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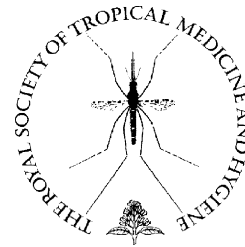**ScienceDirect**

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Density-dependent host choice by disease vectors: epidemiological implications of the ideal free distribution

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Summary   The proportion of vector blood meals taken on humans (the human blood index, h) appears as a squared term in classical expressions of the basic reproduction ratio (R_0) for vector-borne infections. Consequently, R_0 varies non-linearly with h. Estimates of h, however, constitute mere snapshots of a parameter that is predicted, from evolutionary theory, to vary with vector and host abundance. We test this prediction using a population dynamics model of river blindness assuming that, before initiation of vector control or chemotherapy, recorded measures of vector density and human infection accurately represent endemic equilibrium. We obtain values of h that satisfy the condition that the effective reproduction ratio (R_e) must equal 1 at equilibrium. Values of h thus obtained decrease with vector density, decrease with the vector:human ratio and make R_0 respond non-linearly rather than increase linearly with vector density. We conclude that if vectors are less able to obtain human blood meals as their density increases, antivectorial measures may not lead to proportional reductions in R_0 until very low vector levels are achieved. Density dependence in the contact rate of infectious diseases transmitted by insects may be an important non-linear process with implications for their epidemiology and control.
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1. Introduction

Transmission models that successfully predict infection prevalence and intensity in host populations are important tools for predicting the impact on transmission dynamics of ecological change as well as for understanding the causes of control failure. The realised or effective (as opposed to innate) vector feeding preference for the host species affected by the pathogen in question (in this paper the human host) is a critical component of models of vector-borne diseases, and in particular of those transmitted by dipteran insects (Randolph, 1998). The proportion of blood meals taken on humans, denoted here by parameter h (Basáñez et al., 2002), is one of the constituents of the per vector biting rate on humans and is also known as the human blood index (Garrett-Jones, 1964).

The basic reproduction ratio (R_0) is the average number of secondary cases arising, during the infectious period, from an infectious case introduced into a wholly susceptible population (Anderson and May, 1991). In such composite measures of pathogen transmission success for vector-borne diseases, the proportion of blood meals taken on humans appears as a squared term, since vectors must bite at least twice to acquire the pathogen and transmit it after completion of the extrinsic incubation period. This signifies that R_0 varies non-linearly with vector host choice. At present, effective host preference is treated in most existing disease transmission models as a fixed proportion of vectors feeding on humans (Bailey, 1982), and as a result R_0 is linearly related to measures of vector density such as the annual biting rate (ABR) (Basáñez and Boussinesq, 1999; Dietz, 1982).

The ABR consists of the product of the vector:human ratio (V/H), the number of bites per unit time per vector and the human blood index h (Dye, 1992), and is usually measured as a compound single parameter by collecting host-seeking vectors coming to feed on human attractants (Duke, 1968; Dye, 1986). Estimations of h are usually based on snapshot samples ignoring its possible temporal and spatial variation. In reality, vectors are probably flexibly anthropophagic or zoophagic, with the human blood index h varying between 0 and 1 depending on intrinsic vector-specific propensities to feed on particular host species. Also, the human blood index will depend on the relative abundance of preferred and maintenance hosts, overall vector abundance, defensive host behaviour and other determinants of density-dependent feeding success (Kelly and Thompson, 2000). It is well known, for instance, that certain species of *Culex* mosquitoes shift host preference seasonally between large mammals, birds and humans, with important consequences to the epidemiology of the viruses they transmit (Apperson et al., 2004).

At its simplest, effective host preference will vary with the relative abundance of non-human and human hosts, and R_0 will exhibit only weak non-linear responses as a result of the squared term (Killeen et al., 2001). However, effective host preference may also vary with the ratio of vectors to hosts (Gurtler et al., 1997). This is predicted to be a strongly non-linear relationship, and R_0 must also vary non-linearly with vector abundance in addition to varying with the ratio of host abundances (Kelly and Thompson, 2000). The question is, therefore, of applied interest. Control strategies that seek to reduce vector abundance will have very different impacts on disease transmission depending on the shape of the relationship between R_0 and the vector:host ratio. The same applies to control through zooprophylactic manipulation of the abundance of alternative hosts (Bruce-Chwatt, 1985; Sota and Mogi, 1989).

Underlying interpretations both of the proximate mechanisms and of epidemiological implications of host choice is the evolutionary theory of optimal foraging, as there must be intense selection pressures on haematophagous insects to feed on those hosts that are more amenable to being bitten. Given the importance of obtaining complete blood meals for lifetime reproductive success, blood-sucking insects would have evolved strategies to minimise their encounters with defensive hosts. However, a point will be reached where the evolved host choice strategy results in a distribution of vectors among hosts such that the effective per fly feeding success is the same upon all possible hosts, i.e. there will be an optimised distribution of vector densities among hosts for which (density-dependent) host defensive behaviour will be the same. Any novel host-seeking strategy that might lead an individual fly to 'move' hosts would cause a decrease in that particular fly's feeding success and could not, therefore, invade (Kelly, 2001). This distribution, known as the 'ideal free distribution' (IFD), is thus an evolutionary stable strategy (Fretwell and Lucas, 1970; Sutherland, 1983, 1996). It is 'ideal' because it assumes perfect knowledge (evolved or learnt) of the quality as a blood resource of all available hosts, and 'free' because it also assumes that there are no travelling costs associated with host-seeking (Sutherland, 1983).

In this paper, and as a case study, we modify a previously described mathematical model for the population biology of *Onchocerca volvulus* (the causative filarial parasite of river blindness) in West African savannah settings (Basáñez and Boussinesq, 1999) to derive theoretical estimates of the proportion of vector blood meals of human origin that would be compatible with observed measures of vector and parasite density in (pre-control) endemic villages of Cameroon, Burkina Faso and Côte d'Ivoire. By assuming that recorded *O. volvulus* microfilarial loads in human skin (our measure of parasite density) correspond to true endemic equilibrium values (before the initiation of antivectorial or antiparasitic measures), and by using an expression for the effective reproduction ratio (R_e) of the parasite (i.e. in the presence of density dependence), we calculate a village-specific proportion of vector blood meals taken on humans, extending preliminary work by Razali et al. (2002). We explore the effects of heterogeneity in host choice by vectors on the R_0 values estimated for this infection and discuss the epidemiological implications of our findings in terms of the IFD of vectors among hosts.

2. Models and methods

2.1. The basic and effective reproduction ratios

For dioecious (separate sexes) helminth parasites, the basic reproduction number R_0 refers not to the number of secondary cases arising from a primary case, but to the number of mature female worms produced, on average, by a female worm during her reproductive lifespan in the absence of

density dependence (Anderson and May, 1991). In this paper we will not address the complications introduced by the mating probability (which is itself a density-dependent function), by assuming that, at endemic equilibrium, all mature female worms would be mated. This assumption seems justified since theoretical studies have shown that the mating probability (denoted by ϕ; see Appendix A) approaches 1 rapidly when parasites are polygamous and non-randomly, but contagiously, distributed in the host population (Anderson and May, 1985), both of which are features of *O. volvulus* (Duerr et al., 2001; Schulz-Key and Karam, 1986). In a contagious (overdispersed) distribution, the majority of the worm population is harboured by a few hosts. The expression for R_0 in the Basáñez and Boussinesq (1999) model is:

$$R_0 = \frac{F(V/H)\beta^2 \delta_{H_0} \delta_{V_0}}{2(\sigma_W + \mu_H)(\sigma_M + \mu_H)[\sigma_{L_3} + \mu_V + (a_H/g)]} \qquad (1)$$

where one-half of the worms are females; F is the per female worm fecundity rate (scaled so as to be expressed in microfilariae per milligram of skin); V/H is the vector:human host ratio; β is the biting rate per fly on humans; δ_{H_0} and δ_{V_0} are, respectively, the per bite probability of inoculated infective (L_3) larvae establishing within the human host and of ingested microfilariae establishing within the vector in the absence of density-dependent constraints; σ_W, σ_M and σ_{L_3} are, respectively, the per worm mortality rates of adult stages, microfilariae and infective larvae; μ_H and μ_V are, respectively, the per host (background) mortality rates of humans and vectors; a_H is the proportion of infective larvae shed per bite; and g is the average duration of the interval between two consecutive blood meals (so that $1/g$ is the per vector number of bites per unit time).

