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Modeling the role of carrier and mobile herds on foot-and-mouth disease virus endemicity in the Far North Region of Cameroon

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ABSTRACT

Foot and mouth disease virus (FMDV) is an RNA virus that infects cloven-hoofed animals, often produces either epidemic or endemic conditions, and negatively affects agricultural economies worldwide. FMDV epidemic dynamics have been extensively studied, but understanding of drivers of disease persistence in areas in which FMDV is endemic, such as most of sub-Saharan Africa, is lacking. We present a spatial stochastic model of disease dynamics that incorporates a spatial transmission kernel in a modified Gillespie algorithm, and use it to evaluate two hypothesized drivers of endemicity: asymptomatic carriers and the movement of mobile herds. The model is parameterized using data from the pastoral systems in the Far North Region of Cameroon. Our computational study provides evidence in support of the hypothesis that asymptomatic carriers, but not mobile herds, are a driver of endemicity.

1. Introduction

Foot and mouth disease virus (FMDV) is an RNA virus that infects cloven-hoofed animals, often produces either epidemic (outbreak followed by extinction) or endemic (persistent disease presence) conditions, and negatively affects agricultural economics worldwide (James and Rushton, 2002; Grubman and Baxt, 2004; Rweyemamu et al., 2008b; Knight-Jones and Rushton, 2013; Brito et al., 2017). The epidemic environment is well-studied and well characterized, having been represented by dynamical models that identified drivers of FMDV transmission and evaluated disease control options. In contrast, the endemic situation is much less studied, leading to a lack of knowledge about endemic drivers (Pomeroy et al., 2017). Alternative hypotheses for FMDV maintenance contend that either host movement (Fèvre et al., 2006; Rweyemamu et al., 2008b; Di Nardo et al., 2011) or carrier animals (Condy et al., 1985; Moonen and Schrijver, 2000; Tenzin et al., 2008) drive continued transmission. Identifying which drivers maintain endemic dynamics is important for model specification, data collection, and targeting veterinary health measures.

One hypothesis asserts that host movement can maintain FMDV transmission (Fèvre et al., 2006; Rweyemamu et al., 2008b; Di Nardo et al., 2011). Infections in disease-free locations might be initiated through movement of infected individuals from locations experiencing outbreaks to locations without cases. Alternatively, infections in locations experiencing outbreaks might be maintained by movement of susceptible individuals from disease-free locations. We see empirical support for the movement hypothesis in the effectiveness of movement bans in FMDV epidemic control (Ferguson et al., 2001; Haydon et al., 2004). We also see empirical support in studies that show increased risk for FMDV infection among mobile pastoralists in Africa with respect to both clinical disease (Bronsvoort et al., 2004) and seropositivity (Megersa et al., 2009). However, in other cases, mobile pastoralism bestows a protective effect against FMDV risk (Ehizibolo et al., 2014). Also, based on disease simulations of FMDV across networks of mobile pastoralists, it seems as if this movement alone is not sufficient to maintain FMDV transmission within mobile pastoralists in the Far North Region (Kim et al., 2016). Because different studies characterize both positive and negative relationships between movement and disease transmission it is important to further examine the role of host movement in endemic FMDV maintenance.

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A second hypothesis for endemic FMDV maintenance contends that carrier animals might maintain FMDV endemicity (Condy et al., 1985; Moonen and Schrijver, 2000; Tenzin et al., 2008; Arzt et al., 2018). Carrier animals are defined as individuals who are infected with FMDV but do not clear the pathogen within 28 days (Van Bekkum et al., 1959); instead, virus can be recovered from the oropharyngeal fluid of some animals (Salt, 1993; Alexandersen et al., 2002). These findings, coupled with historical reports that implicated cattle recovered from FMDV infection as the source of new outbreaks, led to the carrier hypothesis (Sutmoller and Casas, 2002). We see some empirical support for infection transmitted to susceptible animals from African buffalo carriers in southern Africa (Condy et al., 1985; Sutmoller and Casas, 2002). We also see some experimental support for infection transmitted to susceptible cattle via direct inoculation with oropharyngeal fluid extracted from persistently infected cattle at 30 days post infection (Arzt et al., 2018). However, in livestock species, it is not clear if carrier animals regularly transmit infection to susceptible animals, especially because there was no evidence of a carrier phenomenon after other experimental attempts (Salt, 1993; Alexandersen et al., 2002; Sutmoller and Casas, 2002; Hayer et al., 2018; Bertram et al., 2018). Taken together, these studies and others show that the contributions from carrier animals is probabilistically low (Bronsvoort et al., 2016).

