African swine fever endemic persistence in wild boar populations: key mechanisms explored through modelling

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Abstract

African swine fever (ASF), is a serious global concern from an ecological and economic point of view. While it is well established that its main transmission routes comprise contact between infected and susceptible animals and transmission through contaminated carcasses, the specific mechanism leading to its long-term persistence is still not clear. Among others, a proposed mechanism involves the potential role of convalescent individuals, which would be able to shed the virus after the end of the acute infection. Using a spatially explicit, stochastic, individual-based model, we tested: 1) if ASF can persist when transmission occurs only through infected wild boars and infected carcasses; 2) if the animals that survive ASF can play a relevant role in increasing ASF persistence chances; 3) how hunting pressure can affect the ASF probability to persist. The scenario in which only direct and carcass-mediated transmission were contemplated had 52% probability of virus persistence 10 years after the initial outbreak. The inclusion of survivor-mediated transmission corresponded to slightly higher persistence probabilities (57%). ASF prevalence during the endemic phase was generally low, ranging 0.1-0.2%. The proportion of seropositive individuals gradually decreased with time and ranged 4.5 – 6.6%. Our results indicate that direct and carcass-mediated infection routes are sufficient to explain and justify the long-term persistence of ASF at low wild boar density and the ongoing geographic expansion of the disease front in the European continent. During the initial years of an ASF outbreak, hunting should be carefully evaluated as a management tool, in terms of potential benefits and negative side-effects, and combined with an intensive effort for the detection and removal of wild boar carcasses. During the endemic phase, further increasing hunting effort should not be considered as an effective strategy. Additional effort should be dedicated to finding and removing as many wild boar carcasses as possible.

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Running title: African swine fever endemic persistence mechanisms. **Summary:** African swine fever (ASF), is a serious global concern from an ecological and economic point of view. While it is well established that its main transmission routes comprise contact between infected and susceptible animals and transmission through contaminated carcasses, the specific mechanism leading to its long-term persistence is still not clear. Among others, a proposed mechanism involves the potential role of convalescent individuals, which would be able to shed the virus after the end of the acute infection. Using a spatially explicit, stochastic, individual-based model, we tested: 1) if ASF can persist when transmission occurs only through infected wild boars and infected carcasses; 2) if the animals that survive ASF can play a relevant role in increasing ASF persistence chances; 3) how hunting pressure can affect the ASF probability to persist. The scenario in which only direct and carcass-mediated transmission were contemplated had 52% probability of virus persistence 10 years after the initial outbreak. The inclusion of survivor-mediated transmission corresponded to slightly higher persistence probabilities (57%). ASF prevalence during the endemic phase was generally low, ranging 0.1-0.2%. The proportion of seropositive individuals gradually decreased with time and ranged 4.5 – 6.6%. Our results indicate that direct and carcass-mediated infection routes are sufficient to explain and justify the long-term persistence of ASF at low wild boar density and the ongoing geographic expansion of the disease front in the European continent. During the initial years of an ASF outbreak, hunting should be carefully evaluated as a management tool, in terms of potential benefits and negative side-effects, and combined with an intensive effort for the detection and removal of wild boar carcasses. During the endemic phase, further increasing hunting effort should not be considered as an effective strategy. Additional effort should be dedicated to finding and removing as many wild boar carcasses as possible.

Keywords : ASF transmission, convalescent, chronic carrier, individual-based model, *Sus scrofa,* virus persistence.

INTRODUCTION

African swine fever (ASF) and its ongoing spread in several European and Asian countries (Depner et al., 2017; Lu et al., 2020; Penrith, 2020) is a serious global concern from an ecological and economic point of view (Guberti et al., 2019; Pitts and Whitnall, 2019). The disease is caused by a highly virulent virus of the *Asfaviridae* family, which affects wild boar (*Sus scrofa*), domestic pigs and African wild suids (Blome et al., 2013; de Carvalho Ferreira et al., 2013), leading to almost 100% lethality of infected individuals (Blome et al., 2013). After its first Eurasian appearance in Georgia in 2007, the disease has spread to the Russian Federation through trans-Caucasian countries, to Belarus and Ukraine, then to Belarus and Ukraine, Lithuania, Estonia, Latvia, Poland, Czech Republic, Hungary, Romania, Bulgaria, Belgium, Slovakia, Greece, Serbia and Germany (Depner et al., 2017; Blome et al., 2020). A similar eastward spreading is occurring in Asia, currently affecting China, Hong Kong, North Korea, South Korea, Laos, Vietnam, Myanmar, Cambodia, Indonesia, Philippines, Timor-Leste, Papua New Guinea, and India (Blome et al., 2020; Penrith, 2020).

At the arrival of the virus in the EU, ASF was expected to exhibit the typical epidemic pattern of highly virulent acute infections, which often generate self-limiting localized epidemic waves with a high probability of a rapid fade-out. Such expectation was justified by the fact that the wild boar was the sole infected host, and by the absence of a competent arthropod vector (Gabriel et al., 2011; Chenais et al., 2019; O'Neill et al., 2020). After few years of field experiences, however, it is now evident that the virus is able to persist in low density wild boar populations several years after the first epidemic outbreak, with an endemic prevalence usually around 1%, although some local variation has been observed (Nurmoja, Schulz et al., 2017; Pautienius et al., 2018). The virus endemic persistence at low wild boar density is enhanced by its stability at a wide range of environmental conditions (Mazur-Panasiuk et al., 2019). ASF virus has been shown to persist in frozen meat for several months, and may persist in carcasses, forest soil and water for several weeks (Mebus et al., 1997) allowing an efficient indirect transmission through both contaminated carcasses and the environment (De Carvalho Ferreira et al., 2014; Probst et al., 2017; Carlson et al., 2020; Fischer et al., 2020). However, the inner mechanism leading to the long-term persistence at both low wild boar density and prevalence is still not clear, as virus persistence in the environment and in wild boar carcasses is highly variable and mediated by wild boar behaviour, while the endemic persistence of the virus is invariably

observed (Blome et al., 2020). Several alternative hypotheses have been advanced and are currently being explored, but no one has been confirmed and validated so far.