The biting rate per fly on humans can be further decomposed into its constituents and written as $\beta = (h/g)$, with h representing our variable of interest, i.e. the proportion of blood meals taken on human hosts or the human blood index.

The expression in Eq. (1) quantifies the basic (intrinsic) potential for a dipteran-borne parasite (a filarial nematode) to invade and establish in a host population, and its value must exceed unity for the infection to become endemic. In reality, as the endemic state is reached, the parasite population will be increasingly regulated by density-dependent processes, and in the absence of perturbations (such as those induced by control interventions) parasite densities are indeed remarkably stable (Basáñez and Boussinesq, 1999; Basáñez et al., 2002). Under conditions of endemic equilibrium, each female worm replaces herself and the effective (in the presence of density dependence) reproduction ratio must be equal to 1. We have tested and confirmed this assumption by fitting models to parasitological data from a number of onchocerciasis-endemic regions, including those used in the present study (Filipe et al., 2005).

For the savannah members of the vector complex responsible for onchocerciasis transmission in West Africa (blackflies belonging to *Simulium damnosum* sensu lato), and assuming that all female worms will be mated in a highly overdispersed and polygamous parasite population that has not been subjected to changes in transmission effected by antivectorial or antiparasitic measures, the expression for the effective reproduction ratio R_e as a function of the mean number of microfilariae per mg of skin (M) is (Basáñez, 1996):

$$R_e(M) = \frac{\rho(M)e(M)[1 + (\delta_{H_\infty}/\delta_{H_0})c_H K(M)e(M)]}{[1 + c_H K(M)e(M)]M} \qquad (2)$$

where:

$$\rho(M) = \frac{F\delta_{H_0}K(M)}{2(\sigma_W + \mu_H)(\sigma_M + \mu_H)},$$

$$K(M) = \frac{(V/H)\beta h}{g[\sigma_{L_3} + \mu_V(M) + (a_H/g)]},$$

$$\mu_V(M) = \mu_V + \alpha_V M, \quad \text{and}$$

$$e(M) = \delta_{V_0}M^{b_V}.$$

The new parameters in this expression, δ_{H_∞} and c_H for humans and α_V and b_V for vectors, describe the severity of constraints on parasite or vector survival, with δ_{H_∞} denoting a reduced fraction of infective larvae establishing within the human host (as intensity of transmission increases); c_H the reciprocal of the transmission intensity value at which the fraction of parasites establishing successfully within the human host declines from δ_{H_0} to δ_{H_∞} (Basáñez et al., 2002; Dietz, 1982); α_V the per microfilaria rate of (linear) excess mortality of the fly (Basáñez and Boussinesq, 1999; Basáñez et al., 1996); and b_V the severity of density dependence in parasite establishment (L_1 uptake) within the simuliid vector, with $b_V = 1$ indicating no density dependence (proportionality) and $b_V < 1$ indicating a non-linear (limitation) relationship (Soumbey-Alley et al., 2004). Table 1 lists the model parameters, their values and sources.

2.2. Incorporation of the extrinsic incubation period (latency) in the vector

The previous equations assume that once skin microfilariae are taken up by the vector, with functional form $e(M)$, they develop instantaneously into infective L_3 larvae. More realistically, we can incorporate two additional equations describing the rates of change with respect to time of L_1 and L_2 larvae. Let ν_1 and ν_2 be, respectively, the (constant) rates of progression from L_1 to L_2 larvae and from L_2 to L_3 larvae within the fly's thoracic muscles, so that the reciprocal of ν_1 and ν_2 are the mean duration of each (non-infective) larval stage within the vector. This implies an exponential decay of the numbers of L_1 larvae with time after larval uptake as they develop into pre-infective L_2 larvae, the number of which builds up also to decline exponentially as they become infective L_3 larvae. The latter accumulate in the thorax, migrating subsequently to the blackfly's proboscis, whereupon a fraction a_H is shed per bite or they can experience mortality at a per larva rate, σ_{L_3}. Fitting the model to fly dissection data has confirmed that the process of *O. volvulus* development within the blackfly vector can indeed be modelled in a fashion similar to that in a susceptible–infected–immune framework (Wetten et al., 2003). Considering that parasite-induced vector mortality takes place early in this process (specifically during microfilarial uptake; Basáñez et al., 1996), and assuming that

Table 1 Parameters used in the river blindness model to obtain theoretical estimates of the human blood index h of savannah members of *Simulium damnosum* s.l. in West Africa

Parameter	Definition	Average value[a]	Source
In human host			
F	Per worm fecundity rate (no. of microfilariae contributed per female worm, per unit time and per mg of skin)	0.6674	Basáñez and Boussinesq (1999)
δ_{H_0}	Maximum proportion of L_3 larvae establishing within humans (in the absence of density dependence)	0.16	Basáñez and Boussinesq (1999)
δ_{H_∞}	Minimum proportion of L_3 larvae establishing within humans (in the presence of density dependence)	0.0032	Basáñez and Boussinesq (1999)
c_H	Shape parameter of the function describing the proportion of establishing L_3 larvae within humans	0.0137	Basáñez and Boussinesq (1999)
μ_H	Per human (background) mortality rate	0.02	Basáñez and Boussinesq (1999)
σ_W	Per worm mortality rate	0.1	Basáñez and Boussinesq (1999)
σ_M	Per microfilaria mortality rate	0.8	Basáñez and Boussinesq (1999)
In vector host			
δ_{V_0}	Maximum proportion of microfilariae establishing within vectors (in the absence of density dependence)	0.04	Soumbey-Alley et al. (2004)
b_V	Severity of density-dependent L_1 uptake by the vector	0.74	Soumbey-Alley et al. (2004)
μ_V	Per fly (background) mortality rate	26 (52)[b]	Basáñez and Boussinesq (1999)
α_V	Per microfilariae (excess) mortality rate of infected flies	0.39	Basáñez and Boussinesq (1999)
ν_1	Rate of progression from L_1 larvae to L_2 larvae	73.5	Wetten et al. (2003)
ν_2	Rate of progression from L_2 larvae to L_3 larvae	116.3	Wetten et al. (2003)
σ_{L_3}	Per infective larva mortality rate	52 (104)[b]	Basáñez and Boussinesq (1999)
a_H	Proportion of infective larvae shed per bite	0.8	Duke (1973)
$1/g$	Biting rate per vector	104	Basáñez and Boussinesq (1999)

[a] Rates are expressed per year; proportions are dimensionless.
[b] Values in parentheses were used to ascertain the sensitivity of the model to increased vector and infective larval mortality.

pre-infective larvae do not die but develop to the next stage, the expression for the basic reproduction ratio R_0 becomes:

$$R_0 = \frac{F(V/H)\beta^2 \delta_{H_0} \delta_{V_0} \nu_1 \nu_2}{2(\sigma_W + \mu_H)(\sigma_M + \mu_H)(\nu_1 + \mu_V)(\nu_2 + \mu_V)[\sigma_{L_3} + \mu_V + (a_H/g)]} \quad (3)$$

and $K(M)$ within Eq. (2) becomes:

$$K(M) = \frac{(V/H)\beta h \nu_1 \nu_2}{g[\nu_1 + \mu_V(M)](\nu_2 + \mu_V)[\sigma_{L_3} + \mu_V + (a_H/g)]} \quad (4)$$

2.3. Estimation of locality-specific values of the human blood index

At the endemic equilibrium microfilarial density (denoted as M^*), each female worm replaces herself and the effective reproduction ratio is equal to 1. The factor $(V/H)\beta$ is the biting rate as measured by entomologists in the field (e.g. the ABR). Therefore, assuming that (i) the observed mean microfilarial load per mg of skin in each village before the commencement of control interventions is our value of M^*, (ii) the recorded value of ABR is the true magnitude of $(V/H)\beta$ expressed in years for each village and (iii) the values of the remaining model parameters do not vary between villages, it is possible to find, for each village, the value of h that satisfies $R_e = 1$ for given M^* and ABR^* (where * denotes endemic equilibrium). Unbiased estimates of feeding preferences by blackflies are notoriously difficult to obtain (Hunter and Bayly, 1991).