We can test these alternative hypotheses for endemic maintenance using models of FMDV transmission. Numerous models have been developed to represent the spatial spread of FMDV transmission in the United Kingdom (Ferguson et al., 2001; Keeling et al., 2001; Green et al., 2006; Kao et al., 2006; Kiss et al., 2006; Tildesley et al., 2006) and other locations with fixed farms (Tildesley et al., 2012). Often, the probability of spreading infection from an infectious farm to other farms within a certain distance can be represented with a spatial kernel (Keeling et al., 2001; Tildesley et al., 2006; Chis Ster et al., 2009, 2012; Tildesley et al., 2012; and reviewed in Pomeroy et al., 2017). This framework represents farm-level transmission, in which groups of livestock are represented with the same disease state (Keeling et al., 2001; Tildesley et al., 2006, 2012), although some recent models have extended the work to individual animal status (Chis Ster et al., 2009, 2012; Pomeroy et al., 2018). Nevertheless, farm-level models coupled with spatial kernels have provided insights into FMDV transmission and control in epidemic settings. We applied a similar framework to the livestock production system in the Far North Region of Cameroon to probe the effect of host movement and possible carrier status in an endemic setting.

There are approximately 650,000 cattle in the Far North Region of Cameroon raised in two different livestock production systems. Approximately 92% of cattle in this province are raised by sedentary pastoralists, while the other 8% are raised by mobile pastoralists (Seignobos, 2000). Mobile pastoralists move their camps, which consist of multiple livestock species, in an annual transhumance pattern and let their livestock graze in pastures that are seasonally available (Scholte et al., 2006; Moritz et al., 2013). Multiple serotypes of FMDV are found in the Far North Region (Ludi et al., 2016). Pastoralists practice preventative and restorative practices to maintain the health of their livestock but, in this region, there is no FMDV vaccination nor are animals culled upon FMDV infection. Data on disease status and livestock location have been collected, analyzed, and modeled in this system (Moritz et al., 2012; Pomeroy et al., 2015; Xiao et al., 2015; Kim et al., 2016; Ludi et al., 2016; Pomeroy et al., 2018).

In this system, we test two hypotheses about FMDV transmission and maintenance using simulations of a spatial model of FMDV transmission dynamics. First, we ask if the livestock movements observed are sufficient to maintain FMDV endemicity in model simulations. Second, we ask if the theoretical presence of carrier animals is sufficient to maintain FMDV endemicity in model simulations. Although our simulations are restricted to the Far North Region with no external introduction of FMDV, we could consider these hypotheses in the context of what Cameroon could do to control FMDV to create a region free of FMDV circulation. Creating such a region could constitute a part of Cameroon's progression in the Progression Control Pathway proposed by Food and Agriculture Organization of the United Nations (FAO) and the World Organization for Animal Health (OIE), based in part on Rweyemamu et al. (2008a) and Paton et al. (2009). In this context we ask whether, if the Far North Region could be isolated from outside introductions, it would be possible to prevent endemicity. While this is somewhat hypothetical, it is useful to see if a regional strategy within Cameroon would even be possible or if local circulation alone would require a high level of vaccination and/or animal control. We focus on a single strain, type O, as there is evidence that it has the highest force of infection but waning immunity (Pomeroy et al., 2015), and that other serotypes are less prevalent in the region (Ludi et al., 2016). This work informs our understanding of the causes of endemic FMDV and can help guide plans for veterinary intervention.

2. Data acquisition and disease parameter estimates

Locations and movements of mobile herds were obtained from a combination of GIS/GPS tracking, and quarterly herder interviews beginning with the 2007–2008 seasonal cycle (Moritz et al., 2013). Location of sedentary herds (see Fig. 2) were obtained through computer vision analysis of digitized topographic maps of the region in which village locations were marked. It was assumed that all villages had cattle.