Given the summer peaks observed in several countries, one hypothesis is that the ASF virus might have found an alternative competent arthropod vector species that could replace the *Ornithodoros* ticks, absent in Eurasia. Soft and hard ticks, different species of flies, tabanids and mosquitoes have been proposed (Bonnet et al., 2020), but arthropods do not influence the spread of the virus in wild boar populations (Herm et al., 2021). Another hypothesis relies on the possibility that during its spreading in recent years, the ASF virus might have gone through a process of attenuation, thus reducing its virulence and lethality (Gallardo et al., 2017; Nurmoja, Petrov et al., 2017). Although different wild boar mortality rates have been observed during the ASF spreading in different parts of Estonia and in Latvia (Zani et al., 2018; Gallardo et al., 2019), suggesting the possibility that moderately virulent variants of the ASF virus might be present in the population, no confirmation has been provided so far that a low virulent ASF virus might play a role in its persistence (Blome et al., 2020). Moreover, modelling work shows that, even if the two variants were both present in a wild boar population, the attenuated ASF virus would rapidly go extinct at the expense of the highly virulent one (Nielsen et al., 2021).

A third proposed mechanism involves the potential role of infectious survivors, which would still be able to shed the virus after the end of the acute infection, thus favouring the long-term persistence of the disease. Current knowledge (Sánchez-Vizcaíno et al., 2015; Ståhl et al., 2019) suggests that ASF survivors (hereafter called convalescents) may still carry and transmit the virus after the acute disease phase, but then fully recover from the infection and become immune for life (i.e. category 2 according to Stahl et al., 2019). The possibility that some of them might develop a persistent infection, accompanied by a subacute, chronic disease, has also been proposed (Arias and Sánchez-Vizcaíno, 2002; Category 1 according to Sthal et al., 2019).

The role of infectious survivors is therefore still discussed. It is known that the virus can still be present in survivors for roughly 60–70 days and up to 91days (Petrov et al., 2018). However, lab experiments suggest a very low probability of infection between convalescent and susceptible individuals, and no virus survival beyond 100 days (Nurmoja, Petrov et al., 2017; Petrov et al., 2018; Ståhl et al., 2019). Other experiments on domestic pigs in a controlled environment, though, seem to indicate that transmission of the ASF virus via infectious survivors does occur at least in a 55 days post-exposure window (Eblé et al., 2019). Lacking a conclusive evidence, though, the possibility that surviving wild boars carrying both virus and antibodies could shed and transmit the virus, even though at a very low rate, cannot be disregarded (Blome et al., 2020).

The lack of a clear and verified persistence mechanism for ASF also has consequences on the available management options for its containment and eradication. Currently, carcass removal and wild boar culling are the two main available strategies implemented in the affected areas (Lange et al., 2018), but their effectiveness strongly depends on the relative importance of the different ASF transmission routes. Wild boar culling, which aims at a reduction in wild boar density, mainly affects virus transmission rates between live individuals; therefore, the effectiveness of culling as a control measure depends on how relevant infected and convalescent individuals are in ASF persistence. Carcass removal, on the other hand, only affects the ASF transmission route which involves dead wild boar; its effectiveness, therefore, strongly depends on the importance of carcass-mediated transmission in ASF persistence. Accordingly, it is of paramount importance that all the ASF persistence mechanisms be determined and ranked.

In this paper, we explored the relative role of different ecological and epidemiological factors in the long- term persistence of ASF in wild boar populations. We first assessed the likelihood of the disease to persist through direct and carcass-mediated infection, but without the contribution of any survivor-mediated transmission; in a second scenario we explored the potential for ASF convalescents to play a role in disease persistence. To this aim, we ran and analysed a spatially explicit, stochastic, individual-based model, which mimicked the demography and spatial dynamics of a wild boar population, the epidemiology of the ASF virus through the different proposed transmission routes, and population management through wild boar harvest. Finally,

we assessed the sensitivity of ASF persistence to changes in all the main ecological, epidemiological, and management-related parameters, including hunting rate, thus ranking them in order of importance as determinants of ASF persistence probability. We discuss the implications of our results for the disease surveillance and control in the affected countries, and for the ongoing effort to limit its spread in new, still unaffected areas.

METHODS

2.1 Model structure

The model we used resembled the structure of a SEIR (susceptible-exposed-infected-recovered) epidemiological model (Anderson and May, 1992), with the inclusion of a spatially-explicit, stochastic, individual-based structure. It mimics the structure of the model presented in Lange et al. (2018), with a particular focus on the mechanisms of virus transmission. We built it and ran it using the software Netlogo 6.1.1 (Wilensky, 1999).

All processes took place in a grid of 120x120 km (area = 14,400 km^2). We divided the grid into 1,600 3x3 km cells, which represented the smaller simulated spatial unit. Such units, covering an area of 9 km^2, corresponded to a reasonable estimate of a wild boar's core home range (Leaper et al., 1999). Each spatial unit was characterized by its local wild boar density, defined as the number of individuals having their home range centred in each cell. This state variable was then used as an input parameter for the reproduction and dispersal processes.

