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Rift Valley Fever – assessment of effectiveness of surveillance and control measures in the EU

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Abstract

Effectiveness of surveillance and control measures against Rift Valley Fever (RVF) in Mayotte (overseas France) and in continental EU were assessed using mathematical models. Surveillance for early detection of RVF virus circulation implies very low design prevalence values and thus sampling a high number of animals, so feasibility issues may rise. Passive surveillance based on notified abortions in ruminants is key for early warning and at present the only feasible surveillance option. The assessment of vaccination and culling against RVF in Mayotte suggests that vaccination is more effective when quickly implemented throughout the population, e.g. at a rate of 200 or 2,000 animals vaccinated per day. Test and cull is not an option for RVF control in Mayotte given the high number of animals that would need to be tested. If the risk of RVFV introduction into the continental EU increases, ruminant establishments close to possible points of disease incursion should be included in the surveillance. An enhanced surveillance on reproductive disorders should be applied during summer in risk areas. Serosurveillance targets of 0.3% animals should be at least considered. RVF control measures possibly applied in the continental EU have been assessed in the Netherlands, as an example. Culling animals on farms within a 20 km radius of detected farms appears as the most effective measure to control RVF spread, although too many animals should be culled. Alternative measures are vaccination in a 50 km radius around detection, ring vaccination between 20 and 50 km and culling of detected farms. The assessment of zoning showed that, following RVFV introduction and considering an $R_0 = 2$, a mean vector dispersal of 10 km and 10 farms initially detected, RVFV would spread beyond a radius of up to 100 km or 50 km from the infected area with 10% or 55% probability, respectively.

Keywords: Rift Valley Fever, Mayotte, EU, control, surveillance, vaccination, vectors, ruminants

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Summary

Rift Valley Fever (RVF) has never been reported in continental Europe or in countries neighbouring the European Union (EU) to date, but in 2018–2019, it reappeared after 10 years in a French overseas Department (Mayotte) with outbreaks involving multiple human cases. Besides this reoccurrence, a legislative process triggered a mandate from the European Commission requesting European Food Safety Authority (EFSA) perform a risk assessment on RVF. The Commission adopted the Commission Delegated Regulation 2020/687 which supplements Part III of Regulation (EU) 2016/429 (Animal Health Law), laying down rules for the prevention and control of transmissible animal diseases, and that replaces existing Directive 92/119/EEC which currently provides for measures to apply in the event of occurrence of certain diseases, which includes RVF. Additionally, in accordance with Commission Implementing Regulation (EU) 2018/1882, RVF is categorised as a Category A disease.

Following the categorisation and the proposed changes to the control measures for RVF, the Commission requested a complete risk assessment on RVF (risk of introduction, exposure and effectiveness of prevention and control measures), since the measures proposed in the Delegated Regulation should be based on the latest scientific knowledge.

Two EFSA assessments have been already produced about the risk of introduction and impact assessment in Mayotte. The present document is about the assessment of i) effectiveness of preventive and control measures in eliminating or reducing the disease impact in Mayotte as well as ii) different surveillance strategies in animals that may be used for detection and possible prediction of RVF recurrence in Mayotte. Finally, while considering the risk of RVF introduction into the EU, iii) the surveillance measures for early detection of the disease as well as iv) the feasibility, availability and effectiveness of the prevention and control measures for RVF, especially the ones foreseen in the above-mentioned Commission Delegated Regulation.

The preventive and control measures for RVF elimination in Mayotte that were assessed were different surveillance scenarios, zoning and different vaccination, stamping out and vector control strategies.

Regarding possible surveillance scenarios, considering that the rainy season in Mayotte is from December to March and this is the period at higher risk for the establishment of an RVF epidemic, two main objectives for active surveillance can be considered, i.e. i) early detection of RVFV circulation, ideally before the steady increase of human and/or animal cases: this implies design prevalence values so low that a very high number of animals must be tested, so feasibility issues may rise; ii) the verification of RVFV circulation during the previous rainy season, which can be achieved testing a limited number of animals, due the higher design prevalence.

Monitoring the seroprevalence will give indication about the occurrence of RVF and the spatial and temporal distribution of infection, and indicate possible areas with higher risk for the re-occurrence of the disease. On the other hand, passive surveillance, based on the notification and testing of aborted fetuses and animals showing clinical signs suggestive of RVF, and at present the only feasible surveillance option, given the high percentage of animals naturally immunised after the 2018–2019 epidemic.

Zoning is not applicable in Mayotte, because, due to the small geographical size of Mayotte and the potential dispersal of mosquitoes over long distances (e.g. > 6 km), the whole island would be considered a single protection zone.

In order to assess vaccination and culling strategies, a stochastic version of a model previously developed to simulate the spread and control of RVFV in Mayotte was used.

The results of the analysis of the impact of vaccination on reducing RVF infections suggested that the vaccination is more effective when applied early before the start of the epidemic and quickly implemented throughout the population. Differing levels of vaccine effectiveness, either 60% or 90%, have a relatively minor impact on the reduction of the expected number of infected animals. In particular, with a rate of 200 or 2,000 animals vaccinated per day, the epidemic is halted within one year regardless of whether vaccination is applied before or after RVF incursion. Moreover, the number of infections is kept under 3% if vaccination is conducted at least 30 days prior to incursion with at least 200 animals vaccinated per day (20% coverage achieved at time of incursion, 100% coverage achieved 120 days post incursion). The same effect is achieved if the vaccination is conducted at 2,000 animals vaccinated per day, started at 60 days post incursion at the latest (100% vaccination coverage would be achieved 75 days after RVF incursion).

A test-and-cull strategy does not seem an alternative for the control of RVF in Mayotte unless high numbers (ca. 2,000 per day) of animals are tested every day and the infected animals are quickly

removed, which is particularly difficult in the rural context of Mayotte, with many small herds scattered in the territory and difficult to be visited.

Considering vector control, some activities are in place in Mayotte, but mainly focused to protect humans and probably have a limited impact on RVFV transmission. Vector control alone does not seem to be a useful alternative for the control of RVF in Mayotte either. Only a reduction of 40% or more in mosquito abundance, a level of vector reduction that would be difficult to achieve, and maintained only for short time, e.g. 2 weeks, can have a measurable effect on the transmission and re-occurrence of the infection, alone or combined with other control measures. Effective vector control, mostly by using larvicides, will require long-term programmes considering the mosquito habitat and climate of Mayotte, whereas the general use of adulticides is unfeasible due to the potential impact on the environment.

The assessment of the possible preventive and control measures to be applied in case of RVF (risk of) incursion into continental EU included an evaluation of different surveillance strategies and of zoning, vaccination and stamping out strategies.

Concerning the surveillance, in case of increased risk of RVFV introduction into continental EU, cattle and small ruminant establishments located in the proximity of the high risk points of disease incursion by vector import (ports, airports, cargo and container yards) should be included in the surveillance. Passive surveillance can be considered as first choice for the early detection of the infection under these circumstances: enhanced surveillance of abortions, stillbirths and neonatal mortality of cattle, sheep and goats, therefore, should be applied during summer and autumn (during the peak of and end of vector season) in the areas at major risk of introduction. Regarding targets for active surveillance programmes, based on the only known and documented case of introduction of RVF into a previously free territory (Saudi Arabia), a target seroprevalence of below 0.3% need to be considered.

The assessment of the various control measures against RVF in case of incursion into the continental EU has been conducted by simulating RVF spread by a mathematical model applied to the Netherlands as a case study, chosen because of the results of the previous EFSA Opinion about the risk of RVF introduction in the EU, where the Netherlands was one of the countries at highest risk of introduction of RVF.

According to the model used, in the absence of vaccination, stamping out of farms (i.e. culling all animals) in a 20 km radius around detected farms appears to be the most effective measure to control RVF spread after introduction in the Netherlands, during the vector season, although its feasibility in terms of the number of animals to be culled should be evaluated.

The next most effective control measures are vaccination in a 50-km radius around detected farms, ring vaccination between 20 and 50 km and culling of detected farms only. The time to protection depends on the type of vaccine used (live or inactivated), and therefore, the results of the model should be evaluated in the light of this aspect as well.

The assessment of the effectiveness of zoning showed that, according to the model used, following RVFV introduction and considering an $R_0 = 2$ (value of basic reproduction number of RVF estimated from the literature), a mean dispersal of vectors of 10 km and 10 infected farms detected inside the restriction zones, the RVFV would spread beyond a radius of up to 100 km from the infected area with a probability of 10%. Under the same conditions, if the radius is 50 km, the probability of RVF spreading beyond this zone would be 55%.

What most influences the probability of spread beyond a restriction zone of a certain radius is the mean dispersal distance of vectors and the number of initial number of farms infected inside the restriction zones, rather than R_0. This suggests that the number of infected farms detected inside the restriction zones should be kept as few as possible, implying that the early warning and early implementation of restriction zones are key measures to contain the spread.

Considering vectors and their control, in the Netherlands, *Aedes vexans* and *Culex pipiens* can be considered as candidates for RVFV transmission. Both species are abundant and widespread in the Netherlands, favouring their vector capacity. The vector role of *Ae. albopictus* remains uncertain, since evidences of RVFV transmission come mainly from laboratory trials only and its presence in the Netherlands is currently also uncertain.

Floodwater potential vectors of RVFV in Europe, such as *Cx. pipiens* and *Ae. vexans,* are regularly controlled in European Member States (MSs), but the efficacy of these vector control measures is highly variable. In general, long-term vector control programmes by using larvicides achieve higher rates (up to 95%) of vector control.

Decrease of transmission of West Nile virus (WNV), transmitted by the same vector species as RVFV, in urban and peri-urban areas, has been achieved by decreasing adult population of vectors, mainly by using adulticides. On average, adulticide control in WNV scenarios achieves around 70% efficacy on mosquito adult population. It is uncertain what would be the effect of the current regular floodwater mosquito control measures of MS, mainly larvicides, on the RVFV transmission among domestic animals. There is an uncertainty about RVFV vector control in and around farms compared to the WNV scenario where flooded areas, peri-urban and urban areas are the main target.

Finally, considering the control of RVF in continental EU, the possible role of wildlife was also considered. Whereas in some southern African countries, wild ruminants are considered to play a role in the maintenance of RVFV infection during the inter-epizootic periods, no data are available about the susceptibility of European wild ruminant species to RVFV, or the capacity of the virus of causing a detectable viraemia in these animals. The density of wild ruminant species in Europe is much lower than domestic ruminants, but a possible involvement of these animals in RVFV transmission in specific geographical areas or epidemiological contexts cannot be excluded.

The EFSA Panel on Animal Health and Welfare identified several limitations in the data available for performing the scientific assessment, mainly related to the current infection and immunological status of the livestock population in Mayotte, the spread dynamics of RVF in newly infected areas in general and in Europe in particular. Given the uncertainty generated by these limitations, the results should be carefully interpreted.

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1. Introduction

1.1. Background and Terms of Reference as provided by the European Commission

General introduction-background information

Rift Valley Fever (RVF) is a disease affecting primarily domestic ruminants (cattle, sheep, goats, camels) and some wild ruminants, that is caused by a single stranded RNA virus of the genus Bunyaviridae.

RVF is a vector borne disease, transmitted primarily through various species of vectors (primarily hematophagous mosquitoes). Certain species of vectors (Aedes mosquitoes) may act as reservoirs of the disease during inter-epidemic periods, thanks to their potential for transovarian (vertical) transmission of the virus to their eggs. As a result, new generations of RVF virus infected mosquitoes may hatch from infected eggs, especially in periods of favourable conditions (e.g. high rainfalls).

Ruminants are infected primarily through infected vector bites. Clinical signs range from sudden deaths and abortions to mild, non-specific symptoms, depending on the virulence of the infecting virus strain and the species, breed and age of the affected animals. Mortality may reach 70–100% in lambs and kids and 20–70% in sheep and calves. Abortion rates may reach 85–100% within the affected herds. RVF in camels can cause abortions and neonatal deaths. Infected wild ruminants usually do not demonstrate any clinical signs.

Humans can become infected by RVF, through the bites of vectors, through contact with infected animals and animal materials (blood, discharges, abortion materials etc.) or through consumption of untreated animal products (meat and milk). No human-to-human transmission has been recorded to date. About 50% of infected humans have no clinical symptoms while the rest may demonstrate flu-like symptoms. A small percentage may develop severe clinical forms, involving haemorrhagic fever with hepatic disease, meningoencephalitis or ocular complications. The total case fatality rate varies between different epidemics (overall less than 1% in those documented).

To date no RVF outbreaks in humans or animals have been reported in EU or countries sharing land borders with the continental areas of the EU. Evidence of RVF nearest to the EU is limited to serological findings from retrospective studies, carried out in Turkey, using blood samples collected from camels, gazelles and buffaloes from 2000 to 2006.

Currently the disease is endemic in large areas of Southern and Eastern Africa, where outbreaks of RVF occur periodically (e.g. every few years), in seasons when weather conditions favour competent vectors. In recent decades, large RVF epidemics have occurred in Egypt (1977–1978, 1993, 2003), Mauritania (2010, 2012, 2015), Madagascar (2007–2009), Comoros (2007) and elsewhere on the African continent (Kenya, Somalia, South Africa, Sudan, Senegal etc.). Egypt currently marks the northernmost limit of RVF spread. The disease moved outside the African continent for the first time in 2000, into the Arab peninsula (Saudi Arabia and Yemen).

On 5 April 2017, EFSA, following a request from the Commission, adopted a scientific opinion on 36 vector-borne diseases, including RVF. The opinion concluded that the risk of introduction of RVF in the EU was estimated to be very low, using a semi quantitative method (modified MINTRISK model).

In Mayotte, a French department in the Indian Ocean, close to the Comoros islands and Madagascar, human cases of RVF were detected for the first time in 2007. Retrospective serological studies demonstrated the presence of RVF in livestock since 2004 (serological evidence). Until recently, the disease appeared to be in remission with no new human cases detected since 2011. However, in 2018, RVF reappeared in Mayotte and between 22 November 2018 and 14 March 2019, more than 101 human cases and more than 60 outbreaks in ruminants have been reported.

