les tendances épidémiologiques dans les pays en développement.

Resumen

Estimación de la mortalidad por rabia humana causada por mordeduras de perro en la República Unida de Tanzania

Objetivo Hacer predicciones cuantitativas sobre la magnitud de la subnotificación de las defunciones por rabia humana en la República Unida de Tanzania.

Métodos Se estimó la mortalidad por rabia humana usando una serie de pasos probabilísticos para calcular el riesgo de desarrollar rabia tras la mordedura de un perro presuntamente rabioso; a ese fin, se incorporaron datos de campo sobre la incidencia de mordeduras, la precisión del diagnóstico de la rabia, la distribución de las mordeduras y el tratamiento posterior a la exposición.

Resultados Según las predicciones efectuadas, usando los datos aportados por la vigilancia activa de las mordeduras la mortalidad ascendía a (a) 1499 defunciones al año (intervalo de confianza (IC) 95%: 891-2238), lo que equivale a una incidencia anual de

4,9 (2,9-7,2) defunciones/100 000; al emplear las estadísticas nacionales sobre mordeduras, en cambio, se obtenían 193 defunciones anuales (32-409), lo que se traduce en una incidencia anual de 0,62 (0,1-1,32) defunciones /100 000. La media anual oficial para el mismo periodo fue de 10,8 (7,7-14,0) muertes por rabia.

Conclusión En la República Unida de Tanzania, la notificación de los casos de rabia humana ha estado muy por debajo de las cifras reales. La información sobre las lesiones por mordedura de perro es una fuente accesible de datos epidemiológicos que pueden utilizarse para estimar la carga de salud pública que supone la rabia y para vigilar las tendencias epidemiológicas en los países en desarrollo.

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