Table 2 presents the data used to estimate h for each of 16 West African villages. Of the 12 Cameroonian villages, 8 were studied by Renz et al. (1987) and 4 by Duke et al. (1975). All four villages in the border between Burkina Faso and Côte d'Ivoire were investigated by Thylefors et al. (1978). All data pertain to pre-control situations, as

Table 2 West African savannah villages for which the human blood index h is estimated

Village	H	ABR	M^*_{obs}	$R_0^\S$	Distance from nearest breeding site[a]		Zoonotic host population (cattle ranking)
					km	River	
Cameroon							
Tcholliré[R]	2000	1000	9.6	1.5	8.0	Mayo Rey	Medium
Douffing[R]	112	2507	21.0	3.8	10.0	Mayo Rey, Mayo Bodo	High
Rey Manga[R]	94	3053	10.2	4.6	9.0	Mayo Rey	Highest
Touboro[R]	1500	8960	56.4	13.4	2.0	Vina	Low/medium
Larki[R]	51	10 700	14.4	16.1	6.0	Benoué	High/highest
Gandi-2[R]	229	14 152	39.0	21.2	2.5	Mayo Rey	Medium
Bonandiga[R]	108	16 850	64.2	25.3	2.0	Vina du Nord, Bome	Lowest
Mbai-Mboum[D]	354	28 500	65.3	42.8	7.0	Mbéré	Medium
Mayo-Galké[R]	145	36 157	60.6	54.2	0.5	Mayo Rey, Mayo Dokday	High
Ndiki[D]	139	81 000	21.0	121.5	25.0	NA	Low
Bédara[D]	166	174 750	119.0	262.1	3.0	Mbéré	Low
Koumbán[D]	307	176 500	67.7	264.8	1.5	Vina du Nord	Lowest
Burkina Faso and Côte d'Ivoire							
Nasso[T]	604	2620	28.0	8.9	NA	Kou	NA
Péndié[T]	442	9674	41.5	32.9	NA	Black Volta	NA
Dangouadougou[T]	251	21 312	54.3	72.5	NA	Léraba	NA
Fétékro[T]	167	47 993	66.0	163.2	NA	Nzi	NA

H: size of human population in village; ABR: annual biting rate; M^*_{obs}: observed mean microfilarial load (assumed to be at endemic equilibrium); $R_0^\S$: values of the basic reproduction number as estimated in Basáñez and Boussinesq (1999) with fixed h (0.3 in Cameroon and 0.7 in Burkina Faso and Côte d'Ivoire); NA: not available; [R]: from Renz et al. (1987); [D]: from Duke et al. (1975); [T]: from Thylefors et al. (1978).
[a] Distances from Renz and Wenk (1987).

Cameroon was not under the umbrella of the Onchocerciasis Control Program (OCP) in West Africa, and the study in Burkina Faso and Côte d'Ivoire was conducted before initiation of the OCP. Although we lack census data on the abundances of other possible blood hosts for the vector (cattle, game, birds), we present an attempt to rank cattle density, from lowest to highest (according to fieldwork notes taken in northern Cameroon by A.R. at the time when parasitological and entomological surveys were conducted).

2.4. Relationship between the basic reproduction number and entomological parameters used in assessing the success of vector control programmes

The values of h thus estimated were used to recalculate R_0 for each village (using Eq. (3)). The resulting values were compared with R_0 estimates obtained previously by Basáñez and Boussinesq (1999) and are presented in Table 3. These authors had assumed a fixed proportion of blood meals of human origin; $h = 0.33$ in Cameroon (Disney and Boreham, 1969; Renz, 1987) and $h = 0.67$ in Burkina Faso and Côte d'Ivoire (Toé et al., 1994). The previous and present R_0 values were plotted against ABR*. (Under the hypothesis of constant h, R_0 varies linearly with ABR.) We also plotted the relationship between the newly estimated R_0 values and the

annual transmission potential (ATP) recorded in the field (a measure of the intensity of transmission in the community that reflects the number of L_3 larvae potentially received by a person maximally exposed to blackfly bites during a year (Duke, 1968)). The ABR and ATP are, respectively, measures of vector density and parasite exposure used for monitoring vector control programmes (Walsh et al., 1978). Finally, in addition to using the nominal parameter values listed in Table 1, we assessed the sensitivity of estimates of h to increased vector and infective larval mortality. This was motivated by the different *S. damnosum* survivorship functions suggested by Le Berre et al. (1964) in Sudan-type (lower fly mortality) versus Guinea-type (higher fly mortality) savannah bioclimes in West Africa.

2.5. Model predictions of the mean infective larval density per vector

The equations of the full model (see Appendix A) were solved numerically using the Berkeley Madonna™ numerical integration package (Macey and Oster, 2000) by imputing village-specific ABR* and the newly estimated h values. The output variable of interest was the mean number of infective larvae per fly in the village. Observed mean numbers of infective larvae per fly were regressed on the

Table 3 Estimated values of the human blood index h, the vector:human ratio V/H, the basic reproduction number R_0 and the mean infective larval load per fly L_3 for each village

Village	h[a]	V/H[b]	R_0[a]	$L^*_{3\,obs}$	$L^*_{3\,pred}$
Cameroon					
Tcholliré	0.31 (0.69)	31	2 (2)	0.017	0.023
Douffing	0.25 (0.54)	97	5 (5)	0.022	0.031
Rey Manga	0.11 (0.23)	274	3 (3)	0.016	0.008
Touboro	0.84 (1.00)	102	59 (31)	0.103	0.197
Larki	0.04 (0.09)	2620	3 (3)	0.007	0.004
Gandi-2	0.18 (0.39)	744	20 (20)	0.033	0.034
Bonandiga	0.58 (1.00)	279	76 (59)	0.099	0.145
Mayo-Galké	0.24 (0.51)	1431	68 (65)	0.036	0.059
Mbai-Mboum	0.35 (0.75)	775	78 (75)	0.061	0.089
Ndiki	0.01 (0.02)	100 890	5 (5)	0.006	0.001
Bédara	0.13 (0.26)	13 337	170 (159)	0.040	0.042
Koumbán	0.06 (0.13)	27 950	83 (79)	0.021	0.016
Burkina Faso and Côte d'Ivoire					
Nasso	0.39 (0.83)	65	8 (8)	0.085	0.059
Péndié	0.33 (0.71)	281	25 (24)	0.099	0.064
Dangouadougou	0.33 (0.69)	627	54 (52)	0.075	0.074
Fétékro	0.21 (0.45)	2157	79 (76)	0.041	0.054

[a] The values of h and R_0 in parentheses are those obtained when increasing vector background and infective larval mortalities (see text). For Touboro and Bonandiga the values of h in parentheses indicate maximum permissible estimates of the human blood index when using these increased mortality rates.
[b] The values of the vector:human ratio (V/H) are all estimated using the nominal values.

predicted means (with heterogeneous or constant h) by way of comparing models and observations. A regression coefficient statistically indistinguishable from 1 would indicate good agreement between observed and predicted means (the slope of the perfect agreement line would be exactly equal to 1). We used the predictions as the 'independent' variable because the observed means are random variables and, therefore, subject to measurement error; regressing predicted on observed means could, therefore, be subject to attenuation of the regression coefficient (Carroll et al., 1995). As an alternative approach, we also plotted the difference between the predicted and observed mean infective larval loads against their average, together with a histogram of the differences for both heterogeneous and fixed h. The mean differences for both sets of assumptions and their 95% CIs were estimated (Bland, 1991; Bland and Altman, 1986).

