Zoonotic pathogens in fluctuating common vole (*Microtus arvalis*)

populations: occurrence and dynamics.

**Authorship**

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SUMMARY

Diseases and host dynamics are linked, but their associations may vary in strength, be time-lagged, and depend on environmental influences. Where a vector is involved in disease transmission, its dynamics are an additional influence, and we often lack a general understanding on how diseases, hosts and vectors interact. We report on the occurrence of six zoonotic arthropod-borne pathogens (Anaplasma, Bartonella, Borrelia, Coxiella, Francisella and Rickettsia) in common voles (Microtus arvalis) throughout a population fluctuation and how their prevalence varies according to host density, seasonality, and vector prevalence. We detected Francisella tularensis and four species of Bartonella, but not Anaplasma, Borrelia, Coxiella or Rickettsia. B. taylorii and B. grahamii prevalence increased and decreased with current host (vole and mice) density, respectively, and increased with flea prevalence. B. doshiae prevalence decreased with mice density. These three Bartonella species were also more prevalent during winter. B. rochalimae prevalence varied with current and previous vole density (delayed-density dependence), but not with season. Coinfection with F. tularensis and Bartonella occurred as expected from the respective prevalence of each disease in voles. Our results highlight that simultaneously considering pathogen, vector and host dynamics provides a better understanding of the epidemiological dynamics of zoonoses in farmland rodents.

Key words: rodent- and arthropod-borne pathogens; mixed infections; population outbreaks; Microtus arvalis; fleas; zoonotic diseases dynamics; Bartonella; Francisella tularensis.
Key findings:

- Common voles are reservoirs for *Francisella tularensis* and several *Bartonella* species.

- *Bartonella* spp. prevalence depended on host density, season and flea infestation.

- *B. taylorii*, *B. rochalimae* and *B. grahamii* were the most prevalent pathogens in voles.

- *Bartonella* spp. prevalence was greater than *F. tularenis* prevalence.

- Coinfection of *Francisella* and *Bartonella* spp. occurred as expected from respective prevalence.
INTRODUCTION

The reservoir of an infectious agent is the natural habitat in which the agent normally lives and multiplies. Reservoirs may include humans, animals, and environmental sources, and they may or may not be the source from which an agent is transferred to a host (CDC, 2012; Bonita et al., 2006). Rodents are important reservoirs of diseases of relevance to livestock and human health (Han et al. 2015), so there is considerable interest in understanding endemic infections in natural rodent host populations. The re-emergence of zoonotic diseases of risk to humans heightens the necessity to understand how infections are maintained and transmitted in ecosystems (Morner et al. 2002). Understanding natural infections requires knowledge on how host density, which may be very variable in space or time, and seasonality influence pathogen prevalence, as well as knowledge on the role that vectors play in pathogen transmission (e.g. Telfer et al. 2007a). In particular, vector-borne pathogens offer the opportunity to determine how vector and pathogen dynamics are linked to host dynamics in order to identify reservoirs and transmission pathways. Rodents are frequently exposed to ectoparasites that transmit pathogens (Gratz, 1994). These are transmitted by arthropods to rodents and from rodents to humans, livestock and domestic animals. Among arthropods, ticks, mosquitoes and fleas are the main vectors of pathogens that constitute a burden to public health. For instance, the dynamics of *Trypanosoma microti*, a flea-borne protozoan, were strongly influenced by flea dynamics in cyclic populations of field voles (*Microtus agrestis*) (Smith et al. 2005), whereas vole host density was more influential than flea abundance in explaining the dynamics of a flea-borne bacterium, *Bartonella* spp. (Telfer et al. 2007a). These findings were attributed to fleas exploiting, and being affected by, several host species in the ecosystem.

Coinfections occur when a host is infected by different parasites, at the same time or sequentially. Parasite interactions can result in co-occurrence or in competition between parasites for a shared resource, such as food or habitat, thus affecting host population and
resulting in direct interactions. The immune response of the host to one parasite may affect the host’s ability to control a second parasite species, and coinfection may favour the transmission and progression of other diseases (Jolles et al. 2008; Telfer et al. 2010). In this case, the presence of a parasite can increase the host susceptibility to be infected with a second parasite or, on the contrary, decrease the probability of infection by another parasite due to an immune response (Cox, 2001). Coinfections not only result from the interactions among parasites, but also from shared risk factors such as environmental and climatic conditions, vectors or groups of vectors, host density or host physiological conditions. Many studies have shown that rodents can be simultaneously infected by more than one pathogen (Meerburg et al. 2009; Buffet et al. 2012; Kallio et al. 2014; Razzauti et al. 2015; Koskela et al. 2017). However, the existence and types of interactions between parasites in natural systems, which may be essential to predict disease dynamics and control parasites, remains poorly known (but see Telfer et al. 2010).

The common vole (M. arvalis) is one of the most abundant and widespread mammals in continental Europe (Jacob and Tkadlec, 2010). Throughout its range, common vole populations typically exhibit regular fluctuations in abundance or irruptive outbreaks (Tkadlec and Stenseth, 2001; Lambin et al. 2006). The species recently colonized ca. 5 million ha of farmland in northwest Spain during a rapid range expansion (<20 years), coinciding with an increase in the surface area of irrigated herbaceous crops, in particular alfalfa (Luque-Larena et al. 2013; Jareño et al. 2015). Large-scale regional vole outbreaks followed this colonisation and occurred every ca. 5 years since early 1980s (Luque-Larena et al. 2013), with very high vole abundances (>1,000 individuals/ha) during peak phases. These outbreaks have caused unprecedented public health risks because voles carry and amplify the bacterium Francisella tularensis, a highly infectious agent causing tularemia (Rossow et al. 2015; Luque-Larena et al. 2017). F. tularensis prevalence in voles was found to increase with vole abundance (direct-density dependence; Rodríguez-Pastor et al. 2017) and human cases of tularemia were found to greatly increase during vole outbreak years (Luque-Larena et al. 2015). As reported in other rodents, common voles from
Northwest Spain could be simultaneously infected by other vector-borne pathogens, but the occurrence, dynamics and coinfection patterns of several pathogens remain empirically unknown for these populations, as well as their interactions with vectors. Ticks and fleas can be found on voles, and both vectors can potentially transmit *F. tularensis* (Hopla, 1974; Bibikova, 1977) as well as other pathogens. Therefore, to obtain a complete understanding of the dynamics of pathogens, it is necessary to take into account not only the dynamics of the hosts, but also the dynamics of vectors, pathogen interactions (coinfections) and their consequences in the environment.

