

MULTIPLE CAUSES OF VARIABLE TICK BURDENS ON SMALL-MAMMAL HOSTS

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Abstract. Blood meals by blacklegged ticks (*Ixodes scapularis*) on vertebrate hosts serve to transmit the agents of several zoonotic diseases, including Lyme disease, human babesiosis, and human granulocytic anaplasmosis, between host and tick. If ticks are aggregated on hosts, a small proportion of hosts may be responsible for most transmission events. Therefore, a key element in understanding and controlling the transmission of these pathogens is identifying the group(s) or individuals feeding a disproportionate number of ticks. Previous studies of tick burdens, however, have focused on differences in mean annual burdens between one or a few groups of hosts, ignoring both the strong seasonal dynamics of *I. scapularis* and their aggregation on hosts. We present a statistical modeling framework that predicts burdens on individual hosts throughout the year as a function of temporal-, site-, and individual-specific attributes, as well as the degree of aggregation in a negative binomial distribution. We then fit alternate versions of this model to an 11-year data set of *I. scapularis* burdens on white-footed mice (*Peromyscus leucopus*) and eastern chipmunks (*Tamias striatus*) to explore which factors are important to predicting tick burdens.

We found that tick burdens are a complex function of many extrinsic and intrinsic factors, including seasonality. Specifically: (1) burdens on mice and chipmunks increased with densities of host-seeking ticks in a manner that suggests hosts become saturated. (2) Chipmunks draw larval ticks away from mice, which are efficient reservoirs of the Lyme disease bacterium, and mice draw nymphs away from chipmunks, which are key nymphal hosts. (3) While individual correlates were statistically important, the relationships were complex, and no group or correlate (sex, age, mass) could explain which hosts fed a disproportionate number of ticks. (4) Ticks were strongly aggregated on hosts within and across groups suggesting that some undiscovered quality of individual hosts was responsible for the aggregation. (5) Those individuals that fed more nymphs than expected, and are thus more likely to be infected with the Lyme disease agent, also tend to feed and infect more larvae than expected. Predicting which individuals those are is not yet possible.

Key words: aggregation; blacklegged ticks; eastern chipmunks; *Ixodes scapularis*; negative binomial distribution; *Peromyscus leucopus*; seasonality; *Tamias striatus*; transmission; vector burden; white-footed mice.

INTRODUCTION

Much like the distribution of other macroparasites on their hosts (Shaw et al. 1998, Wilson et al. 2002), vector burdens or biting rates are often extremely heterogeneous such that a few hosts feed many vectors while others feed very few (Woolhouse et al. 1997). This aggregated distribution of blood meals often conforms to the so-called 80–20 rule, whereby roughly 80% of blood meals come from 20% of the hosts. This further implies that most transmission of vector-borne pathogens is focused on a relatively small proportion of the host population.

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Ticks in the *Ixodes ricinus* complex, for instance, are highly aggregated on their vertebrate hosts (Ostfeld et al. 1996b, Shaw et al. 1998, Perkins et al. 2003), and apparently follow the 80–20 rule (Perkins et al. 2003). As they feed on these hosts, *Ixodes* ticks can become infected with and transmit zoonotic pathogens such as *Borrelia burgdorferi*, *Babesia microti*, and *Anaplasma phagocytophilum*, the agents of Lyme disease, human babesiosis, and human granulocytic anaplasmosis, respectively. Host species vary dramatically in their propensity to transmit these pathogens to feeding ticks (see e.g., LoGiudice et al. 2003). The strong aggregation of ticks, and hence blood meals, on individual hosts suggests that individuals also vary dramatically in their contribution to pathogen transmission (Woolhouse et al. 1997, Perkins et al. 2003): Those hosts responsible for feeding most ticks are both highly likely to be infected, and to subsequently infect many naïve ticks. Therefore, a key element in understanding and controlling the transmis-

sion of these diseases is identifying the group(s) or individuals with disproportionately large tick burdens.

A number of studies of Lyme disease risk in the United States have explored the intrinsic and extrinsic factors responsible for variation in burdens of *I. scapularis* on their small-mammal hosts, principally white-footed mice (*Peromyscus leucopus*; see Plate 1) and chipmunks (*Tamias striatus*). For instance, males are commonly found to have higher mean burdens than females (Ostfeld et al. 1996b, Schmidt et al. 1999), and mean burdens tend to increase with the density of ticks questing for hosts (Lyon et al. 1996, Ostfeld et al. 1996b). These relationships, however, are complex. Ostfeld et al. (1996b), for instance, observed the lowest burdens on mice in the year with the highest density of questing ticks. This year also had the highest density of mice, which apparently "diluted" burdens as the many ticks were spread across more hosts (Schmidt et al. 1999). Site characteristics, like vegetation structure and microhabitat composition (e.g., Adler et al. 1992, Lindsay et al. 1999, Randolph and Storey 1999) have also been found to contribute to differences in tick burdens, perhaps via effects on tick survival and population size, or perhaps because of how hosts encounter questing ticks.

There are two important limitations to these studies of tick burdens. First, *Ixodes* ticks, like many vector species, have strongly seasonal life histories (Wilson and Spielman 1985, Fish 1993). In the northeastern and north-central United States, larval ticks hatch in the late summer and quest for hosts for a single blood meal from a mammal or bird, after which they drop to the ground to molt into nymphs and overwinter. The following spring or early summer, these nymphs again quest for a mammal or bird host for a single blood meal. After this second meal, they drop to ground, molt into adults, and emerge later in the year to find a deer or other larger mammal host for a final blood meal and to mate. Nymphal tick burdens have a single peak in the early summer, while larval burdens are characterized by a small early-summer peak (of uncertain origins) and a much larger peak in the late summer (Wilson and Spielman 1985, Fish 1993, Ostfeld et al. 1996a, Goodwin et al. 2001). Thus, an observation in mid June, for instance, cannot be directly compared with one in August. For this reason, most studies have focused on explaining differences in mean annual burdens, both among years and among sites. This focus on mean burdens, however, ignores the strong aggregation in the observed distributions of tick burdens (e.g., Davidar et al. 1989, Mannelli et al. 1993), which tend to follow a negative binomial distribution. An infection's potential rate of spread in a host population, R_0 , increases with the degree of vector aggregation (Woolhouse et al. 1997). Control efforts failing to account for such aggregation will tend to be ineffective (Woolhouse et al. 1997, Lloyd-Smith et al. 2005). Thus, the degree of aggregation of tick burdens among individuals within

a population can be just as important to transmission potential as are the mean values.

Secondly, these studies focus on only one or a few potential explanatory variables and so cannot evaluate the relative importance of each. A large number of extrinsic and intrinsic factors potentially influence tick burdens and may interact, therefore testing just one or a few factors may mask important causes of variation. Although simultaneous tests of multiple factors are desirable, such tests are often limited by the availability of sufficient data.

Here we present a statistical modeling framework that predicts the expected tick burden on individual hosts throughout the year, as well as the degree of aggregation of ticks among these hosts, based upon temporal-, site-, and individual-specific attributes. We used this framework to test hypotheses about the importance of these attributes in predicting tick burdens using an 11-year data set of *I. scapularis* burdens on white-footed mice and eastern chipmunks. Specifically, we built increasingly complex models testing whether: (1) annual variation in densities of host-seeking ticks explained differences in the seasonal dynamics of burdens seen among years; (2) densities of host conspecifics and competitors influenced individual tick burdens; (3) we could identify the type(s) of hosts that feed most ticks based on individual correlates such as sex, age, and/or mass; (4) the degree of aggregation varied by host sex and age, or with expected burdens; and (5) certain individuals consistently fed more ticks than would be expected given all else we knew of these animals.

