Published by Associazione Teriologica Italiana
Hystrix, the Italian Journal of Mammalogy
Volume 28 (2): 202–207, 2017
OPEN ACCESS
Available online at:
http://www.italian-journal-of-mammalogy.it
doi:10.4404/hystrix-28.1-12299

Research Article

EBHS in European brown hares (*Lepus europaeus*): disease dynamics and control

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Keywords:
European Brown Hare Syndrome
brown hare
SIR model
population dynamics

Article history:
Received: 23 December 2016
Accepted: 26 May 2017

Acknowledgements
The authors gratefully acknowledge the local hunters (Ambito Territoriale di Caccia Unico di Brescia, Brescia Province, Northern Italy); without their cooperation, the validation of this study would not have been possible. The authors wish to thank Dr. Lesley Benyon (ScienceDocs) for the editing of this manuscript.

Abstract

Brown hares have undergone a substantial population decline in Europe during recent decades, caused by, among other factors, the occurrence of European Brown Hare Syndrome (EBHS). To improve our knowledge regarding EBHS epidemiology, we developed a mathematical model that takes into consideration both brown hare biology and the infection dynamics of the EBHS virus (EBHSV). The model consists of eight ordinary differential equations simulating the spread of the virus in a closed hare population. Simulations showed that EBHSV's transmission has complex dynamics, which are strongly affected by the hare density. In particular, a density threshold of 7 individuals/km^2 was identified, determining two opposite epidemiological patterns: the extinction of the EBHSV below the threshold and its endemic stability when the hare population density is above the threshold, with a seroprevalence proportional to the population density. The model was validated using serological data collected in different areas in the province of Brescia (Northern Italy). The results suggested that the maintenance of the endemic circulating viral level through density control mechanisms is the best strategy for reducing EBHS's impact.

Introduction

European brown hare (*Lepus europaeus*) is an important game species that is subjected to specific hunting management and restocking programs. In the last decades, a progressive decline in the hare population has occurred in Italy, as well as in the rest of Europe (Edwards et al., 2000). One major cause of this decline is the occurrence of European Brown Hare Syndrome (EBHS), a highly contagious disease, that emerged in the '80s and is now considered endemic in all European countries (Duff and Gavier-Widén, 2012). EBHS can be transmitted by direct contact with infected animals, or indirectly through infected materials or equipment used during capture operations, because of the high environmental resistance of the causal virus (EBHSV). An EBHSV infection can achieve almost 100% morbidity when the virus is introduced into a naive brown hare population, and the induced mortality is age-dependent and varies from 40 to 70% (Cammi et al., 2003; Duff and Gavier-Widén, 2012). The disease has not been observed in hares younger than 2–3 months of age, because if they come into contact with the virus, the resulting infection leads to the development of lifelong immunity, without the exhibition of any clinical symptoms (Zanni et al., 1993; Lavazza et al., 1997).

Targeted EBHS surveillance is commonly based on the assessment of the immunological status of the population using serological determination of anti-EBHSV titres (Paci et al., 2011). On the basis of survey data, Lavazza et al. (1997) hypothesized that the spread and circulation of EBHSV are linked to the hare's population density. In particular, they considered the presence of a density threshold, between 8 and 15 hares/km^2, that determines which of two opposite scenarios occurs. One scenario is characterized by a low EBHSV circulation (i.e. a high number of seronegative hares) below the threshold, and the other by a high EBHSV prevalence (i.e. high number of seropositive hares) above the threshold.

To explore the heterogeneity involved in these field observations, the role of population abundance in the epidemiological pattern of EBHS should be investigated using an appropriate epidemiological modelling approach. Because of the importance of the host age in viral transmission and occurrence of disease outbreaks, as well as the age related contact rate of the host, elements of the population ecology of the species, such as host's social behaviour and dimensions of the home range, should be included in the model. This results in the consideration of an eco-epidemiological model of EBHS dynamics.

Dynamical models inspired by an eco-epidemiological approach have been proposed to investigate the transmission of infectious wildlife disease-causing agents, focusing in particular on those that have a zoonotic impact (Iwami et al., 2007), can be transmitted to livestock (Keeling, 2005; Gilioli et al., 2009) or threaten endangered wildlife populations (White et al., 2014). For example, models involving wildlife infections include rabies in fox (Anderson et al., 1981), sarcoptic mange among chamois (Lunelli, 2010), and tuberculosis in badgers (Anderson and Trewhella, 1985; Cox et al., 2005) and white-tailed deer (McCarty and Miller, 1998).

To the best of our knowledge, there are no published models describing the relationship between the disease prevalence and the population abundance for the EBHS. The lack of modelling tools and the need to account for the ecology of the host in the disease dynamics motivated the model-based exploration of the dependence of epidemiological patterns on the hare's population abundance.