In response to the RVF resurgence, the competent authorities of Mayotte are implementing surveillance and biosecurity measures, coupled with vector control/protection measures, aiming to limit the overall disease spread and prevent animal-to-human transmission. In addition, movements of ruminants and raw meat and milk thereof, originating from Mayotte, have been prohibited.

The Commission is empowered to adopt delegated acts supplementing the rules laid down in Part III of Regulation (EU) 2016/429 on transmissible animal diseases (Animal Health Law) on disease control measures for listed diseases as referred to in point a), b) and c) of its Article 9 (category A, B and C diseases). Therefore a draft Commission Delegated Regulation laying down rules for the prevention and control of certain diseases has been developed and the draft is in consultation.

The rules laid down in the abovementioned draft Commission Delegated Regulation are largely superseding the rules currently in force concerning the disease control measures in the event of animal

diseases with serious effects on the livestock. Consequently, animal disease control measures laid down in existing Directives will be, if not already done by the Animal Health Law, replaced by the rules provided in that Delegated Regulation. This is also the case of Directive 92/119/EEC, which currently provides for measures to apply in the event of occurrence of certain diseases. This includes Rift Valley fever, which is in accordance with Commission Implementing Regulation (EU) 2018/1882, categorised as Category A disease.

In this regard, the existing rules of Directive 92/119/EEC will cease to apply for Rift Valley fever as from the date of application of the Animal Health Law and its complementing legislation, i.e. from 21 April 2021. The proposed measures for the prevention and control of RVF should be assessed in order to ensure that they are updated based on the latest scientific knowledge in this new set of legislation.

Terms of reference

1) RISK OF ENTRY OF RVF INTO THE CONTINENTAL PARTS OF THE EU

   1.1) Provide an update of the global epidemiological situation in relation to RVF with emphasis on areas posing a higher risk for the EU.
   1.2) Provide an updated assessment of the overall risk of introduction of RVF (combined rate of entry, vector transmission and establishment), separately for each one of the EU regions potentially at risk, as specified in the 2017 EFSA scientific opinion on Vector-borne diseases (VBD).
   1.3) Provide a separate risk assessment of the risk of introduction of RVF for specific Member States that may be at particular risk.

2) IMPACT OF RVF IN THE DEPARTMENT OF MAYOTTE AND RELEVANT CONTROL MEASURES

   2.1) Assess the probability of overwintering of RVF in the department of Mayotte as well as the risk of RVF spreading from Mayotte to other areas including other French departments in the Indian Ocean or Metropolitan France.
   2.2) Assess the impact of the disease (as defined in the 'VBD opinion'), with emphasis on animal health and farm production in Mayotte from the time of its initial occurrence to date.
   2.3) **Assess the possible short and long term effectiveness, of different control measures, in eliminating or reducing the disease impact in Mayotte (as per TOR 2.2 above), namely:**

      2.3.1) Stamping out of RVF outbreaks;
      2.3.2) Establishment of a protection and a surveillance zone around RVF outbreaks;
      2.3.3) Biosecurity measures, such as the ones currently in place in Mayotte, coupled with personal sanitary protection measures related to human-animal contact, including measures to prevent consumption of potentially infected meat and milk;
      2.3.4) Vector control and protection measures;
      2.3.5) Vaccination of livestock.

   2.4) **Assess the possible effectiveness of different surveillance strategies in animals that may be used for RVF detection and possible prediction of RVF recurrence in Mayotte in the future, in view of the diagnostic methods currently available.**

3) **SURVEILLANCE AND CONTROL MEASURES FOR RVF [IN CASE OF OCCURRENCE OR HIGH RISK OF RVF INCURSION IN EUROPE]**

   3.1) **In case of high risk of RVFV introduction in Europe assess and describe the surveillance measures necessary to ensure early detection of the disease**
   3.2) **In case of RVF occurrence in Europe, assess the effectiveness of the main available disease prevention and control measures for RVF, including the relevant measures provided for in the draft Commission Delegated Regulation on rules for the prevention and control of certain listed diseases under Part III of Regulation (EU) 2016/429 on transmissible animal diseases (Animal Heath Law), namely their potential to:**

      – **limit the geographical spread of the disease**

- **reduce the number of outbreaks**
- **reduce the overall impact of the disease being present in an area for prolonged periods (e.g. in case overwintering is possible)**

In particular, assess the feasibility, availability and effectiveness of:

3.2.1) **the general measures set out in the enacting terms of Part I and II of draft Commission Delegated Regulation**

3.2.2) **the disease-specific measures set out in Annexes I to X to draft Commission Delegated Regulation**

3.2.3) **vaccination of listed species, including assessment of possible:**

- **risk mitigating measures necessary to be put in place for animals and products of animal origin thereof, following vaccination**
- **surveillance performed after vaccination.**

2. Data and methodologies

2.1. Assessment of the effectiveness of restriction zones

To estimate the zone size required for surveillance, we applied the methods developed in Schley et al. (2009), which allows calculation of the probability of RVFV escaping a zone of a given radius. The size of the surveillance zone can be defined as the minimum radius of zone for which the probability of escape is below a predefined threshold value. The escape probability, $p_E(r)$, is given by,

$$p_E(r) = 1 - \exp\left(-IR_0 \int_r^{\infty} k(s)ds\right),$$

where

$$k(r) = \frac{rK(r)}{\int_0^{\infty} rK(r)dr}$$

is the probability of transmission at distance r, K(r) is the transmission kernel, R_0 is the basic reproduction number, here assumed to be 2, based on previous epidemics in Mayotte (Métras et al., 2017, 2020). On the other side, for EU, the calculation with different R_0 values is provided, since the R_0 under the EU condition is not known: it is reported to vary between 2.3 and 6.8 as from modelled values or from epidemics reported in Africa (Braks et al., 2017) and I is the number of infected animals in the zone (in the best-case scenario assumed to be at least one). Recall that R_0 is the average number of cases an infectious animal will generate in a homogeneously mixed naïve population. Therefore, the total number $N_{\leq}(r)$ of those cases contained within the circular surveillance zone of radius r is given by, $N_{\leq}(r) = R_0 \int_0^r k(s)ds$, and those outside that zone is, $N_{>}(r) = R_0 \int_r^{\omega} k(s)ds$. Consequently, the escape probability can be rewritten as $p_E(r) = 1 - \exp\{-IN_{>}(r)\}$ and be interpreted as the probability of finding cases outside the surveillance zone. It follows from this that the fraction of total cases contained in the surveillance zone is simply given by (for $I = 1$),

$$\frac{N_{\leq}(r)}{R_0} = 1 + \ln(1 - p_E).$$

An exponential kernel, $K(r) = \exp(-r/L)$, was assumed, where L is the mean transmission distance mainly attributed to dispersal distance of hosts (vectors and animals). This means that very long-range transmission events, such as over 20–30 km, usually attributed to animal movements and not to vectors (EFSA, 2019) are highly unlikely, which was deemed appropriate, because we are principally concerned with transmission, when animal movement restrictions are put in place within the restriction zones. For such an exponential transmission kernel, the escape probability (for $I = 1$) is given by,

$$p_E(r) = 1 - \exp\left\{-R_0\left(1 + \frac{r}{L}\right)e^{-r/L}\right\}$$

and the radius r of the circular surveillance zone is therefore obtained as a positive solution of,

$$\left(1 + \frac{r}{L}\right)e^{-r/L} = -\frac{\ln(1 - p_E)}{R_0}.$$

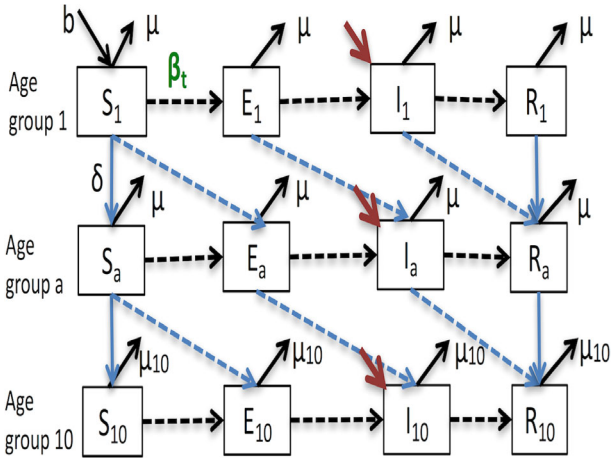
2.2. Assessment of the effectiveness of control measures for RVF in Mayotte: spread model

To model the spread and control of RVFV in Mayotte, we used a stochastic version of a model previously developed by Métras et al. (2017, 2020).

Mayotte is a small island so treating it as a single homogeneously mixed population is a reasonable approximation. The *SEIR* model (Susceptible–Exposed–Infectious–Recovered) used for Mayotte is an approximation of the extended *SEIR-SEI* model used for the EU (see Section 2.3) in the limit of stationary vector population in terms of both population level and prevalence on infection. This is reasonable for Mayotte which is tropical and where RVFV is endemic, but not for Europe.

This is an age-structured *SEIR* model with the force of infection between animals driven by precipitation to reflect seasonal variation in vector abundance. The model treats all susceptible livestock species (cattle, sheep and goats) in Mayotte as a single homogeneously mixed population (i.e. all species are equally susceptible and there is no spatial structure in the population). The model has been fitted to data on RVFV IgG seroprevalence in Mayotte from 2005 to 2016 (Métras et al., 2017) and from 2018 to 2019 (Métras et al., 2020).

The model is presented as in Figure 1 by Métras et al. (2017).



The black arrows represent the state transitions within the same yearly age group, while the blue arrows also account for the ageing of animals. The dashed lines correspond to disease stage transitions. The red arrows are the import of infectious animals, and the transmission parameter β_t in green is driven by climate variables. Reproduced from Métras et al. (2017).

Figure 1: SEIR age-stratified model diagram (10 yearly age groups, with a $\in$ [2–9] on the diagram)

And it is described by the following equations. For age class 1 (comprising animals 0–1 years old), the number of susceptible (S), exposed (E), infectious (I) and recovered (R) animals on day t + 1 is given by,

$$S_1(t+1) = b_t + (1 - \lambda_t)(1 - d)\alpha S_1(t)$$

$$E_1(t+1) = \lambda_t + (1 - d)\alpha S_1(t) + (1 - p_1)(1 - d)\alpha E_1(t)$$

$$I_1(t+1) = p_1(1 - d)\alpha E_1(t) + (1 - p_R)(1 - d)\alpha I_1(t)$$

$$R_1(t+1) = p_R(1-d)\alpha I_1(t)$$

For age classes a = 2, 3, …, 9 (comprising animals 1–2, 2–3, …, 8–9 years old, respectively), the numbers are given by,

$$S_\alpha(t+1) = (1-\lambda_t)(1-d)\alpha S_\alpha(t) + (1-\lambda_t)d\alpha S_{\alpha-1}(t),$$

$$E_\alpha(t+1) = \lambda_t(1-d)\alpha S_\alpha(t) + \lambda_t d\alpha S_{\alpha-1}(t) + (1-p_1)(1-d)\alpha E_a(t) + (1-p_I)d\alpha E_{\alpha-1}(t),$$

$$I_\alpha(t+1) = p_1(1-d)\alpha E_\alpha(t) + p_1 d\alpha E_{\alpha-1}(t) + (1-p_R)(1-d)\alpha I_a(t) + (1-p_R)d\alpha I_{\alpha-1}(t),$$

$$R_a(t+1) = p_R(1-d)\alpha I_\alpha(t) + p_R d\alpha I_{\alpha-1}(t).$$

Finally, for age class 10 (comprising animals > 9 years old), they are given by,

$$S_{10}(t+1) = (1-\lambda_t)\alpha_{10}S_{10}(t) + (1-\lambda_t)d\alpha S_9(t),$$

$$E_{10}(t+1) = \lambda_t\alpha_{10}S_{10}(t) + \lambda_t d\alpha S_9(t) + (1-p_1)\alpha_{10}E_{10}(t) + (1-p_I)d\alpha E_9(t),$$

$$I_{10}(t+1) = p_I\alpha_{10}E_{10}(t) + p_1 d\alpha E_9(t) + (1-p_R)\alpha_{10}I_{10}(t) + (1-p_R)d\alpha I_9(t),$$

$$R_{10}(t+1) = p_R\alpha_{10}I_{10}(t) + p_R d\alpha I_9(t).$$

The number of births, b_t, is chosen to maintain a constant population size, N.

Note that in the stochastic implementation of the model, each of the terms in an equation becomes a series of binomial probabilities. For example, the first term in the equation for $S_1(t)$ is implemented in two steps: the first is to determine the number of animals surviving ($N_s \sim$ Binomial ($S_1(t)$, α) and the second to determine the number of these which become infected ($I \sim$ Binomial(N_s, λ_t)).

In the equations above, α and α_{10} are daily survival probabilities and d is the daily ageing probability. The latent and infectious periods were assumed to follow exponential distributions. Accordingly, the daily probability of completing the latent period (and so becoming infectious) is given by $p_I = 1 - \exp(-1/\mu_E)$, where μ_E is the mean latent period (which was chosen to account for both the intrinsic (i.e. within-host) and extrinsic (i.e. within-vector) incubation periods). The daily probability of completing the infectious period (and so recovering) is given by $p_R = 1 - \exp(-1/\mu_I)$, where μ_I is the mean infectious period. The probability of infection, λ_t, is given by,

$$\lambda_t = 1 - \exp\left(-\frac{R_t^{(S)}}{\mu_I N}\sum_{\alpha=1}^{10} I_a(t)\right),$$

where

$$R_t^{(S)} = \exp(b_0 + b_1 P(t-14)),$$

is the seasonal reproduction number, which is assumed to depend on daily precipitation, P, with a time lag of 14 days (i.e. at day t – 14) to reflect the lag between rainfall and change in mosquito abundance. Parameters and their estimates are summarised in Table 1. Parameters in the model for the transmission of RVFV in Mayotte (from Métras et al., 2020). Data on animal populations and farm management that have been used for this Opinion were derived from the websites of the Statistic and Prospective Service of the French Ministry of Agriculture and Food (Service de la statistique et de la prospective, Ministère de l' Agriculture et de l' Alimentation[1]) and from the Direction of Food, Agriculture and Forestry (Direction de l' Agriculture de l' Alimentation et la Forêt, DAAF) of Mayotte.[2] Data and information on the epidemiology of RVF in Mayotte, in relation to the outbreaks and cases in animals and humans, were obtained from World Organisation for Animal Health (OIE), Animal Disease Notification System (ADNS), French Veterinary Authorities. Monthly precipitation data for July 2018 to

[1] Résultats du recensement agricole 2010, Mayotte : Synthèse illustrée du recensement agricole 2010 – Élevage – juin 2011 (PDF : 1.4 Mo) – 13/9/2011; http://agreste.agriculture.gouv.fr/IMG/pdf_D97611A05.pdf

[2] DAAF:http://daaf.mayotte.agriculture.gouv.fr/Statistiques

June 2019 were obtained from METEO FRANCE[3] and converted to daily precipitation by dividing each monthly total by the number of days in the month. This was done based on the assumption that in a tropical area rainy days are concentrated in rainy months with almost uniform distribution over the month. Furthermore, the same precipitation data were used for each year of the simulations. This was the only data set available, nevertheless, unless 2018–2019 was abnormally dry or wet, the simulations should be representative and, in any case, the relative impact of the strategies is unlikely to be affected.