The infectious period for FMDV in individual cattle is 4–5 days, on average (Mardones et al., 2010). As we are modeling herds as a single unit, we must extend the duration of the infectious period to the herd level. Mardones et al (2010) estimated the distribution of infectious periods (in days) for individual cattle to be Gamma with shape parameter 3.969 and rate parameter 1.107. Assuming that all cattle in a herd become infectious at the same time and lose infectiousness independently, approximately 99.5% of cattle in a herd would no longer be infectious after 10 days, which we use as a lower bound for the herd-level infectious period. As a sensitivity analyses, we also investigated herd-level infectious periods of 20 and 30 days, the latter being consistent with the modeling results of Hayer et al. (2018) for an outbreak in a large herd in India. The duration of immunity in individual cattle for serotype O is estimated to be approximately 4 years (Pomeroy et al., 2015). Due to the introduction of susceptible cattle, the herd-level duration of immunity is likely shorter. Moritz (2010) notes that few animals die or are sold each season, so we expect this turnover to have little impact. Nonetheless, as a sensitivity analysis we investigated duration parameters ½, 1, 2, and 4 years at the herd level. The modeling results of Bronsvoort et al. (2016) suggest that there is extremely low probability ($< 1\%$) of recovering virus from cattle more than 12 months after an outbreak, and Hayer et al. (2017) observed a mean virus extinction time of 13 months in infected cattle. We investigate mean herd-level "carrier" state durations of 2, 4, 8, and 16 months, with the 16-month model yielding a 90^{th} percentile of herd carrier state durations of approximately 36 months.

Base infectiousness (between an infectious herd and adjacent susceptible herd) is chosen to roughly match the rate of spread observed in the 2001 UK FMDV outbreak using transmission kernel parameters for the same outbreak as estimated by Chis Ster and Ferguson (2007). This kernel was chosen due to the movement bans in place during the period for which this kernel was estimated, and is intended to reflect the lower bound for transmission rate across space in the hypothetical scenario in which the mobile herds are the only movement. As a sensitivity analysis, a variety of kernels more permissive of long-distance disease transmission was investigated. The relative infectiousness of carrier herds is unknown, but the relative infectiousness of individual carrier animals, if extant, is thought to be small (Salt, 1993; Alexandersen et al., 2002; Sutmoller and Casas, 2002). Therefore, we explored levels of relative infectiousness from carrier herds on the order of 10^{-4} to 10^{-2}, with the lower bound derived from estimated transmission rates for

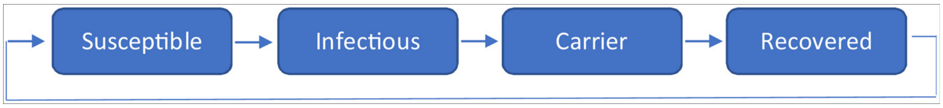

Fig. 1. Compartmental cycle of farm-level disease state.

carriers in the 2001 UK outbreak of 0.002 per day (Parthiban et al., 2015) and an equal estimated upper bound in an experimental setting in Vietnam (Bertram et al., 2018) versus 10.15 per day for acute transmission (Nelson et al., 2017).

3. Model formulation

We use a continuous-time Markov model for disease dynamics. Mathematically, parameters are defined on a timescale in days, but when appropriate we report them explicitly in more natural units. Due to the rapid spread of FMD within herds, it is reasonable to consider the herd as the modeling unit (Ferguson et al., 2001). In our model, herds are considered to be identical and are classified as one of susceptible (S), infectious (I), carrier (C), and recovered (R), based on their ability to react to and transmit FMDV. For example, an infectious herd is one that transmits FMDV at the full rate, a carrier herd is one that has at least one carrier animal and transmits at the reduced rate, and a susceptible herd is one that can be made infectious by transmission from an infectious or carrier herd. A recovered herd is one in which all individuals are immune to FMDV. The cyclic transitions between these compartments are modeled as Poisson processes (Fig. 1). Post-infection compartment transition processes have fixed rate parameters, while the rate of infection events for each susceptible herd is determined by the states of and Euclidean distances to infectious and carrier herds. Simulation of the model is done via a modified Gillespie algorithm (Gillespie, 1976). The observed locations of mobile herds and the dates of arrival are incorporated by instantaneously changing the location of each mobile herd at the recorded date of arrival. Below, we refer to any group of animals, whether sedentary or mobile, as "herds," and qualify by "sedentary" or "mobile" when a specific type is meant.