2.6. Density dependence of the human blood index and the ideal free distribution

Values of h were plotted against ABR[*] and also used to obtain model-derived estimates of total vector abundance (V) and of the vector:human ratio (V/H) for each village. Total vector abundance, V [= (ABR[*]·H·g)/h], was plotted against the distance from each village to its nearest *S. damnosum* s.l. breeding site, and h was plotted against the vector:human ratio, V/H [= (ABR[*]·g)/h]. In the former case it would be expected that V would decrease with distance from the breeding site, and in the latter case a non-linear relationship would suggest density dependence of the proportion of blood meals of human origin with V/H, a prediction of IFD theory (Kelly and Thompson, 2000).

3. Results

Table 3 summarises the resulting values of the proportion of vector blood meals of human origin (h), the vector:human ratio (V/H) and the new R_0 values (calculated with heterogeneous h) for all 16 villages in the data set. The average human blood index for all Cameroonian villages as estimated from our model is 26%, ranging from 1% in Ndiki to 84% in Touboro. For those communities studied by Renz et al. (1987) the average value was 32%, whilst for those studied by Duke et al. (1975) the value was 14%. For the more western localities in Burkina Faso and Côte d'Ivoire the theoretical estimate of the human blood index ranged from 21% in Fétékro to 39% in Nasso (mean of 31%). Renz (1987) had estimated that only 20—40% of all blood meals taken by *S. damnosum* s.l. in northern Cameroon were of human origin.

Table 3 also shows (in parentheses) the estimates of parameter h and R_0 resulting from increasing the values ascribed to the background vector mortality rate (μ_V) from 26 per year (every 2 weeks) to 52 per year (every week), and of infective larval mortality rate (σ_{L_3}) from 52 per year (every week) to 104 per year (every 3.5 days) by way of illustrating the sensitivity of the human blood index estimates to changing vector parameters. More generally, increasing the severity of any density-dependent process or the magnitude of the mortality rates, or decreasing the rates of parasite establishment in humans and vectors, led to an increase in the values of the proportion of human blood meals. (The degree of vector anthropophagy must increase to compensate for stronger constraints, higher loss terms or lower gain terms in order to preserve the endemic equilibrium.) However, there were restrictions to the variability in parameter values that could be allowed, as some parameter

combinations resulted in the human blood index having to be (non-permissibly) greater than 1. Table 3 exemplifies this point by allocating a maximum of $h = 1$ to Touboro and Bonandiga as it was not possible to obtain sensible estimates for these localities with any parameter combination different from that in Table 1. In general, the nominal parameter values listed in Table 1 provided the best overall estimates for parameter h. However, and interestingly, the use of higher fly and larval mortality values for the western villages investigated by Thylefors et al. (1978) yielded estimates of the human blood index ranging from 45% to 83% (with a mean of 67%), closer to the value used by Basáñez and Boussinesq (1999), and motivated by the proportion of filarial larvae borne by *S. damnosum* s.l. that were of human origin according to *O. volvulus*-specific molecular probes (Toé et al., 1994).

The estimates of the basic reproduction ratio were largely insensitive to variation in the parameter values, as a higher human blood index is compensated for by the higher mortality rates. The same applied to the predicted values of infective larval load per fly, for which only the model solutions obtained with the nominal values of Table 1 are shown in Table 3.

Figure 1a plots the estimated human blood index versus the ABR (as given in the published accounts referred to in Table 2, but see also Basáñez et al. (2002) for adjustments to the ABR estimates corresponding to Koumbán and Bédara), using a logarithmic scale for both variables. Figure 1b plots the two model-derived estimates of parameter h against V/H. The fitted line in Figure 1b is the best monotonically decreasing trend line with equation $2.74(V/H)^{-0.40}$ ($R^2 = 0.62$), which gives a value of approximately 12 flies per person as the vector:human ratio for which the maximum human blood index is achieved ($h = 1.0$). In other words, according to our modelling assumptions, when there are ~12 (savannah) *S. damnosum* flies per human host, all of them are able to obtain their blood meal from humans. As V/H increases, the fraction of flies that are able to feed on humans would decrease. (Notice that by multiplying ABR by (g/h) to obtain the vector:human ratio, we are making the already inverse relationship between parameter h and ABR (Figure 1a) more distinct, not causing it.)

Figure 2 depicts the relationship between the model-derived estimate of absolute vector abundance (V) as a function of the distance between the village and the nearest *S. damnosum* breeding site. In general, the closer the village to the breeding place the higher the value of V. Since Ndiki is situated more than 25 km from the closest breeding place and most of the flies were nulliparous at the time of collection (which according to Duke et al. (1975) explains the inconsistency between a very high biting rate and a very low intensity of microfilarial infection), this village was not included in the plot.

Figure 3a compares the values of the basic reproduction number for *O. volvulus* estimated using constant h and village-specific h as a function of the ABR. In the former case the relationship between R_0 and ABR is linear, whereas in the latter it is strongly non-linear. Figure 3a also shows the R_0 values as estimated by Basáñez and Boussinesq (1999) with $h = 0.33$ for Cameroon and $h = 0.67$ for Burkina Faso and Côte d'Ivoire. As can be seen, the values estimated with heterogeneous h range from 2 to 170, whereas
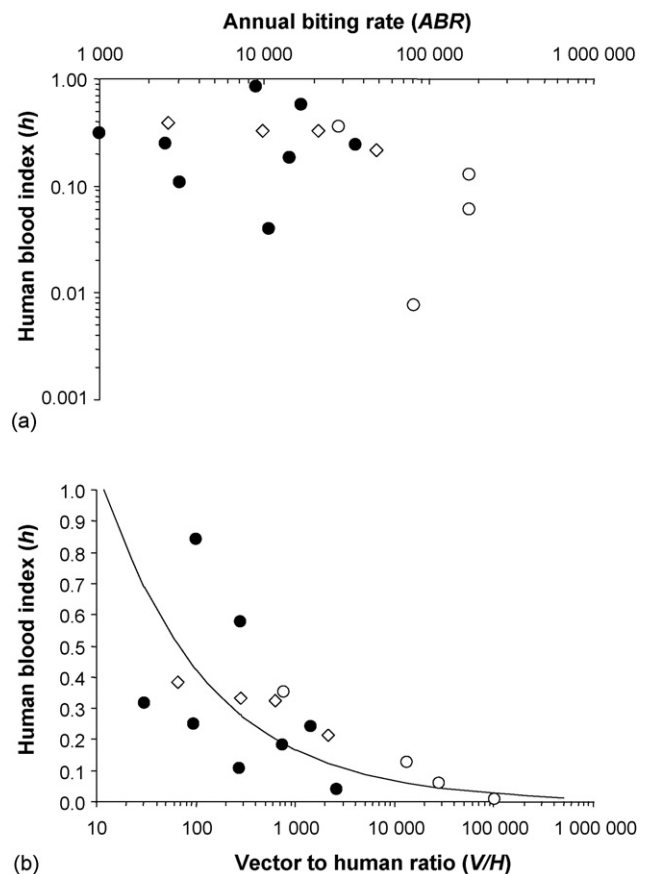

Figure 1 Model-derived estimates of the human blood index h of *Simulium damnosum* s.l. against (a) the annual biting rate (ABR) recorded at each of 16 West African villages presented in Table 2 and (b) the vector:human ratio estimated as $V/H = (ABR \cdot g)/h$, with ABR as measured in the field, $g = 3.5$ days (average interval between two consecutive blood meals according to Crosskey, 1990) and h as estimated in this paper. Circles indicate localities in northern Cameroon, with solid circles for those in Renz et al. (1987) and open circles for those in Duke et al. (1975); open diamonds identify those villages in Burkina Faso and Côte d'Ivoire investigated by Thylefors et al. (1978). The fitted line in (b) has equation $h = 2.74(V/H)^{-0.40}$ ($R^2 = 0.62$), with $h \approx 1$ when $V/H \approx 12$ (see text).

the previously estimated values ranged from 2 to 265 (see Tables 2 and 3).