Table 1: Parameters in the model for the transmission of RVFV in Mayotte (from Métras et al., 2020)

Parameter	Symbol	Estimate
Population size	N	30,000
Number of animals in each age class (a = 1, . . ., 10)	N_a	{8,820, 6,180, 4,320, 3,030, 2,130, 1,500, 1,050, 720, 510, 1,740}
Simulated proportion of immune animals in each age class on 1 October (i.e. post-epidemic)	–	{0.30, 0.54, 0.64, 0.66, 0.66, 0.66, 0.68, 0.71, 0.70, 0.78}
Daily survival probability		
Age class 1–9	A	0.9988
Age class 10	α_{10}	0.9992
Daily ageing probability	d	1/365
Seasonal reproduction number		
Intercept	b_0	0.299
Precipitation	b_1	0.026
Mean latent period (days)	μ_E	7
Mean infectious period (days)	μ_I	7
Precipitation in 2018–2019 (mm)		Median: 51.3; quantiles (25–75%): 21.2–273.1; range: 5.6–336.6

In order to evaluate surveillance and control measures, the model was used to simulate incursions of RVFV to Mayotte on 1 January, 1 April, 1 July or 1 October, assuming either: i) a completely naïve population (except for pre-emptive vaccination) or ii) a population with immunity equal to that after the 2018–2019 epidemic (specifically, the median simulated proportion of immune animals on 1 October 2019). For each of the eight scenarios, 100 replicates of the model were run until the end of the second year after the incursion (i.e. day 1,095, where day 0 is 1 January in the first year of the simulations).

Surveillance: The time course for the proportion of recovered animals (assumed to be equivalent to IgG seroprevalence) from the 'no control measures' scenario was used to estimate either the time to detection (in days) for a given design prevalence or the design prevalence required to detect an incursion by a specified number of days post introduction. The value of test sensitivity is obtained from the literature, and sample size is calculated using the RIBESS tool.[4]

Vaccination: When implemented as a control measure, the following assumptions were made about vaccination:

- vaccine is deployed at a constant rate, i.e. number of animals per day, until the whole population has been vaccinated;
- animals are vaccinated independently of their infection status, though previously vaccinated animals are not revaccinated;
- vaccination has no effect on animals that are already infected or have been infected (i.e. are in the E, I or R classes) as these animals will clear the virus and subsequently become (naturally) immune;

[3] Meteo France : http://www.meteofrance.yt/climat/description-du-climat; and http://www.meteofrance.yt/climat/suivi-climatique-recent/an-2019

[4] https://zenodo.org/record/167306#.XuHs6kX7TD4

- susceptible animals are protected after vaccination with probability given by the vaccine efficacy; the model assumed that there was no delay between vaccination and protection (this is the day of protection).

In this case, the number of susceptible and vaccinated (and protected) animals on day $t + 1$ is,

$$S_\alpha(t+1) = S_\alpha(t+1) - V_\alpha^{(new)}(t),$$

$$V_1(t+1) = (1-d)\alpha V_1(t) + V_1^{(new)}(t),$$

$$V_\alpha(t+1) = (1-d)\alpha V_\alpha(t) + d\alpha V_{\alpha-1}(t) + V_\alpha^{(new)}(t),$$

$$V_{10}(t+1) = \alpha_{10} V_{10}(t) + d\alpha V_9(t) + V_{10}^{(new)}(t),$$

where the number of newly vaccinated, protected animals in each age class is given by,

$$V_\alpha^{(new)}(t) = \nu_E \frac{S_\alpha(t)}{\sum_{\alpha=1}^{10} S_\alpha(t) + E_\alpha(t) + I_a(t) + R_\alpha(t)} n_V$$

and n_V is the number of animals vaccinated per day and v_E is the vaccine efficacy. We considered three rates at which animals were vaccinated (20, 200 or 2,000 animals per day – see Section 3.3.2.3 about the choice of these scenarios, which are the numbers that could feasibly be vaccinated each day by 1, 10 or 100 vaccination teams, see Section 3.3.2.3); five time points at which vaccination started (60 or 30 days prior to the incursion and 30, 60 or 90 days after the incursion) and two vaccine efficacies (60% or 90%; Njenga et al. 2015).

Culling: Culling of infected animals (i.e. those in the exposed (E) and infectious (I) classes) was assumed to be part of a test and cull strategy (using a test with an assumed sensitivity and specificity of 100%, a best-case scenario) in which a number of animals is tested each day and all infected animals detected are culled. In this case, the number of exposed and infectious animals is given by

$$E_a(t+1) = E_\alpha(t+1) - E_\alpha^{(cull)}(t),$$

$$I_a(t+1) = I_\alpha(t+1) - I_\alpha^{(cull)}(t),$$

where the number of animals culled is

$$E_\alpha^{(cull)}(t) = \frac{E_\alpha(t)}{\sum_{\alpha=1}^{10} S_\alpha(t) + E_\alpha(t) + I_\alpha(t) + R_\alpha(t)} n_T,$$

$$I_\alpha^{(cull)}(t) = \frac{I_\alpha(t)}{\sum_{\alpha=1}^{10} S_\alpha(t) + E_\alpha(t) + I_\alpha(t) + R_\alpha(t)} n_T$$

and n_T is the number of animals tested each day. Animals culled as part of control are assumed not to be replaced. We considered three rates at which animals were tested (20, 200 or 2,000 animals per day selected randomly from the population; cf. vaccination) and three time points at which testing and culling started (30, 60 or 90 days after the incursion).

Vector control: Vector control was assumed to reduce vector abundance and, hence, the seasonal reproduction number, $R_t^{(s)}$, which is proportional to abundance (see, e.g. Smith et al., 2012). We considered a range of scenarios in which abundance and, hence, the seasonal reproduction number was reduced by between 10% and 90%. The broad range is due to lack of specific information on the reduction in abundance that could be achieved by vector control measures.

Combined measures were also considered, namely vaccination combined with reduced mosquito abundance through vector control measures, and test and cull combined with vector control measures. Vaccination is not compatible with a test and cull strategy unless DIVA vaccines with available DIVA diagnostic tests are used.

2.3. Assessment of the effectiveness of control measures for RVF in EU: modelling the transmission of Rift Valley fever virus within and between farms in Europe

In order to assess the effectiveness of surveillance and control measures against RVF in the continental EU, a mathematical model was used to simulate the spread of RVF after introduction into the EU, and then to assess the effectiveness of surveillance and control measures such as vaccination or animal culling.

However, there are very limited data on transmission of RVFV between holdings in endemic countries and none for Europe specifically. To provide an assessment of spread and control, we selected one country, the Netherlands, from those identified as being at highest risk of RVFV introduction (EFSA AHAW Panel, 2020a) and geographically homogeneous to have a simpler scenario to be simulated, since the model used does not take into account environmental elements such as geographical barriers.

The main aim of the RVF spread model applied to the continental EU context is to provide a basic tool for making inferences on the magnitude of the duration of an epidemic after introduction of infection and implementation of control measures and to allow the relative comparison of the various control measures, for obtaining informative suggestions on their relative effectiveness. The estimation of the disease impacts in terms of absolute number of e.g. infected animals, abortions, deaths is not the purpose of the current model and it cannot be applied as such to assess these aspects. The description of the data used, the model structure, the underlying assumptions and the scenarios chosen are described in the Sections 2.3.1, 2.3.2 and 2.3.3.

2.3.1. Data

2.3.1.1. Demographic data

The location of and number of cattle, sheep and goats on each farm were obtained from the national authorities from the Netherlands. There are 65,740 farms and 6,244,938 animals in the population used for the Netherlands simulations.

2.3.1.2. Climate data

Temperature data were obtained from the European Commission Joint Research Centre MARS Meteorological Database, which provides daily meteorological data spatially interpolated on a 25 km by 25 km grid. Specifically, we extracted the daily mean temperatures for 2018. Farms used the temperature data for the grid square in which they are located.

2.3.2. Within-farm transmission of Rift Valley fever virus

The dynamics of RVFV within a farm are described using a stochastic compartmental model that includes a single ruminant host (cattle, sheep and goats are assumed to be equivalent) and a single mosquito vector genus (*Culex* spp.) considered to widely transmit RVFV according to the knowledge from epidemics in Africa.

The host population is assumed to be constant (H), except for disease-associated mortality, and is subdivided into the number of susceptible (i.e. uninfected), infected and recovered animals, denoted by X, Y and Z, respectively. To allow for a more general gamma distribution for the duration of viraemia, the infected host population, Y, is subdivided into a number of stages, with newly infected hosts entering the first stage and then passing through each successive stage. If the time spent in each stage follows an exponential distribution with mean 1/nr, the total length of time spent in the n stages follows a gamma distribution, with mean 1/r and variance $1/nr^2$ (Anderson and Watson, 1980).

The vector population (N) is subdivided into the number of adult female mosquitoes that are susceptible (i.e. uninfected), latent (i.e. infected, but not infectious) and infectious, denoted by S, L and I, respectively. To allow for a more general gamma distribution for the extrinsic incubation (i.e. latent) period (EIP), the latent class is subdivided into a number of stages in a similar approach to that described above for the duration of host viraemia. Vector mortality occurs at the same rate in all classes and is balanced by the recruitment of susceptible vectors, so that the total vector population remains constant. No transovarial transmission is considered in mosquitoes.

The force of infection for the host, λ_H, is given by,

$$\lambda_H(t) = bam\theta(t)\frac{I(t)}{N},$$

where b is the probability of transmission from an infected vector to a host, a is the reciprocal of the time interval between blood meals for the vector (assumed to be equal to the biting rate), m (= N/H) is the vector-to-host ratio and I/N is the proportion of bites which are from infectious vectors. For the Netherlands, mosquitoes were assumed to be active from April to October (Ibañez-Justicia et al., 2015), so the activity on day t is given by,

$$\theta(t) = \begin{cases} 0 & \text{otherwise} \\ 1 & 91 \leq t \leq 304 \end{cases}$$

Vector–host preference has been not considered because mosquitoes of the genus *Culex* (i.e. *Cx. pipiens* s.l.) are considered ornithophilic, but also generalist and opportunistic mammalophilic with no specific preference for any of the domestic animal species considered in this opinion (Brugman et al., 2018).

The force of infection for vectors, λ_V, is

$$\lambda_V(t) = \beta a\theta(t)\frac{Y(t)}{H},$$

where β is the probability of transmission from an infected host to a vector and Y is the total number of infected animals. Parameters in the model are summarised in Table 2 and their values were extracted from the published literature.

Table 2: Parameters in the model for the transmission of Rift Valley fever virus within a farm

Description		Symbol	Estimate or function	Comments and references
Probability of transmission from vector to host		b	1	Turell et al. (2008)
Probability of transmission from host to vector		β	0.1	Brustolin et al. (2017); Lumley et al. (2018); Vloet et al. (2017)
Vector to host ratio		m	Gamma(s_V,μ_V/s_V)	Varies amongst farms
Mean vector to host ratio		μ_V	20	Gachohi et al. (2016)
Shape parameter for vector to host ratio		s_V	2	–
Number of animals on farm		H	–	Obtained from national farm data
Reciprocal of the time interval between blood meals		a	a(T) = 0.0173(T – 9.6)	Depends on temperature (Madder et al., 1983)
Duration of viraemia	Mean	1/r	6	Bird et al. (2009); Pepin et al. (2010)
	No. stages	n	3	
Disease-associated mortality rate		d	0.01	Assumes 5–30% of livestock die of disease (Bird et al., 2009)
Extrinsic incubation period (EIP)	Mean	1/ν	ν(T) = 0.0071(T – 14.6)	Depends on temperature (Turell et al., 1985; Barker et al., 2013)
	No. stages	k	3	
Vector mortality rate		μ	μ(T) = 1/(69.1 – 2.14T)	Depends on temperature (Fischer et al., 2013)
Vector recruitment rate		ρ	–	For simplicity, assumed to be equal to vector mortality rate, so the vector population is constant
Vector population size		N	–	For simplicity, assumed to be constant; given by N = mH

Population sizes in the model take integer values, while transitions between compartments are stochastic processes (Table 3). The number of transitions of each type during a small time interval δt

was drawn from a binomial distribution with population size n and transition probability q (the appropriate per capita rate multiplied by δt) (Table 3). However, binomial random variables are computationally expensive to simulate and an approximating distribution was used wherever possible. If: (i) $nq(1-q) > 25$; (ii) $nq(1-q) > 5$ and $0.1 < q < 0.9$; or (iii) $\min(nq, n(1-q)) > 10$, an approximating normal variate with mean nq and variance $nq(1-q)$ was used, while if $q < 0.1$ and $nq < 10$, an approximating Poisson variate with mean nq was used (Forbes et al., 2011).