Each wild boar was characterized by a series of state variables, which defined its role and behaviour in the model. First, a wild boar was assigned a sex and classified into one of the three age classes: juveniles (0-1-year-old), yearlings (1-2 years old); adults (older than 2 years). Additional individual state variables were the reproductive state (only for females) and the dispersal state (only for yearlings). Finally, each individual could be classified in one of the eight model compartments: susceptible, exposed, infected, convalescent, immune, infectious carcass, non-infectious carcass, hunted. The "convalescent" compartment included the individuals which survived the acute phase of the disease and were passing through the recovery process. In such phase they were still able to transmit the infection for a limited amount of time, until total recovery. The duration of the infectious period in convalescents was controlled by parameter χ, whose value was determined through a numerical optimization process (see below for details). The "infectious carcass" compartment included the individuals which succumbed ASF and whose decomposing bodies could still transmit the virus. Once a carcass lost its potential infectiousness it was transferred to the absorbing "non-infectious carcass" state. The duration of a carcass infectious period was controlled by parameter$I$, also derived from the optimization process. Such period was by default 50% shorter in summer than in winter.

The analytical framework included two scenarios, one in which disease transmission occurred only through direct contact between susceptible and infected individuals, or between susceptible individuals and infected carcasses, another in which we added a third possible transmission route, which involved the role of ASF convalescents, while keeping the other two transmission mechanisms in place. Transmission routes are shown in Fig. 1.

2.2 Virus transmission and disease course

For each of the three transmission pathways, we considered two different contact probabilities, depending on the spatial location of the virus source and of the susceptible individual: 1) a first potential transmission occurred with probability $P_{i,i}$, between individuals whose home range centres fell both in cell i.This parameter referred mainly to those wild boars which were likely to belong to the same social group; 2) a second potential transmission occurred with probability $P_{i,j}$, between individuals whose home range fell in the two neighbouring cells $i$and j , respectively. This parameter referred to the wild boars which were likely to belong to different but neighbouring social groups.

After infection, individuals were moved into the "exposed" state to allow for a 3-day period of incubation and latency (Blome et al., 2013), then transferred into the "infected" compartment. There, an infected wild

boar had a γ probability to die because of the ASF acute infection within a 5-day period, whose value was optimized before model running. The individuals which did not survive the disease were transferred each day into the "infectious carcass" compartment. In the first scenario, survivors were directly moved to the "immune" state and could neither be re-infected, nor transmit the disease to others (Fig. 1). In the second scenario, ASF survivors we moved into the "convalescent" state at 5 dpi, became seropositive at 15 dpi and remained in that compartment until full recovery, according to parameterχ . Then, if still alive, they were transferred into the "immune" state (Fig. 1).

2.3 Mortality, reproduction, dispersal

Besides lethality, we considered also natural and hunting mortality rates. For natural mortality we applied a 0.18 annual rate to juveniles and 0.12 to the other two age classes (Toïgo et al., 2008). Individuals who died of natural causes were transferred directly to the "non-infectious carcass" compartment of the model. Hunting rate in the post-recruited population was initially set at 0.3 for all age classes. Then, to test for the effect of an increased hunting pressure on virus persistence probability, we also ran additional scenarios in which hunting pressure ranged from 0.4 to 0.6.

At the beginning of each year, each female wild boar was assigned a reproductive state, controlled by an age and density-dependent reproduction probability. All reproductive females were assigned a delivery reproduction day, ranging from 1 to 60, to allow for a uniform distribution of births during the birth season. Litter size was set to 4 for juveniles, 5 for yearlings, 6 for adults (Bieber and Ruf, 2005). Then, in the assigned day, they gave birth to the age-specific number of piglets with a 50:50 sex ratio. The piglets coordinates initially corresponded to those of their mother.

At the beginning of the dispersal season, all yearling individuals were assigned a dispersal state, generated through a sex-specific dispersal probability (0.7 for males, 0.4 for females; Truvé et al., 2004), a dispersal starting day, ranging from 1 to 40, and a dispersal duration ranging from 1 to 14 days for males, from 1 to 7 days for females (Truvé et al. 2004). Then, each day and for the entire duration of the dispersal season, each dispersing individual moved from its current cell to the neighbouring cell with the lowest wild boar density, thus mimicking the effort by dispersing animals to avoid intra-specific competition for resources. All model parameters are summarized in Tab. 1.

2.4 Model initialization

We initialized the model with a starting population of 43,200 wild boar, corresponding to a density of 3.0 individuals / km^2. The initial coordinates of all individuals were randomly generated within the grid limits, thus producing a homogeneous spatial distribution of wild boar density. We set sex ratio at 50:50, whereas age classes were attributed according to the stable age distribution estimated by Bieber and Ruf (2005): 60% juveniles, 20% yearlings, 20% adults. All individuals except one (randomly picked) were initially assigned to the "susceptible" state. The remaining individual was defined as "infected" and placed in the centre of the simulated grid. The model proceeded in daily time-steps for a period of 10 years. Reproduction took place each year for a period of 60 days during the months of April and May. Natal dispersal occurred for a period of 40 days and started on June 1^{st}. The hunting season lasted for 150 days between October and February. Each day, model processes were performed according to the following order: density update, disease incubation, virus transmission, disease-related mortality, recovery, carcass decomposition, hunting, reproduction, dispersal, aging.

2.5 Parameter optimization

For several of the main parameters, known to play a role in ASF persistence, there was no reliable estimate obtained in the field from the affected wild boar populations. In particular, virus transmission rates mediated by infected or convalescent individuals, or by wild boar carcasses, are substantially unknown. A few experimental estimates exist but with different virus genotypes (de Carvalho Ferreira et al., 2013; Eblé et al., 2019) and obtained mainly on pigs and in controlled conditions. The applicability of such estimates to the complex eco-epidemiological conditions of a natural wild boar population are therefore dubious. Similar

considerations can be done for other crucial parameters, such as the duration of carcass infectivity in the field or the disease lethality rate in the field.