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Methods

Model description

To simulate the eco-epidemiology of EBHS in a closed age-structured hare population, we developed a compartmental model, combining demographic and disease transmission processes.

The demographic structure of the hare population is based on three age classes: newborn (N), younger than 3 months, young (Y), from 3 to 6 months, and adult (A), older than 6 months. A density-dependence in hare demography is assumed to take place on host fecundity, whereas no evidence of relation between hare density and mortality/survival rate were described (Frylestam, 1979; Marboutin et al., 2003; Schmidt et al., 2004). Demographic processes, including development, mortality and fecundity, are represented by fluxes in the diagram in Fig. 1.

The number of individuals in the three classes changes due to demographic processes, including development and mortality. Moreover, adults reproduce, contributing to the renewal of the newborn class.

The EBHSV infection process changes the status of the individuals from susceptible to infected and infectious, and finally to immune or recovered. To model the infection dynamics, individuals in each age class were further classified into three categories: susceptible (S), infected and infectious (I) and recovered/immunised/immune (R). Since hares younger than 2–3 months of age do not develop symptoms or die from EBHS, the class of the infected/infectious newborn hares was omitted. Newborn hares are considered to be susceptible (N_S) after birth, at least after the disappearance of maternal immunity, and when they come into contact with the virus they pass to the recovered class (N_R). Those newborn hares not exposed to the virus within three months develop into susceptible young hares (Y_S) and then, after three months, into susceptible adults (A_S). Susceptible individuals that come into contact with infected and infectious individuals, either young or adult, also become infected and infectious (Y_I or A_I respectively). They can either die from EBHS at a stage-specific mortality rate k_i ($i = Y, A$) or recover at a rate r and join the recovered class (Y_R or A_R, respectively). Recovered hares do not contribute to the transmission of the virus and remain immune to further infections. Since the infection from EBHSV has typically a short clinical course, hares spend proportionally little time in the infected class: for this reason the demographic processes (natural mortality, development and reproduction) involving infected hares (both young and adult) were assumed to be negligible and were not considered in the model. The population dynamics and disease processes illustrated above can be described by the following system of eight ordinary differential equations (ODEs), in which the variables are expressed in terms of the number of animals per unit area:

$$\frac{dN_S}{dt} = f\left(1-\frac{A_S+A_R}{K}\right)(A_S+A_R) - i_N\left(1-e^{-\mu_N(Y_I+A_I)}\right)N_S + \\ - d_N N_S - m_N N_S \tag{1}$$

$$\frac{dY_S}{dt} = d_N N_S - i_Y\left(1-e^{-\mu_Y(Y_I+A_I)}\right)Y_S - d_Y Y_S - m_Y Y_S \tag{2}$$

$$\frac{dA_S}{dt} = d_Y Y_S - i_A\left(1-e^{-\mu_A(Y_I+A_I)}\right)A_S - m_A A_S \tag{3}$$

$$\frac{dY_I}{dt} = i_Y\left(1-e^{-\mu_Y(Y_I+A_I)}\right)Y_S - (k_Y+r)Y_I \tag{4}$$

$$\frac{dA_I}{dt} = i_A\left(1-e^{-\mu_A(Y_I+A_I)}\right)A_S - (k_A+r)A_I \tag{5}$$

$$\frac{dN_R}{dt} = i_N\left(1-e^{-\mu_N(Y_I+A_I)}\right)N_S - d_N N_R - m_N N_R \tag{6}$$

$$\frac{dY_R}{dt} = d_N N_R + rY_I - d_Y Y_R - m_Y Y_R \tag{7}$$

$$\frac{dA_R}{dt} = d_Y Y_R + rA_I - m_A A_R \ , \tag{8}$$

where: f, maximum fecundity; $d_N = d_Y$, development rate (newborn and young); $m_A = m_Y$, natural mortality (young and adult); m_N, natural mortality (newborn); r, recovery rate; i_N, maximum infection rate for newborn hares; μ_N, density dependent infection parameter (newborn); i_Y, maximum infection rate for young hares; μ_Y, density dependent infection parameter (young); i_A, maximum infection rate for adult hares; μ_A, density dependent infection parameter (adult); k_Y, EBHS-induced mortality (young); k_A, EBHS-induced mortality (adult); K, carrying capacity of the environment.