Table 3: Transitions, probabilities and population sizes in the model for the transmission of Rift Valley fever virus within a farm

Description	Transition	Probability	Population size
Hosts			
Infection	$\begin{cases} X \to X-1 \\ Y_1 \to Y_1+1 \end{cases}$	$\lambda_H \delta t$	X
Completion of infection stage j (j = 1, …, n − 1)	$\begin{cases} Y_j \to Y_j-1 \\ Y_j \to Y_j+1 \end{cases}$	$Nr\delta t$	Y_j
Mortality during infection stage j (j = 1, …, n)	$Y_j \to Y_j$ - 1	$D\delta t$	Y_j
Recovery	$\begin{cases} Y_n \to Y_n-1 \\ Z \to Z+1 \end{cases}$	$Nr\delta t$	Y_n
Vectors			
Infection	$\begin{cases} S \to S-1 \\ L_1 \to L_1+1 \end{cases}$	$\lambda_V \delta t$	S
Completion of extrinsic incubation period (EIP), stage j (j = 1, …, k − 1)	$\begin{cases} L_j \to L_j-1 \\ L_{j+1} \to L_{j+1}+1 \end{cases}$	$Kv\delta t$	L_j
Vector mortality during EIP (j = 1, …, k) (and compensatory recruitment)	$\begin{cases} L_j \to L_j-1 \\ S \to S+1 \end{cases}$	$M\delta t$	L_j
Completion of EIP	$\begin{cases} L_k \to L_k-1 \\ I \to I+1 \end{cases}$	$Kv\delta t$	L_k
Mortality of infectious vectors (and compensatory recruitment)	$\begin{cases} I \to I-1 \\ S \to S+1 \end{cases}$	$M\delta t$	I

2.3.3. Transmission of Rift Valley fever virus between farms

2.3.3.1. Modelling approach

To describe the spread of RVFV between farms, a stochastic, spatially explicit model with a daily time-step was used. The probability that susceptible farm j (i.e. one with no infected hosts or vectors present) acquires infection from infected farm k at time t was given by,

$$p_{jk}(t) = 1 - \exp(-\lambda(x_{jk}, t)),$$

where $\lambda(x, t)$ is the force of infection and x_{jk} is the (Euclidean) distance between farms. This is given by,

$$\lambda(x_{jk}, t) = \gamma\theta(t)\, I_k(t)\, K(x_{jk}),$$

where γ is the transmission parameter, $I_k(t)$ is the number of infectious vectors on farm k (from the within-farm model) and K(x) is the kernel. Two functional forms were considered for the kernel, K(x), namely,

fat-tailed kernel K(x) = (1 + (x d02))-1 exponential kernel K(x) = exp (- x d0)

where d_0 is the length scale. These represent different assumptions about how transmission depends on distance. In particular, a fat-tailed kernel results in a much higher probability of transmission at longer distances than an exponential kernel.

2.3.3.2. Parameters

There are only very limited data available on transmission of RVFV between herds in endemic countries and none that are directly applicable to Europe. Accordingly, we explored a range of scenarios for the transmission parameter (γ) and kernel distance scaling (d_0). First, these parameters for the fat-tailed and exponential kernels were estimated by fitting the force of infection to data on outbreaks reported to the OIE from Tanzania in 2007 using a conditional likelihood approach (Szmaragd et al., 2009). Second, two estimates for the transmission parameter were computed based on the force of infection within a herd, but applied to between-herd transmission, $\gamma = baI_{max}/N$ and $\gamma = bamI_{max}/N$, where I_{max} is the maximum number of infected mosquitoes based on simulations of the within-herd model. Finally, a shorter length scale ($d_0 = 6$ km) was assumed for the exponential kernel, based on reported dispersal distances (EFSA AHAW Panel, 2020a).

In total, nine scenarios were considered representing combinations of three transmission parameters ($\gamma = 1 \times 10^{-5}$, 3×10^{-4} and 1×10^{-3}) and three kernels (fat-tailed, $d_0 = 1.6$ km; exponential, $d_0 = 6$ km; and exponential, $d_0 = 13.7$ km).

2.3.4. Control measures

2.3.4.1. Detection of infected premises

Infected premises (IPs) were assumed to be detected if they reported infection or if an animal died of RVF. Reporting was modelled by assuming that there was a daily probability (0.05) of an infected farm reporting disease. This corresponds to a mean time to reporting of 20 days, selected considering that the incubation period for clinical sings is around 4–7 days, and considering the time for the development of serious signs and to have more animals affected, to get the farmer's attention).

2.3.4.2. Vaccination

At the animal level, vaccination was assumed to reduce the probability of transmission for vector to host (to reflect the protective effect of vaccination) and the probability of transmission from host to vector (to reflect reduced viral titres in infected, vaccinated animals). The probabilities were assumed to decrease linearly over time until full protection was reached, so that,

$$b(t) = \begin{cases} b & t < t_{vacc} \\ b\left(1 - \left[\frac{t - t_{vacc}}{t_{FP}}\right]\varepsilon\right) & t \geq t_{vacc}, t < t_{vacc} + t_{FP} \\ b(1-\varepsilon) & t \leq t_{vacc} + t_{FP} \end{cases}$$

and

$$\beta(t) = \begin{cases} \beta & t < t_{vacc} \\ \beta\left(1 - \left[\frac{t - t_{vacc}}{t_{FP}}\right]\varepsilon\right) & t \geq t_{vacc}, t < t_{vacc} + t_{FP} \\ \beta(1-\varepsilon) & t \leq t_{vacc} + t_{FP} \end{cases}$$

where ε is the vaccine efficacy (assumed to be 90%; as best-case scenario, see Table 4), t_{vacc} is the time of vaccination and t_{FP} is the time to full protection (assumed to be 21 days; see Table 4).

At the herd level, vaccination was assumed to be implemented in zones around known IPs. Once an infected herd was detected, all farms within the zone (and all animals on a farm) were assumed to be vaccinated in a random order over the 14 days after the IP was detected. Two zones were considered: the first was a circular zone with a 50 km radius around an IP (i.e. vaccination in the PZ and SZ); and the second was a ring with inner radius of 20 km and outer radius of 50 km (i.e. vaccination in the SZ only).

2.3.4.3. Stamping out

Stamping out was assumed to be implemented so that either: i) all animals on a reported IPs were culled; or ii) all animals on farms within a circular zone of radius 20 km (i.e. with the PZ) were culled. Where farms other than the IP were culled, farms were culled in a random order over the 14 days after the IP was detected.

2.3.5. Incursion

For all simulations, RVFV was assumed to be introduced on 1 July to the same (large) farm near Amsterdam Airport Schiphol (EFSA AHAW Panel, 2020a).

2.4. Uncertainty analysis

Sources of uncertainty in the scientific assessment performed for Mayotte and the EU were identified at two levels: inputs for the assessment (i.e. parameters used in the models) and methods used in the assessment (here, disease spread models themselves). The limitations on the evidence for the parameters used as inputs for the model were assessed by the WG and taken into consideration in the modelling (see below) and in the interpretation of the results.

For the assessment of the uncertainty associated with the models, for each of the scenarios considered in Mayotte different values/distributions were considered for several parameters (transmission distance, dates of RVF incursion, immunity level of the population and time of implementation of the control measures), thus generating distributions for the expected outcomes (number of infected farms/animals, time to extinction of an outbreak) reflecting the uncertainty on each expected outcome for a given scenario.

Similarly, when modelling the spread of the disease in Europe, a series of scenarios have been considered, taking into account different values of transmission parameter and the type of the transmission kernel aiming at simulating different spread characteristics.

3. Assessment

Two different mathematical models are used to assess the control and prevention measures for RVF in Mayotte (Section 3.3) and in case of incursion into EU (Section 3.4).

Firstly, the performance of diagnostic tests and vaccines is discussed, since this will serve as inputs for the mathematical model (Sections 3.1 and 3.2).

3.1. Diagnostic test for RVF early detection

Different laboratory diagnostic tests can be used for RVF early detection under different scenarios. In case of investigations on clinical suspicions, direct tests, such as real time PCR (RT-PCR) or virus isolation, performed on blood and other tissues taken from animals showing clinical signs suggestive of RVFV infection are the best option. In the framework of a random active surveillance programme based on blood sampling, RT-PCR might not be the best alternative, given the limited time window on which infected animals are viraemic or with detectable RVFV's genome in blood (Pepin et al., 2010; Paweska, 2015) and the cost of a survey based on this molecular technique, especially when a large number of animals must be tested. In this context, the test of choice in a psopulation free from infection (unvaccinated animals) is the one identifying the immune response, which is, in case of RVF, the enzyme-linked immunosorbent assay (ELISA) detecting IgM and IgG towards RVFV (Williams et al., 2011). The laboratory diagnostic tests for RVF have been reviewed in Nielsen et al., 2020. The commercially available ELISA test, e.g. ID Screen® Rift Valley Fever Competition Multi-species set for bovine, ovine, caprine, horses, dogs, cats, human (ID Vet), has diagnostic sensitivity and specificity estimated at 100% (CI95%: 91.24–100%; n = 40) and 100% (CI 95%: 99.58–100%; n = 920), respectively (El Mamy et al., 2011; Comtet et al., 2010). In the assessment, the lower CI for Se will be considered.

3.2. Effectiveness of RVF vaccines

A number of live-attenuated and formalin-inactivated vaccines, based on various RVFV strains (Smithburn and Clone 13 strains), are currently licensed in African countries only and commercially produced for livestock vaccination against RVF. These vaccines are produced by three different laboratories: Onderstepoort Biological Products (OBP) in South Africa, Kenya Veterinary Vaccine

Producing Institute (KEVEVAPI) and Egypt's Veterinary Serum and Vaccine Research Institute. In Table 4, the main characteristics of these vaccines are summarised.

Table 4: Characteristics of RVF vaccines commercially available

	Live-attenuated vaccine Clone 13 strain	**Live-attenuated vaccine Smithburn strain**	**Formalin-inactivated vaccines**
Effectiveness (%)	Field condition: • 67% in cattle • 91% small ruminants (Njenga et al., 2015a)	Highly immunogenic Variable response in cows: • 100% in pregnant aborted (induced by vaccine) • 44% in non-pregnant cows (Botros et al., 2006) Herd immunity tested by ELISA from 95% to 66.7% after 1 year, to 0% after 7 years	Cattle (controlled trial): 80% after first dose, 90% after booster 4 weeks after (Lagerqvist et al., 2012)
Interference with passive/ maternal immunity	Yes	Yes, cross reaction till 6 months (according to the producer[5])	No
Time to protection (days)	21 days (according to producer[6])	21 days (according to producer)	30 days after boost at day 21 (Lagerqvist et al., 2012)
Duration of immunity (months)	At least 18 months following vaccination in sheep and cattle after a single inoculation (Coackley et al., 1967). Annual revaccination is advised according to the producer[6] above	Long lasting, although annual revaccination is advised according to the producer[5]	It requires the administration of booster doses 3–4 weeks after initial vaccination to ensure adequate long-term protection, up to 38 weeks, and annual revaccination (Lagerqvist et al., 2012; Barnard, 1977). Long-term neutralising antibodies may persist for 21 months after a booster dose at any age and any stage of pregnancy (Rusnak et al., 2011)
Use in pregnant animals (safety)	Yes (Dungu et al., 2010) Recently vaccine virus detected to cross the ovine placental barrier and spread to the fetus resulting in malformations and stillbirth (Makoschey et al., 2016)	No: abortion and death of fetus at parturition, but also caused harmful changes in internal organs (Botros et al., 2006; Kamal, 2009)	Yes
Risk of recombination	Possible recombination of Clone 13 and RVFV field strains (Bouloy et al., 2001)	Possible recombination between RVFV field strains and the Smithburn strain has been described in mammals (Grobbelaar et al., 2011) and mosquitoes (Turell et al., 2011) (one reassorted isolate out of over 200 collected from 16 African countries over 60 years)	None
DIVA	No	No	Possible
Cost	Live vaccines are cheaper than inactivated ones		

[5] https://www.obpvaccines.co.za/resources/products/X5Q2767Q298MMNA3/2153_RVFLive_PI.pdf
[6] https://www.obpvaccines.co.za/resources/productInserts/RVF%20CLONE%2013%20VACCINE%20FOR%20CATTLE%20SHEEP%20AND%20GOATS.pdf

	Live-attenuated vaccine Clone 13 strain	Live-attenuated vaccine Smithburn strain	Formalin-inactivated vaccines
Shelf-life	Up to 12 months if stored at +4°C (Daouam et al., 2014)	At –20°C: 2 years; at 2–8°C: 1 month[7] 6 months to 4 years[8] (Bardosh, 2016)	At least 1 year (OIE, 2019)

However, in the African context, several challenges for the utilisation of vaccines in the management of RVF outbreaks have been described (Gachohi et al., 2012).

First, there may be an issue for vaccine availability. The inter-outbreak period of the disease (approximated at 3 ± 7 years) is much longer than the shelf-life of the currently available vaccine (Smithburn vaccine; 4 years), what may hamper the maintenance of vaccine stocks due to the risk of expiration. Therefore, most of these vaccines are often manufactured on order, and this may be a problem for timely intervention. This may be an issue also for EU, in case mass vaccination would be needed.

Second, the heavy rains during the high-risk periods limit access and hence the delivery of vaccines to the rural areas.

Third, small ruminants, which are highly susceptible to the disease and hence would benefit from vaccination, have a high population turn-over rates, limiting the maintenance of herd immunity. Vaccinating dams may also help to provide certain degree of protection through passive immunity to lambs and kids.

Key messages:

- Commercially available live-attenuated vaccines lack safety, especially in pregnant animals, and do not support DIVA.
- The commercially available inactivated vaccine requires multiple doses or annual revaccination to provide protection which renders the use of this vaccine not feasible in endemic zones due to high costs and especially in remote areas where it is difficult to track animals, but suitable for emergency vaccination in not at-risk areas or at least in valuable breeding animals.
- The above-mentioned drawbacks of currently available vaccines indicate the need for vaccine development in the near future to fill the gap in safety and immunogenicity.
- Validated vaccine combined with related DIVA test should be considered in future researches.
- Vaccine availability in short time may be an issue in case of need of a high number of vaccine doses, due to the limited stocks available and to the production on demand of the manufacturers.