Savill et al. (2006) show that Euclidean distance is a very good determinant of relative risk of transmission, more so than shortest-distance or shortest-time determinants where there is no physical or geographic boundary (e.g., mountains). The relationship between distance and relative risk may be encapsulated in a transmission kernel $k(r)$ where r is the Euclidean distance between two herds. The exact shape of the transmission kernel for FMD in the study region remains unknown, but we employ a parametric power law form

$$k(r) = \frac{1}{1 + (r/r_0)^{\alpha}},$$

with primary parameter estimates $r_0 = 1400$ meters and $\alpha = 2.7$ chosen to fit the estimated transmission distance distribution from the 2001 UK FMD epidemic by Chis Ster and Ferguson (2007). As the kernel originates from an outbreak during which movement bans were enforced, we use it to encapsulate transmission mechanisms separate from animal movement, for example aerosols, rodents, and foot traffic. While there is likely less aerosol transmission in the African setting compared to the UK for all but the rainy season, there is also likely more foot traffic in the Cameroon setting. Nonetheless, the UK transition kernel is similar to those calculated in Uruguay, the Netherlands, and Japan (Pomeroy et al., 2017), and we perform sensitivity analyses with respect to kernel parameters.

Assuming no carrier herds, the force of infection on a susceptible herd at position x_i is then given by

$$f(x_i) = \beta \sum_{j \in I} k(|x_i - x_j|),$$

where I is the index set for infectious herds and β is the rate of transmission from an infectious herd to an adjacent susceptible herd, here set to $\beta = 0.01$ transmissions per day to approximate the observed rate of FMDV spread in the 2001 UK outbreak (Ferguson et al., 2001). The sum of the forces of infection over all susceptible herds gives the total rate of infection events, and the probability that a specific herd is infected is proportional to the force of infection on it. If desired, the probability of a particular infectious herd being the transmitter is proportional to the transmission kernel between the infectious and susceptible herds.

Alternatively, the specific transmission rate of an infectious herd at location x_i is given by

$$g(x_i) = \beta \sum_{j \in S} k(|x_i - x_j|),$$

where S is the index set for susceptible herds. The total rate of infection is the sum of the specific transmission rates over all infectious herds, the probability that an infection event originates from a specific infectious herd is proportional to its specific transmission rate, and given the transmitter, the probability that a specific susceptible herd is infected is proportional to the transmission kernel between the infectious and susceptible herds.

Hypothetical carrier herds are modeled as infectious herds with infectiousness discounted by a factor c. Mobile herds are modeled as herds with instantaneous changes in location. Thus, for example, the specific transmission rate for an infectious or carrier herd at position $x_i(t)$ is

$$g[x_i(t)] = [\mathbb{1}(i \in I) + c\mathbb{1}(i \in C)]\, \beta \sum_{j \in S} k(|x_i(t) - x_j(t)|),$$

where $\mathbb{1}(i \in I)$ is 1 if $i \in I$ and 0 otherwise, and similarly for $\mathbb{1}(i \in C)$.

Transitions from the infectious to carrier, carrier to recovered, and recovered to susceptible compartments are governed by transition rate parameters γ, δ, and μ, respectively. For example, while $|I|$ herds are infectious, the transition process from the infectious to carrier compartment is a Poisson process with rate parameter $\gamma|I|$, and similarly for the other transitions. The modified Gillespie algorithm proceeds as follows.

1 Compute the total rate of the overall transition Poisson process at time t,

$$\lambda(t) = \left(\sum_{i \in I \cup C} g[x_i(t)] \right) + \gamma\, |I| + \delta\, |C| + \mu |R|$$

2 The next transition occurs before the next movement at time τ_{move} with probability $\lambda(t) e^{-\lambda(t)(\tau_{move} - t)}$. Equivalently, we draw the next transition time from an exponential distribution with rate $\lambda(t)$ and, if the next transition is before the next movement, the transition occurs. Otherwise, the next movement occurs and, due to the memoryless property of the Poisson process, a new next transition time may be simulated independently at the new time and location configuration.
3 The type of the next transition (e.g., infection) is selected with probability proportional to the event rate of that transition type.
4 The herd undergoing the transition is selected uniformly from the herds in the starting compartment, unless the transition is an infection, in which case the herd i is selected with probability proportional to $f[x_i(t)]$, accounting for current position and carriers.
5 If the transition is an infection, the transmitting herd j may be selected from among the infectious and carrier herds with probability proportional to