METHODS

Data

We used 11 years of data from a small-mammal trapping program in the oak-dominated forests on the Institute of Ecosystem Studies campus in southeastern New York (Schmidt et al. 1999, Ostfeld et al. 2006). This data set includes 23 095 observations of 10 283 individual white-footed mice (*Peromyscus leucopus*) and 5360 observations of 2155 individual eastern chipmunks (*Tamias striatus*). Visual examination of nymphal burdens at the beginning of trapping in three years (1999, 2000, and 2004) indicated we might have missed the peak in nymphal burdens. To be conservative, we therefore excluded observations from these three years from the analyses of nymphal burdens, leaving 16 226 observations of 7690 individual mice and 3949 observations of 1603 individual chipmunks. (All 11 years were used for larval burdens.)

In brief, the data were collected as follows. There were six permanent trapping grids, each consisting of 242 of Sherman traps arranged in pairs along an 11 × 11 grid (10 × 12 grid in one case) covering ~2.25 ha. Each grid was trapped for two consecutive nights (equaling one trapping session) between 6 and 16 times per year between April and October, depending upon the year, from 1995 through 2005, for a total of 84–99 trapping

sessions per grid over the 11 years. (Since 2000, the trapping regime was more regular, with seven to nine trapping sessions per year at intervals of three or four weeks.) In 1995, 1997, and 1998, the small-mammal density on three of the six grids was manipulated. In 1995, both mice and chipmunks were removed during June and July, and in 1997, mice were removed from mid-June through July, and in 1998 chipmunks were removed from June through August (Schmidt et al. 1999).

Upon first capture, mice and chipmunks were given numbered ear-tags for later identification. On first capture in a trapping session, each animal was weighed, sexed, aged according to pelage (juvenile, subadult, adult; mice only), and the larval and nymphal *I. scapularis* on their heads and ears were counted. We have observed a strong relationship between these field counts and whole-body burdens for mice ($R^2 = 0.79$ for larvae, $R^2 = 0.19$ for nymphs, presumably due to low counts) and for chipmunks ($R^2 = 0.67$ for larvae and $R^2 = 0.87$ of nymphs) (Schmidt et al. 1999).

Abundances of mice and chipmunks were estimated separately for each of the six trapping grids using the closed-population robust design (Kendall and Nichols 1995, Kendall et al. 1995, 1997) as implemented in Program MARK (White and Burnham 1999). The same basic model was used for both mice and chipmunks on all trapping grids. The probability of recapture (c) was set equal to the probability of capture (p) (i.e., no trap-shy or trap-happy animals), which was constant in each year, but allowed to vary among years. Survival (S) was constant during the trapping seasons, but the overwintering survival rates were allowed to vary among years. Lastly, the probabilities of emigration (γ') and immigration ($1 - \gamma'$) were allowed to vary from each other and among years, allowing for potential emigration off of the trapping grids when, for example, densities were high. In this way, we estimated abundance of both mice and chipmunks for each grid during every trapping session.

Densities of host-seeking nymphs and larvae were measured by the standard drag-cloth method (Falco and Fish 1992) two to three times during both the nymphal and larval periods each year. The highest density observed on a grid during a year was considered the peak density for that grid in that year.

Models

Our modeling approach was to first create basic phenomenological models to account for the strong seasonal dynamics in nymphal and larval tick burdens (Fig. 1), and then create sets of alternate versions of the nymphal and larval models to examine specific hypothesis about the extrinsic temporal (year-to-year and within season) and spatial (among-grid) and intrinsic (individual-specific) factors that influence tick burdens (Tables 1 and 2). Alternate versions of each model were compared using AIC_c (Akaike's information criterion, corrected for sample size; Burnham and Anderson

2002), and the models or subsets of models best supported by the data were determined by AIC_c weights.

Basic model of nymphal burdens.—The expected nymphal burden during a particular week of a particular year was described by a right-shifted log-normal curve (Fig. 1a):

$$E[\text{burden}] = H \times \exp\left(-1/2[\ln([\text{week} - \text{shift}_y]/\mu_y/\sigma_y)]^2\right). \quad (1)$$

where $H = \beta_{\text{year}} + \beta_{\text{grid}} + \beta_{\text{sex}} + \beta_{\text{age}} + \beta_{\text{mass}} \times \text{mass} + \dots$ is a linear function of the year-, grid-, and individual-specific covariates. H controls the height of the expected burden, and the year-specific shift term controls the position of the curve along the x -axis. Observations earlier in the year than shift were given an expected burden of 0.001. This model has considerable flexibility in its shape, particularly in how sharply the curve rises (small μ produces a sharp rise) and falls (a small μ and/or small σ produces a sharp decline), which fit the observed interannual variation in seasonal trends in nymphal tick burdens (Fig. 1c, d).

In the basic model (model A in Table 1) and all subsequent models of nymphal tick burdens, the timing of the peak (determined by shift and μ) and its shape (controlled by parameters μ and σ) were allowed to vary from year to year. The height of these curves (i.e., the peak expected burden) varied both by year and by trapping grid ($H = \beta_{\text{year}} + \beta_{\text{grid}}$). In this way, we allowed for year-to-year differences in weather or other factors that might, for instance, have led to an earlier or later emergence of nymphs, as well as differences among the trapping grids (e.g., vegetative structure; Adler et al. 1992) without assuming specific relationships or mechanisms. There are ways we might have reduced the number of parameters in these models, but they involve making assumptions about relationships between variables. In most cases, we have no empirical basis for assuming particular relationships. Moreover, we have sufficient data to support these large models and test for particular relationships among variables. Other more mechanistic models could easily be incorporated into this framework in the future.

Basic model of larval burdens.—Larval burdens were modeled in a similar fashion, only with two curves: a normal to account for the much smaller early summer peak and then a log-normal to describe the larger late summer peak:

$$E[\text{burden}] = H_1 \times \exp\left(-1/2\ln([\text{week} - \text{mean}_y]/\text{variance}_y]\right) + H_2 \times \exp\left(-1/2[\ln([\text{week} - \text{shift}_y]/\mu_y/\sigma_y)]^2\right). \quad (2)$$