To overcome this limitation and provide the model with appropriate values of the missing parameters, we used an optimization process based on a series of demographic and epidemiological criteria regarding the evolution of the disease in a wild boar population. In particular, we optimized model parameters to mimic the evolution of the ASF spread in Latvia during the period 2014-2019, as described in Olşevskis et al. (2020). First, we selected all parameters for which we had no field-based reliable estimate. They were the three ASF infection probabilities (direct, carcass, convalescent), the duration of a carcass infectious period, the duration of a convalescent infectious period, disease lethality rate and the ratio between the infection rate within and between wild boar social groups. Then, we ran 1,000 iterations of our model, each time with a randomly selected value for each of the parameters to be optimized. For each iteration, we reported the number of days of disease persistence, the maximum virus prevalence and seroprevalence during the 10-year period and the minimum observed population density. Finally, we picked the iterations which satisfied all of the following criteria, derived from the Latvian study case (Olşevskis et al., 2020):

1. The virus was still circulating in the population at the end of the simulated study period
2. The highest observed virus prevalence ranged 2-5%
3. The highest observed seroprevalence ranged 5-10%
4. Population density decreased by at least 70% during the epidemic

The parameter values which maximized the probability of all the four criteria to be met were picked as input values for our model, thus assuring the highest ASF persistence chances and a realistic epidemiological and demographic evolution of the study system. The values for each parameter, resulting from the optimization process, are shown in Tab. 1, whereas the density probability functions associated to each parameter are available in Figs. S1 and S2 in the Online Supporting Information.

2.6 Analysis of model results

After the parameter optimization process, we performed the actual model runs and compared the disease course under the sole direct and carcass-mediated transmission (scenario 1), and under the action of all three mechanisms (direct, carcass-mediated, convalescents; scenario 2). For each scenario, we ran the model 1,000 times. In each iteration and at each time step, we recorded the number of infected individuals (ASF^+), seropositive individuals (Ab^+), and the number of both virus and seropositive wild boar (ASF^+ & Ab^+). We also kept track of the number of infected carcasses and of total population size. We stopped model running as soon as the virus disappeared from the population and had no more chances to be transmitted through the pathways considered in that specific scenario. In such a case we also recorded the year and day of virus extinction. For each simulated day, we also recorded the number of ASF infections occurring through each of the three transmission routes, thus obtaining an estimate of how relevant each source of infection was in virus transmission and persistence.

2.7 Sensitivity analysis

To more fully explore the relative importance of each model parameter in affecting ASF persistence, we also performed a regression-based global sensitivity analysis (Saltelli et al., 2008; but see Nsoesie et al., 2012 for an application on individual-based epidemiological models). Once more, we ran 1,000 iterations of the model, this time randomly selecting each parameter from a uniform distribution ranging from the optimized parameter value to its 150% values. For each iteration, we recorded the number of days of virus persistence in the population. Then, we visually checked the linearity of the relationship between the input parameter and the resulting virus persistence. Following, we standardized all input parameter values using the z-score method (Kreyszig, 1979), and performed a generalized linear regression using virus persistence as the response variable and the standardized model parameters as predictors. To account for the overdispersion in the data we used a quasi-Poisson distribution for the response variable. The regression coefficients of each predictor provided an estimate of the sensitivity of ASF persistence to changes in that parameter (Saltelli et al., 2008). The z-score standardization made all regression coefficients comparable, although the initial

model parameters were measured on different scales.

RESULTS

3.1 ASF dynamic

In both simulated scenarios, ASF exhibited an infection dynamic which could be characterized in four distinct phases (Guberti et al., 2019): invasion (years 1-2), first epidemic wave (years 3-4), endemic phase (years 5-7), second epidemic wave (years 8-10). During the initial invasion phase, the disease remained rather localized with a low virus prevalence, in average 0.01%, and a mild reduction in wild boar density (Tab.2 and Fig. 2). This was also the phase during which the ASF virus had the highest chances to disappear from the wild boar population: when simulating only transmission through direct and carcass contacts, the virus failed in reaching the endemic status in 40% of the model runs after two years; when adding the survivor-mediated infection, the extinction probability after the first two years was slightly reduced to 34% (Fig. 3).

During the first epidemic wave (years 3-4), the ASF virus exhibited a rapid geographic spread and a progressive increase in both prevalence and seroprevalence. In scenario 1 (two transmission pathways) the ASF prevalence and seroprevalence were in average 1-2% (Tab. 2), with peaks of 2.87% in virus prevalence and 6.52% in seroprevalence (Fig. 2). When accounting for role of convalescents in disease transmission (scenario 2), the average virus and seroprevalence slightly increased, with peaks of 4.52% and 6.61%, respectively. During this phase, the virus faded out in 1% of the iterations in both scenarios, corresponding to a 59% persistence probability and 65% in scenario 2 (Fig. 3).

After spreading across the whole study area, ASF entered its endemic phase in years 5-7, during which virus prevalence was in average lower than 0.5% in both scenarios (Tab. 2). Seroprevalence progressively decreased during the endemic years, averaging 1.79% and 2.11% in the two scenarios, respectively (Fig. 2). This period was also the one during which the population reached its lowest density, in average about 0.8-0.9 individuals / km^2, depending on the scenario (Tab. 2).

Despite the low virus prevalence, ASF had low probabilities to disappear from the population during the endemic phase: extinction rate during this period was 1% in scenario 1 and 2% in scenario 2, so that at the end of seventh year the ASF virus was still present in 58% of the iterations in scenario 1 (only direct and carcass-mediated transmission) and in 63% of cases in scenario 2 (all three transmission pathways included).

The last phase of the ASF dynamic occurred in years 8-10, during which a second lower epidemic wave emerged (Fig. 2), with average prevalence and seroprevalence ranging 1-2% and 2-3%, respectively. At the end of the 10-year simulated period, the ASF virus was still present in the wild boar population in 52% of the iterations in scenario 1 and in 57% in scenario 2 (Tab. 2, Fig. 3).