$$[\mathbb{1}(j \in I) + c\mathbb{1}(j \in C)]k(|x_i(t) - x_j(t)|).$$

Selecting the transmitting herd is not necessary to update the state of the simulation, but can provide additional information if desired, at the cost of some speed. At an even greater penalty to speed, information about transmissions to non-susceptible herds may also be obtained by including those transmissions in the overall rate computation

$$\lambda(t) = \left(\sum_{i \in I \cup C} [\mathbb{1}(i \in I) + c\mathbb{1}(i \in C)]\, \beta \sum_{all\, j} k(|x_i(t) - x_j(t)|) \right) + \gamma\, |I| + \delta\, |C| + \mu\, |R|,$$

and if a transmission event occurs, selecting the transmitter and receiver regardless of the receiver's status.

We simulate realizations of FMDV transmission histories by fixing parameter values and setting one herd in the relatively densely-populated region around Maroua to be infectious, and all other herds to be susceptible. The evolution of the disease population is updated via a modified Gillespie algorithm, and the disease is determined to be either present (endemic) or extinct after ten simulated years. The four parameters of interest are: (1) the presence (or absence) of mobile herds; (2) the relative infectiousness of carrier herds (including the possibility of 0 relative infectiousness, representing the absence of carrier herds); (3) the duration of immunity at the herd level; and (4) the duration of carrier status at the herd level. When mobile herds are simulated, each follows its observed path, repeated annually. When no mobile herds are simulated, we fix those herds' positions to their positions at the start of the season (near Mindif in the South). We then relate the probability of endemicity (disease presence after ten years) to the presence of mobility and the properties of carrier herds. The stochastic disease spread process is simulated 100 times in each scenario.

4. Simulation results

Fig. 2 displays the primary local reproduction number R_0, defined as

$$R_0(x_i) = \frac{g(x_i)}{\gamma},$$

where γ is the rate of transition from the infectious compartment to the carrier compartment, set to $\gamma = 0.1$ In the Poisson process model, $1/\gamma$ is the expected length of the infectious period, here 10 days. Note that the basic local R_0 does not account for infectiousness in the carrier state, and is thus independent of the relative infectiousness of carrier herds. For all locations and all tested values of relative infectiousness (maximum 1%), the local R_0 for the carrier state is less than 1.

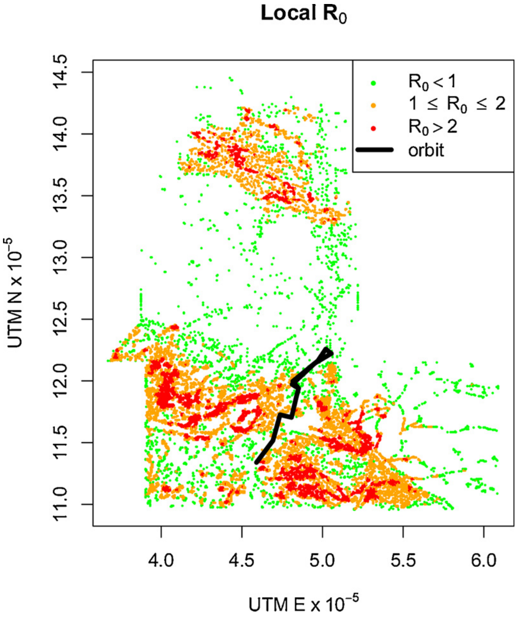

Fig. 2. Spatial variability of basic reproduction number, and annual orbit of typical mobile herd.

Although between the northern and southern high- R_0 regions there is a substantial gap with herds with $R_0 < 1$, a full outbreak in the south is likely to result in infections in the north, independent of the movement of mobile herds. In particular, the expected number of primary infections among the herds in the northern region with $R_0(x) \ge 1$ during an outbreak in which all herds in the southern region with $R_0(x) \ge 1$ become simultaneously infectious is

$$\frac{\beta}{\gamma} \sum_{x_i \in U} \sum_{x_j \in L} k(|x_i - x_j|) \approx 6.25,$$

where U and L are the sets of herds with $R_0(x) \ge 1$ in the northern (upper) and southern (lower) regions, respectively. Thus, an outbreak in the southern region has the potential to cause an outbreak in the northern region as well. This property is symmetric, and thus the quantity and conclusion hold for transmission from the north to the south.