This model was constrained such that the normal curve

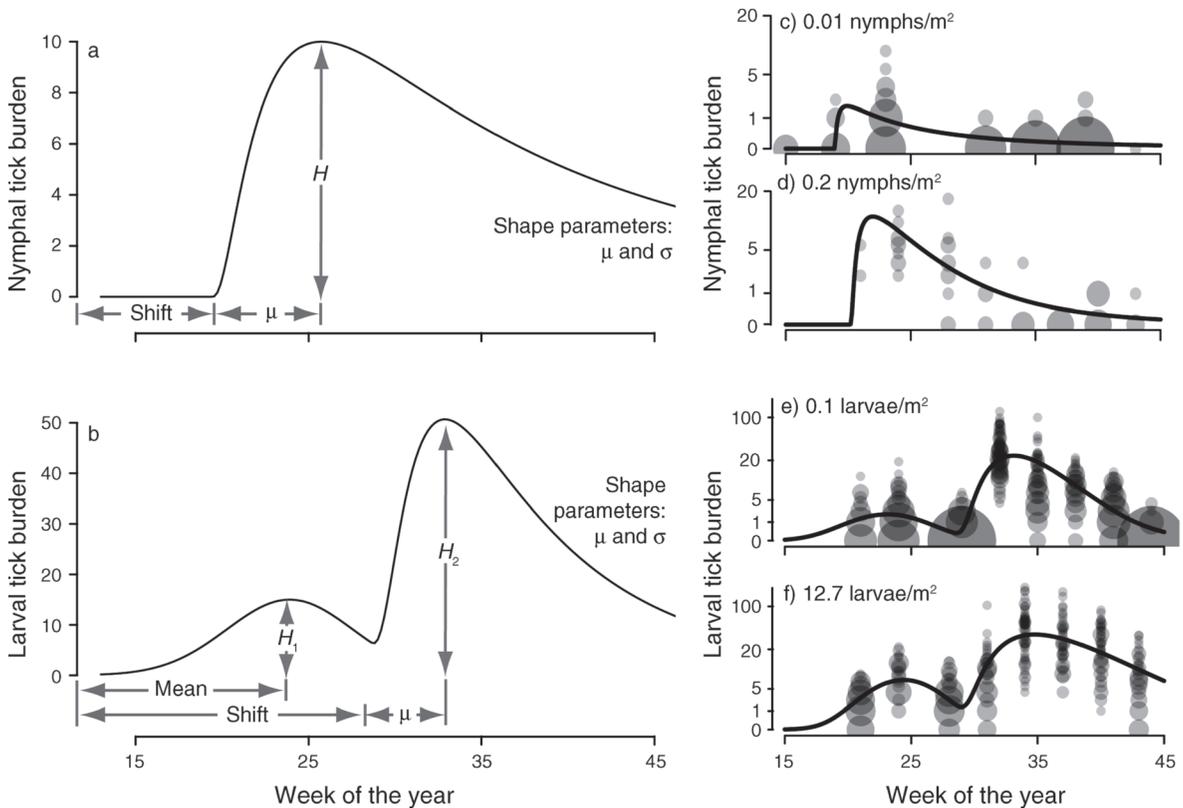


FIG. 1. The (a) nymphal and (b) larval tick (*Ixodes scapularis*) burden models describing the expected burdens on hosts at any given week of the year. The timing of the peak burden (position along the x-axis) is determined by the right shift of the log-normal curve and μ ; the size of the burden (height of the curve) is determined by (a) the parameter H or (b) the parameters H_1 and H_2 ; and the shape of the curve is determined by the parameters μ and σ . The models account for the variable burden dynamics from grid-to-grid and year-to-year, e.g., nymph burdens on chipmunks found on the (c) Henry Control grid in 1995 and the (d) Henry Experimental grid in 2003, and larval burdens on mice on the (e) Green Control grid in 2002 and the (f) Henry Control grid in 2003. The areas of the circles in (c)–(f) are proportional to the sample size. Note that the shapes of the log-normal curves vary with the density of questing ticks.

occurred left of (earlier in the year than) the log-normal (Fig. 1b). H_1 and H_2 , in Eq. 2, were linear functions of the year-, grid-, and individual-specific covariates, controlling the heights (peak larval burdens) of the two curves.

Again, in the base model (model A in Table 2) and all subsequent models, the parameters that control the timing (mean, and shift and μ) and the shapes of the two curves (variance, and μ and σ) were allowed to vary across the years, and the heights of the curves varied by year and grid ($H_1 = \beta_{1\text{year}} + \beta_{1\text{grid}}$; $H_2 = \beta_{2\text{year}} + \beta_{2\text{grid}}$; Fig. 1e, f).

Alternate versions of these models including different covariates were fitted to the data sets of nymphal and larval burdens on mice and chipmunks with a negative binomial error structure by maximizing the log likelihood using a simulated annealing routine (Goffe et al. 1994) implemented in R (R Development Core Team 2005) by L. Murphy and C. Canham (likelihood package available online).² The best-supported models

from one set of models (e.g., those in which questing tick densities influenced the shape and height parameters) served as the base model for the next set of models (e.g., those testing for the influence host densities), as indicated in Tables 1 and 2.

Question 1: densities of host-seeking ticks

Seasonal dynamics varied among years such that, in some years, there was a short, intense peak of burdens and, in others, a much longer, gradual peak. We hypothesized that the shape of the curve would depend upon the density of ticks questing for hosts. In years with many questing ticks, we suspected that hosts would be saturated and tick burdens on hosts would decline slowly. We formulated models in which the shape parameters of the log-normal curves were a function of the year in question and the \log_{10} of the appropriate peak questing nymph or larvae density [$\mu = \mu_y + \mu_{\text{ticks}} \times \log_{10}(\text{questing ticks} + 1)$ and $\sigma = \sigma_y + \sigma_{\text{ticks}} \times \log_{10}(\text{questing ticks} + 1)$] (B models). The normal curves (early peak) in larval burden models were left unchanged.

² http://www.ecostudies.org/lme_R_code_tutorials.html

TABLE 1. Support for models of nymphal tick (*Ixodes scapularis*) burdens on white-footed mice (*Peromyscus leucopus*) and eastern chipmunks (*Tamias striatus*).

Model	Mice					Chipmunks				
	Model letter	<i>p</i>	AIC _c	Δ_i	w_i	Model letter	<i>p</i>	AIC _c	Δ_i	w_i
Dispersion										
<i>k</i> is a function of expected burden	Q	48	21 840.9	0	1	Q	45	12 776.6	0	0.85
<i>k</i> varies by sex	P	47	22 008.3	167.4	0	P	44	12 780.0	3.4	0.15
<i>k</i> varies by age	O	48	21 980.2	139.3	0	O
Best model from below	<i>L</i>	<i>46</i>	<i>22 002.8</i>	<i>161.9</i>	<i>0</i>	<i>G</i>	<i>43</i>	<i>12 793.6</i>	<i>17.0</i>	<i>0</i>
Height of burden and individual-level factors										
<i>H</i> is a function of sex and age and mass	N	46	22 005.9	3.1	0.18	N
<i>H</i> is a function of sex and mass	M	45	22 045.3	42.4	0	M	45	12 794.2	0.7	0.23
<i>H</i> is a function of sex and age	L	46	22 002.8	0	0.82	L
<i>H</i> is a function of age and mass	K	46	22 051.4	48.6	0	K
<i>H</i> is a function of sex	J	44	22 045.3	42.4	0	J	44	12 793.5	0	0.32
<i>H</i> is a function of mass	I	44	22 080.4	77.6	0	I	44	12 795.2	1.7	0.14
<i>H</i> is a function of age	H	45	22 048.9	46.1	0	H
Best model from below	<i>G</i>	<i>43</i>	<i>22 079.0</i>	<i>76.1</i>	<i>0</i>	<i>G</i>	<i>43</i>	<i>12 793.6</i>	<i>0.1</i>	<i>0.31</i>
Height of burden and host density										
<i>H</i> is a function of mouse and chipmunk populations	G	43	22 079.0	0	1	G	43	12 793.6	0	0.61
<i>H</i> is a function of chipmunk population	F	42	22 160.8	81.8	0	F	42	12 816.9	23.3	0
<i>H</i> is a function of mouse population	E	42	22 121.9	42.9	0	E	42	12 794.9	1.3	0.31
<i>H</i> is a function of rodent population	D	43	22 144.9	66.0	0	D	43	12 797.7	4.1	0.08
Best model from below	<i>C</i>	<i>41</i>	<i>22 175.3</i>	<i>96.3</i>	<i>0</i>	<i>C</i>	<i>41</i>	<i>12 817.4</i>	<i>23.8</i>	<i>0</i>
Height of burden and nymph density										
<i>H</i> is a function of log ₁₀ (QND)	C	41	22 175.3	0.2	0.85	C	41	12 817.4	0	0.93
Best model from below	<i>B</i>	<i>40</i>	<i>22 178.7</i>	<i>3.6</i>	<i>0.15</i>	<i>B</i>	<i>40</i>	<i>12 822.7</i>	<i>5.3</i>	<i>0.07</i>
Seasonal dynamics										
μ and σ are a function of year and log ₁₀ (QND)†	B	40	22 178.7	0	0.97	B	43	12 822.7	0	1
μ and σ are a function of year†	A	38	22 185.8	7.1	0.03	A	38	12 850.5	27.8	0

Notes: Results are grouped from bottom to top into (1) models addressing seasonal dynamics (shape parameters, μ and σ), (2) those in which the burden curve peak height parameter, *H*, is a function of questing nymph densities (QND), (3) those in which height changes with host densities (rodent population = mice + ϕ chipmunks), (4) models including individual-level factors, and (5) those in which the dispersion parameter, *k*, varies. In each case, the best model from the set below (shown in italics) was the basis for more complex models above. Abbreviations are: *p*, the number of parameters; AIC_c, Akaike's information criterion corrected for sample size; Δ_i , difference in AIC_c; and w_i , AIC weight (Burnham and Anderson 2002). Ellipses indicate that the model was not run because no data on the age of chipmunks were available.