Here, we investigated the occurrence and dynamics of six vector-borne pathogens of zoonotic risk to humans in fluctuating populations of common voles in Northwest Spain across a sectional study of two years. Specifically, we screened every four months the occurrence of three tick-borne bacteria (*Anaplasma phagocytophilum*, *Borrelia* spp., and *Coxiella burnetii*), and three flea- and tick-borne bacteria (*Bartonella* spp., *Rikettsia* spp. and *F. tularensis*) that are often reported in voles species (including the common vole) across Europe (Barandinka *et al.* 2007; Telfer *et al.* 2010; Buffet *et al.* 2012; Silaghi *et al.* 2012; Kallio *et al.* 2014; Rossow *et al.* 2014; Rodríguez-Pastor *et al.* 2017; Fischer *et al.* 2018). We also investigated whether the prevalence of these pathogens in common voles varied with vole population density and the density of other coexisting potential hosts (the wood mouse *Apodemus sylvaticus*, and the Algerian mouse *Mus spretus*). Common voles typically occur at much greater abundances than coexisting mice (Lambin *et al.* 2006; Rodríguez-Pastor *et al.* 2016), so we expected pathogen prevalence to be more heavily influenced by vole density (positive density-dependence). We also looked for associations between vector (flea) and pathogen prevalence to assess whether vectors participated in pathogen transmission. Finally, we investigated coinfection patterns and tested whether the infection probability by a given pathogen varied depending on the presence of a second pathogen.
MATERIAL AND METHODS

We held all the necessary licenses and permits for conducting this work: JLL, FM and RRP held official animal experimentation licenses of level B-C for Spain, and capture permission (permit number 4801646) was provided by the Dirección General del Medio Natural, Junta de Castilla-y-León, Spain.

Study area

The study was conducted in an 80-km² area of farmland located in Palencia province, Castilla-y-León autonomous region, north-western Spain (42°01’N, 4°42’W), which is recurrently affected by common vole outbreaks (Luque-Larena et al. 2013). We sampled voles between March 2013 and March 2015, when vole abundance increased region-wide, peaked to outbreak densities in July 2014, and thereafter declined (Luque-Larena et al. 2015; Rodríguez-Pastor et al. 2017). Pre-outbreak vole abundance data (2009-2013) were also available (Rodríguez-Pastor et al. 2016), allowing us to investigate delayed-density dependent patterns.

Bacterial zoonoses and small mammals in Spain: background

Six vector-borne pathogens (A. phagocytophilum, Bartonella spp., Borrelia spp., C. burnetii, F. tularensis and Rickettsia spp.) were studied in common voles. Empirical data about the role of the common vole as reservoir of zoonotic bacteria are very scarce in Spain, although information is available from other sympatric small mammals (Oporto et al. 2003; Gil et al. 2005; Barandika et al. 2007). In northern Spain, tick-borne zoonotic bacteria, such as Borrelia spp., A. phagocytophilum and C. burnetii have been detected in small mammals, but not the spotted fever group rickettsiae (Barandika et al. 2007). All these pathogens are considered as agents of emerging human diseases (Table S1).

Common vole sampling
Common vole abundance, as well as pathogen and vector prevalence were monitored every 4 months during March, July and November. Voles were live trapped using LFAHD Sherman© traps (8 cm × 9 cm × 23 cm) baited with carrots. At each seasonal sampling, trap lines were set in 24 randomly selected fields and their adjacent margins. Thirty-five traps per trap line spaced by 2 m between each other were operated, with 10 traps set along a margin and 25 traps set perpendicularly inside the field (see Rodríguez-Pastor et al. 2016 for more details on the trapping scheme). Traps were opened in the morning and checked the following morning, with a constant vole trapping effort (840 traps set for 24h per seasonal sampling, making up a total sampling effort of 5,880 trap night). Since our trapping method was extractive, we avoided sampling the same fields during consecutive trapping events in order to minimize any potential impact on host populations. Common voles live in sympatry with other rodent species in the area, but the majority of captures were voles (76%; 929/1221), followed by A. sylvaticus (18.5%; 226/1221) and M. spretus (5%; 66/1221). From a total of 929 voles captured between March 2013 and March 2015, a subset of 240 voles (105 males and 135 females) was used for pathogen and vector screening. The selection was based on a representative sample of captured voles that arrived alive at the laboratory and was stratified by seasonal sampling event and vole gender.

**Laboratory procedure**

Each vole was sexed, weighed and euthanatized through medical CO₂ inhalation, following a protocol approved by our institution ethics committee (CEEBA, Universidad de Valladolid; authorisation code: 4801646). Immediately after death, each individual was examined for ectoparasites (fleas and ticks) through careful visual inspection and by gently blowing the vole’s fur while holding the animal over a white plastic tray (520 × 420 × 95 mm) filled with water. Collected ectoparasites were counted and preserved at room temperature in individually labelled tubes filled with 70% ethanol. Fleas were subsequently identified to species level using a binocular microscope (x10 and x40 magnification; Nikon Optiphot-2) based on morphological
traits following Gómez et al. (2004). Three flea species were identified (Ctenophthalmus apertus, Nosopsyllus fasciatus and Leptopsylla taschenbergi). Ticks were rarely found and collected on voles, so we did not identify ticks to genus and/or species levels, or record the developmental stage (i.e., larva, nymph, or adult). Vole carcasses were kept frozen at -23°C until dissection, which followed standard protocols. The spleen and liver were kept separately in labelled tubes and stored at -23°C until used for molecular detection of pathogens.