Also displayed is the annual orbit of a typical mobile herd. The mobile herds from the south (Mindif area) do not enter the northern orange-and-red region (above 1,300,000 N UTM), and for the most part remain in more sparsely-populated areas.

Table 1 presents the ranges of parameter values investigated in the simulation study. Ranges identified as the primary focus are those that we consider to be most likely, and are used most frequently when varying other parameters. Sensitivity analyses expand these ranges to evaluate the effects of deviations from assumed parameter ranges, usually by one or two parameters at a time.

The probability of an outbreak resulting in endemicity depends on, among other factors, the relative infectiousness of carrier herds compared to newly infectious herds, and the length of the immune period (Fig. 3). As may be expected, higher relative infectiousness and shorter immune periods result in a higher probability of endemicity. For example, when the length of the immune period was set to 1 year, the probability of endemicity was 9% at a relative infectiousness of 0.1%, and surpassed 50% for all values of relative infectiousness of 0.4% and higher. At 0.3% relative infectiousness of carriers, the probability of endemicity for immune periods of ½, 1, 2, and 4 years was 81%, 47%, 0%, and 0%, respectively. For a 4-year immune period, relative infectiousness below 7% resulted in a low probability of endemicity. At extremely low relative infectiousness (0.01%, not shown), 64% of simulations with an immune period of 6 months and no movement resulted in endemicity, versus 53% with movement (fewer simulations with movement resulted in endemicity, though the difference was not statistically significant at the 5% significance level). With a 1-year immune period no simulations resulted in endemicity without movement, versus 4% with movement. No simulations with longer immune periods resulted in endemicity at extremely low relative infectiousness, and no comparisons between scenarios with and without movement were significant at the 5% level. Alterations of the base infectiousness resulted in no initial outbreak (0.1 times estimated value) or rapid spread followed by extinction (10 times estimated value).

A small suite of simulations were also run with herds bypassing the carrier state entirely. This model is different from a model simply setting the relative carrier infectiousness to zero because it results in a shorter average duration of immunity, and changes the distribution of times between leaving the infectious state and returning to the susceptible state from a sum of independent, non-identical exponential variables to a single exponential variable. With an average immune duration of 6 months, 87% of simulations without movement and 86% with movement resulted in endemicity. With an average immune duration of 12 months, 16% without movement and 17% with

Table 1

Simulation parameters. Simulations end after 10 years, or when no infectious or carrier herds are present.

Parameter type	Primary focus	Sensitivity analyses
Infectiousness	Average infectious period 10 days; base infectiousness 1 transmission per 100 days per nearby susceptible herd	Average infectious period 10–30 days; base infectiousness 0.1 and 10 transmissions per 100 days per nearby susceptible herd
Carrier state	Average carrier period 2–16 months; relative infectiousness 10^{-3} to 10^{-2}	No carrier state; relative infectiousness 10^{-4} to 10^{-1}
Immunity	Average immune period 6–48 months	
Transmission kernel	$\alpha = 2.7$; $r_0 = 1400\,m$	α from 1 to 3; r_0 from 1 to 10 km

movement resulted in endemicity.

Related to the length of the immune period, the length of the carrier period also has an effect on the probability of endemicity. Fig. 4 displays probabilities of endemicity at various carrier periods, with a relative infectiousness of 0.3%. A longer carrier period results in a higher probability of endemicity, counteracting the effect of long immune periods.

The inclusion of movement does not substantially affect the probability of endemicity. In particular, movement alone is not sufficient to result in endemicity. For example, Fig. 5 (left) displays the probabilities of endemicity at various levels of carrier relative infectiousness and an immune period of 1 year, with and without movement. As a sensitivity analysis, we compared models with and without movement in scenarios with longer herd-level infectious periods (up to 30 days), as well as larger range parameters (up to 10 km) and smaller decay powers ($\alpha = 1, 2, 3$). For decay power parameters smaller than in our primary simulations ($\alpha = 2.7$), the probability of endemicity was near 100% for all scenarios, with or without movement. Fig. 5 (right) displays results for $\alpha = 3$, which indicate that any potential effect of movement is small, even as the probability of endemicity predictably increases with longer infectious periods and larger range parameters.