† The height of the curve, *H*, is a function of year and grid.

We also suspected that densities of questing ticks would directly influence the heights of the curves, i.e., the size of the expected burdens, and so we let *H*, and *H*₁, and *H*₂ vary with log₁₀-transformed densities of questing nymphs and larvae, respectively (C models).

Question 2: host densities

With more hosts collecting and feeding ticks we expected the burden on each to decrease, so we examined three models in which the expected burdens varied with host abundance. In the absence of host behavior and/or tick preferences, all rodent hosts should be equivalent, and so in the first formulation (D models), expected burdens changed with the sum of mouse and chipmunk population sizes. Since chipmunks are larger than mice, and might be expected to support more ticks, we used a "conversion" factor, ϕ , such that *H*, and *H*₁ and *H*₂ were modeled as $\beta_{\text{rodents}} \times (\text{mice} + \phi\text{chipmunks})$. The influence of mouse and chipmunk population sizes may not be equivalent, however. In

particular, we might expect strong effects of competitor densities on host behavior. We therefore formulated models where expected burdens were a function of mouse population size (E models), chipmunk population size (F models), or both independently (*H*, and *H*₁ and *H*₂ specified by $\beta_{\text{mice}} \times \text{mice} + \beta_{\text{chipmunks}} \times \text{chipmunks}$) (G models).

Question 3: individual correlates

At an individual level, we predicted larger, older males would have larger burdens than smaller, younger, females. Sex-biased parasite loads are common, although not ubiquitous, among mammals, as are age-intensity relationships, either of which may be rooted in behavior or physiology (Scott 1988, Moore and Wilson 2002, Wilson et al. 2002). Male mice, for instance, often have larger home ranges (e.g., Ostfeld et al. 1996b, Ribble et al. 2002) and greater activity rates (e.g., Rehmeier et al. 2006), potentially exposing them to greater numbers of questing ticks than females. Males

TABLE 2. Support for models of larval tick tick (*I. scapularis*) burdens on white-footed mice (*P. leucopus*) and eastern chipmunks (*T. striatus*).

Model description	Mice					Chipmunks				
	Model letter	<i>p</i>	AIC _c	Δ _i	<i>w_i</i>	Model letter	<i>p</i>	AIC _c	Δ _i	<i>w_i</i>
Dispersion										
<i>k</i> is a function of expected burden	Q	102	124 077.3	0	1	Q	100	19 035.8	0	0.68
<i>k</i> varies by sex	P	102	124 292.5	215.2	0	P	99	19 037.3	1.5	0.32
<i>k</i> varies by age	O	102	124 281.2	203.8	0	O
Best model from below	N	102	124 290.5	213.2	0	I	98	19 053.3	17.5	0
Height of burden and individual-level factors										
<i>H</i> ₁ and <i>H</i> ₂ are a function of sex and age and mass	N	102	124 290.5	0	1	N
<i>H</i> ₁ and <i>H</i> ₂ are a function of sex and mass	M	98	124 337.3	46.8	0	M	100	19 056.9	3.5	0.15
<i>H</i> ₁ and <i>H</i> ₂ are a function of sex and age	L	100	124 500.0	209.5	0	L
<i>H</i> ₁ and <i>H</i> ₂ are a function of age and mass	K	100	124 806.7	516.2	0	K
<i>H</i> ₁ and <i>H</i> ₂ are a function of sex	J	96	124 494.0	203.5	0	J	98	19 074.2	20.9	0
<i>H</i> ₁ and <i>H</i> ₂ are a function of mass	I	96	124 786.7	496.2	0	I	98	19 053.3	0	0.85
<i>H</i> ₁ and <i>H</i> ₂ are a function of age	H	98	124 922.1	631.6	0	H
Best model from below	F	94	124 950.2	659.7	0	G	96	19 070.6	17.3	0
Height of burden and host density										
<i>H</i> ₁ and <i>H</i> ₂ are a function of mouse and chipmunk populations	G	96	124 954.5	4.3	0.10	G	96	19 070.6	0	0.97
<i>H</i> ₁ and <i>H</i> ₂ are a function of chipmunk population	F	94	124 950.2	0	0.90	F	94	19 085.5	14.9	0
<i>H</i> ₁ and <i>H</i> ₂ are a function of mouse population	E	94	125 000.0	49.8	0	E	94	19 078.0	7.4	0.02
<i>H</i> ₁ and <i>H</i> ₂ are a function of rodent population	D	95	124 994.4	44.3	0	D	95	19 080.1	9.5	0.01
Best model from below	C	92	124 996.9	46.7	0	C	92	19 084.0	13.4	0
Height of burden and nymph density										
<i>H</i> ₁ and <i>H</i> ₂ are a function of log ₁₀ QLD	C	92	124 996.9	0	1	C	92	19 084.0	0	1
Best model from below	B	90	125 083.0	86.1	0	B	90	19 119.6	35.6	0
Seasonal dynamics										
μ and σ are a function of year and log ₁₀ QLD†	B	90	125 083.0	0	1	B	90	19 119.6	0	1
μ and σ are a function of year‡	A	88	125 289.8	206.8	0	A	88	19 183.9	64.3	0

Note: See Table 1 for information on the organization of the table and an explanation of abbreviations. *H*₁ is the height of the earlier, normal curve; and *H*₂ is the height of the later, generally larger, log-normal curve.
 † The heights of the curves, *H*₁ and *H*₂, are functions of year and grid; variance is a function of year.

may also be more susceptible to tick infestations (Hughes and Randolph 2001).

We formulated separate versions of the nymphal and larval models for mice with these three correlates included in the height terms (*H*, and *H*₁ and *H*₂, respectively) both separately (models H–J) and in combination (models K–N). We had no independent estimates of the age of chipmunks, so we used only sex and mass separately (models I and J) and together (model M).

Question 4: varying aggregation

Both nymphal and larval ticks are highly aggregated on their hosts as measured by the variance/mean ratio of tick burdens (Ostfeld et al. 1996b) or by the dispersion parameter, *k*, of the negative binomial (see Results: Question 4). The variance of the negative binomial is μ(1 + μ/*k*), so as *k* decreases, the variance increases faster with the mean, implying greater dispersion, or aggregation. Increasing values of *k* mean less aggregation, or a more random, Poisson-like distribution. When *k* approaches ~20, the negative binomial and Poisson distributions are essentially indistinguishable. The estimates of *k* for tick burdens on mice and chipmunks are

well below that limit (see Results: Question 4). The degree of aggregation, however, may be exaggerated when distinct groups (e.g., sexes or age classes) are lumped together (Shaw et al. 1998). We therefore estimated separate *k*'s for the groups that we could distinguish: sex for both chipmunks and mice (P models), and age classes for mice (O models). In addition, the degree of aggregation has been found to decrease as average burdens increase (Shaw et al. 1998, Wilson et al. 2002), suggesting that individual differences in tick burdens, and their influence on disease transmission, becomes relatively more pronounced when mean burdens are low. We therefore formulated models that allowed *k* to vary as a function of the expected burden for each individual observation *i* ($k = k_0 + \beta_k \times E[\text{obs}_i]$) (models Q).