**DNA extraction and multiplex PCR-Reverse Line Blot**

DNA was extracted from a homogenized mix of liver and spleen (ca. 25 mg) using commercial kits (QIAamp® DNA Mini Kit, Qiagen, Hilden, Germany) according to the standard procedures of the manufacturer. A multiplex Polymerase Chain Reaction (PCR) was set up for the simultaneous detection of six vector-borne pathogens (A. phagocytophilum, Bartonella spp., Borrelia spp., C. burnetii, F. tularensis and Rickettsia spp.) combined with a reverse line blotting (RLB), as previously described (Anda et al. 2012). Sensitivity of the multiplex PCR was between 10 and 100 GE (Genome Equivalents) and specificity with unrelated bacteria, mammals and arthropods was 100% (Anda et al. 2012). All positive samples to any given pathogen were further tested separately using specific probes with an individual PCR and subsequent RLB.

**Detection of F. tularensis**

We used a phylogenetically informative region of gene lpnA (231 bp) that was amplified by conventional PCR and further hybridization with specific probes by RLB as previous described in Escudero et al. (2008). Positive samples were tested using a real-time multitarget TaqMan PCR, using tul4 and ISFtu2 assays (Versage et al. 2003). A negative PCR control as well as a negative control for DNA extraction was included in each group of samples tested. For real-time PCR using tul4, ISFtu2, a type A positive control was used, as type A strains are restricted to North America. Rodriguez-Pastor et al. (2017) previously screened 243 common voles for a single pathogen (F.
Here, we screened 240 (99%) of these voles for 6 pathogens (including *F. tularensis*) using the multiplex PCR (Escudero et al. 2008).

**Identification of Bartonella species infecting voles**

*Bartonella* positive samples were further analysed using a multiplex PCR targeting the 16S rRNA and the intergenic transcribed spacer (ITS) 16S-23S rRNA. Subsequently, amplicons were analysed with a RLB that included 36 probes for the identification of the different genotypes and species of *Bartonella* (Garcia-Esteban et al. 2008; Gil et al. 2010).

**Statistical analyses**

We focused on *Bartonella* and *F. tularensis* because the other pathogens screened were not detected in voles. We used Generalized Linear Models (GLM) with a binomial error structure and logit link for all the analyses of prevalence, which were done with R v3.4.1 (R Development Core Team, 2017). Model selection was performed using the Aikake Information Criterion for small sample size (Δ-AICc) with the “AICcmodavg” package in R and compared. In order to evaluate hypotheses on pathogen prevalence, we calculated time-varying host population-level covariates and individual-level vole host covariates. The former included mean vole abundance, mean mouse abundance (wood mouse and Algerian mouse pooled) per seasonal sampling (mean rodent abundances were estimated as the average number of captures per 100 traps per 24h for a given seasonal sampling period), and mean prevalence of *F. tularensis* and *Bartonella* spp. for each seasonal sampling (hereafter, *Bartonella* spp. refers to all species of *Bartonella*).

Seasonal sampling-specific pathogen prevalence was calculated as the number of voles positive for a particular pathogen, over the total number of voles analysed. Individual level covariates included vole sex; *F. tularensis* PCR result (0/1); *Bartonella* spp. PCR result (0/1); overall flea prevalence (0/1) and flea burden (number per host); species-specific flea prevalence and flea burden (i.e., *C. apertus*, *N. fasciatus* and *L. taschenbergi* separately); tick prevalence and tick...
burden. Burdens of ectoparasites were estimated as the number of fleas, or ticks, collected per individual vole.

Density-dependence: host-pathogen interactions

The probability of a vole being infected (categorical variable: “0” vs. “1”, as dependent variable) at time \( t \) was tested according to vole abundance (at time \( t \)), previous vole abundance (4 months before, times \( t-4 \)) and mouse abundance (wood mouse and Algerian mouse abundance at time \( t \)). As host abundance changed seasonally and by sex, the categorical variables season (spring/March, summer/July and winter/November) and sex (male and female) were also included in the initial models. Correlation between vole and mouse abundances at times \( t \) and \( t-4 \) was tested. In order to address collinearity issues and improve model fitting to the data, vole abundances were log-transformed when included as explanatory variables (\( \rho \) between Log (vole abundance \( t \)) and Log (vole abundance \( t-4 \)) = 0.28; \( \rho \) between Log (vole abundance \( t \)) and mouse abundance \( t \) = 0.46; \( \rho \) between Log (vole abundance \( t-4 \)) and mouse abundance \( t \) = -0.35). We built a series of GLMs with a binomial error including these different explanatory variables.

Flea-pathogen interactions

We considered flea prevalence (whether or not a vole had fleas) and vole sex as explanatory variables. These models were also fitted for each Bartonella species in turn to examine species-specific relationships. We further tested which flea species better explained the prevalence of Bartonella spp., as well as that of each Bartonella species separately.

Pathogen-pathogen interactions

We used Bartonella spp. prevalence as dependent variable and F. tularensis prevalence, vole abundance at time \( t \) and sex, and the 2-way interaction between F. tularensis prevalence and
vole abundance as explanatory variables. We similarly tested for associations between *F. tularensis* and each *Bartonella* species separately.

**RESULTS**

*Pathogens prevalence in common vole*

Among the six pathogens screened, only *F. tularensis* and *Bartonella* spp. were detected using PCRs. *Bartonella* spp. prevalence averaged 47% (112/240), with marked differences between seasonal samplings: prevalence was maximum during the summer peak in vole density (July 2014), when 69% (70/101) of voles were infected (Fig. 1). For *F. tularensis*, we also confirmed that 20% (49/240) of voles were infected on average, and that in July 2014, prevalence peaked at 34% (34/101; Fig. 1).

*Bartonella species infecting voles*

Five *Bartonella* species were identified among infected voles (Table 1): *B. taylorii*, *B. grahamii*, *B. rochalimae*, *B. doshiae*, and *B. clarridgeiae*. The most frequent species was *B. taylorii*, which was detected in 65% (72/111) of the *Bartonella*-positive voles. Mixed infections with different *Bartonella* species were detected in 59% (65/111) of the positive voles (Table 1). Moreover, a mix of three different *Bartonella* species was found in 8% (9/111) of the positive voles. One of the samples reacted with the 16S rRNA probe, but not with any of the other 36 *Bartonella* species-specific ITS probes (Table 1). Attempts to sequence the ITS amplicon were unsuccessful and the sample was classified as belonging to an unknown *Bartonella* species.