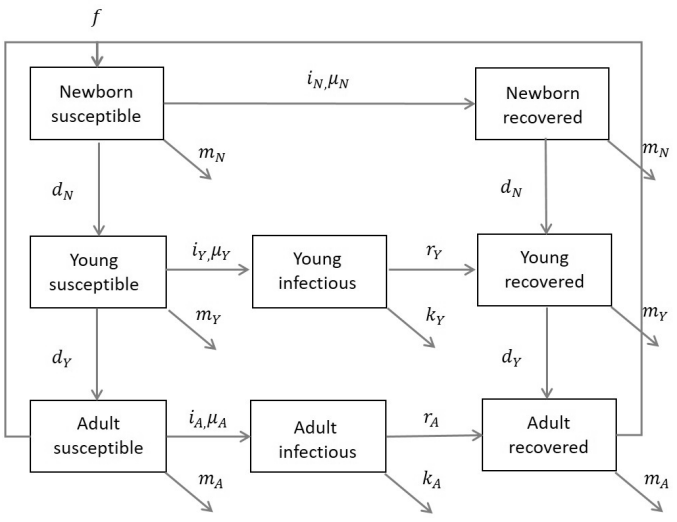

Figure 1 – The compartmental model, combining both demographic and EBHS epidemiological processes. The demographic structure of the hare population is composed of three age classes: newborn (N), younger than 3 months, young (Y), 3–6 months, and adult (A), older than 6 months. Demographic processes, including development, survival and fecundity, are represented by vertical fluxes in the diagram. In the figure f, represented the maximum fecundity; $d_N = d_Y$, the development rate (newborn and young); $m_A = m_Y$, the natural mortality (young and adult); m_N, the natural mortality (newborn); r, the recovery rate; i_N, the maximum infection rate for newborn hares; μ_N, the density dependence infection parameter (newborn); i_Y, the maximum infection rate for young hares; μ_Y, the density dependence infection parameter (young); i_A,the maximum infection rate for adult hares; μ_A, the density dependence infection parameter (adult); k_Y, the EBHS-induced mortality (young); k_A, the EBHS-induced mortality (adult) and K, the carrying capacity of the environment.

Model parameter definitions and estimations

The model parameters were taken from published literature regarding the biological characteristics of the European hare, except for the two parameters involved in the transmission process, i an μ, which were calibrated using field data. All of the parameters, together with their definitions and values, are listed in Tab. 1.

Demographic parameters include development, mortality and recruitment rates. Development depends on the stage-specific development rates d_N and d_Y, which describe the rate of individuals transferred from N to Y classes and from Y to A classes, respectively. Development rates were estimated to be equal to $\frac{1}{90}\text{days}^{-1}$ in our model because, according to the biological data, hares are supposed to spend 3 months (90 days) in both the N and Y classes (Trocchi and Riga, 2005). Mortality is described by a linear function with age-specific mortality rates. Mortality rates (0.0022 days^{-1} for young and adult hares and 0.0033 days^{-1} for newborn hares) were derived from the mortality statistics reported by Trocchi and Riga (2005).

The recruitment is described by a density-dependent fecundity rate function, in which the maximum fecundity rate f, which corresponds to an average of 13 leverets per female per year (Trocchi, *personal data*, Bologna 2010–2015), is multiplied by the term $\left(1-\frac{A_S+A_R}{K}\right)$, which depends on the carrying capacity K. This carrying capacity-dependent component that appears in the fecundity rate function was chosen to simulate the decrease in fecundity that occurs once a population is close to K.

Disease-specific parameters include the infection and the recovery rates, as well as the disease-induced mortality. The recovery rate $r = \frac{1}{3}\text{days}^{-1}$ was estimated from Frölich and Lavazza (2008), who reported 72 h as the average duration of infection. EBHS-induced mortality rates, 0.2 days^{-1} for adult hares and 0.46 days^{-1} for young hares, were estimated from survey data by Cammi et al. (2003).

Table 1 – Hare demographics and EBHSV infection parameters in the transmission model. Parameters were estimated from published literature on the European hare or calibrated using field data.

Parameter	Description	Value	References
f	Maximum fecundity	13 (leverets/female)/year	Trocchi, *personal data* Bologna 2010–2015
$d_N = d_Y$	Development rate (newborn and young)	(1/90) / days	Frölich and Lavazza (2008); Trocchi and Riga (2005)
$m_A = m_Y$	Natural mortality (young and adult)	0.0022 / days	Trocchi and Riga (2005)
m_N	Natural mortality (newborn)	0.0033 / days	Trocchi and Riga (2005)
r	Recovery rate	(1/3) / days	Frölich and Lavazza (2008)
i_N	Maximum infection rate for newborn hares	0.3040 / days	Calibration
μ_N	Density dependent infection parameter (newborn)	1.0507 / (hares/km^2)	Calibration
i_Y	Maximum infection rate for young hares	0.3040 / days	Calibration
μ_Y	Density dependent infection parameter (young)	1.0507 / (hares/km^2)	Calibration
i_A	Maximum infection rate for adult hares	0.3040 / days	Calibration
μ_A	Density dependent infection parameter (adult)	0.2139 / (hares/km^2)	Calibration
k_Y	EBHS-induced mortality (young)	0.46 / days	Cammi et al. (2003)
k_A	EBHS-induced mortality (adult)	0.2 / days	Cammi et al. (2003)
K	Carrying capacity of the environment	$5 \leqslant K \leqslant 100$ hares/km^2	Trocchi and Riga (2005)