Question 5: super-spreading individuals

Lastly, we wanted to know whether those individuals that feed more nymphs than expected also feed more larvae than expected. If so, the same individuals most likely to be heavily inoculated by infected nymphs are also most likely to feed a large number of uninfected larvae. Again, because burdens change annually, spa-

tially, and especially seasonally, we could not simply compare raw burdens to test for correlations between nymphal and larval burdens. Instead, we used the residuals from the appropriate model; first those from the models with all extrinsic factors included (model F for larval burdens on mice, model G for all else) and then those from the fullest supported models where both extrinsic and intrinsic factors were included. Moreover, since burdens are strongly overdispersed, single observations are unlikely to provide a realistic estimate of an individual's average burden. We therefore divided the year into nymphal and larval seasons (weeks of the year 10–29 and 30–46, respectively) and restricted our analyses to individuals for which there were at least three observations in each period ($n = 289$ mice, $n = 104$ chipmunks). We then calculated the correlation between the mean nymphal residuals during the nymphal season and mean larval residuals later, during the larval season.

RESULTS

Question 1: densities of host-seeking ticks

Densities of host-seeking ticks strongly influenced tick burdens on hosts. Models in which the shape of the log-normal curve varied with $\log_{10}(\text{questing tick density [QTD]})$ were strongly favored over those in which shape variables changed only with year (compare models A and B; Tables 1 and 2). In each case, the shape parameters, μ and σ , changed in such a way that, when densities of host-seeking nymphs and larvae were higher, the expected burdens declined more slowly (e.g., Fig. 1c–f).

The models improved even more when the heights of the curves were allowed to change with the densities of questing ticks (models C; Tables 1 and 2). The \log_{10} -transformed QTD provided a moderately to much better fit than the untransformed tick densities (results not shown), suggesting a saturating relationship between the density of host-seeking ticks and actual tick burdens (e.g., Fig. 3b, f).

Question 2: host densities

Models in which the expected burdens were a function of host densities were strongly supported over those without host density (compare models C–G; Tables 1 and 2). The models in which mice and chipmunks were treated as essentially equivalent hosts (D models) were never favored, suggesting that rodents do not simply passively encounter and feed ticks. Rather, models where burdens varied with the abundances of individual host species were favored, although which host abundances were important varied with host species and tick life history stage.

In the case of nymphal burdens, mouse abundance was a better predictor than chipmunk abundance (compare models E and F in Table 1), although the G models including abundances of both hosts were

strongly (nymphal burdens on mice) or moderately supported (nymphal burdens on chipmunks). In the case of larval burdens, it appears that abundance of the alternative (non-focal) host was a better predictor than abundance of the focal host (compare models E and F; Table 2). Indeed, adding mouse abundance to the model with chipmunk abundance already included provided no added information about larval burdens on mice ($\beta_{\text{mice}} = 0$ for both H_1 and H_2 ; model G for mice; Table 2). For larval burdens on chipmunks, however, there was substantial support for including abundances of both mice and chipmunks (model G for chipmunks; Table 2).

Generally, the trend was for increasing nymphal burdens with increasing abundances of chipmunks, and decreasing nymphal burdens with increasing numbers of mice (Fig. 2a, e), but for larval burdens the results were more complex. Larval burden on mice decreased with increasing number of chipmunks, while larval burdens on chipmunks increased with *both* mice and chipmunks (Fig. 3e).

Question 3: individual correlates

Individual host characteristics were not good predictors of nymphal burdens on chipmunks: The evidentiary weight was equivalent for model G, without any individual characteristics, and models I, J, and M with them (Table 1), meaning that there was little support for including covariates. Models using an individual's sex and age to predict nymphal burden on mice, however, were strongly supported, although the actual effect sizes were relatively small (model L; Table 1, Fig. 2c, d). Although the model that also included the mass of the mice was not as strongly supported (model N), the effect of mass ended up being much stronger in the final model, Q (Fig. 2d). Larger, older mice had fewer nymphs.

Individual host characteristics were generally better predictors of larval burdens on mice and chipmunks (Fig. 3c, d, g) than of nymphal burdens. The larval model including chipmunk masses was strongly supported (model I; Table 2), but there was little or no support for including their sex (models J and M; Table 2). This relationship was negative such that the smallest chipmunks were expected to have 5.5 more larvae than the largest chipmunk (Fig. 3g). In the case of larvae on mice, the model including all covariates (an individual's age and sex and mass) was strongly supported (model N; Table 2). Based on AIC_c values, sex appeared to be a better predictor than mass, which was a better predictor than age, although the effect sizes in the final model, Q, were not necessarily in this order of importance. Males had larger larval burdens than females, and, in contrast to nymphal burdens on mice and larval burdens on chipmunks, larger mice had greater burdens than smaller ones (Fig. 3c, d). Age, however, had the largest effect on expected burdens: Subadults had much larger burdens than adults and juveniles (Fig. 3d).