**Density-dependence: host-pathogen interactions**

The models that best explained variation in *Bartonella* ssp. prevalence in voles included vole abundance (direct, positive density-dependence), mouse abundance (direct, negative density-dependence) and season (see model selection in Table 2 and Fig. 2). Both mouse abundance and vole abundance were statistically significant: vole abundance influenced prevalence positively
(slope ± standard error (S.E.): 3.45 ± 0.80), but mouse abundance influenced prevalence negatively (-0.39 ± 0.09; Fig. 2). In addition, pathogen prevalence in voles was relatively higher in winter than in summer or spring (Fig. 2).

Two models explained *B. doshiae* prevalence in voles equally well, and included season and mouse abundance, or these variables plus vole abundance (Δ-AICc < 2; Table 2). Prevalence decreased with increasing mouse abundance (slope ± S.E.: -0.19 ± 0.09), was higher in winter (estimate ± S.E.: 3.12 ± 1.18) and summer (2.02 ± 1.10) than in spring (-3.35 ± 1.09) and increased with vole abundance.

For *B. rochalimae*, two models also explained equally well prevalence variation in voles (Δ-AICc < 2; Table 2). One model included contemporary and previous vole densities, while the other model also included mouse abundance. However, mouse density was marginally significant, and the omission of this variable improved the significance of vole densities (Table 2). *B. rochalimae* prevalence increased with current vole density (slope ± S.E. = 0.88 ± 0.48) and with vole density 4 months before (slope ± S.E. = 1.27 ± 0.55). This was the only species of *Bartonella* that showed a positive delayed density-dependence and its prevalence did not differ between seasons.

*B. grahamii* and *B. taylorii* prevalence varied like *Bartonella* spp. prevalence. In both species, prevalence in voles increased with vole density (slope ± S.E.: 3.20 ± 1.26, for *B. grahamii*; and 3.61 ± 1.11, for *B. taylorii*) and decreased with mouse density (-0.40 ± 0.16, for *B. grahamii*; and -0.50 ± 0.15, for *B. taylorii*) (Table 2). *B. grahamii* prevalence was higher in winter (estimate ± S.E.: 1.88 ± 0.88) than in summer (0.53 ± 0.77) and lowest in spring (-3.72 ± 1.09). *B. taylorii* prevalence in voles was lower in spring (estimate ± S.E. = -2.27 ± 0.79) than in winter (1.54 ± 0.69) and there was a null effect in summer (coefficient not significant).

**Flea-pathogen interaction**
Almost all (94%; 225/240) the voles that were screened during this study arrived alive to the laboratory. Among them, 56% (125/225) were females and 44% (100/225) were males. A total of 153 (68%) voles were infested with fleas, with 643 fleas collected from 70 male voles and 83 female voles. By contrast, only 5 (2%) voles were infested with ticks, considering both larvae and nymphs (29 ticks collected from 4 females and 1 male). The community of fleas was dominated by C. apertus (62%), followed by N. fasciatus (37%), and with L. taschenbergi (1%) occurring in a minor proportion. Details about flea prevalence and tick prevalence on voles at each sampling period are shown in Table 3.

*Bartonella* spp. prevalence was positively correlated with flea prevalence (estimate ± S.E. = 0.60 ± 0.29). *Bartonella* spp. prevalence was 1.4 fold higher in voles carrying fleas than in voles without fleas. Considering species-specific prevalence, B. doshiae and B. rochalimae prevalence were not related to flea prevalence, while B. grahamii and with B. taylorii prevalences were 3.5 and 1.8 fold higher when voles had fleas as compared with voles without fleas, respectively (*B. grahamii*: estimate ± S.E. = 1.49 ± 0.46; *B. taylorii*: 0.79 ± 0.34).

At flea species level, *Bartonella* spp. prevalence was 1.4 fold higher when voles had *N. fasciatus*, but did not differ according to the prevalence of other flea species. This positive association between *Bartonella* prevalence and *N. fasciatus* was found in *B. grahamii* (estimate ± S.E. = 0.75 ± 0.33) and in *B. taylorii*, but marginally significant, (estimate ± S.E. = 0.51 ± 0.29; p = 0.07). There was a positive association between *B. doshiae* prevalence and *C. apertus*, but marginally significant (estimate ± S.E. = 1.14 ± 0.64, p = 0.07).

**Pathogen-pathogen interaction**

The presence of both *F. tularensis* and *Bartonella* spp. was detected in 13% (31/240) of the screened voles (Table 3). Coinfection rate (*F. tularensis* and *Bartonella* spp) reached a maximum of 24% (24/101 voles) in July 2014 when voles reached their maximum density (Table 4). Overall, the probability of a vole being infected by both pathogens was not different from that predicted
from the prevalence of each pathogen at a given sampling time (Table 3). Coinfection rate was
15% (20/135) in female voles and 10% (11/105) in male voles (Table 4). We observed that the
probability of being infected with both pathogens was not different from the predicted
prevalence of each pathogen in voles ($\chi^2 = 6.81$, $p < 0.05$; Table 3). Evidences for association
were found for $B. grahamii$ with $F. tularensis$ ($\chi^2 = 8.24$, $p < 0.05$), $B. taylorii$ with $F. tularensis$
($\chi^2 = 7.94$, $p < 0.05$), $B. grahamii$ with $B. taylorii$ ($\chi^2 = 34.24$, $p < 0.05$), $B. doshiae$ with $B.$
rochalimae ($\chi^2 = 9.12$, $p < 0.05$) and $B. rochalimae$ with $B. taylorii$ ($\chi^2 = 15.40$, $p < 0.05$). When
vole abundance and sex were considered in the model, the probability of infection with
$Bartonella$ spp. did not depend on $F. tularensis$ prevalence, but only depended on vole density
(slope ± S.E. = 0.03 ± 0.01). This positive association with vole density was found for $B. grahamii$
(slope ± S.E. = 0.05 ± 0.01) and $B. taylorii$ (0.03 ± 0.01).