Figure 3b plots R_0 versus the intensity of transmission in the community as measured by the ATP. The relationship, which is also non-linear, is linearized by taking logarithms in both axes (note that the trend line fitted, i.e. $R_0 = 0.14 \cdot ATP^{0.80}$; $R^2 = 0.89$) should not be extrapolated beyond the data points). Although it would seem tempting, at first sight, to suggest that this relationship indicates a threshold ATP value of 12 L$_3$ per person per year for R_0 to be greater than 1, this interpretation would be misleading, as our model does not take into account possible transmission breakpoints.

Figure 4a presents the observed values of the mean number of L$_3$ larvae of *O. volvulus* per fly in each village versus the predicted values, both for fixed h (0.3 for Cameroon and 0.67 for Burkina Faso and Côte d'Ivoire) and heteroge-

Table 4 Ratio of flies with *Onchocerca volvulus* L_3 larvae to the total number of infective flies (with all *Onchocerca* spp.) and model-derived estimates of the human blood index *h*

Village	Dissected flies	Ratio of infective flies	Proportion of *O. volvulus*-infective flies (95% CI)	Parameter *h*	
				Nominal mortality rates	High mortality rates
Rey Manga	5321	49/99	0.49 (0.39–0.60)	0.11	0.23
Mayo-Galké	40 660	712/1300	0.55 (0.52–0.58)	0.24	0.51
Douffing	5185	39/59	0.66 (0.53–0.78)	0.25	0.54
Bonandiga	1917	60/60	1.00 (0.94–1.00)	0.58	1.00
Touboro	5304	139/139	1.00 (0.97–1.00)	0.84	1.00

neous *h*. Allowing *h* to vary between villages significantly improves the agreement between data and model outputs (with a regression coefficient of 0.71); however, the 95% CIs for this coefficient (0.56–0.87) did not include 1, indicating that the model tends to overestimate transmission. Figure 4b and its inset illustrate, respectively, the difference between the predicted and observed mean infective larval loads for heterogeneous and fixed *h*, and a frequency histogram of such differences. The mean difference for the model with heterogeneous *h* was 0.009 L_3/fly (95% CI −0.007 to 0.025), whereas the value for fixed *h* was 0.032 L_3/fly (95% CI 0.002–0.061). This indicates that the mean difference between predictions and observations is not significantly different from zero when allowing for heterogeneity in the human blood index. The model with a constant proportion of human blood meals overestimates transmission (the histogram of differences is more markedly skewed to the right). Although accounting for heterogeneity in host choice significantly improves model predictions, the model still shows a tendency for overestimating infective larval load.

In Figure 5 the villages have been (arbitrarily) split between those with high observed numbers of infective larvae per vector (>0.07 L_3/fly: Touboro and Bonandiga in Cameroon; Nasso, Péndié and Dangouadougou in Burkina Faso/Côte d'Ivoire) and the remaining villages with low

(a)

(b)

Figure 3 Model-derived estimates of *Onchocerca volvulus* basic reproduction ratio R_0 against (a) the annual biting rate (ABR) and (b) the annual transmission potential (ATP) recorded at each of 16 West African villages. In (a), symbols (as in Figure 1) correspond to heterogeneous *h*. R_0 varies linearly with ABR for fixed *h* (= 0.33; thin line) but non-linearly for heterogeneous *h* (thick line) ($R_0 = a[1 − \exp(−b \cdot ABR)]$, with $a = 112$ and $b = 0.34 \times 10^{-4}$). In (b), symbols are as in Figure 1 and the trend line ($R_0 = 0.14 \cdot ATP^{0.80}$; $R^2 = 0.89$) highlights the non-linearity between these two variables, but it is not interpretable with regard to transmission breakpoints (i.e. a threshold value of ATP below which R_0 is < 1) (see text).
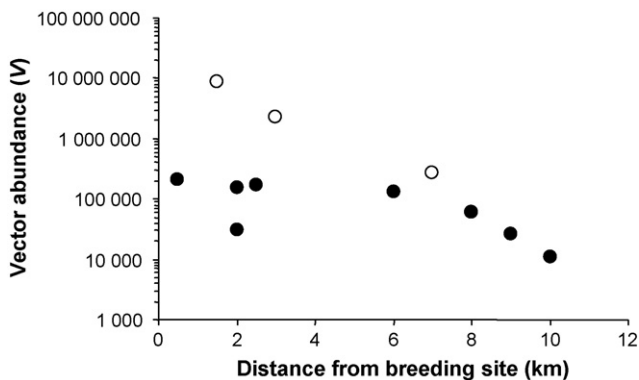

Figure 2 Model-derived estimates of absolute blackfly vector abundance (estimated as $V = (ABR \cdot H \cdot g)/h$, with annual biting rate (ABR), *g* and *h* as in Figure 1b and *H* being the size of the human population) versus the distance between the village and its nearest breeding site (Table 2). Symbols as in Figure 1 (distances from villages to nearest breeding sites not given by Thylefors et al., 1978).
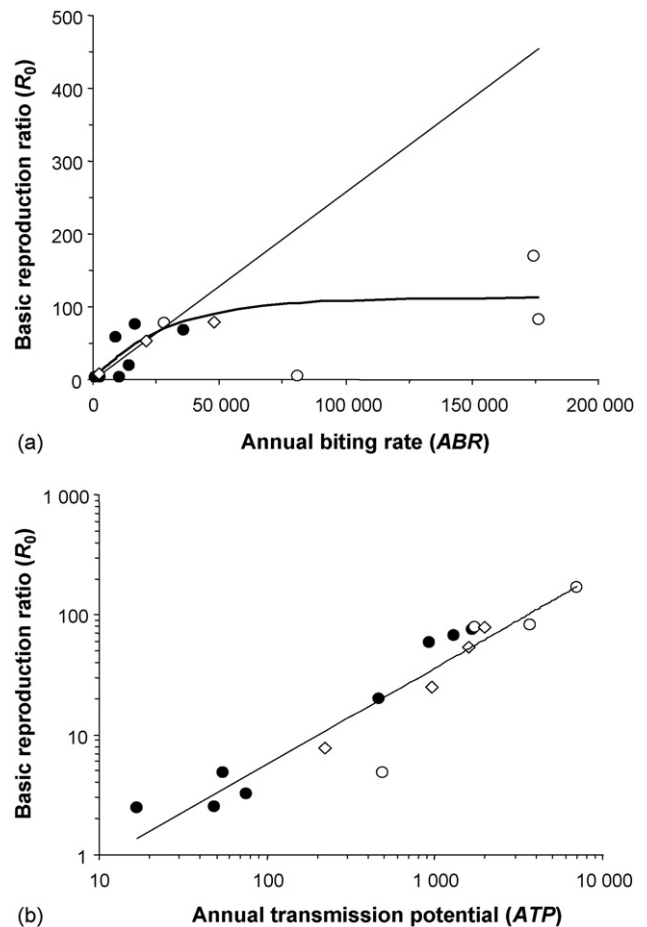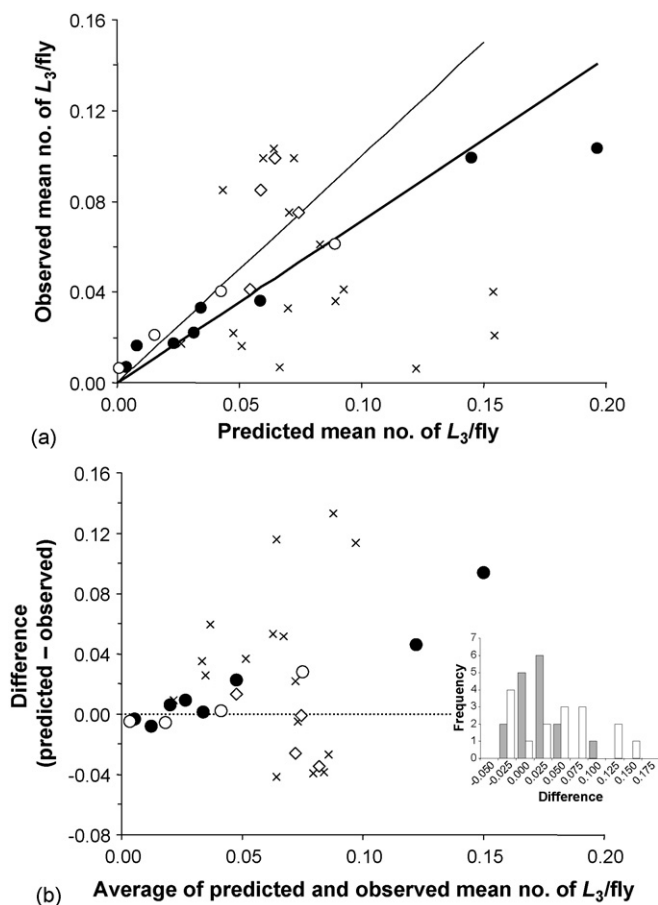
(a)