3.3. Control measures against RVF in Mayotte

3.3.1. Control measures put in place in Mayotte against RVF in 2018–2019 and considerations about their effectiveness and feasibility

The epidemics of RVF in Mayotte started in November 2018, with a first human case that was admitted at the hospital on 22 November 2018, the date considered as the onset of the symptoms, and RVF confirmed in December, 1 month later. On 10 January 2019, RVF was confirmed in animals and notified to the Animal Disease Notification System (ADNS) of the EU. Until August 2019, 121 outbreaks in ruminants from Mayotte were reported in ADNS, plus four outbreaks in December 2018 retrospectively reported by French veterinary services, i.e. a total of 125 outbreaks (EFSA AHAW Panel, 2020b).

3.3.1.1. Stamping out

No animal stamping out was applied in Mayotte during the RVF epidemic because it was considered not possible since, very quickly after the confirmation of the first RVF cases in animals, it was evident that the infection was present across the whole island. Furthermore, according to livestock experts having worked in Mayotte (Dommergues, personal communication), it was assumed that stamping out would have increased the risk of underreporting of suspected cases and possible illegal introduction of

[7] https://kevevapi.or.ke/product/riftvax-tm/
[8] https://www.oie.int/doc/ged/D12326.PDF

ruminants. In addition, since there are no rendering plants in Mayotte, the elimination of culled livestock would have been difficult.

3.3.1.2. Establishment of a protection and a surveillance zone around RVF outbreaks

No surveillance and protection zone were established in Mayotte around RVF outbreaks in animals.

The first RVF confirmation by RT-PCR in animals occurred in January 2019 in the commune of Tsingoni in the centre of Mayotte (Figure 4). A protection zone of at least 20 km radius (as foreseen in Regulation (EU) 2016/429 and annexes[9]) around Tsingoni would have covered most of the island surface and a surveillance zone of 50 km radius would have included the whole island.

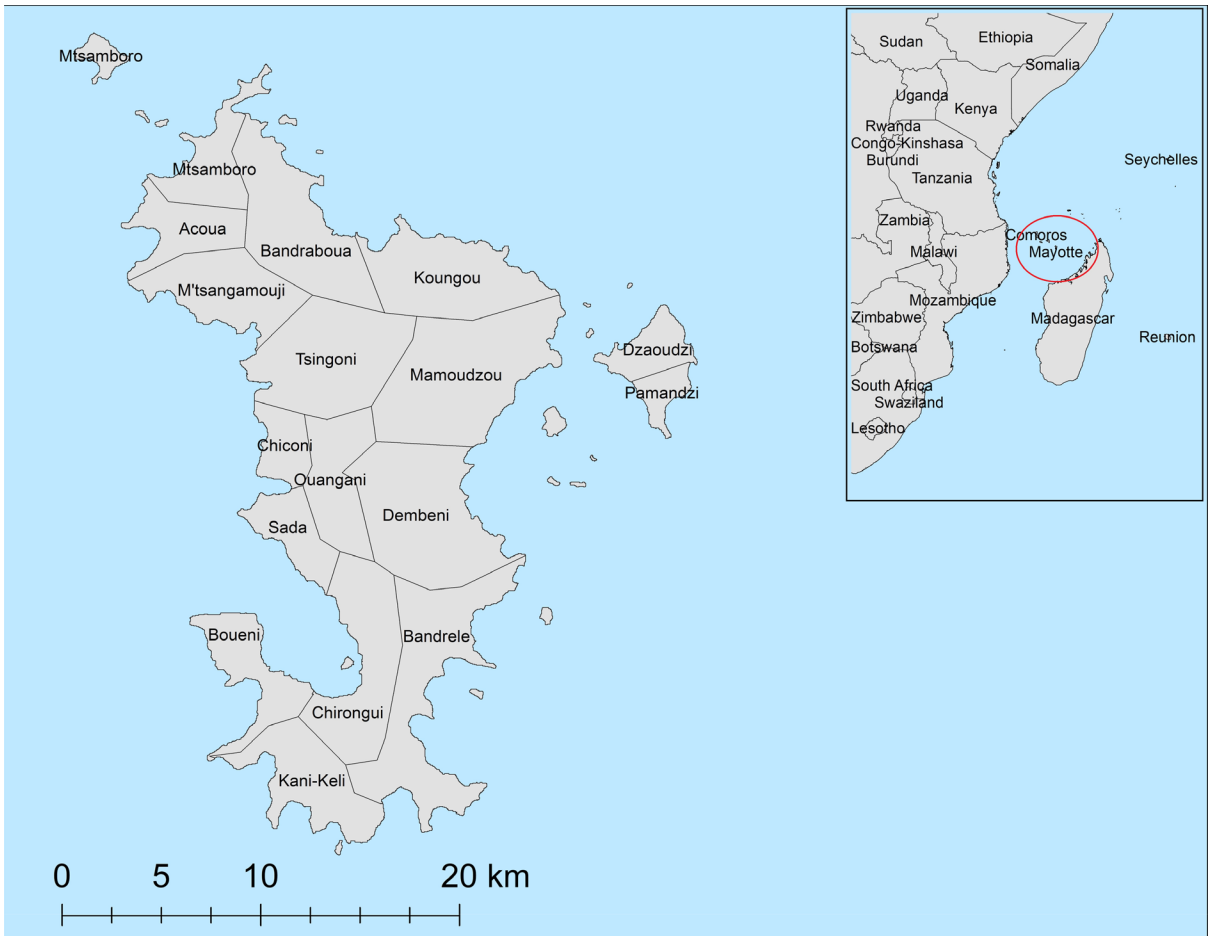


Figure 2: Map of Mayotte with location of communes (in the square top right the location of Mayotte in the Indian Ocean, in the red circle)

At the time of the first RVF confirmation in an animal in 2019, five human cases had already been detected and they lived in various places from Mamoudzou (on the East coast of the island) to Chiconi (on the West coast). In addition, serological evidence of RVFV circulation in livestock at least since August 2018 indicated that the virus might have been circulating undetected in livestock for a few months. Therefore, it was probable that RVF had already spread in Mayotte and that a surveillance zone would not prevent the disease from reaching apparently uninfected communes.

Furthermore, controls at the border of a surveillance zone would have been very difficult to achieve. In case on control on roads, people would have been able to move animals on foot through forests or cultivated areas.

[9] https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=PI_COM:Ares(2019)3908627

3.3.1.3. Biosecurity measures including sanitary protection measures related to human–animal contact

In Mayotte, most animals are raised outdoors and biosecurity measures aiming at isolating animals from the environment were considered impossible to achieve quickly. To protect animals suspected of RVFV infection from vectors, veterinarians were asked to treat them with deltamethrin (pour-on).

Due to the difficulties in confining the spread in animals, the priority was set on preventive measures related to animal to human transmission and to vector control. Awareness messages were broadcasted on TV, radio and the newspapers (Figure 3).

Farmers were advised to use individual protective equipment (masks, gloves and goggles) and to report abortions to the veterinarian. Selling raw milk was forbidden by the local authority (Préfet). The farmer coop (CoopADEM) implemented trainings to teach farmers to pasteurise milk.

The general population was advised to:

- Boil the milk
- Cook the meat
- Keep out mosquitoes
- Eliminate mosquito larval breeding habitat

Figure 3: Example of awareness material distributed in Mayotte for RVF prevention (Source: Prefecture of Mayotte, France[10])

[10] http://www.mayotte.gouv.fr/

3.3.1.4. Vector control and prevention measures

The surveillance protocol written at the beginning of the epidemic stated that when an animal case was confirmed in a village, disinsectisation around the outbreak farm should be implemented by the vector control service of the public health authorities. When an animal case was confirmed outside a village, that is in cultivated areas or in forests, the environment should not be treated against vectors, but breeding sites should be destroyed if possible.

At some point, the vector control service stopped visiting farms with confirmed cases in animals, because they became too numerous and they focused their work on human households.

For each suspicion in animals, the veterinarian had to protect the animal with insecticide treatment and to leave insecticide (deltamethrin) to the farmer to be used on the other animals. Limited information provided in a report about activity against vectors in Mayotte at the time of RVF epidemic has been issued by the Health Agency of Indian Ocean.[11]

3.3.1.5. Vaccination of livestock

No vaccination was implemented in the Mayotte epidemic, because no vaccine was authorised in the EU. In the surrounding countries such as Kenya, Comoros and Madagascar, no mass vaccination campaigns were in place.

3.3.1.6. Reasons for limited measures taken

The main reason why limited measures were taken to control RVF in animals in Mayotte was due to the fact that the disease was already widespread at the time of confirmation, linked to the delay between onset of symptoms and RVF laboratory confirmation/reporting. This delay was due to:

- The time between the onset of symptoms and the call of the owner to the veterinarian can take a few days. For example, in case of an abortion the expulsion of the foetus might occur a few days after the onset of symptoms in the cow
- The time between the call of the owner and the effective visit of the veterinarian: resources are limited and there were only two vet practices in Mayotte and both vet practices cover the whole island so the visit can be delayed by one day
- The time between the notification of the suspicion by the veterinarian and results of the laboratory: samples were sent only once a week to Reunion Island, and therefore, confirmation analysis can be delayed by 1 week

As a result, RVF was usually confirmed about 10–15 days after the onset of symptoms.

The other reason for limited measures applied is farm size and accessibility: even if Mayotte is a small island, most farms are located in forest areas accessible only by a four-wheel drive vehicle or on foot. Therefore, any intervention on a single farm requires almost half a day. Since the average herd size is five animals, most farms had only one infected animal. Very soon after the beginning of the epidemic, the number of people available at the veterinary services or in veterinary practices was not enough to implement control measures in all infected farms.

Key messages:

- During the RVF outbreak in Mayotte, priority was put on protection measures related to animal to human transmission, because animal cases became too many and uncontrollable.
- No stamping out, no protection zones and no vaccination were implemented.
- The only measures applied were very limited biosecurity and some vector control measures.
- The main reasons for limited measures applied were the delayed disease reporting, lack of personnel to visit many small and isolated farms, cost of stamping out and vaccination and inability to prevent animal movement (no protected zones (PZs)) as many animals were neither housed nor corralled.

[11] https://www.mayotte.ars.sante.fr/system/files/2019-11/Rapport%20annuel%20d%27activit%C3%A9%202018%20de%20l%E2%80%99ARS%20Oc%C3%A9an%20Indien.pdf

3.3.2. Scenarios of possible surveillance and control measures to be applied in Mayotte and their effectiveness

3.3.2.1. Size of restriction zones

The radius of the surveillance zone as defined by the model applied herein depends on the basic reproduction number, the threshold probability of escape (i.e. the risk of finding cases outside of the surveillance zone) and the mean dispersal distance of mosquitoes (Figure 4). Active flight of mosquitoes can be over distances from 50 m to 50 km, with average flight range of up to 6 km (EFSA AHAW Panel, 2020a). For R_0 = 2 and a mean dispersal distance of mosquitoes of 6 km, the radius of the circular surveillance zone would be 34 km, 45 km and 60 km for probabilities of escape of 0.05, 0.01 and 0.001, respectively, corresponding to 95%, 99% and 99.9%, respectively, of cases from a source farm contained within the surveillance zone (Figure 4). In the context of Mayotte (area = 376 km^2, i.e. a radius of about 11 km), the whole of the island would be covered by a single zone for all these sizes and, hence, the use of restriction zones was not considered further.

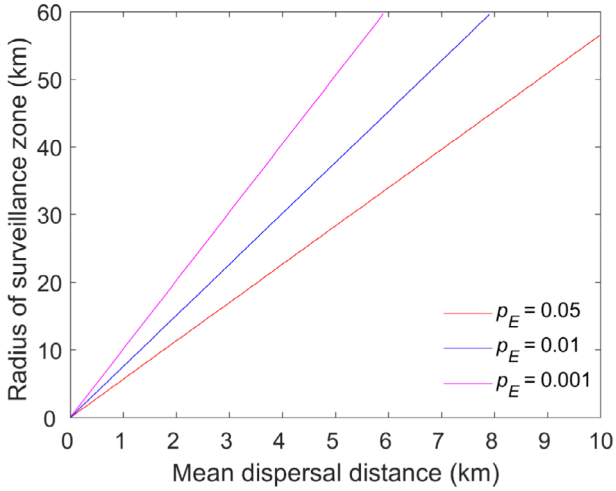


Figure 4: Radius of surveillance zone required for different mosquito dispersal distances for R_0 = 2. The probability of RVFV escaping the zone through mosquito dispersal alone (in restriction zones, animal movements are forbidden) is 0.05 (red), 0.01 (blue) or 0.001 (magenta)

Key messages:

- Due to the small geographical size of Mayotte and the potential dispersal of mosquitoes over long distances (e.g. > 6 km), the whole island can be considered a single protection zone; thus, the use of restriction zones was not considered further.

3.3.2.2. Surveillance scenarios for RVF in Mayotte

Assuming a completely naive population at the time of incursion, the seroprevalence at around 40–50 days from disease incursion is about 0.1%, whereas at around 110–170 days is 3% (Table 5). The time to detection depends on the time of the incursion, with incursions in January or April that can be detected earlier than those in July or October (Table 5). This reflects the seasonal pattern of rainfall in Mayotte (rainy season is from December to March) and, hence, vector abundance and potential for spread. Although all possible timing during the year for RVFV incursions are considered, those happening at the early stages of the rainy season (from September to December) have in general the maximum probability of resulting in larger epidemics, as observed in 2108–2019 and described in a previous EFSA opinion (EFSA AHAW Panel, 2020b).

To ensure early detection of an incursion in a completely naïve population e.g. by 30 days after incursion, the surveillance system requires a design prevalence of around 0.04–0.05%, regardless of the time of incursion (Table 5). For longer times to detection (60, 90, 120 days), the required design prevalence is higher and depends on the time of incursion (Table 6).