**DISCUSSION**

Prevalence of $F. tularensis$ and $Bartonella$ spp. has been studied in small mammals other than
common voles from Mediterranean areas (Márquez et al. 2008; Gil et al. 2010; Cevidanes et al.
2017; Rodríguez-Pastor et al. 2017), although the relationship between the dynamics of hosts,
pathogens and vectors, as well as the interactions between pathogens, have not been studied
previously. Our study shown a significant association between host and pathogen dynamics, and
that the probability of infection with $Bartonella$ spp. increased with flea prevalence, which is
consistent with $Bartonella$ spp. being a flea-borne pathogen. We also provided evidence that
the occurrence of one zoonotic pathogen ($Bartonella$ spp.) was not dependent on the
occurrence of the other ($F. tularensis$) in vole populations. Our study was cross-sectional and
relatively limited in terms of duration (2 years), so, in order to better tease apart the relative
importance of density-dependence and seasonality, a longer-term investigation of host-
pathogen dynamics should follow up, complemented by longitudinal studies that follow
infection dynamics at individual level over time. Despite these limitations, we were able to provide novel insights that we discuss below.

**Bartonella infection in voles**

*Bartonella* spp. was the most prevalent bacteria in voles, infecting almost half (47%) of all the voles analysed, while just a fifth (20%) of all the voles were infected with *F. tularensis*. This *Bartonella* spp. prevalence falls within the range (between 11 and 72 %) of those previously reported in rodents from other European countries (Gutiérrez et al. 2015). *B. taylorii*, *B. rochalimae* and *B. grahamii* were the most prevalent pathogens in voles, and there was a high percentage of mixed infections (59%), with dual infections among *B. taylorii* and *B. grahamii* being most frequent. This relatively high percentage may be reflecting a host specificity of these species. However, to assert this, it will be necessary to screen the prevalence of the species of *Bartonella* in other rodents that cohabit with voles.

**Density-dependence of Bartonella prevalence in voles**

An effect of host density on *Bartonella* spp. prevalence has been demonstrated in several rodent species. For instance, in a study of a Mediterranean peri-urban environment without voles, *Bartonella* spp. occurrence was positively correlated with wood mouse abundance, the most abundant small mammal of the community, but not with Algerian mouse abundance, despite prevalence being higher in autumn than in spring for both rodent species (Cevidanes et al. 2017). In that case, density-dependence was tested considering a pool of various species of *Bartonella*, so the density-dependent pattern may have been masked by the most prevalent species of *Bartonella*. In another study in a moist Atlantic climate using long-term data from field voles, which also experience abundance outbreaks and are infested by fleas, Telfer et al. (2007a) found that different species of *Bartonella* exhibited contrasting dynamics in two alternative hosts: field voles and wood mice. The probability of infection with *B. doshiae* and *B. taylorii* increased with field vole density, while *B. doshiae* and *B. grahamii* increased with wood mouse density. In
another study with different rodent hosts (bank voles, *Myodes glareolus*, and wood mice), *B. taylorii* and *B. doshiae* were more prevalent in wood mouse, while *B. birtlesii* was more prevalent in bank vole (Telfer *et al.* 2007b). This suggests that the distribution and abundance of each *Bartonella* species do not follow common patterns and that their response to host density depends on the most abundant, preferred host. These findings highlight that each species of *Bartonella* has its distribution pattern and abundance, host specificity, seasonality and response to host density. Therefore, studying the relationship between pathogen and host dynamics requires considering each species of *Bartonella* separately (Telfer *et al.* 2007b). In agreement with previous findings by Telfer *et al.* (2007a, b), we provided evidence for a density-dependence response that differed among *Bartonella* species and rodent hosts: i.e., *B. taylorii* and *B. grahamii* responded to both vole and mouse densities, while *B. doshiae* responded to mouse density (direct response), and *B. rochalimae* to vole density (direct and delayed responses). The positive direct density-dependence to vole density suggests that the pathogen spreads quickly between individuals, and that voles may have low resistance to pathogen infection. Moreover, the negative relationship with mouse density suggests that voles may influence infection prevalence in other coexisting rodent species.

**Seasonal variations of Bartonella prevalence in voles**

Factors such as seasonality can also determine variation of pathogen prevalence in reservoir hosts. *Bartonella* spp. prevalence in small mammals follows a seasonal pattern, although results differ among studies: *Bartonella* spp. prevalence can peak in summer (Paziewska *et al.* 2012) or in autumn (Cevidanes *et al.* 2017). However, these seasonal patterns are based on a pool of *Bartonella* spp., not on the prevalence at species level (but see Telfer *et al.* 2007b). Overall, we found that *Bartonella* spp. prevalence in voles was highest during winter (Fig. 2) when taking into account host densities. Altogether, more fleas were collected in spring and summer than during winter. An increase in the infection probability with *Bartonella* spp. in winter could be
the result of an increase in the occurrence of infected alternative hosts, increasing the infection probability in voles. However, we need to know the *Bartonella* spp. prevalence of the alternative rodent hosts (mice) as well as prevalence in the main vector (fleas) in order to better understand these interactions. At the species level, the infection probability with *B. grahamii*, *B. taylorii* and *B. doshiae* in voles followed a marked seasonal variation, i.e., increased in winter and lowest in spring. *B. rochalimae* was the only species whose prevalence did not vary seasonally, but was also the one with the lowest prevalence in voles. A seasonal pattern for *B. grahamii* has been also found in other vole species, but not for *B. taylorii* and *B. doshiae* (Telfer et al. 2007a). Such seasonal differences may be due to the dynamics and phenology of the fleas that transmit *Bartonella* spp.

**Ectoparasite vectors and Bartonella prevalence in voles**

Pathogen prevalence also varies with vector dynamics. *Bartonella* spp. prevalence has been previously shown to be higher in mice carrying greater flea burdens (Cevidanes et al. 2017). In our studied common vole population, *B. taylorii* and *B. grahamii* were the most prevalent species and the infection probability increased when voles were infested by fleas, independently of the flea burden. This positive relationship between flea and pathogen was found between *N. fasciatus* and both species of *Bartonella*, providing evidence for vector specificity: these bacteria were likely transmitted by *N. fasciatus*. Indeed, both *B. taylorii* and *B. grahamii* have been previously detected in *N. fasciatus* collected from rodents (Silaghi et al. 2016). However, we need to confirm the role of fleas in the transmission process, because when host density and flea prevalence were simultaneously considered, variation in pathogen infection was explained by host dynamics rather than flea prevalence. A lack of effect of flea prevalence on *Bartonella* dynamics has been previously shown in voles (Telfer et al. 2007a). Therefore, our findings should be considered with caution because we do not know which proportion of fleas becomes infected, what species of *Bartonella* occur in fleas, and whether there are other vectors or
modes of transmission. Some species of Bartonella are transmitted by ticks, and others can be transmitted vertically between mother and offspring (Kosoy et al. 1998; Chang et al. 2001). A relatively weaker role of fleas in modulating Bartonella prevalence over time could also be explained by a delayed-density dependence response of flea burden to common vole density as we observed in our study system (a lag of 8 months; unpublished data), but more work is needed to test this hypothesis.