5. Discussion

We consider the influence of carrier animals and herd movement on the dynamics of endemicity in the Far North Region of Cameroon in a scenario in which the region is isolated from outside introductions as part of a control plan. Under this condition of no external virus introductions and a short (up to 1 month) herd-level infectious period, our simulations support the hypothesis that carrier animals maintain FMDV endemicity, but not that the movement of mobile herds support endemicity. Without carriers, the rapid spread of an FMDV outbreak and long immune period generally results in all herds losing infectiousness before previously-infected herds lose immunity. Carriers constitute a longer-term reservoir of FMDV, and, if the relative infectiousness of carriers is not too small, re-infect herds that have lost immunity. In contrast, mobile herds do not provide the necessary opportunity for FMDV to persist beyond the immune period.

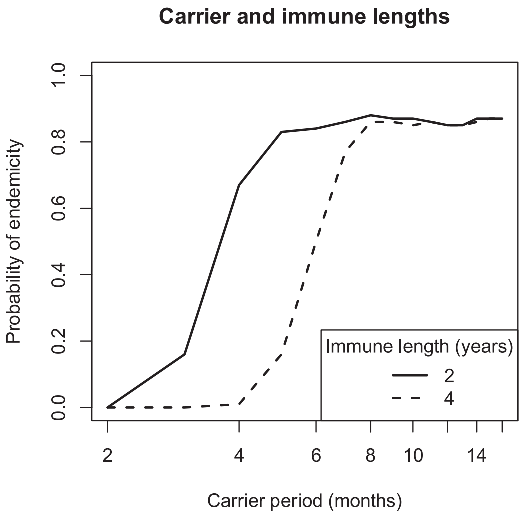

Fig. 4. Relative infectiousness 0.3%, 10-day average infectious period. Long carrier periods counteract the effect of long immune periods.

In most of our simulations, all herds exit the infectious compartment before a sufficient number of herds have lost immunity to sustain a second-wave outbreak. One exception is the scenario in which there is no carrier compartment at all (versus carriers having very low relative infectiousness), which allows some herds to lose immunity very shortly after the end of their infectious period. Another is the scenario under which very long distance transmissions are made more likely by a more permissive transmission kernel, thereby lowering the number of susceptible herds necessary to sustain another outbreak. Although transmission by carrier cattle has not been observed in our setting, the generalized notion of a carrier herd (i.e., simply a lowered level of infectiousness following the initial period of full infectiousness) offers a potential mechanism for sustaining endemicity. Heuristically, there needs to be sufficient force of infection from remaining carrier herds to infect herds that have lost immunity. This force of infection could be due to sufficient relative infectiousness (if any) of carrier herds, or by a

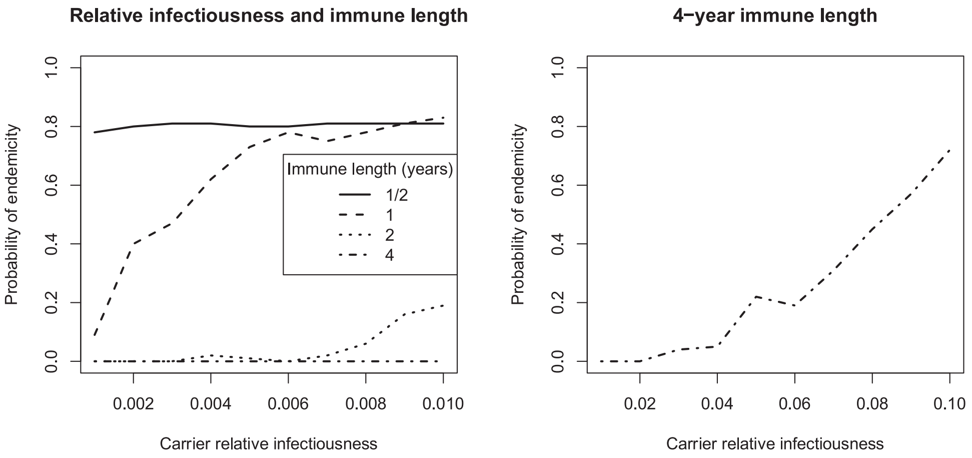

Fig. 3. Average carrier period 8 weeks, average infectious period 10 days. Probability of endemicity increases with relative infectiousness of carrier herds and decreases with longer immune periods (left). Sufficiently high relative infectiousness can result in endemicity even with long immune period. Shaded bands are 95% equal posterior probability pointwise credible bands from independent Beta(½, ½) priors.