Model calibration

A calibration process based on a least squares method was used to estimate the parameters involved in the infective agent's transmission process. The infection process is described by a monotonically increasing, convex and uniformly bounded function, following the Ivlev functional response (Ivlev, 1961). The Ivlev functional response, a non-linear density-dependent function, is a simple function derived from prey-predator models and describing the outcome of a search/contact process. This function has two positive parameters: i_k $(k = N,Y,A)$, which represents the maximum infection rate and μ_k $(k = N,Y,A)$, which regulates the relationship between disease transmission and hare density. This non-linear density-dependent model of infection was introduced to account for the action of several density-related factors, such as the persistence of the virus in the environment, the host's social behaviour and the dimension of the home range, that play a role in the disease transmission process (Pearce et al., 2006; Preedy et al., 2007).

Since there is no evidence of an influence of age on the infection rate, the value of the parameter i_k, representing the susceptibility to the infection, was assumed to be the same for all the ages.

As for the density, both newborn and young hares seem to be particularly sensitive, because they tend to stay in the familiar group home range until they reach sexual maturity. On the contrary, because of their solitary habits, adult hares seem to be less sensitive to density-dependent EBHSV-associated factors. Therefore, an increase in population density is more likely to affect the average contact rates of newborn and young animals rather than that of adults. Thus, the parameter μ_k for newborn and young hares was assumed to be equal and higher than that of the adults. Both i and μ_k were estimated using the model and published biological data obtained from field surveys (Paci et al., 2011; Chiari et al., 2014).

Simulation results were compared with serological data, collected from free-ranging hares captured for restocking reasons between December and January over seven consecutive years (2006–2013), that estimated the disease prevalence. The samples were collected in seven protected, but open, "breeding for restocking" grounds (BfRGs) in the province of Brescia (Northern Italy) characterized by different density values. Chiari et al. (2014) reported that in areas with density values higher than 15 hares/km^2 the recovered fraction was greater than 60% during six out of seven surveyed years. The calibration procedure was based on data derived from the BfRG in Quinzano because a constant brown hare density was reported in this BfRG over a long survey period. The set of parameters found to minimize the distance between the model output and the field data in the sense of least squares was: i=0.3040 (95% CI: 0.2947–0.3133); $\mu_N = \mu_Y$=1.0507 (95% CI: 0.9952–1.1041); μ_A=0.2139 (95% CI: 0.205–0.2230). Figure 2 shows the model fitting field data used to estimate the infection parameters.

Sensitivity analysis

The aim of the sensitivity analysis was to describe how an infinitesimal change in the model parameters could affect the output variables. The sensitivity estimation was performed as described by Keeling and Gilligan (2000):

$$S = \lim_{P \to P_0} \frac{\log\left(\frac{V(P)}{V(P_0)}\right)}{\log\left(\frac{P}{P_0}\right)} = \frac{P_0}{V(P_0)} \frac{\partial V}{\partial P} \quad , \tag{9}$$

where S represents the sensitivity with respect to the parameter P (whose default value is P_0) and V represents the model output. In the present work the fraction of A_R represents the output variable, and the sensitivity of the model was explored with respect to the K and the parameters involved in the infection transmission, i and μ_k.

Simulations

Simulations were run to investigate the hare population and the disease dynamics. The equations (1–8) were numerically solved using Matlab ODE solvers (Release 2014a).