**Coinfections with Bartonella and F. tularensis**

Coinfections with more than one pathogen seems to be common in wildlife. We found coinfection between Bartonella spp., a flea-borne bacterium, and *F. tularensis*, a facultative flea-borne bacterium. In the absence of tick-borne infection, the pairwise combination was limited, and the pattern of infection was consistent with concurrent exposure rather than variation in susceptibility. Around 13% of all the common voles screened here were simultaneously infected with *F. tularensis* and Bartonella spp., and this percentage of coinfection reached 24% during the population peak in July 2014 (see Table 3). The high percentage of individuals infected with two pathogens suggested that there could be some type of interaction modulated by characteristics of the host and the environment. Coinfections by both bacteria may occur non-randomly and thus, the infection with *F. tularensis* may increase the probability of infection with Bartonella spp. or vice-versa. According to Rossow et al. (2014), field voles and bank voles experimentally and naturally infected with *F. tularensis* ssp. *holarctica* readily developed lethal tularemia with similar severity and lesions, which suggests that there is not a chronic or latent infection in voles. On the other hand, experimentation has showed that common voles are less susceptible to be infected with a wild strain of *F. tularensis* ssp. *holarctica* than either BALB/c mice (*M. domesticus*) or yellow-necked mouse (*A. flavicollis*) (Bandouchova et al. 2009). Thus, these experimental studies suggest that *F. tularensis* can be potentially fatal to common voles. Bartonella spp. provokes lasting chronic infection in woodland rodents and can be detected in
rodent's blood for several weeks (Birtles et al. 2001). Thus, \textit{F. tularensis} is expected to cause an acute and lethal infection in common voles, and \textit{Bartonella} spp. a more chronic but non-lethal infection (Harms and Dehio, 2012). However, we do not know the average duration of infection by both bacteria in common voles. Voles could be initially infected with \textit{Bartonella} spp. and later with \textit{F. tularensis}, killing the animal. However, the initial association among the two bacteria disappeared when we considered host density. The lack of correlation between both pathogens reflected the similarity of percentages of coinfection to those expected by multiplying the percentage of infected individuals by each pathogen independently (see Table 3), so we have no clear evidence of pathogen interaction. This preliminary result about coinfection should be confirmed by experimental studies focusing on interactions between \textit{Francisella} and \textit{Bartonella}, and some measures of infection duration in common voles.

\textbf{Other pathogens}

The lack of detection of \textit{Rikenetsia} spp., \textit{A. phagocytophilum}, \textit{Borrelia} spp., and \textit{C. burnetii} in the studied voles could be due to the climatic conditions (seasonally semi-arid Mediterranean climate) and the habitat type (agricultural landscape) of the study area, which may be related to the absence of other more suitable vectors, such as ticks (that infested around 2\% of sampled voles). In contrast to our study, and in a region with an Atlantic climate (mild temperature and significant precipitations) in areas surrounding farms, forested and recreational areas, Barandika et al. (2007) were able to study the prevalence and diversity of \textit{Borrelia} spp., \textit{A. phagocytophilum}, \textit{C. burnetii}, and the spotted fever group rickettsiae infecting several species of small mammals: the wood mouse, the yellow-necked field mouse (\textit{A. flavicollis}), the bank vole, the crowned shrew (\textit{Sorex coronatus}), the white-toothed shrew (\textit{Crocidura russula}), the house mouse (\textit{M. domesticus}) and the European mole (\textit{Talpa europaea}). They found that infection rates with \textit{Borrelia}, \textit{Anaplasma} and \textit{Coxiella} differed between small mammal species,
although like in our study, *Rickettsia* spp. was not detected. In this other study, however, all the small mammals were heavily infested by ticks.

All the results shown in our study came from one 80-km² area, so caution should be exercised before generalizing to other common vole populations. Notwithstanding, we found that voles were infected with four species of *Bartonella*, which had different dynamics according to host density (vole and mice), season and flea infestation. Moreover, voles were infected with *Bartonella* spp. and *F. tularensis*, but we did not find a clear pattern of association among pathogens. Future studies could focus on identifying other suitable reservoirs as well as the effect that these pathogens may have on individual voles and how the infective process happens.

**ACKNOWLEDGEMENTS**

We thank José Luis Guzman for helping with fieldwork and Fabio Flechoso for helping with ectoparasite counts and flea identification.

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**COMPETING INTERESTS**

The authors declare that they have no competing interests.

**REFERENCES**


Kallio, E. R., Begon, M., Birtles, R. J., Bown, K. J., Koskela, E., Mappes, T. and Watts, P. C. (2014). First report of Anaplasma phagocytophilum and Babesia microti in rodents in


Telfer, S., Begon, M., Bennett, M., Bown, K. J., Burthe, S., Lambin, X., Telford, G. and Birtles, R. (2007a). Contrasting dynamics of Bartonella spp. in cyclic field vole populations: the


Table 1. Species-specific occurrence of *Bartonella* species in infected common voles (n=111) according to infection type: single *Bartonella* species infection, or mixed-*Bartonella* species infection.