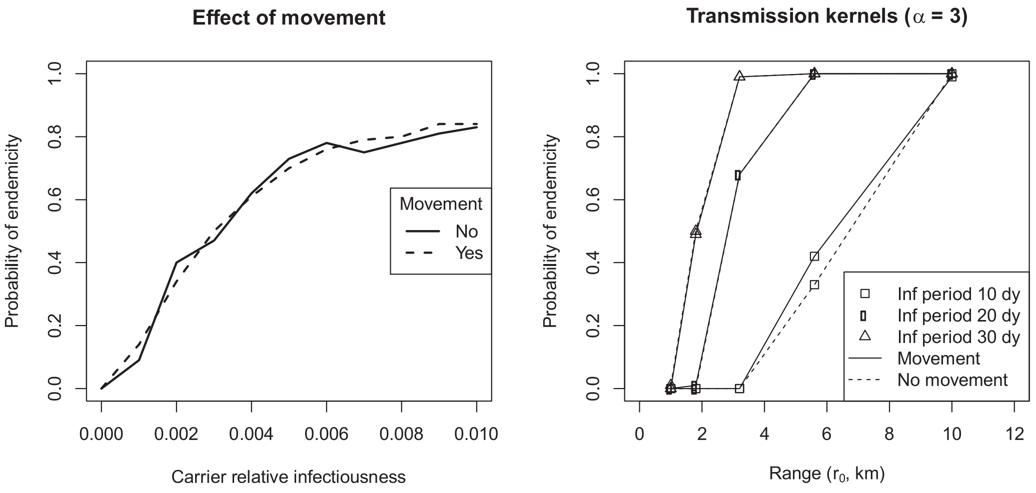

Fig. 5. Left: Average carrier length 2 months, average immune period 12 months. Movement does not have a significant effect on probability of endemicity when carriers are absent (zero relative infectiousness) or present. Right: Average carrier period 3 months, average immune period 2 years, relative infectiousness 0.1%. Movement does not have a significant effect for a range of infectious periods and transmission kernels with a variety of range parameter values.

large number of carrier herds arising from a long enough carrier period relative to the immune period.

The inclusion of mobile herds does not appear to substantially affect the probability of disease persistence. Two factors contributing to this lack of effect are evident. First, as illustrated in Fig. 2, the orbits of the mobile herds do not connect regions that are not already connected by continuous or near-continuous paths of densely-populated land, and therefore do not provide a new path for disease spread. Second, the limiting factor in an outbreak resulting in endemic disease does not appear to be the initial spread of the disease, but rather the remaining force of infection when herds eventually lose immunity, which is not strongly affected by the transit of mobile herds.

While our work illustrates the qualitative effects (or lack thereof) of hypothesized components of endemicity, there is room for improvement in scope and parameter estimation. The treatment of herds as identical (aside from location) atomic units is a dramatic simplification, and, while such approaches have been used before in epidemic situations, the implications in the endemic situation are unknown. Additionally, we restrict the spread of the disease to our study region, which is not an island (e.g., Great Britain), but in fact surrounded by neighboring regions in which the disease may easily spread, and fairly small (less than 35,000 km^2). Introduction of FMDV from external sources or circulation of infection among areas in a larger study region could result in different conclusions. The presence of multiple FMDV strains may also increase the likelihood of at least one strain becoming endemic, even if the dynamics of each strain individually are unmodified. Finally, we consider only the herds themselves, and not possible wildlife susceptible to FMDV, which may yield an effect similar to that of the hypothesized carrier animals. These expansions of the model, along with more reliable estimates of relevant parameter values in Cameroon and elsewhere, present an opportunity for future research.

Previous studies have applied transmission kernels to initial FMDV outbreaks and epidemics, but have not been applied to areas in which FMDV is endemic. Our work illustrates a computational approach for investigating FMDV endemicity in spatially heterogeneous settings, as well as potential drivers of endemicity. In particular, we have used the approach to provide evidence in support of the hypothesis that carrier herds are a driver of endemicity in the Far North Region of Cameroon, and against the hypothesis that mobile herds are a driver of the same.

Ethics approval

The collection of movement data used in this study was approved by the Institutional Review Board (IRB) at The Ohio State University (2010B0004) and the Ministry of Scientific Research and Innovation (MINRESI), the École de Fauna de Garoua, and the University of Maroua in Cameroon.

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Declaration of Competing Interest

Declarations of interest: none.

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