(b)

Figure 4 (a) Relationship between observed and model-predicted mean numbers of infective larvae per fly and (b) the difference between predictions and observations against the mean larval load with a frequency histogram of such differences. Symbols (as in Figure 1) correspond to heterogeneous h estimated in this paper. Crosses indicate results using constant h (1/3 for Cameroon and 2/3 for Burkina Faso and Côte d'Ivoire). In (a), the thin line represents perfect agreement between observations and predictions, and the thick line is the regression of the observed values ($L_{3\,obs}$) on the newly predicted values ($L_{3\,pred}$) with equation $L_{3\,obs} = 0.71 \times L_{3\,pred}$ ($r = 0.78$; d.f. 16, $P = 0.0003$; 95% CI for the regression coefficient 0.56−0.87). The regression of the observations on predictions with fixed h (not shown) was not significant ($r = 0.23$; d.f. 16, $P = 0.4$; 95% CI for the regression coefficient −0.74 to 0.31). In (b), the thin dotted line indicates no difference between predictions and observations, with mean difference for heterogeneous $h = 0.009$ (95% CI −0.007 to 0.025) and mean difference for fixed $h = 0.032$ (95% CI 0.002−0.061). The inset frequency histogram for the differences is markedly more skewed to the right for constant h (white bars) than for heterogeneous h (grey bars).

numbers of infective larvae per vector (<0.07 L_3/fly). The average value of the estimated human blood index in the high infectivity villages is 0.49 (using the lower vector and larval mortalities) and 0.85 (using the higher mortalities). The average estimated proportions of human blood meals in the low infectivity villages are, respectively, 0.17 and 0.37. The curves are the model solutions for the equilibrium mean number of infective larvae per vector as a function of the
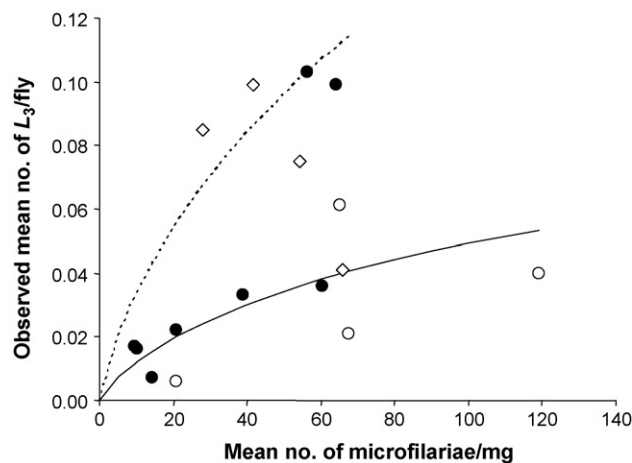

Figure 5 Relationship between observed mean number of infective larvae per fly and mean microfilarial load per mg of skin in the villages where the flies have been collected. The infective larval load was classified into high (>0.07 L_3/fly) and low (<0.07 L_3/fly). The lines correspond to Eq. (A.6) in the Appendix A, used to estimate (by minimising the χ^2 between predictions and observations) the values of the human blood index that best fitted high (broken line) and low (solid line) infectivity villages. For vector and larval mortality rates $\mu_V = 26$ per year and $\sigma_{L_3} = 52$ per year, respectively, the values of h were 0.44 for high infectivity villages and 0.16 for low infectivity villages. Using $\mu_V = 52$ per year and $\sigma_{L_3} = 104$ per year, the values were $h = 0.95$ and $h = 0.34$ for high and low infectivity villages, respectively.

equilibrium mean number of microfilariae per mg of skin (see Appendix A).

Allowing Eq. (A.6) for $L_3^*(M^*)$ in the Appendix A to estimate the values of parameter h (by minimising the χ^2 between the observed and predicted L_3 values), the results are very close to those obtained by averaging the village-specific estimates, i.e. $h = 0.44$ (using the lower vector and larval mortalities) and $h = 0.95$ (using the higher mortalities) for the high infectivity villages, and $h = 0.16$ and $h = 0.34$, respectively, for the low infectivity villages.

The proportion of flies with infective larvae of human origin among the total number of infective flies in a sample has been used to estimate human blood indices from such samples at particular localities (WHO, 1976). This would assume implicitly that both *O. volvulus* and other *Onchocerca* spp. have the same ability to infect and develop within *S. damnosum*, so differences in the proportions of infective flies reflect host choices. Table 4 presents the (ranked) fraction of flies with *O. volvulus* L_3 larvae together with the values of h estimated in this paper for those Cameroonian localities in Renz (1987) whose total number of infective flies exceeded 50 as a way of minimising biases due to small sample sizes. Although the figures are by no means equivalent, there is a positive relationship between the ratio of *O. volvulus*-infective flies and the estimates of h we have obtained.

4. Discussion

Modifying a previously developed onchocerciasis transmission model (Basáñez, 1996; Basáñez and Boussinesq, 1999)

to allow for between-village variation in the human blood index of *S. damnosum* s.l. populations in West Africa, we have obtained estimates of the human blood index that are compatible with the few direct (one fly with human blood in three; Disney and Boreham, 1969) or indirect (20—40% of all blood meals taken from humans; Renz, 1987) estimates available. With the nominal parameter values for the mortality rates of vectors and parasite infective larvae, the average proportion of human blood meals was 27%. Using the higher mortality rates, this fraction increased to 67% for localities situated in Burkina Faso and Côte d'Ivoire. Toé et al. (1994) have shown that the proportions of human- and non-human-derived *Onchocerca* larvae, identified by DNA probes, indicate a lower proportion (approximately one-third) of *O. volvulus* in Mali and Senegal, and a higher proportion (approximately two-thirds) in Burkina Faso, Côte d'Ivoire, Ghana and Togo. Since the most eastern country in the OCP was Benin, we do not have comparable data for Cameroon.

However, more interesting than the averages is the between-population heterogeneity in host choice that the results suggest. One intuitively plausible interpretation of these data is that host defensiveness increases more rapidly with biting density in humans than in alternative blood-meal hosts such as cattle (Kelly and Thompson, 2000). The IFD solution to this behaviour is for individual *S. damnosum* to exhibit an increasing tendency to bite non-human hosts as the vector:human ratio increases. This is because, when formulated according to the IFD, the human blood index would be a complex function of the relative density of vectors and hosts, the relative feeding success by vectors on human and non-human hosts and the relative responsiveness by the hosts to vector bites elicited by the probing of particular vector species (Kelly and Thompson, 2000). If the degree of human responsiveness (irritability, sensitisation, avoidance) to a particular vector species increases with vector population size at a faster rate than that of non-human hosts for the same vector species, this will lead to a non-linear decrease in the effective (realised) human blood index. Assuming that recorded values of the ABR provide an accurate representation of vector density, Figure 1 suggests that there may indeed need to be a (negative) density-dependent relationship between the human blood index and vector abundance (Figure 1a) or vector:human ratio (Figure 1b) if the observed (endemic) microfilarial loads are to be mirrored by the model. Using the nominal parameter values in Table 1, it is predicted that when there are approximately 12 flies per person on average, all flies would be able to feed on human blood, with the human blood index decreasing as the number of flies per person increases. A subsidiary prediction of the model is that of absolute vector abundance, which, as may be expected, decreases with distance from the village to the nearest blackfly breeding site (Figure 2).