<table>
<thead>
<tr>
<th>Bartonella species</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>B. taylorii</em></td>
<td>19 (17)</td>
</tr>
<tr>
<td>with <em>B. grahamii</em></td>
<td>27 (24)</td>
</tr>
<tr>
<td>with <em>B. rochalimae</em></td>
<td>17 (15)</td>
</tr>
<tr>
<td>with <em>B. rochalimae</em> and <em>B. grahamii</em></td>
<td>4 (4)</td>
</tr>
<tr>
<td>with <em>B. rochalimae</em> and <em>B. doshiae</em></td>
<td>3 (3)</td>
</tr>
<tr>
<td>with <em>B. doshiae</em> and <em>B. grahamii</em></td>
<td>2 (2)</td>
</tr>
<tr>
<td><em>B. rochalimae</em></td>
<td>14 (13)</td>
</tr>
<tr>
<td>with <em>B. doshiae</em></td>
<td>4 (4)</td>
</tr>
<tr>
<td>with <em>B. grahamii</em></td>
<td>3 (3)</td>
</tr>
<tr>
<td>with <em>B. clarridgeae</em></td>
<td>1 (1)</td>
</tr>
<tr>
<td><em>B. grahamii</em></td>
<td>11 (10)</td>
</tr>
<tr>
<td>with <em>B. doshiae</em></td>
<td>4 (4)</td>
</tr>
<tr>
<td><em>B. doshiae</em></td>
<td>1 (1)</td>
</tr>
<tr>
<td><em>Bartonella</em> spp.</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Total</td>
<td>111 (100)</td>
</tr>
</tbody>
</table>
**Table 2.** Results of the Generalized Linear Models (GLMs) describing how host density, sex and season influenced *Bartonella* spp. prevalence in common voles. The best models (lowest AICs) are highlighted in bold. Vole abundances were log-transformed. Vole Ab: contemporary vole abundance (at time \(t\)); Vole Ab4: previous vole abundance (4 months before, time \(t-4\)); Mouse Ab: contemporary mouse abundance (wood mouse and Algerian mouse, at time \(t\)); Sex: female vs. male common vole; Season: spring (from March to July), summer (from July to November) and winter (from November to March).

<table>
<thead>
<tr>
<th>Model Description</th>
<th>k</th>
<th>AIC</th>
<th>AICc</th>
<th>Δ-AICc</th>
<th>Pseudo-R²</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Bartonella</em> spp. ~ Season + Mouse Ab + Log Vole Ab</td>
<td>5</td>
<td>288.33</td>
<td>288.59</td>
<td>0.00</td>
<td>0.266</td>
</tr>
<tr>
<td><em>Bartonella</em> spp. ~ Season + Mouse Ab + Log Vole Ab + Sex</td>
<td>6</td>
<td>289.59</td>
<td>289.95</td>
<td>1.36</td>
<td>0.269</td>
</tr>
<tr>
<td><em>Bartonella</em> spp. ~ Season + Mouse Ab + Log Vole Ab + Log VoleAb4 + Sex</td>
<td>7</td>
<td>291.26</td>
<td>291.74</td>
<td>3.15</td>
<td>0.271</td>
</tr>
<tr>
<td><em>B. doshiae</em> ~ Season + Mouse Ab</td>
<td>4</td>
<td>104.08</td>
<td>104.25</td>
<td>0.00</td>
<td>0.121</td>
</tr>
<tr>
<td><em>B. doshiae</em> ~ Season + Mouse Ab + Log Vole Ab</td>
<td>5</td>
<td>104.77</td>
<td>105.02</td>
<td>0.77</td>
<td>0.135</td>
</tr>
<tr>
<td><em>B. doshiae</em> ~ Season + Mouse Ab + Log Vole Ab + Sex</td>
<td>6</td>
<td>105.48</td>
<td>105.84</td>
<td>1.59</td>
<td>0.150</td>
</tr>
<tr>
<td><em>B. doshiae</em> ~ Season + Mouse Ab + Log Vole Ab + Log VoleAb4 + Sex</td>
<td>7</td>
<td>106.38</td>
<td>106.87</td>
<td>2.62</td>
<td>0.162</td>
</tr>
<tr>
<td><em>B. grahamii</em> ~ Season + Mouse Ab + Log Vole Ab</td>
<td>5</td>
<td>215.89</td>
<td>216.15</td>
<td>0.00</td>
<td>0.264</td>
</tr>
<tr>
<td><em>B. grahamii</em> ~ Season + Mouse Ab + Log Vole Ab + Sex</td>
<td>6</td>
<td>217.06</td>
<td>217.42</td>
<td>1.27</td>
<td>0.268</td>
</tr>
<tr>
<td><em>B. grahamii</em> ~ Season + Mouse Ab + Log Vole Ab + Log VoleAb4 + Sex</td>
<td>7</td>
<td>218.73</td>
<td>219.22</td>
<td>3.07</td>
<td>0.270</td>
</tr>
<tr>
<td><em>B. rochalimae</em> ~ Mouse Ab + Log Vole Ab + Log VoleAb4</td>
<td>4</td>
<td>228.50</td>
<td>228.67</td>
<td>0.00</td>
<td>0.091</td>
</tr>
<tr>
<td><em>B. rochalimae</em> ~ Log Vole Ab + Log VoleAb4</td>
<td>3</td>
<td>228.83</td>
<td>228.93</td>
<td>0.26</td>
<td>0.076</td>
</tr>
<tr>
<td><em>B. rochalimae</em> ~ MouseAb + Log VoleAb4 + Log Vole Ab + Sex</td>
<td>5</td>
<td>230.08</td>
<td>230.34</td>
<td>1.66</td>
<td>0.094</td>
</tr>
<tr>
<td><em>B. rochalimae</em> ~ Season + Mouse Ab + Log Vole Ab + Log VoleAb4 + Sex</td>
<td>7</td>
<td>234.02</td>
<td>234.50</td>
<td>5.83</td>
<td>0.094</td>
</tr>
<tr>
<td><em>B. taylorii</em> ~ Season + Mouse Ab + Log Vole Ab</td>
<td>5</td>
<td>264.90</td>
<td>265.15</td>
<td>0.00</td>
<td>0.217</td>
</tr>
<tr>
<td><em>B. taylorii</em> ~ Season + Mouse Ab + Log Vole Ab + Sex</td>
<td>6</td>
<td>266.77</td>
<td>267.13</td>
<td>1.98</td>
<td>0.218</td>
</tr>
<tr>
<td><em>B. taylorii</em> ~ Season + Mouse Ab + Log Vole Ab + Log VoleAb4 + Sex</td>
<td>7</td>
<td>268.76</td>
<td>269.25</td>
<td>4.09</td>
<td>0.218</td>
</tr>
</tbody>
</table>
Table 3. Prevalence of fleas, ticks, *F. tularensis*, *Bartonella* spp. and co-infections (with both *F. tularensis* and *Bartonella* spp.) in common voles at each sampling time. Note that sample sizes differ for ectoparasite and pathogen prevalence because only those common voles that did not die in traps were considered for ectoparasite prevalence.