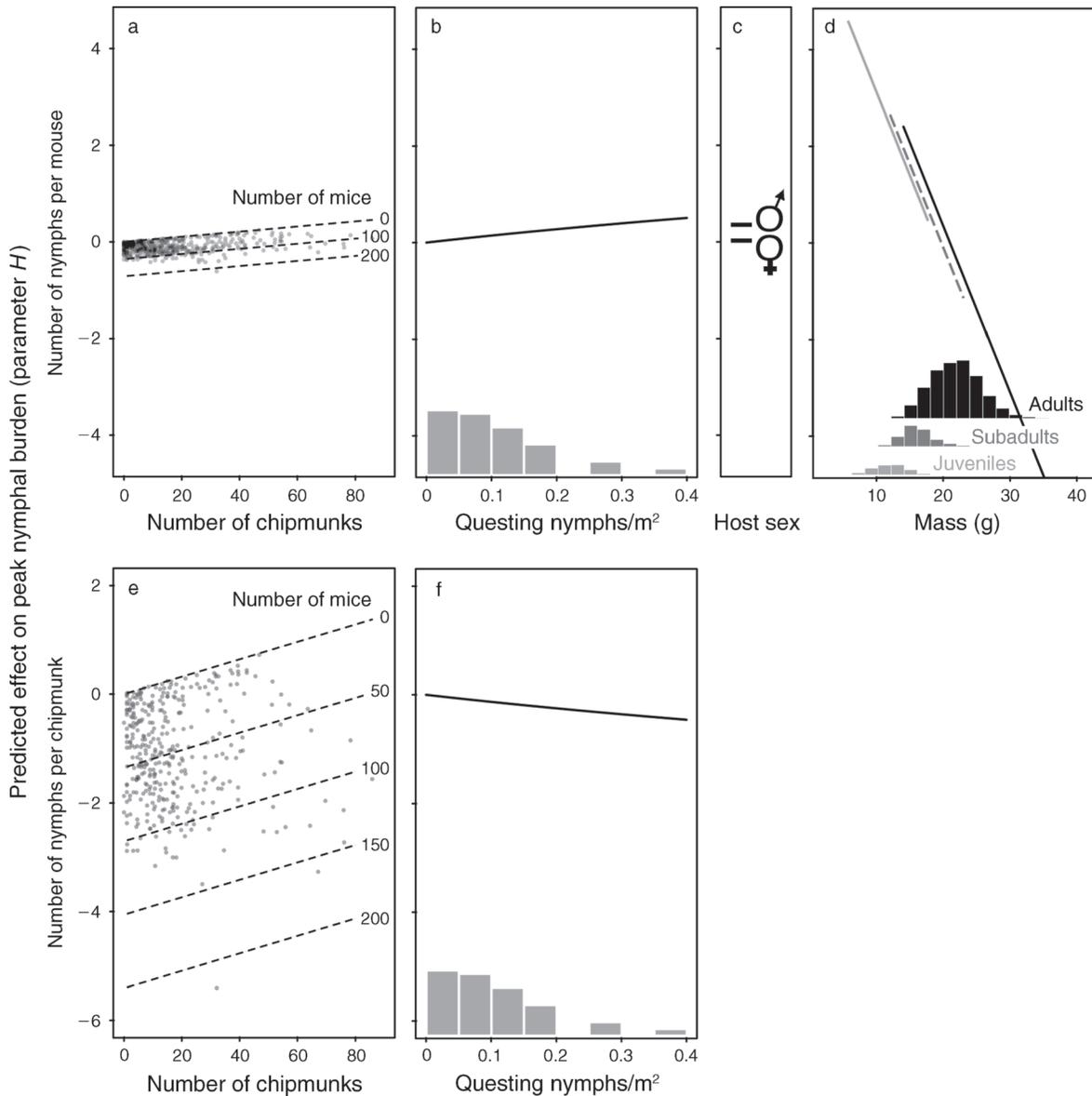


FIG. 2. The effect of (a, e) host abundance, (b, f) densities of questing nymphs (*Ixodes scapularis*), (c) host sex, and (d) host mass and peltage-age (juveniles, light gray line; subadults, dark gray dashed line; and adults, black line) on the predicted peak nymphal burdens on (a–d) white-footed mice (*Peromyscus leucopus*) and (e, f) eastern chipmunks (*Tamias striatus*), as represented by their influence on parameter H (see Fig. 1a) in Q models. Each dot in (a) and (e) represents a particular number of mice and chipmunks found during each sampling period on each grid, data input into the model. Gray histograms in panels (b) and (f) show the frequency of peak questing nymph densities on the six grids over 11 years. Histograms in panel (d) represent the frequency of individual masses of juvenile (light gray), subadult (dark gray), and adult (black) mice.

Question 4: varying aggregation

Estimates of the shape parameter, k , were always < 2 , indicating strongly aggregated tick burdens. Models in which k varied by age class, but not by sex (models O and P, respectively, in Tables 1 and 2), were favored for mice, with lower values of k (greater aggregation at a given mean burden) for younger mice ($k_J = 0.33$, $k_{SA} = 0.48$, and $k_A = 0.68$ compared to the common $k = 0.56$ for nymphs; $k_J = 0.75$, $k_{SA} = 1.00$, and $k_A = 1.28$

compared to the common $k = 1.19$ for larvae; J, juvenile; SA, subadult, A, adult). For chipmunks, there was relatively strong support for different degrees of aggregation between the sexes (P models): Females had lower values of k than males ($k_M = 1.52$ and $k_F = 1.11$, compared with the common $k = 1.23$ for nymphs; $k_M = 0.72$ and $k_F = 0.68$, compared with the common $k = 0.68$ for larvae). The estimated values of k , however, were always low and the difference between sex- and/or age-

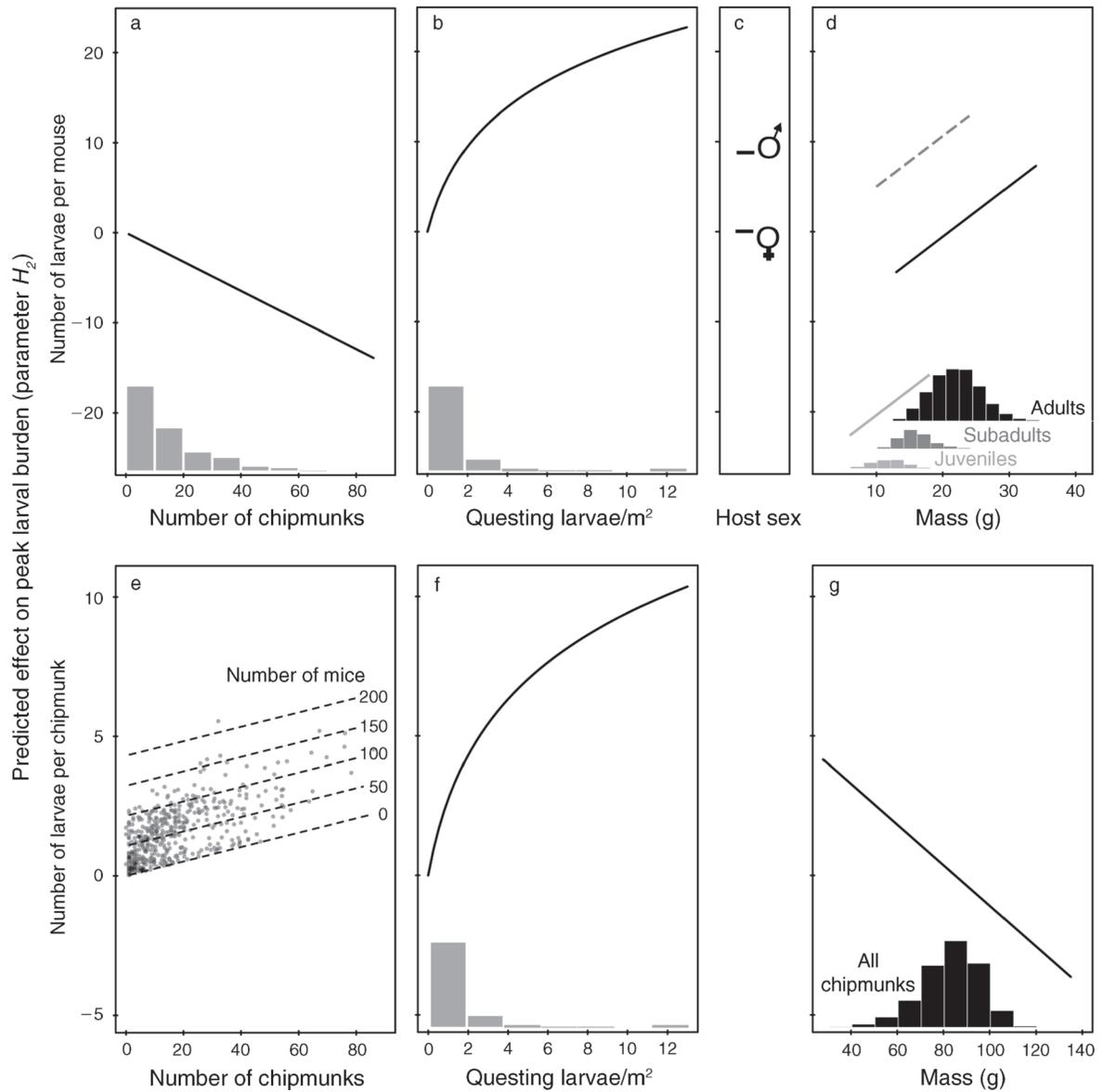


FIG. 3. The effect of (a, e) host abundance, (b, f) densities of questing larvae (*I. scapularis*), (c) host sex, and (d, g) host mass and peltage-age (juveniles, light gray line; subadults, dark gray dashed line; adults, black line) on the predicted peak larval burdens on (a–d) white-footed mice (*P. leucopus*) and (e, f) eastern chipmunks (*T. striatus*), as represented by their influence on parameter H_2 (see Fig. 1b) in Q models. The histogram in panel (a) shows the frequency of chipmunk abundances among sampling periods on the six grids. Similarly, each dot in panel (e) represents the number of mice and chipmunks in a sampling period on a grid. Gray histograms in panels (b) and (f) show the frequency of peak questing larval densities on the six grids over 11 years. Histograms in panel (d) represent the frequency of individual masses of juvenile (light gray), subadult (dark gray), and adult (black) mice. The histogram in panel (g) shows the frequency of masses for all chipmunks observed.

specific estimates were quite minor, deviating little from the common estimates of k . This suggests that the large degree of aggregation commonly observed in tick burden data (e.g., Davidar et al. 1989, Mannelli et al. 1993) is not a result of distinct groups of hosts being lumped together.