Table 5: Number of days to detection (median and 95% prediction interval) for a specified design prevalence for RVFV in Mayotte assuming a completely naïve population

	Design prevalence		
	0.1%	**1%**	**3%**
Time of incursion			
1 January	42 (28, 109)	87 (65, 170)	111 (85, 204)
1 April	41 (30, 95)	106 (74, 196)	145 (102, 227)
1 July	53 (32, 112)	132 (96, 222)	172 (128, 249)
1 October	52 (30, 98)	118 (84, 184)	142 (111, 210)

Table 6: Design prevalence (%) (median and 95% prediction interval) required for a specified number of days to detection for RVFV in Mayotte in a completely naïve population

	Days to detection			
Time of incursion	**30**	**60**	**90**	**120**
1 January	0.05 (0.02, 0.12)	0.26 (0.02, 0.78)	1.11 (0.02, 3.85)	4.35 (0.02, 13.61)
1 April	0.05 (0.02, 0.10)	0.22 (0.02, 0.56)	0.62 (0.02, 1.99)	1.46 (0.02, 5.06)
1 July	0.04 (0.01, 0.08)	0.11 (0.02, 0.33)	0.26 (0.02, 0.83)	0.55 (0.02, 2.02)
1 October	0.04 (0.02, 0.10)	0.12 (0.02, 0.39)	0.31 (0.02, 1.20)	0.95 (0.02, 4.43)

If a certain level of pre-existing immunity is present in the population (equal to that following the epidemic in 2018–2019; Table 1), the time to detection is longer than in a completely naïve population, being 78–100 days to detect a prevalence of 0.1% (Table 7). Furthermore, the prevalence of newly infected animals seldom exceeds 0.2% before the virus dies out, meaning a design prevalence of 1% or 3% will not allow an incursion to be detected. To ensure early detection of an incursion in a partially immune population within 30 days after incursion, the surveillance system requires a design prevalence of around 0.02%, thus lower than in a completely naïve population, and the required design prevalence does not increase greatly for longer times to detection (Table 8). This reflects the slow rate of spread in the population due to the presence of immune individuals.

Table 7: Number of days to detection (median and 95% prediction interval) for a specified design prevalence for RVF in Mayotte assuming a partially immune population (from pre-existing immunity)

	Design prevalence
	0.1%
Time of incursion	
1 January	78 (50, 160)
1 April	80 (39, 156)
1 July	100 (54, 172)
1 October	88 (53, 122)

Table 8: Design prevalence (%) (median and 95% prediction interval) required for a specified number of days to detection for RVFV in Mayotte assuming a partially immune population (from pre-existing immunity)

	Days to detection			
Time of incursion	**30**	**60**	**90**	**120**
1 January	0.02 (0.003, 0.04)	0.03 (0.003, 0.11)	0.04 (0.003, 0.32)	0.04 (0.003, 0.32)
1 April	0.01 (0, 0.05)	0.02 (0.003, 0.10)	0.03 (0.003, 0.17)	0.03 (0.003, 0.20)
1 July	0.01 (0.003, 0.04)	0.02 (0.003, 0.09)	0.02 (0.003, 0.12)	0.02 (0.003, 0.12)
1 October	0.01 (0.003, 0.04)	0.02 (0.003, 0.08)	0.02 (0.003, 0.15)	0.02 (0.003, 0.21)

RVF surveillance was described in a previous EFSA opinion (EFSA AHAW Panel, 2020b). In livestock, surveillance was mainly based on repeated cross-sectional sero-surveys and on monitoring the number of abortions reported via the national brucellosis surveillance system. RVF seroprevalence was computed yearly, aggregating data from July on year N to June on year N + 1 in order not to split the rainy season in two parts. Results were displayed in the previous opinion.

In Table 9, the characteristics and performance of different active surveillance strategies in animals that may be applied for RVF detection and possible prediction of RVF recurrence in Mayotte in the future are reported, considering the diagnostic methods currently available and a naïve population. An active surveillance programme based on random sampling is not feasible in the scenario of a high proportion of population naturally immune as foreseen after the 2018-–2019 epidemic due to the extremely low required design prevalence (Table 9).

Passive surveillance, based on the systematic testing of aborted fetuses and notifications of clinical cases, remains a pillar for the detection of virus circulation.

Two main objectives for the active surveillance have been considered:

- Early detection of virus circulation, ideally before having a significant number of human and animal cases (i.e. steep increase in the number of cases, from the mathematical point of view the point when the derivative of the epidemic curve assumes its maximum value can be considered), in order to apply control measures. In this case, the best period of testing is represented by September–December, at the beginning of the rainy season. Different values of expected prevalence of infection can be considered in this period of the year, according to the time of viral incursion to the island. In case of incursion on 1 July, the expected prevalence can vary from 0.11% in September to 0.55% in November (Table 9). In case of incursion on 1 October, the expected prevalence can vary from 0.04% in November to 0.12% in December (Table 6).
- To monitor the level of virus circulation after the rainy season, when the expected prevalence of infection, in case of virus circulation, is maximum. Therefore, for this objective, the best period of testing is in May–June, after the rainy season. Under this scenario, the main assumption is that the virus circulation occurred mainly during the rainy season, and therefore, it is assumed that the viral incursion in the island occurred in January at latest. This would correspond to a value of expected prevalence of 4.35% or more (Table 6).

For both objectives of the surveillance, the target population is represented by non-immune animals born after the end of previous epidemics, to be tested after 3–4 months of age, when the probability of interference with maternal antibodies is lower.

Concerning the diagnostic tests, IgG ELISA is the best option to have the maximum probability of detecting the infected animals. Positive samples should be tested also for the presence of IgM and viral genome (RT-PCR) to provide more information about the timing of infection.

Since the exact time of incursion of RVFV into the island cannot be predicted, but considering that the period from September to December (at the beginning of rainy season) is the most risky for the establishment of a new epidemic, we could also calculate from the model a mean value of design prevalence for that period of time which would be equal to around 0.24%. This would imply a sample size of 1,371 animals to be tested once or, as alternative, the repeated monthly testing of 343 randomly selected animals (preferably from different farms), in order to assure the same sensitivity of the surveillance system (Cameron et al., 2020).

The characteristics of the surveillance scenarios are presented in Table 9.

Table 9: Surveillance scenarios for early detection of RVF in Mayotte considering a naïve population

Objective of surveillance	**Early detection of virus circulation (ideally before having a significant number of human and animal cases)**	**To verify whether the virus circulated during the previous rainy season**
Diagnostic tests	ELISA IgG (sensitivity = 91%) Positive samples should be tested also for the presence of IgM and viral genome (RT-PCR)	
Target population	Not vaccinated animals and born after the end of previous epidemics. To be tested after 3–4 months of age, when the probability of interference with maternal antibodies is lower	
Period of testing	September–December (at the beginning of rainy season)	May–June (after the rainy season)

Objective of surveillance	Early detection of virus circulation (ideally before having a significant number of human and animal cases)		To verify whether the virus circulated during the previous rainy season
Design prevalence ranges according to the time of incursion	Time of incursion		
	1 July 0.11%–0.55%	1 October 0.04%–0.12%	1 January 4.35%
	Mean value for the period September–December: 0.24%		
Sample size (95% C.L.)	2,992–598	3,500–2,742	75
Sampling frequency	With 0.24% design prevalence: 1,371 animals to be tested once or, repeated monthly testing (September–December) of 343 randomly selected animals (Cameron et al., 2020)		

Key messages:

- Considering that the rainy season in Mayotte is from December to March and this is the period at higher risk for the establishment of an RVF epidemic, according to surveillance objectives, two possible scenarios for active surveillance can be considered:
  - Early detection of RVFV circulation, ideally before the occurrence of a significant number of human or animal cases. This implies that a substantial number of animals need to be tested to detect as early as possible RVFV incursions. Feasibility issues may rise.
  - Verification of RVFV circulation during previous rainy season, which can be achieved testing a limited number of animals, due to the higher required design prevalence.
- Monitoring the seroprevalence will give an indication about the occurrence of RVF and the spatial and temporal distribution of infection and indicate possible areas with higher risk for the re-occurrence of the disease.
- Passive surveillance, based on the notification and testing of aborted fetuses and animals showing clinical signs suggestive of RVF, is the pillar of any early warning system and at present the only feasible surveillance option, given the high percentage of animals naturally immunised after the 2018–2019 epidemic.

3.3.2.3. Vaccination against RVFV in Mayotte

Vaccination can reduce the size and duration of an epidemic provided it is implemented early enough and deployed quickly enough (Figure 5. Simulated dynamics of Rift Valley fever virus showing the impact of vaccination assuming a vaccine efficacy of 60% (Figures 6 and 7).

In order to depict realistic vaccination rate scenarios (number of animals that can be realistically vaccinated per day in Mayotte), given the experience gathered in Mayotte, it can be considered that one team composed of one vet and one technician moving across the island by 4WD car can vaccinate between five and 80 animals a day, with an average of about 20. Although the island is very small, many factors hamper to reach higher vaccination rates:

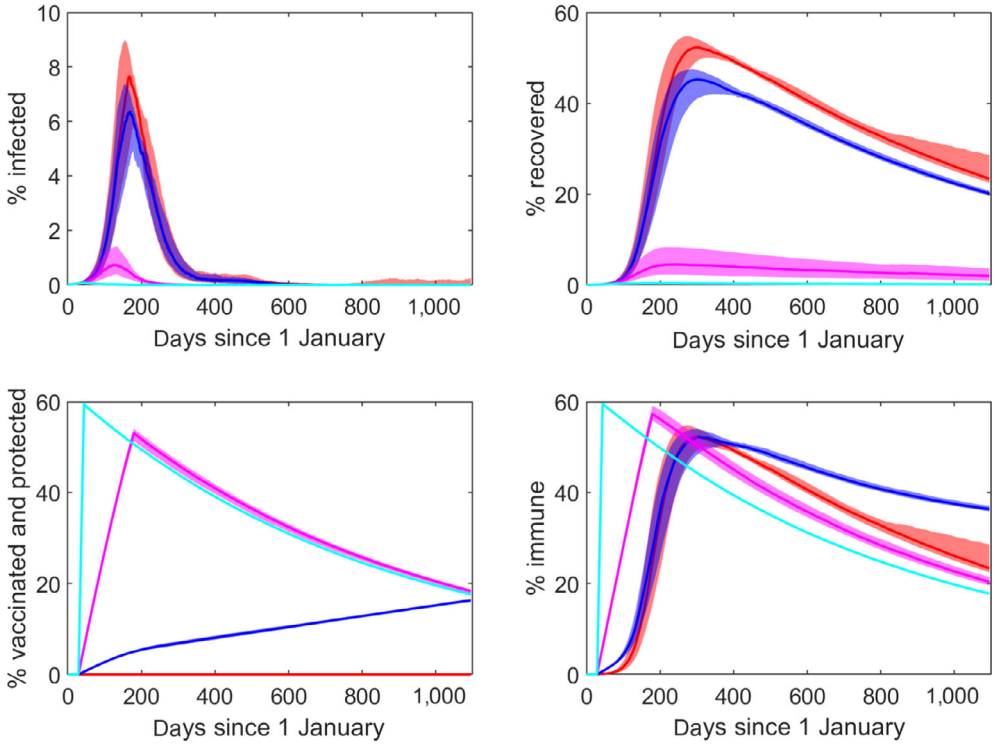
- farm accessibility and farm size: often the vaccination team must drive 45 min and walk 20 min only to vaccinate two cows.
- Difficulty to localize and reach cattle breeders in order to localise animals in the forest.

It must be considered that during the FMD vaccination campaign in 2019–2020, four or five teams contributed to vaccination.

Therefore, vaccination rates of 20, 200 and 2,000 animals vaccinated per day were considered as possible scenarios by cross checking with veterinary personnel having worked there and by considering the local reality in Mayotte such as the dispersal of small farms and the logistics available to the veterinary services.

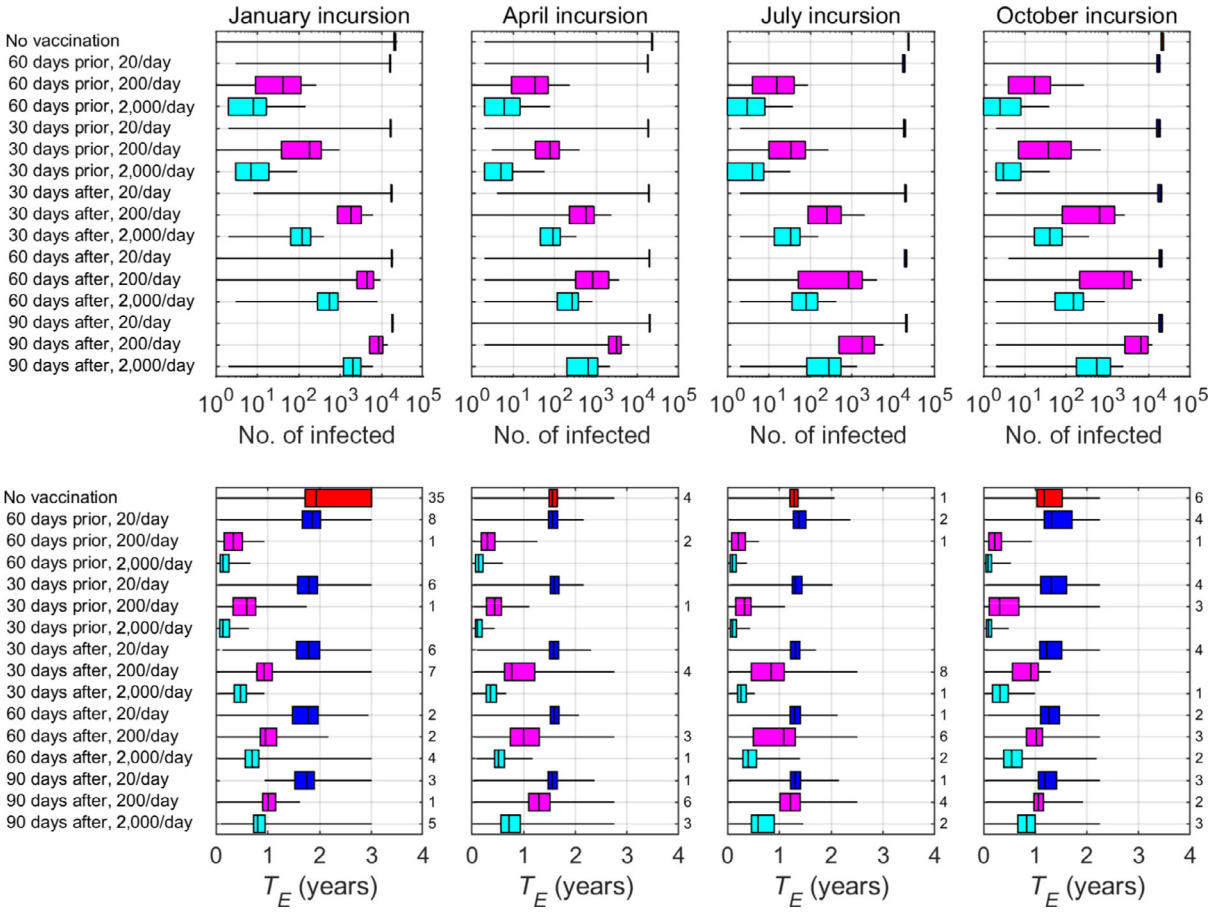
As it could be expected, when only 20 animals are vaccinated each day the impact on the number of infected animals is minimal, though an effect can be expected on the number of epidemics lasting beyond the end of the second year after the introduction of RVFV. If 200 or 2,000 animals are vaccinated each day, both the number of infected animals and time to extinction are reduced, with

bigger reductions seen with earlier deployment. The magnitude of any reduction for any scenario was greater for a vaccine efficacy of 90% (Figure 7) compared with 60% (Figure 6).