Population dynamics in the absence of infection were investigated by running simulations over a period of 10 years. The initial condition of the population was supposed to be half K, which varies in the range of 5–100 hares/km^2, with an initial age ratio of $\frac{N+Y}{A}$=1.5, being close to the 1.53 value reported by Trocchi and Riga (2005). Infection dynamics

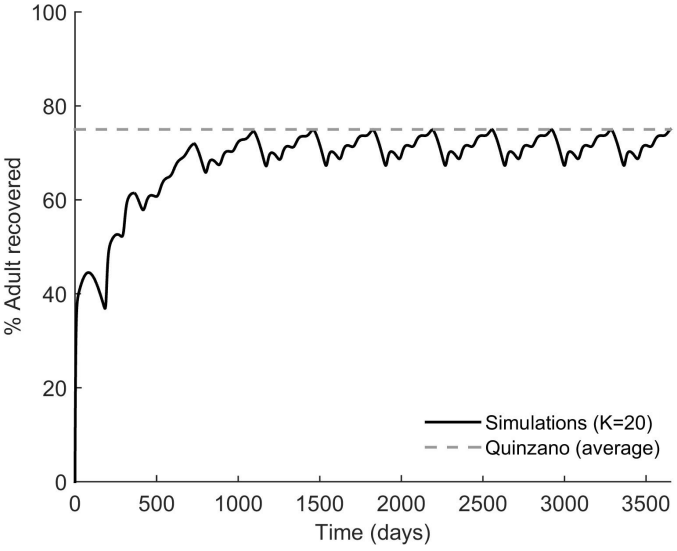

Figure 2 – Result of the fitting procedure used to estimate the infection parameters i and $\mu_N = \mu_Y$ and μ_A.

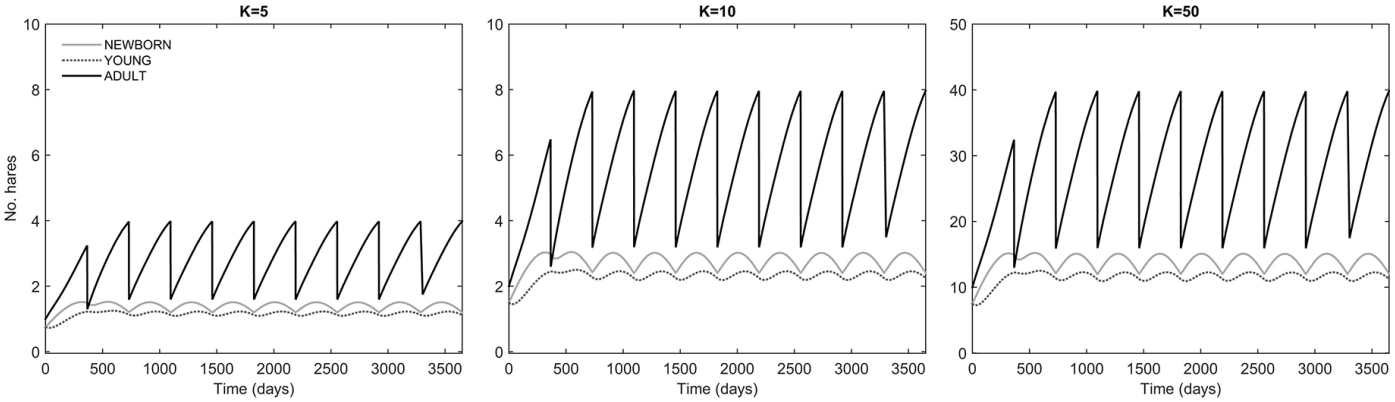

Figure 3 – Time evolution of the hare population model without infection ($Y_I = A_I = 0$) at carrying capacity (K) values of 5, 10 and 50 hares/km^2.

were simulated over the same time period and within the same range of K. Initial conditions were chosen as above, but one adult hare was assumed to be infectious at day zero. In both simulations a total of 60% of adult hares were removed yearly from the population to simulate the regular hare translocation (i.e., captured in protected areas, transported and released in public hunting areas), which takes place every winter in each BfRG.

Basic reproduction number

The basic reproduction number R_0 is a key concept in epidemiology and in the study of infection dynamics. It is defined as the expected number of secondary infections arising from a single infectious individual in a completely susceptible population; for this reason, it is commonly used as a threshold parameter that predicts whether an infection will spread. In particular, when R_0>1 the infection is expected to invade the susceptible population, whereas if R_0<1 the infection will probably die out in the long run. There are several common methods of formulating R_0 as well as means of estimating its value from epidemiological data. Following Heffernan et al. (2005), R_0 was estimated at different density values from the final fraction of susceptibles $S(\infty)$:

$$R_0 = \frac{\log S(\infty)}{S(\infty) - 1} \quad . \tag{10}$$

Such an approach is appropriate for any model with a closed population, where the infection leads either to immunity or death, as in the case of EBHS (Heffernan et al., 2005).

Results

Because of the complexity of the system, the properties of the model were investigated from a numerical point of view only. Simulations were run at different K values to investigate the presence of thresholds that determine regime shifts in the epidemiological pattern (from endemic stability to disease extinction in local and isolated populations).

Population dynamics

Population dynamics were first investigated in the absence of infection (Y_I and A_I=0) within a K range from 5 to 100 hares/km^2. The time evolution of the model at three different K values (5, 10 and 50 hares/km^2) is reported in Fig. 3.