<table>
<thead>
<tr>
<th>Time</th>
<th>Voles sampled for ectoparasites</th>
<th>% infested by fleas</th>
<th>% infested by tick</th>
<th>Voles sampled for pathogens</th>
<th>% infected with <em>F. tularensis</em></th>
<th>% infected with F. tularensis + <em>Bartonella</em> spp.</th>
<th>% infected with F. tularensis + <em>Bartonella</em> spp.</th>
<th>% infected with co-infection (F. tularensis + <em>Bartonella</em> spp.)</th>
<th>% infected with F. tularensis + <em>Bartonella</em> spp.</th>
<th>% infected with co-infection (F. tularensis + <em>Bartonella</em> spp.)</th>
<th>% infected with <em>B. rochalimae</em></th>
<th>% infected with <em>B. grahamii</em></th>
<th>% infected with <em>B. doshiae</em></th>
<th>% infected with <em>B. taylorii</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>March 2013</td>
<td>2</td>
<td>50</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>July 2013</td>
<td>14</td>
<td>71</td>
<td>7</td>
<td>15</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>November 2013</td>
<td>31</td>
<td>35</td>
<td>0</td>
<td>31</td>
<td>16</td>
<td>16</td>
<td>6</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>13</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>March 2014</td>
<td>58</td>
<td>43</td>
<td>0</td>
<td>63</td>
<td>14</td>
<td>40</td>
<td>6</td>
<td>6</td>
<td>0</td>
<td>8</td>
<td>24</td>
<td>25</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>July 2014</td>
<td>101</td>
<td>87</td>
<td>4</td>
<td>101</td>
<td>34</td>
<td>69</td>
<td>24</td>
<td>23</td>
<td>8</td>
<td>42</td>
<td>23</td>
<td>48</td>
<td>48</td>
<td>48</td>
</tr>
<tr>
<td>November 2014</td>
<td>12</td>
<td>92</td>
<td>0</td>
<td>18</td>
<td>6</td>
<td>50</td>
<td>6</td>
<td>3</td>
<td>22</td>
<td>14</td>
<td>22</td>
<td>33</td>
<td>33</td>
<td>33</td>
</tr>
<tr>
<td>March 2015</td>
<td>7</td>
<td>100</td>
<td>0</td>
<td>8</td>
<td>0</td>
<td>38</td>
<td>0</td>
<td>0</td>
<td>13</td>
<td>13</td>
<td>0</td>
<td>25</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Total</td>
<td>225</td>
<td>68</td>
<td>2</td>
<td>240</td>
<td>20</td>
<td>47</td>
<td>13</td>
<td>95</td>
<td>6</td>
<td>22</td>
<td>19</td>
<td>30</td>
<td>29</td>
<td>30</td>
</tr>
</tbody>
</table>
Table 4. Occurrences of co-infections with both *F. tularensis* and *Bartonella* spp. in studied common voles (n=240). “Positive” = voles with the pathogen(s); “Negative” = voles without the pathogen(s). Percentages are indicated in parentheses.

<table>
<thead>
<tr>
<th></th>
<th>F. tularensis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Negative</td>
<td>Positive</td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>59 (25)</td>
<td>14 (6)</td>
</tr>
<tr>
<td>Positive</td>
<td>42 (18)</td>
<td>20 (8)</td>
</tr>
<tr>
<td><strong>Bartonella spp.</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>51 (21)</td>
<td>4 (2)</td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>39 (16)</td>
<td>11 (5)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>191</td>
<td>49</td>
</tr>
</tbody>
</table>
**FIGURE CAPTION**

**Figure 1.** Temporal changes in rodent abundance and in pathogen prevalence in common vole during the course of the study (March 2013 to March 2015). Common vole abundance (captures/100 traps/24 h) = black solid line and black circles; mouse abundance (wood mouse and Algerian mouse; captures /100 traps/24 h) = black dashed line and white circles; *F. tularensis* prevalence = thick black dashed line and black triangles; *Bartonella* spp. prevalence = black dashed line and white triangles.

**Figure 2.** *Bartonella* spp. prevalence in common vole populations according to current common vole abundance (at time *t*), current mouse abundance (wood mouse abundance and Algerian mouse abundance, at time *t*) and season. The graphs show model outputs (Table 2), with grey shades denoting 95% confidence intervals of the predicted curves.
Table S1. Background information on the pathogens screened in the studied common voles, based on the best available knowledge for infections in rodents.

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Mode of transmission</th>
<th>Infection length</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>A. phagocytophilum</em></td>
<td>Ticks</td>
<td>Self-limiting (4 to 8 weeks)</td>
<td>Johns et al. 2009</td>
</tr>
<tr>
<td><em>Bartonella</em> spp.</td>
<td>Hematophagous</td>
<td>Self-limiting (4 to 8 weeks)</td>
<td>Birtles R.J. 2005;</td>
</tr>
<tr>
<td></td>
<td>arthropods (fleas)</td>
<td></td>
<td>Telfer et al. 2007a</td>
</tr>
<tr>
<td><em>B. burgdorferi</em></td>
<td>Ticks</td>
<td>Prolonged persistence</td>
<td>Gern et al. 1994</td>
</tr>
<tr>
<td><em>C. burnetii</em></td>
<td>Ticks</td>
<td></td>
<td>Barandika et al. 2007</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Murine rodents, used as animal models, are poorly susceptible to C. burnetii infection, and consequently a high dose of this bacterium is necessary to induce organ lesions.</td>
<td></td>
</tr>
<tr>
<td><em>F. tularensis</em></td>
<td>Arthropods, water and air</td>
<td>Rapid infection (5-10 days)</td>
<td>Rosow et al. 2014; Bandouchova et al. 2009</td>
</tr>
<tr>
<td><em>Rickettsia</em> spp.</td>
<td>Ticks, fleas, lice, mites</td>
<td>The epidemiology of Rickettsia species has not been investigated in detail, but small mammals are considered to play a role as reservoirs of the rickettsioses</td>
<td>Fischer et al. 2018</td>
</tr>
</tbody>
</table>
Figure 2.