The proportion of blood meals taken on humans decreases as the cattle:human host ratio increases. The localities of Touboro, Larki and Gandi, on the one hand, have similar vector densities (approximately 10 000 bites per person per year) but differ in the sizes of their human populations (Touboro > Gandi > Larki). Cattle abundance follows the opposite trend (Larki > Gandi > Touboro). It would be expected that the cattle:human and the vector:human

ratios follow Larki > Gandi > Touboro. In accordance with our expectations, the predicted human blood index follows Touboro > Gandi > Larki. The percentage of flies carrying infective larvae of human origin is approximately 1% in Larki and Gandi but approximately 3% in Touboro (Renz, 1987) where all infective larvae were indistinguishable from *O. volvulus* (Table 4). Bonandiga, Mayo-Galké and Bédara, on the other hand, have similar human population sizes (100—200 people) but differ in their vector densities (Bédara > Mayo-Galké > Bonandiga). Bonandiga, with the lowest vector density of the three villages and the lowest cattle:human ratio, has the highest predicted proportion of blood meals of human origin; in fact, 100% of the infective larvae were indistinguishable from *O. volvulus*. In Bédara, with a comparable cattle:human ratio but a much higher vector:human ratio, the expected human blood index is the lowest. In Mayo-Galké, with a higher cattle:human ratio, the parameter *h* is intermediate as is the fraction of *O. volvulus*-infective flies (Table 4).

A strongly non-linear relationship is apparent between the endemic intensity of microfilarial infection in the community and the ATP or the ABR that such a community is exposed to (Basáñez et al., 2002). This has been solely attributed to density-dependent constraints operating at various points in the parasite's life cycle (Basáñez and Boussinesq, 1999; Duerr et al., 2004, 2005). We propose that evolutionary-driven, density-dependent vector feeding success could be an additional factor contributing to this non-linearity, whereby vectors are less able to obtain human blood meals as vector abundance increases (because of host defensive behaviour, avoidance of locales with high vector densities, between-vector interference, etc.).

It must be stressed, however, that our calculations assume that the measures of ABR reported in the studies used for this analysis represent accurate estimates of human exposure to blackfly bites in the communities. More likely they represent fly landing rates that either overestimate true exposure (as they are recorded for full exposure to vectors from dawn to dusk throughout the year) or underestimate it (as fly catchers may not be able to capture and count all the flies that alight to bite on the attractant, particularly in high vector density localities). An overestimation of the ABR would lead to an underestimation of parameter *h* (for a given endemic microfilarial load) and vice versa. Since the human blood index forms part of the ABR, errors in estimating the latter could explain some of the variation in the former.

The values reported by Renz et al. (1987), however, were tightly estimated, as for each village they represent a weighted mean of the biting rates recorded at a number of catching sites distributed throughout the village, taking into account annual variations in vector density during three consecutive years (from 1976—1978). The weights included the daily visiting frequency (the estimated number of person-hours spent at each site). The decreasing trend of the human blood index with increasing vector:human ratio is very noticeable in the data collected by Renz and co-workers, lending support to the conjecture of a true density-dependent effect. Interestingly, and in agreement with our results, indirect estimations by Renz (1987) suggest that the villages of Touboro and Bonandiga would have the highest proportion of blood meals taken on humans.

Notwithstanding the operation of vector density-dependent effects, we cannot discard the possibility that some of the variation in vector anthropophagy predicted by our model could be due to the fact that the vector is not a homogeneous entity across the study areas, but that these actually differ in the proportions of the different members of the *S. damnosum* complex biting humans. Renz and Wenk (1987) observed that higher *O. volvulus* infective larval loads were recorded in localities and seasons in which the vector population mainly comprised *S. damnosum* sensu stricto (e.g. Touboro and Bonandiga with 91–93% of the blackfly larvae at breeding sites belonging to *S. damnosum* s.s.), as opposed to Tcholliré (with 27% *S. sirbanum* in the dry season). These vector species could differ in their intrinsic preference to bite on humans or in their vector competence for the parasite. In fact, recent analyses support the latter hypothesis (Soumbey-Alley et al., 2004) and suggest that *S. sirbanum* allows a lower number of ingested microfilariae to succeed in traversing its peritrophic matrix and proceed to larval development than *S. damnosum* s.s. This may have implications for the analysis of the relationship between L_3 load in the flies and microfilarial load in the skin mediated by density dependence and vector anthropophagy as discussed below.

Allowing for variation in the fraction of blood meals of human origin makes the relationship between R_0 and ABR strongly non-linear (Figure 3a). Although the expression fitted would suggest a threshold biting rate of ~260 bites per person per year above which R_0 is >1 (a value very similar to that of ~288 estimated by Dietz (1982) and of ~306 calculated by Basáñez and Boussinesq (1999)), it should not be overinterpreted beyond its role as an empirical relationship highlighting the non-linearity between the newly estimated values of the basic reproduction ratio and the ABR. The village-specific values of R_0 range between 2 and 170 (or between 2 and 159 with the higher mortality rates). Even when these estimates are considerably lower than previously presented values for the same localities (from 2 to 265; Basáñez and Boussinesq, 1999; see also Dietz, 1982), they contrast sharply with those reported by Filipe et al. (2005) using an age- and sex-structured onchocerciasis model. These authors estimated R_0 to be approximately 8 in northern Cameroon (analysing together 37 communities with an endemic average microfilarial load of 39 microfilariae/mg and assuming an average ABR of 42 800 bites per person per year, with one-third of vector blood meals taken on humans). Since R_0 estimates thus obtained are model-dependent, these authors may have underestimated density dependence and therefore R_0 (Klaus Dietz, personal communication).

The non-linear relationship between R_0 and ABR suggests that decreasing the biting rate in vector-borne infections would have little impact on the basic reproduction ratio of the pathogen until much greater reductions in vector density are achieved. Plotting the values of R_0 estimated in this paper against recorded levels of parasite transmission (as measured by the ATP) also indicates a non-linear relationship (Figure 3b), according to which the minimum number of infective larvae received per person per year would be approximately 12 for the basic reproduction ratio to exceed 1. Again, this is merely an empirical function that cannot be interpreted in a population dynamics context. Since our model does not contain any Allee effects (i.e. facilitating

density dependence at low parasite densities), such as an explicit function for the mating probability (Churcher et al., 2005) or the probability of finding undamaged microfilariae in the blood meal when vectors possess a well developed cibarial armature (Basáñez and Ricárdez-Esquinca, 2001), which could give rise to unstable equilibria, we cannot discuss formally the existence of transmission breakpoints (non-zero parasite densities below which R_0 is < 1). In the model used in this paper there is a single, locally and globally stable equilibrium (the endemic worm burden) when vector density exceeds the threshold biting rate ($R_0 > 1$) (Basáñez, 1996; Basáñez et al., 2002). Below the threshold biting rate ($R_0 < 1$) the parasite population would disappear (the trivial equilibrium of zero parasite densities in humans and flies is stable).

The model with heterogeneous *h* also performs better at predicting parasite load in vectors (Figure 4), with less variability at the lower end of the spectrum. We have already demonstrated that mean-based models tend to overestimate transmission compared with those incorporating the interplay between density dependence and parasite frequency distribution (Churcher et al., 2005), a complexity not considered here.