Overall, about 58% of the virus transmissions occurred directly between an infected and a susceptible wild boar, 38% by mean of an infected carcass, 4% due to a convalescent wild boar (Fig. 4a). These proportions, though, were not constant over the 10 simulated years. Direct transmission was relatively more frequent in the initial years of the epidemic, when about 65% of the infections occurred using this pathway; carcass-mediated transmission, instead, was relatively less frequent at the beginning of the simulated period, when it accounted for only about 20% of the infections, but became progressively more important, especially during the endemic phase. In those years, in fact, it represented 40% of all ASF transmissions. Moreover, carcass-mediated virus transmission was strongly correlated to wild boar density. As shown in Fig, 5, this infection pathway accounted for only about 20% of all virus transmission when wild boar density was around 3 individuals / km^2, but it increased to 60% when density decreased to 1.0 / km^2 or lower values. The proportion of survivor-mediated virus transmission remained rather constant during the simulated period, ranging 2-4% of all infections. Finally, the proportion of infections occurring within and between social groups was also rather constant during the study period, with about 55% of the virus transmission taking place within the same 3x3 km cell, the remaining 45% between two neighbouring cells (Fig. 4b).

During the 10 simulated years, the ASF force of infection exhibited a seasonal cycle, with a peak in spring and summer at about 1.05, after newly born piglets entered the susceptible compartment. The force progressively

decreased during the following seasons, exhibiting negative values (0.95 – 1.00) throughout winter, starting a new cycle at the onset of the successive reproductive season. The temporal trend in the force of infection is shown in Fig. S3 in the Online Supporting Information.

3.2 Sensitivity analysis

After visually inspecting the relationship between the input parameters and the resulting ASF persistence, all of them appeared as clearly linear, except for the annual hunting rate, whose effect was not. As shown in Fig. 6, the effect of hunting, expressed as the resulting lowest wild boar density observed during the 10-year period, could be broken down into two segments of different slopes. For this reason, we estimated two different sensitivity values for the hunting rate parameter, one for the rates corresponding to a minimum wild boar density < 0.75 individuals / km^2, one for the rates corresponding to a wild boar density > 0.75 individuals / km^2.

The global sensitivity analysis revealed than not all the input parameters had a significant effect on ASF persistence. Of the infection probabilities related to each of the three transmission pathways, direct and carcass-mediated transmission exhibited significantly different from zero sensitivity values (Tab. 3), whereas the sensitivity of survivor-mediated transmission was not significant. Similarly, increasing the duration of a carcass infectivity period significantly increased the ASF persistence, whereas increasing the duration of a convalescent wild boar infectivity period did not (Tab. 3). ASF lethality exhibited a significant but negative sensitivity value (Tab. 3), implying that an increase in the proportion of fatal disease outcomes produced a reduction in virus persistence, because of the reduced time available for infected wild boars to transmit the disease. The proportion of reproducing females in the population, on the contrary, exhibited a positive and significantly different from zero sensitivity value (Tab. 3), suggesting that an increased reproductive performance at the population level corresponded to an increased probability of disease persistence over time.

When analysing the effect of hunting rate in the two different density segments, the results of the sensitivity analysis exhibited rather different relationships. The sensitivity of ASF persistence to changes in hunting rate when wild boar density was higher than 0.75 / km^2 was the highest among all tested parameters, whereas the same parameter did not exhibit any significant effect on ASF persistence when wild boar density was lower than 0.75 / km^2 (Tab. 3 and Fig. 6). At 1.5 wild boars / km^2 ASF was expected to persist in the population at least 10 years, but a reduction of wild boar density to its half corresponded to an expected persistence of about three years (Fig. 6), which resulted in a disease fade-out at the end of the first epidemic wave. On the contrary, further increasing hunting effort to reduce wild boar density to even lower values did not result in any further reduction in the expected duration of the epidemic (Fig. 6).

DISCUSSION

Our model captured well both the epidemiological and the demographic dynamics observed in the affected areas during the first years of the epidemic, in terms of population size reduction, average prevalence and seroprevalence, and long-term persistence of the disease at low wild boar density during the endemic phase. Although we used the epidemiological data reported for Latvia (Oļševskis et al., 2020) as a reference for model parameterization, the dynamics emerging from our study were typical for ASF in wild boar in most of the surveillance data reported for northern and eastern Europe since the ASF initial outbreak: ASF reduced infected populations by 70-80% during the first 4-5 years of the epidemic, as reported in most of the Baltic countries and in Poland (Depner et al., 2017; Oļševskis et al., 2020; Nielsen et al., 2021); peaks in the ASF virus prevalence were usually around 5%, with the average prevalence during the whole period ranging 1-2 % (Depner et al., 2017; Nurmoja, Schulz et al., 2017); seroprevalence peaked at values around 10% and then progressively decreased during the endemic phase, as recently reported for Estonia and Latvia (Nielsen et al., 2021). Moreover, the additional parameters selected through the optimization procedure were all in the range of values obtained from field and laboratory data during these years, even though no a-priori information was used to select them (Tab. 1, Figs. S1 and S2). The model exhibited a rather slow dynamic, especially during the initial period after virus release (years 1-2), when prevalence remained well

below 1% and raised slowly towards a clear first epidemic wave. Besides from being an intrinsic property of the system, such pattern was determined by the large area used for simulation, which caused a dilution effect of the epidemiological parameters during the initial years. Data estimated exclusively on the initially infected area would have shown higher prevalence and faster spread of the virus. This should be taken into account when comparing model dynamics with surveillance data reported from small affected areas, shortly after the initial virus detection.