At 5 hares/km^2, the system reached K within the first 2 years with an age ratio $\frac{N+Y}{A}$=1.46 after the last sampling. At 10 and 50 hares/km^2 the equilibrium was reached within 2 years with an age ratio of 1.42 after the last sampling (Fig. 3). Density values mentioned in this section refer to pre-breeding values and account for the three age-classes together, unless otherwise specified.

Epidemiological patterns

EBHSV transmission dynamics were investigated for the same K values that had been evaluated in the disease-free dynamics. The dynamics of the epidemiological system at the three selected K values are reported in Fig. 4.

Since two distinct behaviours of the model at 5 and 10 hares/km^2 were found, the intermediate values were carefully evaluated. Simulations revealed that the system had a threshold-like behaviour. In particular, a density threshold of approximately 7 individuals/km^2 that separated two opposite epidemiological patterns, the extinction of the disease in the hare population below the threshold and the persistence above, was identified.

With a value of K of 5 hares/km^2 at the equilibrium the whole population was susceptible to the infection, and there were no infected or recovered individuals. In this simulation, the virus underwent a rapid extinction.

However, above the carrying capacity threshold of 7 individuals/km^2, the fraction of infected hares was always different from zero and the dynamics of the EBHSV infection progressively converged toward an endemic equilibrium. At a density of 10 hares/km^2 the population was mostly susceptible at the end of simulated time horizon, but a significant fraction of recovered (42%), and a small amount of infected individuals, were constantly present (Fig. 4).

When the K value was set at 50 hares/km^2 the population was mostly recovered (89%).

Overall, the fraction of the population recovered at equilibrium was positively related to K, ranging from 16% at a density value of 7 hares/km^2 to 95% at the highest density studied (100 hares/km^2). The expected seroprevalence of young and adult hares as a function of K is reported in Fig. 5.

Sensitivity analysis

K was determined to be the most sensitive parameter, as concluded by Lavazza et al. (1997) (Tab. 2). Thus, small changes in this parameter produce large variations in the A_R fraction. It should be emphasized that in our model hare populations tend to saturate the different carrying capacity values. Different K values were tested to verify the effects on the output variable (fraction recovered). In particular, the impacts of small changes in the parameters on the model's behaviour were found to be greater at low K values rather than at high values. The infection rate i and the parameters $\mu_N = \mu_Y$ and μ_A were found to be less sensitive.

Table 2 – Sensitivity analyses of the model parameters. The carrying capacity (K) was the most sensitive parameter. The infection rate i, and the parameters $\mu_N = \mu_Y$ and μ_A, were found to be less sensitive.

Parameter	Description	Sensitivity
K	Carrying capacity	35
i	Infection rate	0.5
$\mu_N = \mu_Y$	Density dependent infection parameter (newborn and young)	0.3
μ_A	Density dependent infection parameter (adult)	0.25