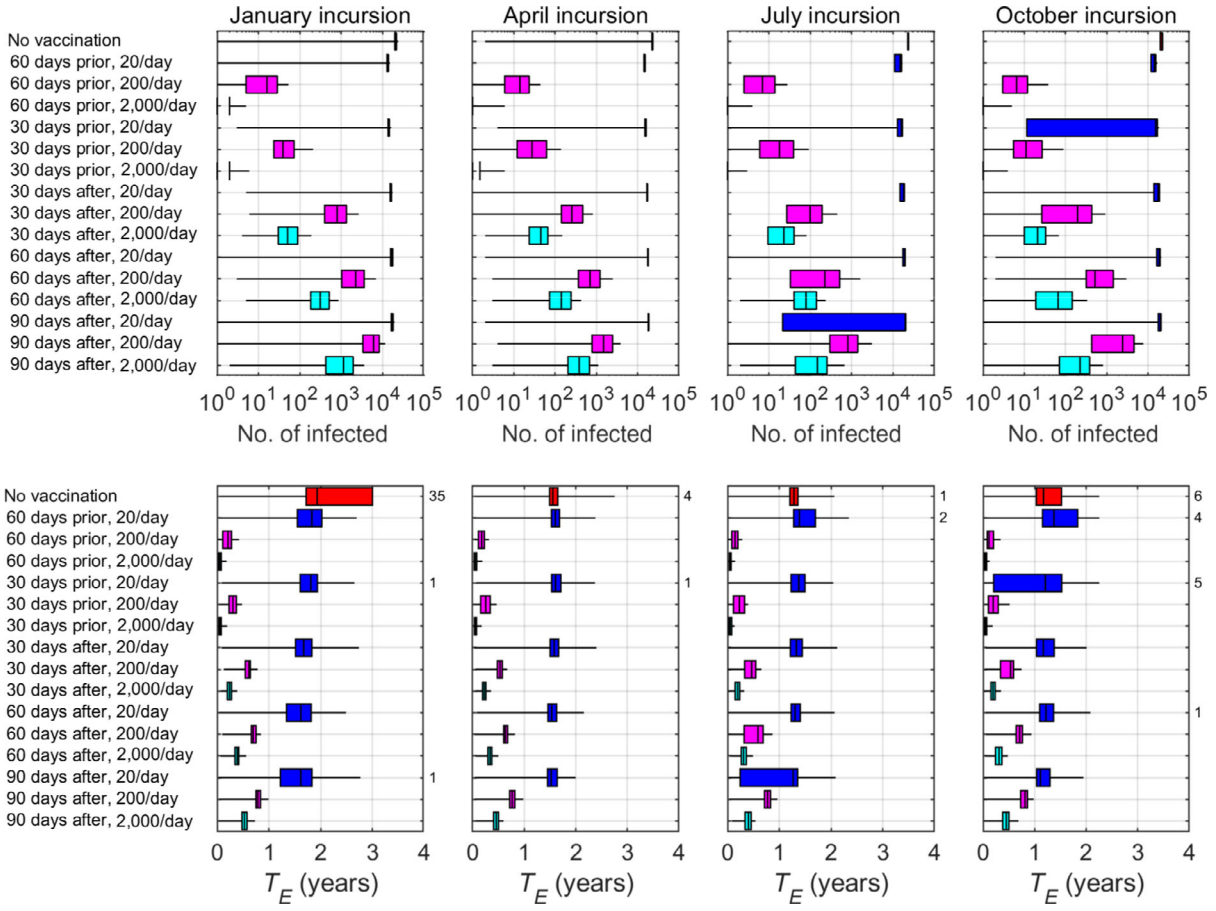
Plots show the median (line) and interquartile range (shaded area) for the percentages of infected animals, recovered animals, vaccinated (and protected) animals and immune animals (i.e. recovered and vaccinated, protected) assuming no vaccination (red) and 20 (blue), 200 (magenta) or 2,000 (cyan) animals are vaccinated each day. Results are based on 100 replicates of the model for an incursion on 1 January.

Figure 5: Simulated dynamics of Rift Valley fever virus showing the impact of vaccination assuming a vaccine efficacy of 60%



The top row shows the cumulative number of infected animals and the bottom row shows the time to extinction (the numbers indicate the number of replicates for which RVFV had not been eliminated by the end of the third year of the simulation). Incursions were simulated in January, April, July and October and assumed a completely naive population (except for any pre-emptive vaccination). Vaccination was implemented 60 or 30 days prior to or 30, 60 or 90 days after the incursion at a rate of 20, 200 or 2,000 animals per day. Box-and-whisker plots show the median (black line), interquartile range (box) and 2.5th and 97.5th percentiles (whiskers) for 100 replicates of the model.

Figure 6: Impact of vaccination on incursions of Rift Valley fever to Mayotte assuming a vaccine efficacy of 60%



The top row shows the cumulative number of infected animals and the bottom row shows the time to extinction (the numbers indicate the number of replicates for which RVFV had not been eliminated by the end of the third year of the simulation). Incursions were simulated in January, April, July and October and assumed a completely naive population (except for any pre-emptive vaccination). Vaccination was implemented 60 or 30 days prior to or 30, 60 or 90 days after the incursion at a rate of 20, 200 or 2,000 animals per day. Box-and-whisker plots show the median (black line), interquartile range (box) and 2.5th and 97.5th percentiles (whiskers) for 100 replicates of the model.

Figure 7: Impact of vaccination on incursions of Rift Valley fever to Mayotte assuming a vaccine efficacy of 90%

In Table 10, the level of vaccination coverage and % infections reached 3 years after RVF incursion with different vaccination rates and different start in relation to disease incursion are reported.

Table 10: Vaccination coverage and % infected reached 3 years after an RVF incursion in January with different vaccination rates and different start in relation to disease incursion

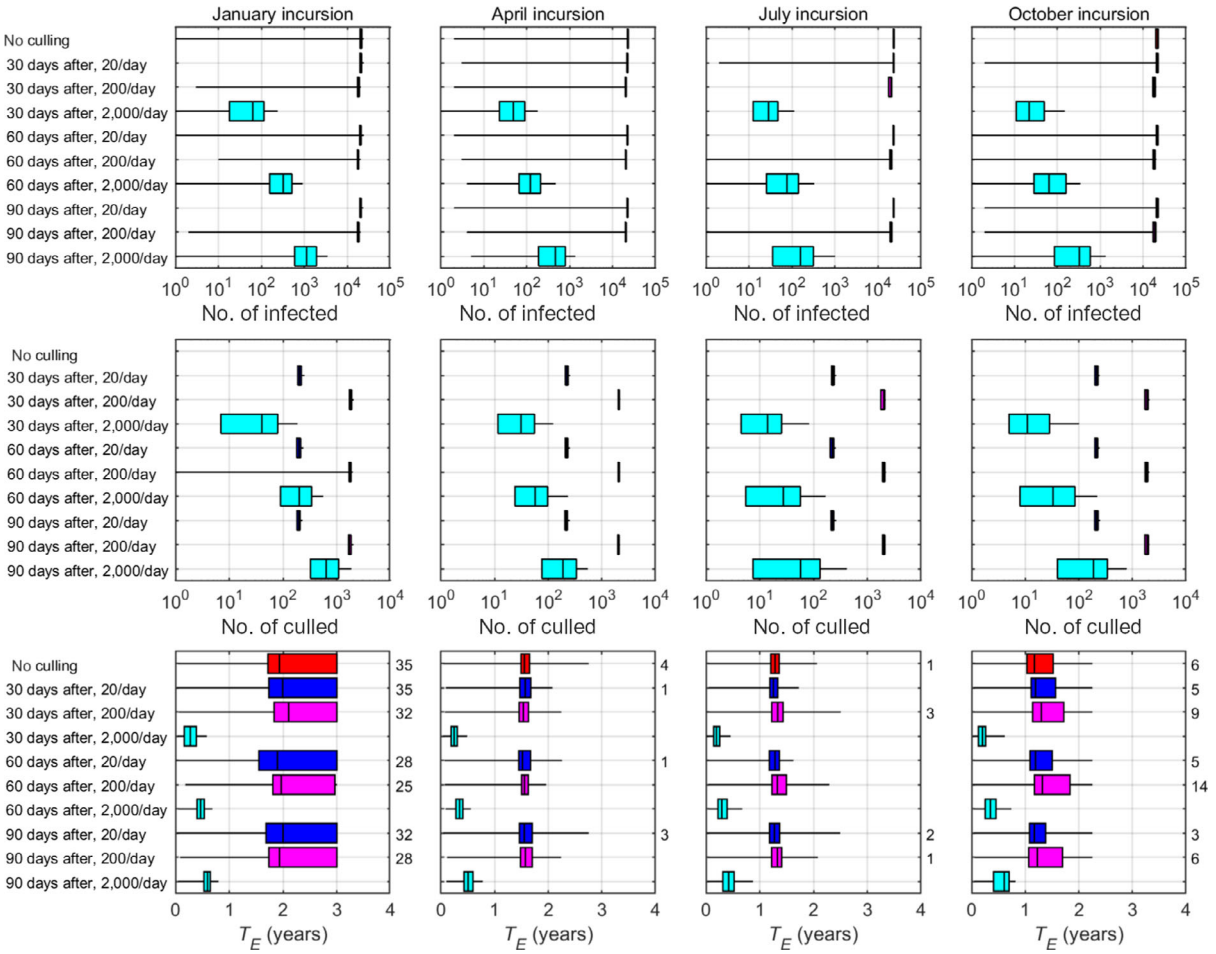
Vaccination rate	Vaccination coverage at time of incursion if started 60 days prior	Median % infection prevalence cases at the end of 3 years		Median duration of the epidemics (years)		Vaccination coverage at time of incursion if started 30 days prior	Median % infection prevalence at the end of 3 years		Median duration of the epidemics (years)	
		60% VE	90% VE	60% VE	90% VE		60% VE	90% VE	60% VE	90% VE
20 animals/day	4%	52.9	44.7	1.86	1.83	2%	54.3	46.7	1.79	1.81
200 animals/day	40%	0.14	0.05	0.34	0.21	20%	0.6	0.13	0.59	0.31
2000 animals/day	100%	0.03	0.003	0.14,	0.05	100%	0.02	0.003	0.14	0.05

Key messages:

- The results of the analysis of the impact of vaccination on reduction of RVF infections suggest that the vaccination is more effective when applied early before the start of the epidemic and quickly implemented throughout the population. Different levels of vaccine effectiveness, either 60% or 90% have a relatively minor effect on the reduction, albeit higher for 90% effectiveness.
- In particular, with a vaccination rate of 200 and 2,000 animals vaccinated per day, the epidemic is halted within 1 year, regardless whether the vaccination is applied before or after the RVF incursion. Moreover, the number of infections is kept under 3% if the vaccination is conducted at least 30 days prior to incursion with at least 200 animals vaccinated per day (20% coverage achieved at time of incursion, 100% coverage achieved 120 days post incursion). The same effect is achieved if the vaccination is conducted at 2,000 animals vaccinated per day, started at 60 days post incursion at the latest, 100% vaccination coverage would be achieved 75 days after RVF incursion.
- On the contrary, with 20 animals vaccinated per day, the epidemic continues for more than 2 years and the whole population would get infected.

3.3.2.4. Culling strategies to control RVFV in Mayotte

When carried out as part of a test and cull strategy, culling is unlikely to be effective at controlling RVF in terms of both number of animals infected and epidemic duration unless large numbers of animals (2,000 per day) can be tested to identify infected animals for culling (Figure 8. Impact of testing and culling on incursions of Rift Valley fever to Mayotte.). Lower levels of testing (20 or 200 per day) had no impact on the number of infected animals or epidemic duration compared with no control (Figure 8).



The top row shows the cumulative number of infected animals (including those which were not detected and those which were detected and culled), the middle row shows the cumulative number of infected animals detected and culled, and the bottom row shows the time to extinction (the numbers indicate the number of replicates for which RVFV had not been eliminated by the end of the third year of the simulation). Incursions were simulated in January, April, July and October and assumed a completely naive population. Culling was implemented as part of a test and cull strategy starting 30, 60 or 90 days after the incursion, with 20, 200 or 2,000 animals tested per day. Box-and-whisker plots show the median (black line), interquartile range (box) and 2.5th and 97.5th percentiles (whiskers) for 100 replicates of the model.

Figure 8: Impact of testing and culling on incursions of Rift Valley fever to Mayotte

Key messages:

- Test and cull strategy does not seem a valid alternative for the control of RVF in Mayotte conditions unless high numbers (ca. 2,000 per day) of animals are tested every day and the infected culled.