As many authors have pointed out (e.g., Scott 1987, Wilson et al. 1996, 2002), estimates of k are not independent of the mean, and so k is not ideal for

comparing the degree of aggregation among groups with different mean burdens. We therefore also calculated ratios of the variance in burdens to the mean (σ^2/μ), which increases with the mean less quickly, among the males and females and between the different age classes (for mice) using the burden data from the three-week period around the predicted peak burden. Consistent with our sex- and age-specific difference in k , the differences in σ^2/μ among the groups were almost



PLATE 1. An adult white-footed mouse (*Peromyscus leucopus*) feeding many larval blacklegged ticks (*Ixodes scapularis*). Photo credit: J. L. Brunner.

always small, and which group showed more aggregation tended to change from year to year. The one exception was larval burdens on chipmunks, which were more aggregated on males in 9 of 11 years (mean σ^2/μ on males = 21.1 and 8.8 on females; Wilcoxon signed rank test, $W = 8$, $P = 0.024$).

The greatest evidentiary support was for models in which k increased with the expected burden on each animal (Q models; Tables 1 and 2). This had the effect of slowing the rate at which aggregation increased with the expected burden, but even at the highest expected burdens ticks were highly aggregated on their hosts ($k \leq 2.5$).

Question 5: super-spreading individuals

There was a moderate positive correlation between the average residual nymphal and residual larval burdens on mice, both when individual covariates were not accounted for (residuals from F and G models, respectively; $\rho = 0.191$, $P = 0.001$) and when they were (residuals from full Q models; $\rho = 0.168$, $P = 0.004$). Similar, although nonsignificant, levels of correlation were found in average nymphal and larval residuals for chipmunks (residuals from models G, without individual correlates, $\rho = 0.175$, $P = 0.075$; residuals from the full models, Q, $\rho = 0.173$, $P = 0.080$).

DISCUSSION

Macroparasites, including the vectors of many pathogens, are often aggregated among their hosts (Wool-

house et al. 1997, Shaw et al. 1998, Wilson et al. 2002), such that some hosts feed many vectors while others feed few. In these cases, mean burdens or biting rates are often misleading indicators of either vector population or pathogen dynamics. The basic reproductive number of a pathogen, R_0 , which indicates how quickly an infection will spread in a naïve population, increases with increasing aggregation of vectors on hosts, even when the mean burden or biting rate does not vary (Woolhouse et al. 1997). When vectors are concentrated on particular individuals or groups of hosts, transmission from infected to naïve vector becomes increasingly likely. Control measures that ignore this heterogeneity are likely to be ineffective, whereas measures that target those hosts that feed a disproportionate number of vectors can more easily reduce transmission to a point where the pathogen fades out (Woolhouse et al. 1997, Perkins et al. 2003, Lloyd-Smith et al. 2005).

Thus, an important goal is to identify the individuals or groups of hosts that feed a disproportionately large number of vectors (e.g., Perkins et al. 2003). Ideally there would be one or a few easily identifiable (and targeted) groups or factors that would account for this variation in vector burdens, allowing us to predict when or where or which hosts will have the largest tick burdens.

Using the long-term data from the Institute of Ecosystem Studies (Millbrook, New York, USA), we found that many factors are important in determining tick burdens on mice and chipmunks. The factor that

had the greatest ability to predict burdens was season (Fig. 1). This is in agreement with several other studies describing the seasonal peaks and troughs of immature tick burdens on rodent hosts (Wilson and Spielman 1985, Fish 1993, Ostfeld et al. 1996a, Goodwin et al. 2001), presumably reflecting tick life history and host-seeking activity. Even after accounting for this strong seasonality, however, we found substantial interindividual heterogeneity in tick burdens. Moreover, no one group or factor adequately predicted tick burdens on mice and chipmunks. Rather, burdens appeared to be a consequence of a complex combination of season, year, questing tick densities, densities of focal and non-focal hosts, as well as individual characteristics such as sex, size, and age. Single-factor explanations were incomplete and, given the correlation between many factors (e.g., age and mass, the abundance of mice and chipmunks) may even suggest spurious relationships. Only by addressing the multiple levels of interacting factors can we begin to understand the causes and consequences of such variable tick burdens on small-mammal hosts.

Question 1: densities of host-seeking ticks

It is clear, if not surprising, that the density of ticks questing for hosts is an important predictor of actual tick burdens on hosts. This is particularly true for larvae, which are much more abundant than nymphs on the ground and on hosts. With greater densities of ticks questing for hosts, tick burdens on hosts increased, but only to a point. Two lines of evidence suggest that hosts can be saturated. First, as questing tick densities (QTD) increased, burdens remained at near-peak levels longer (Fig. 1d, f). Second, there was strong support, at least for larval burdens, for models relating the heights of these curves to the $\log_{10}(\text{QTD})$, which started to saturate at higher densities (Fig. 3b, f), over models with a simple linear relationship (not shown). This is important because it suggests that many questing ticks fail to find a host, at least in some years or locations. It implies that hosts might be limiting and therefore regulate vector populations (e.g., Ostfeld et al. 2006). It also suggests that transmission rates of tick-borne pathogens such as *Borrelia burgdorferi* will saturate when vector densities are very high.

Question 2: host densities

The abundance of hosts also influenced tick burdens on mice and chipmunks, often strongly, but not always in a consistent direction. These two host species were clearly not just different-sized versions of the same kind of host, passively acquiring ticks. If that were the case, the "rodent population" models (D) would have been supported. Instead, the two host species interacted in a way that suggests some behavioral interaction between hosts, perhaps altered movement or space use (e.g., Schnurr et al. 2004), or changes in grooming behavior

when densities increase. At a given mouse abundance, increasing the number of chipmunks increased the nymphal burdens on both mice and chipmunks and the larval burdens on chipmunks. Larval burdens on mice, however, decreased sharply with increasing chipmunk abundances (Fig. 3a), as would be expected if chipmunks were intercepting ticks that otherwise would have fed on mice. Similarly, nymphal burdens on chipmunks declined with increasing numbers of mice (Fig. 2e), suggesting that mice draw nymphs away from chipmunks.

These results are highly relevant to human risk of exposure to Lyme disease. Mice are high-quality hosts for larval ticks, meaning that larvae feeding on them have a high probability of surviving and molting. They are also highly efficient reservoirs for *B. burgdorferi* (Lane et al. 1991, LoGiudice et al. 2003, Brisson and Dykhuizen 2004). Chipmunks, which are less competent reservoirs for *B. burgdorferi*, are thought to be key blood-meal hosts for nymphal ticks in eastern and central North America (Mannelli et al. 1993, Schmidt et al. 1999). Our results suggest that abundant populations of alternate hosts can reduce encounters between ticks and their primary hosts (mice for larvae, chipmunks for nymphs). Termed "encounter reduction" by Keesing et al. (2006), this deflection of tick meals away from hosts that are important to either tick populations or pathogen transmission provides a mechanism by which changes in host community composition can reduce disease risk.