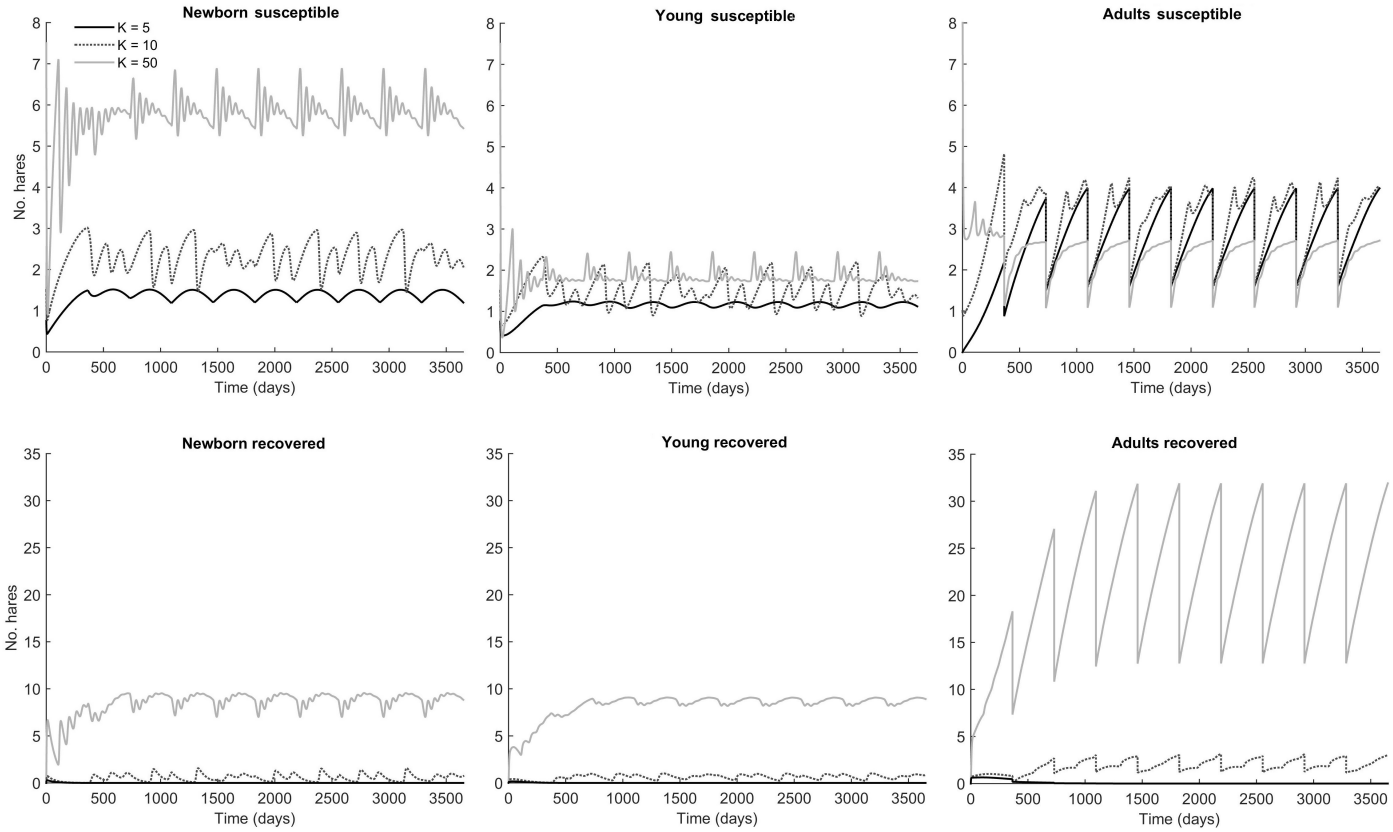

Figure 4 – Time evolution of EBHSV transmission dynamics at carrying capacity (K) values of 5, 10 and 50 hares/km^2.

Basic reproduction number

The basic reproduction number R_0 was found to vary with the carrying capacity K; in particular, its value was found to be approximately one around the threshold of 7 hares/km^2 and to increase above it.

Estimates of the basic reproduction number R_0 for different carrying capacity values are reported in Tab. 3.

Table 3 – Estimation of the basic reproduction number R_0 at different carrying capacity values.

Carrying capacity K	Basic reproduction number R_0
50	2.15
20	1.65
10	1.29
8	1.21
7	1.03

Discussion

We investigated the impact of hare density on EBHSV infections within a wide density range (5–100 hares/km^2), which was consistent with the biological hare data estimated in Italy and Europe (Trocchi and Riga, 2005). Our model focused on the role of population density because it was considered the main factor influencing EBHSV transmission (Lavazza et al., 1997).

To analyse the impact of EBHS, population dynamics simulations in the absence of the disease were first considered. Despite the percentage of adult hares (60%) removed every year from the model to better simulate hare management in BfRGs, K was reached in all of the disease-free scenarios investigated. The resulting age structure at equilibrium after the last sampling was always close to the natural age ratio reported in Italian and other European brown hare populations (Trocchi and Riga, 2005; Pepin, 1987).

Further simulations that included the introduction of infected hares into the original susceptible population were run to evaluate the conditions for EBHS maintenance. The system was highly sensitive to variations in the parameters of the infection function. In particular, the parameter μ was found to influence the relationship between the infection probability and the hare density and, therefore, the pattern of the epidemics. This fact suggests that the transmission cannot be determined only by random contact, but that more sophisticated mechanisms are involved. For example, the high resistance of EBHSV in the environment (Frölich and Lavazza, 2008) might influence the transmission of the disease. Moreover, the habit of sharing shelter and the dimension of the home range may play a role in the transmission of EBHSV.

Lavazza et al. (1997) hypothesized the presence of a double-threshold behaviour: in areas where the hare density is lower than 8 hares/km^2 the virus transmission is reduced and irregular, while in areas where the density is greater than 15 animals/km^2 the virus is endemically maintained.