Taken as a whole, the apparently 'humped' relationship between the data for mean infective larval load per fly and mean microfilarial load per mg of skin portrayed in Figure 5, with low levels of infective larvae in flies for the lowest and highest microfilarial densities in humans, has been interpreted as an indication of strong parasite-induced vector mortality (Basáñez, 1996; Dietz, 1982). Here we suggest, as an alternative explanation, that the observed patterns may also be due to heterogeneity in the human blood index. By subdividing localities into those with high (>0.07 L_3/fly) and low (<0.07 L_3/fly) larval load in vectors, and using a power relationship between larval output and microfilarial input (Soumbey-Alley et al., 2004), we were able to obtain, respectively, high and low estimates of vector anthropophagy, compatible with the model-derived averages for these two groups of localities. To the group with high *O. volvulus* infective larval load belong the villages Touboro and Bonandiga in Cameroon, and Nasso, Péndié and Dangouadougou in Burkina Faso. As mentioned earlier in this paper, *S. damnosum* s.s. was nearly the only species present at Touboro and Bonandiga, but at Péndié the vector species was almost exclusively *S. squamosum* (Thylefors et al., 1978).

The values presented in Table 4 indicate that, in dissected samples, as the ratios of *O. volvulus*-infective flies to any *Onchocerca* spp.-infective flies increase, so do our estimates of the human blood index. Unfortunately, we lack census data on the abundances of other blood hosts for the vectors such as cattle, game or birds at the time of the field studies, and therefore it is not possible to undertake a rigorous quantitative analysis of the variation in human blood index with the ratio of non-human to human blood hosts. In one such analysis with regard to malaria transmission, Killeen et al. (2001) found that the proportion of human blood meals taken by *Anopheles arabiensis* and *A. gambiae* s.l. decreased with an increasing ratio of cattle to humans, but not that of *A. funestus* or *A. gambiae* s.s., which persistently bit nearly only humans regardless of cattle abundance; this study, however, did not investigate variations of *h* with vector density.

The central idea behind the IFD theory is to provide a link between the foraging behaviour of individuals and the population consequences of such behaviour, making it possible to derive population ecology and population dynamics inferences from first evolutionary principles (Sutherland, 1996). Kelly and Thompson (2000) were the first to apply the IFD to vector-borne infections, where the resource in question is vertebrate blood, hosts differ in their quality as a blood resource, and the density and distribution of vectors and hosts change in time and space. In this paper, we use a parasite population dynamics model to infer vector biting behaviour (measured as the human blood index) and interpret our results in light of the IFD. Following Sutherland (op. cit.), models of behaviour can be used to predict density dependence. Our results suggest that the proportion of blood meals of human origin taken by *S. damnosum* in West African savannah would decline with increasing vector density and with the ratio of vectors to human hosts, i.e. the biting rate per fly on humans would be negatively density-dependent. We then extend these density-dependent relationships to models of parasite population size, in particular to the estimation of the basic reproduction ratio of the infection and the intensity of larval infection in vectors. We conclude that if such density dependence were confirmed in field studies, the basic reproduction ratio of the parasite would not decrease linearly with reductions in vector abundance. We propose, as a plausible conjecture, that simuliid flies would switch to cattle, game, birds or other non-human blood hosts as human defensive behaviour, avoidance or vector interference increases with vector density, but we cannot, at present, ascertain the consequences that this would have in terms of blackfly reproductive fitness or vector population dynamics. We have fixed the mortality rate of vectors and explored the consequences of lower and higher mortality rates, but have not allowed these to vary with vector or host density. For a modelling approach allowing a theoretical exploration of the influence of vector mortality by host-seeking mosquitoes on outcomes of zooprophylaxis or zoopotentiation, see Saul (2003). In the case of simuliids, and in practice, fly parity rates as assessed by dissection could be used as indicators of fly survival, but this would be confounded by the differential dispersal of nulliparous and parous flies from their breeding sites (Duke, 1975).

We have instead focused on the population consequences for the parasite transmitted between humans and flies. Whether or not flies switch between humans and cattle will be important for the epidemiology of human onchocerciasis not only because of its effects on the basic reproduction ratio as described above, but also because *S. damnosum* s.l., as shown in Table 4, is known to transmit *Onchocerca* spp. of animal origin, and in particular *O. ochengi* among cattle (Omar et al., 1979; Wahl et al., 1998a). It has been suggested that human populations exposed to *O. ochengi* may be cross-protected against *O. volvulus*, highlighting its zooprophylactic potential (Renz et al., 1994; Seidenfaden et al., 2001; Wahl et al., 1998b) and the complexity of the interactions between helminth species, vectors and human and animal hosts (Bottomley et al., 2005). In West Africa, cattle abundance varies considerably from village to village and during the year as nomadic herds are moved between pastures. Realised host preference of blackfly vector populations in villages must therefore have a substantial effect on the transmission potential of *O. volvulus* both in time and space.

Vector and/or host density dependence in the contact rate of infectious diseases transmitted by insects in general, and dipteran vectors in particular, may be understood in the context of evolutionary stable strategies that may underlie important non-linear processes. In this paper we have strived for a synthesis of evolutionary theory and infectious disease modelling, as such processes and the mechanisms driving them will have yet unexplored implications for the epidemiology and control of vector-borne infections.

Conflicts of interest statement

Acknowledgements

Appendix A

The full model modifies the system of ordinary differential equations presented by Basáñez and Boussinesq (1999) by assuming a power relationship between L_1 uptake by vectors and skin microfilarial load of humans (Soumbey-Alley et al., 2004) as well as exponentially distributed incubation times in vectors (Wetten et al., 2003). The new system of equations describes the rates of change with respect to time of the mean number of adult worms (W) per human, microfilariae (M) per mg of skin and first stage larvae (L_1), pre-infective larvae (L_2) and third-stage infective larvae (L_3) per blackfly vector:

$$\frac{dW(t)}{dt} = \frac{V}{H}\beta\left\{\frac{\delta_{H_0} + \delta_{H_\infty} c_H(V/H)\beta L_3(t)}{[1 + c_H(V/H)\beta L_3(t)]}\right\} L_3(t)$$
$$- (\sigma_W + \mu_H)W(t) \tag{A.1}$$

$$\frac{dM(t)}{dt} = \left(\frac{1}{2}\phi F\right) W(t) - (\sigma_M + \mu_H)M(t) \tag{A.2}$$

$$\frac{dL_1(t)}{dt} = \beta\delta_{V_0} M(t)^{b_V} - [\nu_1 + \mu_V + \alpha_V M(t)]L_1(t) \tag{A.3}$$

$$\frac{dL_2(t)}{dt} = \nu_1 L_1(t) - (\nu_2 + \mu_V)L_2(t) \tag{A.4}$$

$$\frac{dL_3(t)}{dt} = \nu_2 L_2(t) - \left[\sigma_{L_3} + \mu_V + \left(\frac{a_H}{g}\right)\right] L_3(t) \tag{A.5}$$

Parameter values are listed in Table 1 (with the exception of the mating probability, denoted by ϕ, and taken to be equal to 1 in highly endemic parasite populations); the annual biting rate (ABR) equals $(V/H)\beta$, and parameter β equals h/g. Once Eqs (2) and (4) of the main text were used to estimate

h (the human blood index), the model above was solved by numerical integration (with fourth-order Runge–Kutta) using Berkeley Madonna™ (Macey and Oster, 2000) to obtain the predicted mean infective larval load per fly (results shown in Figure 4).

The curves fitted to the data presented in Figure 5 are the equilibrium solutions (denoted by asterisk) of the mean number of infective larvae per fly as a function of mean microfilarial load, $L_3^*(M^*)$, with equation:

$$L_3^*(M^*) = \frac{h\delta_{V_0} M^{*b_V} \nu_1 \nu_2}{g(\nu_1 + \mu_V + \alpha_V M^*)(\nu_2 + \mu_V)[\sigma_{L_3} + \mu_V + (a_H/g)]}$$

$$(A.6)$$

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