In terms of mechanistic disease dynamics, our model results indicate that the two transmission pathways so far considered as the main infection routes, namely direct and carcass-mediated, are sufficient to explain and justify the long-term survival of the ASF virus at low wild boar density and the ongoing geographic expansion of the disease front in the European continent. The addition of a third transmission mechanism, mediated by ASF survivors during their convalescent phase, did not change drastically the disease dynamics, nor substantially increased the ASF virus persistence probabilities. Three specific results clearly indicate that survivors play a minor role in virus persistence: 1) the temporal trend in the main epidemiological parameters (prevalence and seroprevalence) was similar in the scenarios with and without the inclusion of survivor-mediated transmission (Tab. 2); 2) persistence probabilities at five and ten years were substantially the same for the two scenarios (Tab. 2); 3) the sensitivity values of all the parameters involved in the survivor-mediated infection were not significantly different from zero (Tab. 3).

The role of different transmission mechanisms in ASF persistence, though, is far from being clarified, and several parallel approaches are being developed to explore the issue. In a recent work, Lange et al. (2021) proposed a comparison of different alternative ASF persistence mechanisms, based on the Estonian case study. They estimated a less than 20% persistence probability after 10 years for a scenario involving only direct and carcass-mediated virus transmission. They also found that the inclusion of convalescents with up to 4 weeks of transient infectivity did not increase ASF persistence rates, unless it was combined with a reduction of disease lethality from 95% to 80% (Lange et al., 2021). Instead, they reported that a small proportion (0.1 – 1.0 %) of life-long infectious carriers would drastically increase ASF long-term persistence probabilities. Alternative mechanisms, such as a shortened protection by maternal antibodies and the possibility of immunity loss after recovery were not related to an increase in ASF persistence in their model (Lange et al., 2021). Using a similar modelling approach and surveillance data for Eastern Poland, Pepin et al. (2020) obtained results which are more in agreement with our findings: they estimated 50-60% ASF persistence rates running an individual-based model which comprised only direct and carcass-mediated infection, but estimated such persistence on a time horizon of only 2 years, which makes the comparison with our study not optimal. Finally, O'Neill et al. (2020) presented a different modelling approach to the study of ASF persistence in wild boar, which made use of a deterministic, population-based, compartmental model (Keeling and Rohani, 2008). They reported that the observed epidemiological patterns of ASF could not be matched when accounting only for infected and carcass-mediated transmission, and that the inclusion of a re-infection probability for ASF survivors allowed to obtain long-term disease persistence and the same epidemiological trends reported in the affected countries (O'Neill et al., 2020). The apparently contrasting results of these different modelling exercises confirms the complexity of the ecological and epidemiological mechanisms on which ASF persistence relies. In such complexity, our results suggest that the main infection routes through which ASF can persist at low wild boar density might have been already unveiled. Although identifying alternative or additional mechanisms is relevant and needed, the main focus should be kept on the role of infectious live wild boar and infectious carcasses, which are likely to explain a large part of the observed dynamics in the affected countries.

In particular, the temporal trend in the proportion of ASF infections occurring with each of the two mechanisms (Fig. 4) shows that direct and carcass—mediated transmissions are likely to play different roles in different phases of the ASF epidemic. During the initial invasion phase, which in our model roughly corresponded to the first two years after virus invasion, almost 70% of the infections occurred directly between infected and susceptible individuals (Fig. 4a), and in particular within the same social group (Fig. 4b). This quantification is substantially different from what reported by Pepin et al. (2020), who estimated that 53-66% of all virus transmission would be due to a contact between a susceptible wild boar and an infectious

carcass. It should be noted, though, that those quantifications were based on an initial wild boar density ranging 0.5-2.0 individuals / km^2, as opposed to the 3.0 / km^2 used in our model. Accordingly, we also observed that carcass-mediated ASF transmission became relatively more frequent and even predominant for decreasing wild boar density values (Fig. 5), suggesting that carcasses are likely to be the most important infection route during the endemic phase, when the wild boar population density has been reduced by 70-80% after the first epidemic wave. After entering its endemic phase, ASF seems to be maintained essentially by infected carcasses, which act as a reservoir for the virus in small pockets, until the wild boar population bounces back to density levels which re-allow an effective virus transmission through direct boar-to-boar contacts.

Such prolonged period of endemicity, which some of the affected countries in north and eastern Europe are experiencing in these years, is likely to be challenging both for disease surveillance and for the efforts of its eradication. One of the most challenging results of our study is the evidence that a long-term disease persistence was compatible with a very low endemic prevalence, which ranged in average from 0.2 to 0.3% (Tab. 2). This means that at any given time during the endemic phase, only 2-3 wild boars out of 1000 in the population were infected. Moreover, our model reported an average of about 40 infected carcasses in the whole study area during the endemic phase, corresponding to a density of about one carcass / 300 km^2. In such conditions, the evidence of ASF presence in a given area can remain substantially invisible to surveillance. In this phase, both passive and active surveillance are likely to be poorly effective in detecting the disease, because the likelihood of hunting an ASF infected wild boar and that of retrieving an infected carcass in the forest are both rather low. On the other hand, seropositive individuals represented about 6% of the wild boar population at the beginning of the endemic period, decreasing to about 1% after three years (Fig. 2), making much more likely to detect seropositive than virus positive animals during the endemic phase. Accordingly, in most of the affected countries the number of virus positive wild boar in hunting bags and the number of infected carcasses detected in the forest rapidly dropped to zero after the end of the first epidemic wave, whereas the number of ASF seropositive cases reported through hunted individuals progressively increased in subsequent years (Boklund et al., 2018; Nielsen et al., 2021). In most of the cases, seropositive animals are the sole reported cases for long periods of time during the endemic phase. Such epidemiological landscape, in which the probability to detect the virus in dead wild boar is extremely low, makes the infection status of the involved wild boar population uncertain.