Our simulation outcomes suggested the presence of a single threshold of approximately 7 individuals/km^2. When the density was lower than the threshold, the system had a disease-free equilibrium and a local extinction of the virus was reported (Fig. 4). This outcome corroborated field data, which indicated that at low density values the virus dies out in the short term (Paci et al., 2011; Chiari et al., 2014). As a consequence of the absence of viral circulation, all of the animals rapidly become susceptible to the infection, and the population is likely to be exposed to recurrent EBHS outbreaks due to reintroductions of the virus. This has occurred in areas where the hare density is constantly below the threshold value (e.g. hunting areas in the north of Italy) and all of the animals sampled were repeatedly seronegative (Paci et al., 2011; Chiari et al., 2014). EBHSV can be easily introduced into such hare populations because it can be transmitted directly by infected animals and indirectly through infected materials or passive vectors, such as predators (Frölich and Lavazza, 2008; Chiari et al., 2016). Our model revealed this particular epidemiological situation, which allows for new epidemics, but the observed recurrent outbreaks due to the reintroduction of the virus were not described. In fact, our model illustrates the evolution of the disease in a closed population after a single intro-

duction of the virus, whereas in the field the virus can be repeatedly reintroduced into the population.

When the hare density exceeded the value of 7 individuals/km^2, the virus was endemically maintained and constantly circulated in the population due to the population's renewal process that ensures a faster recruitment of newborn hares. In this scenario most individuals acquired the infection in early life and seroconverted before becoming susceptible to the disease, leading to an endemic equilibrium (Fig. 4). The fraction of recovered/immune animals predicted by the model at different K values was consistent with the available field data. For instance, simulations showed a fraction of the 78% adult and young hares recovered at a density of 25 individuals/km^2, which was similar to field data that reported an average of 75% recovered in high-density areas during the annual capture operation (Paci et al., 2011; Chiari et al., 2014).

The simulated seroprevalence of young and adult hares as a function of K is reported in Fig. 5.

When comparing field values reported by Chiari et al. (2014) with simulated seroprevalence values, the former resulted in a higher seroprevalence value than the latter at the same carrying capacity K. In addition, in few cases a BfRG reported a density value higher than 7 hares/km^2 and a seroprevalence lower than the one predicted by the model (Fig. 5). It should be emphasized that in the model the seroprevalence is described as a function of K, whereas field data usually refer to hare density because K cannot be easily estimated in the field. This fact might explain possible discrepancies between simulation results and field data, even when the density reported is likely much lower than the K of the BfRG. Thus, the field data were generally consistent with the simulated seroprevalence.

The analysis of the basic reproduction number (Tab. 3) further supports numerical results.

R_0 was found to be related to the carrying capacity, in particular its value grows as K increases. Moreover, the critical value of R_0 coincides approximately with the critical density threshold of 7 hares/km^2. Both these facts are consistent with the supposed influence of the density on the infection dynamics of EBHS and with the presence of the two opposite scenarios described above.

Conclusions

The model's results suggested that the brown hare population density directly influenced the transmission of EBHSV, which is a main cause of the hare decline in Europe (Duff and Gavier-Widén, 2012). Because a density-dependent mechanism in EBHSV transmission was demonstrated and a threshold of 7 hares/km^2 was estimated, hare management should promote this minimal density to minimize the impact of EBHS. High density values (>20 hares/km^2) are difficult to achieve, especially in hunting areas and where the K of the environment is limited. However, our results, showing that the higher the hare density value, the lower the susceptible fraction of the population, should be taken into consideration. Because the eradication of EBHS in a wild hare population is not feasible (Chiari et al., 2014), the only way to reduce the disease impact is to maintain EBHSV in the hare population through a high hare population density, thus avoiding recurrent disease outbreaks.

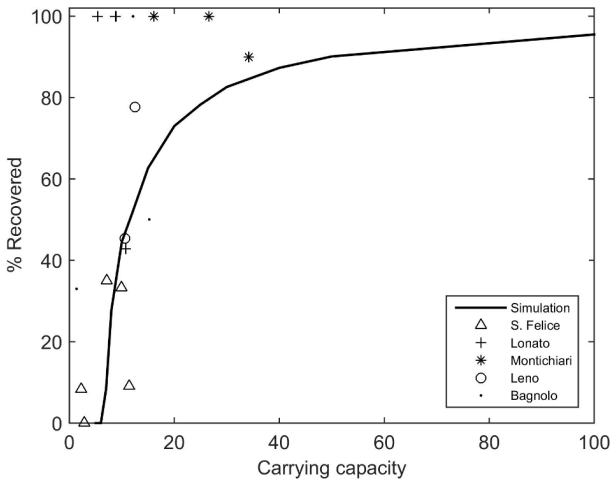

Figure 5 – Comparison of field seroprevalence values reported by Chiari et al. (2014) with simulated seroprevalence ones. The expected seroprevalence values of young and adult hares are reported as a function of the carrying capacity (K).

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Associate Editor: N. Ferrari