One other interesting finding is that, even after accounting for the dramatic year-to-year variation in densities of hosts and host-seeking ticks (Goodwin et al. 2001, Schaubert et al. 2005, Ostfeld et al. 2006), the year effect on the expected burdens (H , and H_1 and H_2) remained large (not shown). There remain some unexplained, but important factor(s) responsible for the large amount of interannual variation in tick burdens.

Question 3: individual correlates

We predicted that individual attributes, such as sex or age or size (mass), would have a strong association with tick burdens, and as such could be used to identify the individual hosts responsible for feeding most ticks. This was not the case. While models with individual attributes were favored in some cases, there was little support for them in others. Male mice, for instance, had larger burdens than females: about 0.3 more nymphs and 8.7 more larvae per host (Figs. 2c and 3c), which is a common finding (e.g., Davidar et al. 1989, Schmidt et al. 1999, Perkins et al. 2003), but sex was not a good predictor of burdens on chipmunks. Mass and age of mice were consistently and strongly associated with tick burdens, but the direction of these associations varied. Smaller, younger mice, for instance, had greater nymphal burdens than larger, older mice (Fig. 2d), but

subadults had greater larval burdens than adults, which had greater larval burdens than juveniles (Fig. 3d). Again, we were not able to determine the age of chipmunks as we could with the pelage of mice, but the general expectation is that older individuals tend to be heavier. Larval burdens on chipmunks tended to decrease with increasing mass (and presumably age), but mass did not explain nymphal burdens on chipmunks: This particular data set had equivocal support for all models with individual correlates and those without. The simplest explanation for these varied and conflicting results is that host behavior probably influences how individuals come into contact with (and potentially remove) questing ticks, but that individual behavior changes with age, sex, size, and likely other unmeasured factors in complex ways.

Unfortunately, these results suggest that it may be impossible to determine a priori which types of individuals or groups should be targeted by disease management or interventions strategies. Readily identifiable groups do not account for enough variation in burdens to warrant special focus. Male mice, for instance, were the most distinct group in terms of larval burdens, but even they only feed ~56.6% of the mouse-fed larval ticks compared with females (found by integrating the curves for model L in Table 2; a similar proportion was found in the raw data), and mice are only one component of the entire community of tick hosts.

Question 4: varying aggregation

Expected burdens, however, are not the whole story. The degree of aggregation can be just as important to pathogen transmission as mean burdens. When vectors concentrate on a relatively few hosts, those hosts are both more likely to become infected and more likely to infect naïve vectors. *Ixodes* ticks are highly aggregated on their hosts (Ostfeld et al. 1996b, Shaw et al. 1998, Perkins et al. 2003). Measures of aggregation, however, can be inflated when data from distinct groups are lumped together, and parasite aggregations often tend to increase with host age (e.g., Pacala and Dobson 1988, Shaw et al. 1998, Wilson et al. 2002). We therefore separately estimated the aggregation parameter, k , for males and females, and for the observable age classes of mice. While there was some moderate support for these models, in particular, partitioning the dispersion by age in mice and by sex in chipmunks, the estimated values of k were all quite low (suggesting a high degree of aggregation) and did not vary a great deal between the groups or from the original common estimate of k . Moreover, with the exception of larval burdens on chipmunks, the variance/mean ratios were only slightly and inconsistently different between males and females, or among age classes for mice. This suggests that the large degree of aggregation observed in tick burden data did not come from combining distinct groups. Rather it

appears that certain, as yet unidentified (perhaps unidentifiable), individual hosts within both sexes and within each age class feed a large number of ticks while most do not. Again, it may be impossible to identify appropriate hosts a priori to target for vaccination or other control strategies.

Another common pattern observed in macroparasite distributions is for estimates of k to increase with the mean, meaning that the variance (and variance/mean ratios) increase more slowly with increasing mean burdens (Shaw et al. 1998, Wilson et al. 2002). In accordance with this pattern, we found the greatest support for models in which k was a linear, increasing function of the expected burden such that ticks were distributed (relatively) more evenly with increasing burdens. As noted earlier, R_0 is inversely related to k (and thus increases in proportion to the degree of aggregation; Woolhouse et al. 1997). This suggests that individual heterogeneity is most important to transmission of *Ixodes* tick-borne diseases when vector burdens are low.

Question 5: super-spreading individuals

Of course, given that *B. burgdorferi* and other pathogens are transmitted from nymphal ticks to vertebrate hosts to larval ticks, we must consider both tick life history stages together. If nymphs tend to feed on certain hosts, and larvae on others, then the potential for transmission is greatly reduced. If instead nymphal and larval burdens are positively correlated, then those hosts most likely to be frequently infected are the same hosts feeding and infecting larval ticks, ensuring transmission from one tick generation to the next.

We found a moderate positive correlation between the mean deviation from expected nymphal and larval burdens for mice, and a similar, but nonsignificant degree of correlation between these nymphal and larval residuals on chipmunks. That is, those individuals that fed more nymphs than expected also tended to feed more larvae than expected. This correlation remained even after we took into account individual correlates, although there is no evidence to suggest that certain groups or individual correlates are associated with increased burdens. Clearly, some unmeasured quality of mice and chipmunks makes certain individuals more likely to feed ticks and thus more important to the transmission of tick-borne diseases like Lyme disease.

Given the large number of mechanisms that can generate aggregated burdens, it is impossible to infer from these analyses the underlying process(es). However, the behavior of hosts appears to be an important aspect of the encounter between questing ticks and hosts. Questing nymphal ticks and, especially, larval ticks are aggregated in space (Daniels and Fish 1990, Ostfeld et al. 1996a, b). Any factor that increases the likelihood that an individual host encounters an aggregation of questing ticks should dramatically increase its tick burden.

Moreover, the spatial heterogeneity of questing ticks is likely to accentuate differences among individuals, making the aggregation more pronounced (Wilson et al. 2002). Host ranging behavior, home range size, time spent moving or immobile, and use of microhabitats favored or avoided by ticks, are all likely to affect host–tick encounter rates as well as the probability of encountering an aggregation.

Individuals may also vary in their ability to remove feeding ticks, either by grooming or via immunological mechanisms. Self-grooming by mice and chipmunks removes substantial numbers of immature ticks (Shaw et al. 2003) and allogrooming, particularly of dependent young by their mothers, might play a role in reducing tick burdens, although this appears not to be true for nymphs on juvenile mice (Fig. 2d). An individual's immune response(s) could also lower its tick burden, either indirectly, by inducing a stronger grooming response, or directly, by attacking and killing embedded ticks (Brossard and Wikel 2004). Behavioral and immunological mechanisms underlying individual heterogeneities remain to be explored.

We began with the objective of identifying the group(s) or characteristics of hosts responsible for feeding most ticks (e.g., male *Apodemus flavicollis* mice feeding *Ixodes ricinus*; Perkins et al. 2003). If they could be found and targeted, for instance, with injectable or bait-delivered vaccine (e.g., Tsao et al. 2004), intervention strategies would be much more effective (Woolhouse et al. 1997, Lloyd-Smith et al. 2005). What we must conclude instead is that tick burdens are a complex function of temporal, spatial, and individual-specific factors. While there is strong evidence that certain individual hosts feed more ticks than expected, we cannot identify them a priori.

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