Our results confirm the possibility for ASF to persist for long times with a very low endemic prevalence, which ranged in average from 0.2 to 0.3%, and at very low wild boar density (Tab. 2). This means that at any given time during the endemic phase, only 2-3 wild boars out of 1000 in the population were infected. Moreover, our model reported an average of about 40 infected carcasses in the whole study area during the endemic phase, corresponding to a density of about one carcass / 300 km^2. In such conditions, the evidence of ASF presence in a given area can remain substantially invisible to surveillance. In this phase, both passive and active surveillance are likely to be poorly effective in detecting the disease, because the likelihood of hunting an ASF infected wild boar and that of retrieving an infected carcass in the forest are both rather low. On the other hand, seropositive individuals represented about 6% of the wild boar population at the beginning of the endemic period, decreasing to about 1% after three years (Fig. 2), making much more likely to detect seropositive than virus positive animals during the endemic phase. Accordingly, in most of the affected countries the number of virus positive wild boar in hunting bags and the number of infected carcasses detected in the forest rapidly dropped to zero after the end of the first epidemic wave, whereas the number of ASF seropositive cases reported through hunted individuals progressively increased in subsequent years (Boklund et al., 2018; Nielsen et al., 2021). In most of the cases, seropositive animals are the sole reported cases for long periods of time during the endemic phase. Such epidemiological landscape, in which the probability to detect the virus in dead wild boar is extremely low, makes the infection status of the involved wild boar population uncertain.

In terms of wild boar population management, our model results confirm that the effort of eradicating or just controlling ASF is a hard challenge, but they also indicate that some options are more likely to be effective than others. In particular, the sensitivity analysis revealed that the effectiveness of wild boar hunting is

limited. Hunting effects are more apparent during the initial invasion and epidemic phases, when wild boar density is still at relatively high values (Fig. 6). However, the main effect of hunting is just to shorten the transition from the epidemic to the endemic condition, through an initial reduction in population density. High hunting pressure might also generate unwanted effects, inducing compensatory population growth rate and accelerated generation time, higher juvenile female contribution to the reproductive set and earlier reproduction (Morelle et al., 2020). Moreover, the potentially limited benefits of increased hunting are likely to be counteracted by several of its side effects, such as increased wild boar movements, virus contamination risks and potential human-related long-distance transport of the ASF virus (Guberti et al., 2019).

Afterwards, when ASF enters its endemic phase, hunting has a negligible role in increasing the overall probability of virus fade out, because during that period ASF is mainly transmitted and sustained through infected carcasses. (Fig. 5). In our modelling conditions, the density threshold marking such loss of hunting effectiveness was estimated at 0.75 wild boar/km^2, but such threshold is likely to be context dependent and difficult to be estimated with the sole hunting data. Additionally, it should be noted that modelling hunting as a fixed proportion of population size, as we did in our model, might reduce model realism at very low population densities. Hunters' effectiveness, in fact, is expected to decrease when a wild boar population is sparser, making it hard to accomplish the same hunting goals achieved at higher population densities.

Therefore, if transmission and persistence mechanisms are different in the different stages of an ASF epidemic, also management actions should be modulated depending on which phase a given affected area is experiencing. To this aim, our study indicates that during the initial years, and especially during the first epidemic wave, hunting as a management tool should be carefully evaluated in terms of potential benefits and negative side-effects, and combined with an intensive effort for the detection and removal of wild boar carcasses. During the endemic phase, when both virus prevalence and wild boar density are low, further increasing hunting effort should not be considered as an effective option. Instead, additional effort should be dedicated to finding and removing as many wild boar carcasses as possible. In epidemiological terms, this would correspond to shortening a carcass' infectious period, a parameter which exhibited a high sensitivity value during all phases of the ASF simulated course (Tab. 3).

Finally, the sensitivity analysis revealed a third relevant ASF persistence mechanism, which offers an additional management opportunity: ASF persistence probability was significantly and positively influenced by spring recruitment, expressed in the model as the proportion of females of all ages giving birth to piglets (Tab. 3). Newly born wild boar, in fact, provide each year a new input of susceptible individuals, potentially suitable for infection and virus transmission, thus allowing the typical increase in ASF prevalence during summer, observed in several of the affected European countries (Boklund et al., 2018). Moreover, an increased reproductive performance also generates a higher population growth rate during the endemic phase of the ASF epidemic, allowing wild boar density to recover quickly, and increasing the chances that a second lower epidemic wave might occur. Ecological theory has long recognized the link between food availability and recruitment in large herbivorous mammals such as wild boar (Gaillard et al., 1998). Therefore, management actions such as winter supplemental feeding, which are a widespread practice in most of the European countries currently affected by ASF (Guberti et al., 2019), should be considered as powerful enhancers of ASF persistence and strongly limited or banned. Other modelling work (O'Neill et al., 2020) has shown that ASF is more likely to persist in wild boar populations with increased reproductive performance and increased carrying capacity, which are the typical demographic and ecological consequences of widespread supplemental feeding. Such population-level effects of artificial feeding are likely to be further magnified by the local spatial and behavioural effect: feeding sites, in fact, increase wild boar spatial aggregation, favour direct or indirect contact between neighbouring social groups, and overall are likely to increase virus transmission rates in the population.

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Conflict of interest statement

The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

ETHICAL statement

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been adhered to. No ethical approval was required as this is a modelling article with no original research data.

DATA AVAILABILITY statement

Data sharing is not applicable to this article as no new data were created or analysed in this study.

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Parameter	Description	Value	Source / Notes
N_0	Initial population size	43,200	-
D_0	Initial density (wild boar / km^2)	3	-
A_0	Initial age-distribution (juveniles, yearlings, adults)	0.6, 0.2, 0.2	Bieber and Ruf 2005
P_d	Direct transmission probability (infected - susceptible)	0.0035	Numerically optimized with data fr
P_c	Carcass transmission probability	0.00016	Numerically optimized with data fr
P_s	Convalescent transmission probability	0.00038	Numerically optimized with data fr
ϵ	Incubation time (days)	3	Blome et al. 2013
γ	Disease lethality	0.946	Numerically optimized with data fr
I	Carcass infectious period (days)	85	Numerically optimized with data fr
χ	Convalescents infectious period (days)	77	Numerically optimized with data fr
M	Natural mortality rate (juveniles, yearlings, adults)	0.18, 0.12, 0.12	Toigo et al. 2008
h	Annual hunting rate	0.3	-
R	Reproduction probability (juveniles, yearlings, adults)	0.3, 0.8, 0.9	Bieber and Ruf 2005
L	Litter size (juveniles, yearlings, adults)	4, 5, 6	Bieber and Ruf 2005
d	Dispersal probability (females, males)	0.4, 0.7	Truvé et al. 2004

Tab. 1 – Summary of the main parameters used to build and run the spatially explicit, stochastic, individual-based model of ASF spread into a wild boar population.

	Scenario 1 (direct + carcasses)	Scenario 2 (direct + carcasses + convalescents
Invasion phase (years 1-2)	Invasion phase (years 1-2)	Invasion phase (years 1-2)
ASFV$^+$	0.05% (0.01 – 0.13)	0.07% (0.01 – 0.17)
ASFV$^+$ & Ab$^+$	0.09% (0.01 – 0.21)	0.04% (0.01 – 0.11)
Ab$^+$	0.06% (0.01 – 0.18)	0.08% (0.01 – 0.21)
Population density (wild boar / km^2)	2.64 (2.58 – 2.69)	2.62 (2.54 – 2.70)
First epidemic wave (years 3-4)	First epidemic wave (years 3-4)	First epidemic wave (years 3-4)
ASFV$^+$	0.67% (0.31 – 0.92)	0.74% (0.42 – 1.14)
ASFV$^+$ & Ab$^+$	0.44% (0.23 – 0.68)	0.49% (0.27 – 0.73)
Ab$^+$	1.32% (1.04 – 2.39)	1.90% (1.19 – 2.55)
Population density (wild boar / km^2)	1.31 (0.94 – 1.51)	1.13 (0.87 – 1.44)
Endemic phase (years 5-7)	Endemic phase (years 5-7)	Endemic phase (years 5-7)
ASFV$^+$	0.10% (0.01 – 0.33)	0.13% (0.02 – 0.35)
ASFV$^+$ & Ab$^+$	0.11% (0.02 – 0.23)	0.09% (0.01 – 0.22)
Ab$^+$	1.64% (1.40 – 2.37)	2.02% (1.61 – 2.46)
Population density (wild boar / km^2)	0.92 (0.55 – 1.02)	0.87 (0.51 – 0.98)
Second epidemic wave (years 8-10)	Second epidemic wave (years 8-10)	Second epidemic wave (years 8-10)
ASFV$^+$	0.50% (0.16 – 0.66)	0.55% (0.17 – 0.60)
ASFV$^+$ & Ab$^+$	0.60% (0.22 – 0.90)	0.36% (0.10 – 0.58)
Ab$^+$	1.95% (1.20 – 2.84)	2.19% (1.30 – 2.92)
Population density (wild boar / km^2)	2.19 (1.91 – 2.59)	2.03 (1.87 – 2.54)
5-year persistence probability	55%	64%
10-year persistence probability	52%	57%

Tab. 2- Summary average statistics corresponding to the two simulated scenarios used to test the different long-term persistence mechanisms of ASF in a wild boar population. 95% Cis are shown in parentheses.

Parameter	Parameter	Sensitivity	SE	p-value
Symbol	Description			
P_d	Transmission probability from infected wild boars	**-0.067**	**0.010**	**< 0.001**
P_c	Transmission probability from infected carcasses	**-0.107**	**0.012**	**< 0.001**
P_s	Transmission probability from ASF survivors	-0.001	0.011	0.88
χ	Duration of ASF survivors' infectivity period	0.016	0.017	0.11
I	Duration of carcasses infectivity period	**0.088**	**0.010**	**< 0.001**
γ	Disease lethality	**-0.042**	**0.011**	**< 0.001**
h	Hunting rate (wild boar density > 0.75 / km^2)	**-0.385**	**0.088**	**0.001**
h	Hunting rate (wild boar density < 0.75 / km^2)	0.006	0.059	0.21
R	Proportion of females reproducing in the population	**0.171**	**0.086**	**0.04**

Tab. 3- Sensitivity of ASF persistence to changes in the main epidemiological and demographic parameters. The values result from a global regression-based sensitivity analysis based on standardized input values. Sensitivity values significantly different from zero are highlighted in bold font.

FIGURE LEGENDS

Fig. 1 – Epidemiological compartments used to build the spatially explicit, stochastic, individual-based model of ASF spread into a wild boar population. In scenario 1 only direct and carcass-mediated transmissions were considered. In scenario 2 the three transmission mechanisms were included. The following notations are used for model parameters: γ = disease lethality; χ = convalescents infectious period; I = Carcass infectious period; M = natural mortality rate; h = hunting rate.

Fig. 2 – Average daily proportions of ASF infected (a) and sero-prevalent (b) wild boars, resulting from a model in which disease transmission occurred either directly (infected-susceptible) or through an infected carcass.

Fig. 3 – Daily virus persistence probabilities associated to each of the two simulated scenarios of the spatially explicit, individual-based model of ASF in wild boar. Scenarios 1 include only direct and carcass-mediated virus transmission, whereas scenario 2 also includes survivor-mediated transmission.

Fig. 4 – Proportion of ASF virus infections occurring with each of the three simulated transmission pathways (a), and their relative distribution within and between wild boar social groups (b).

Fig. 5 – Functional relationship between wild boar population density and the proportion of ASF infections occurring through infected carcasses.

Fig. 6 – Relationship between the minimum observed wild boar density during the simulated 10-year period and the ASF persistence expressed in days.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Fig. S1 – Results of the optimization process for the three ASF transmission rates

Fig. S2 – Results of the optimization process for four additional model parameters.

Fig. S3 – Temporal trend in the ASF force of infection.