3.3.2.5. Impact of vector control on RVFV in Mayotte

In theory, vector control in RVFV endemic areas may contribute to decrease transmission of the disease by controlling adult mosquitoes, breeding sites, engage general public and predict and monitor of RVFV high-risk areas (Anyamba et al., 2010; Chevalier et al., 2010). However, in reality, there have been few attempts at controlling vectors of RVFV in endemic areas in Africa. In the 90s, Linthicum et al. (1989) showed promising results in a semi-field controlled trial where a single treatment of IGR Methoprene (5.6 kg/ha) was able to control *Aedes* and *Culex* spp. for 2 weeks in a dambo[12] area in Kenya after 3 and 1 day after flooding. Subsequently, Logan et al. (1990) tried to control floodwater mosquito vector species in Kenya by treating with Methoprene (4%) the dambos habitat 5, 3 and 1

[12] class of complex shallow wetlands in central, southern and eastern Africa.

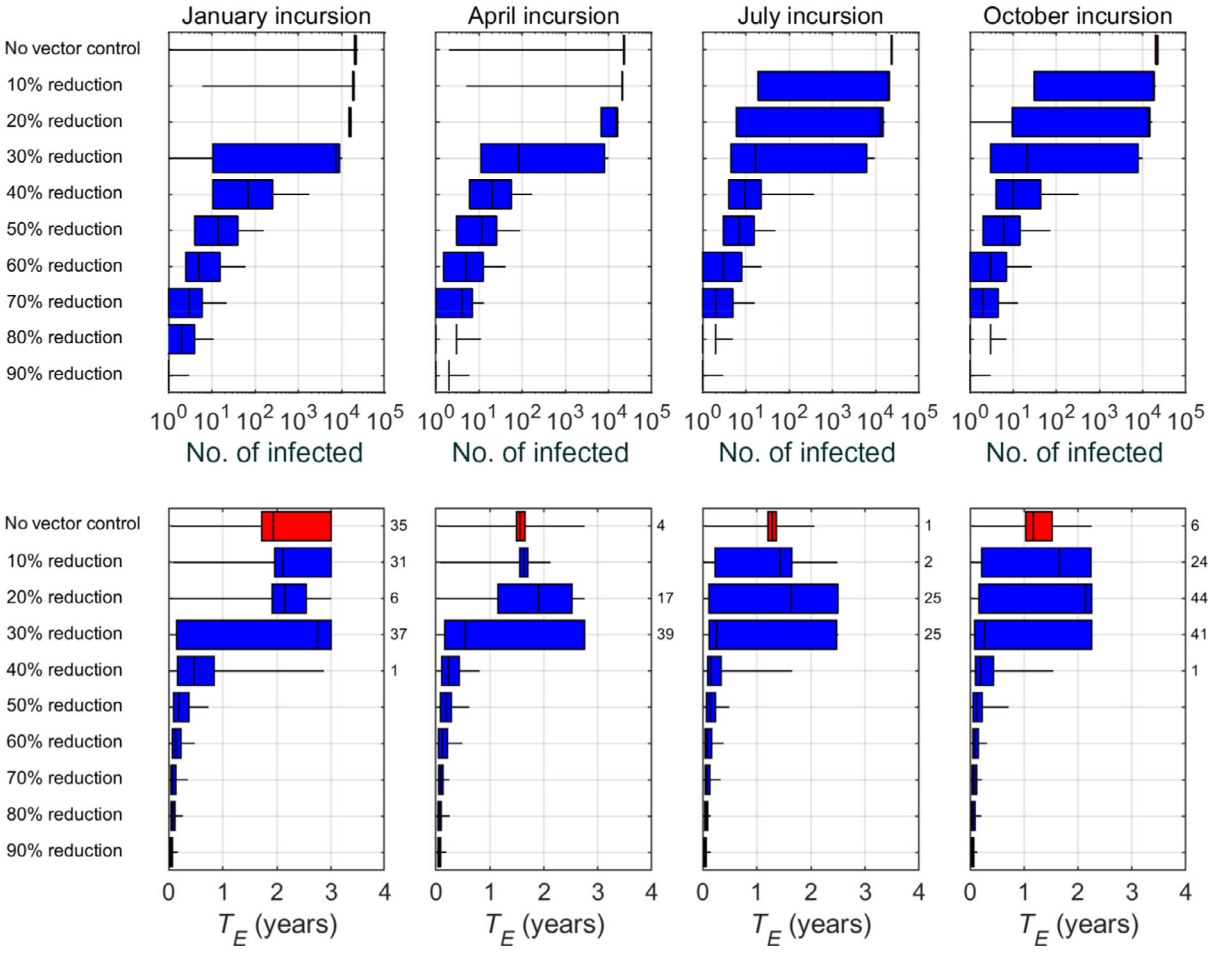
week before flooding and 1 day after. Treatment performed 5 weeks before flooding showed to reduce *Aedes* spp. adults by 98% and 100% if treatment was conducted 1 day after flooding. Treatments conducted 3 and 1 week before flooding reduced *Aedes* spp. adults by 88% and 84%, respectively. None of the treatments was effective against *Culex* spp. In a similar approach, Logan and Linthicum (1992) used *Bacillus thuringiensis* var. *israelensis* (Bti) in briquet formulation in different doses during 30 days and 13 days after flooding in a dambo area in Kenya. The doses of 1 briquet/9 m^2 showed to significantly increased *Aedes* spp. larval mortality by 36% compared to the control (8%). The treatment even at higher doses failed to control *Culex* spp. larvae when compared to the control site. In a different strategy conducted in Senegal (Diallo et al. 2008), a bull-calf treated with 25 mg/m^2 of deltamethrin showed to reduce the average number of mosquitoes attracted during the first 2 weeks post-treatment for the main RVFV vector species in the area (*Ae. vexans, Ae. ochraceus, Cx. poicilipes, Cx. neavei* and *Ma. uniformis*). In addition, the number of blood engorged females was reduced by 64.1%, while mortality rate of collected mosquitoes decreased by 43.8%.

Despite the potential effect of larvicides, adulticides and repellents on mosquito populations, up to now, there is no evidence on their effect on the transmission of RVFV in endemic countries. Therefore, it is difficult to determine the level of vector control that should be achieved for an effective decrease of disease transmission. In addition, the fact RVFV is transmitted by a multi-species mosquito fauna (*Aedes* spp. and *Culex* spp.) with different ecological and behavioural traits, makes difficult to effectively control their populations.

In the case of Mayotte, there is a lack of information about the vector control procedures during the recent RVFV outbreaks. However, mosquito control has been a regular activity in the island since the 50s because of the presence of human diseases such as malaria and Bancroftian filariasis, as well as the outbreaks of dengue and chikungunya in different decades (Pocquet et al., 2014). Therefore, main control efforts are conducted on *Cx. pipiens/quinquefasciatus*, *Anopheles gambiae*, *Ae. albopictus* and *Ae. aegypti*, all potential vectors of RVFV except *An. gambiae*. However, current mosquito control in the island is constrained by the European legislation, that reduced the number of formulates available for mosquito control and more importantly, by the protection of ecosystems. Insecticides used in the island were the larvicides temephos (an organophosphate) from 1973 to 2012 and currently the larvicide Bti as well as the adulticide deltamethrin (pyrethroid) since 1984 in indoor residual spraying and/or on long-lasting insecticide-treated nets. Since all these treatments are intended for the control of human VBD and therefore applied around human settlements, there are no evidences of their impact on other potential vector species of RVFV in Mayotte.

Provided they are able to reduce mosquito abundance (and, hence, the seasonal reproduction number) by 40% or more, vector control measures have the potential to reduce both the number of animals infected and epidemic duration (Figure 9). If the reduction in abundance is lower (10–30%), however, vector control can potentially increase the duration of an epidemic, even though it reduces the total number of animals infected during its course (Figure 9). In this case, vector control reduces the seasonal reproduction number, but not to below one, effectively flattening the epidemic curve.

There are no previous studies showing the effect of vector control on the reduction of transmission of RVFV in endemic countries. In fact, considering the diversity of vector species in Mayotte (EFSA AHAW Panel, 2020b), as well as the wide variety of breeding sites and suitable climatic conditions, controlling mosquito abundance by 40% or more seems rather unfeasible when conventional methods (i.e. larvicide and adulticide treatments) are used. As commented above for other RVFV endemic countries in Africa, while effective control can be achieved for some species (i.e. *Aedes* spp.), control for other species (i.e. *Culex spp.*) seems to be very limited. In addition, the impact of treatments in natural and agricultural areas (i.e. impact on pollinators) may preclude any vector control on those areas. The data about vector control measures taken during the epidemics in Mayotte in order to protect animals and humans, as well as its efficacy, are unavailable. In consequence, there is no baseline data to estimate the level of impact of the vector control procedures applied in Mayotte to be compared with the model produced here.



The top row shows the cumulative number of infected animals and the bottom row shows the time to extinction (the numbers indicate the number of replicates for which RVFV had not been eliminated by the end of the third year of the simulation). Incursions were simulated in January, April, July and October and assumed a completely naive population. Vector control measures were assumed to reduce abundance by 10–90%. Box-and-whisker plots show the median (black line), interquartile range (box) and 2.5th and 97.5th percentiles (whiskers) for 100 replicates of the model.

Figure 9: Impact of reduced mosquito abundance through vector control measures on incursions of Rift Valley fever to Mayotte

Key messages:

- There are few examples of control of RVFV vectors in endemic African countries, but none of them showed an effective control of all mosquito species involved in RVFV transmission.
- There are vector control activities in Mayotte mainly against human VBD with probably none or limited impact on the RVFV vector species.
- Vector control alone does not seem to be a valid alternative for the control of RVF in Mayotte. Only a reduction of 40% or more of mosquito abundance (which is achievable for short time, e.g. 2 weeks, according to experience from Kenya using larvicides against *Aedes* spp., can have a measurable effect on the transmission and re-occurrence of the infection).
- Effective vector control, mostly by using larvicides, will require long-term programmes considering the mosquito habitat and climatology of Mayotte. General use of adulticides is unachievable due to the potential impact on the environment.
- Lesser rates of mosquito reduction (10–30%, which may also be levels very challenging to achieve) may reduce the total number of animals infected during its course but also flatten the epidemic curve, thus increasing the duration of the whole epidemic.

3.3.2.6. Impact of pre-existing immunity on RVFV control

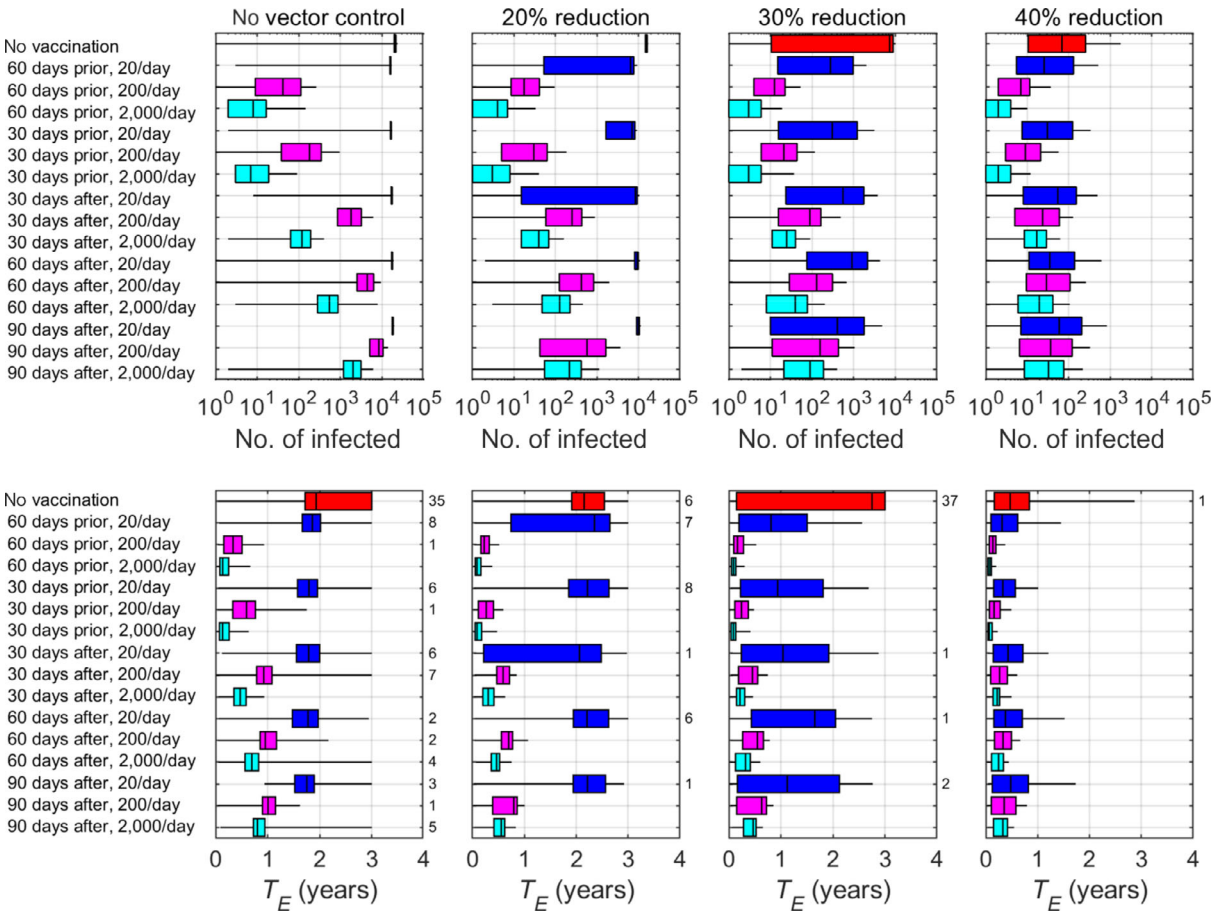
If there is a high level of pre-existing immunity (see Table 1) on the population as a result of a previous epidemic, it is unlikely that a new epidemic will occur, even in the absence of control measures. Accordingly, vaccination, culling and vector control all have limited impact on the (small; median < 10 animals) number of infected animals or time to elimination of the virus from the population in this scenario (see Annex A).

3.3.2.7. Impact of combination of control measures

In the real situation, a combination of different strategies can put in place. However, a systematic use of vaccination is not compatible with a test and culling strategy, unless DIVA vaccines with available DIVA diagnostic tests are used. Vaccination and test-and-culling strategies can be therefore considered alternative approaches, while the control of vector population can be usually applied in all situations. Therefore, two realistic combinations of control strategies above reported can be considered:

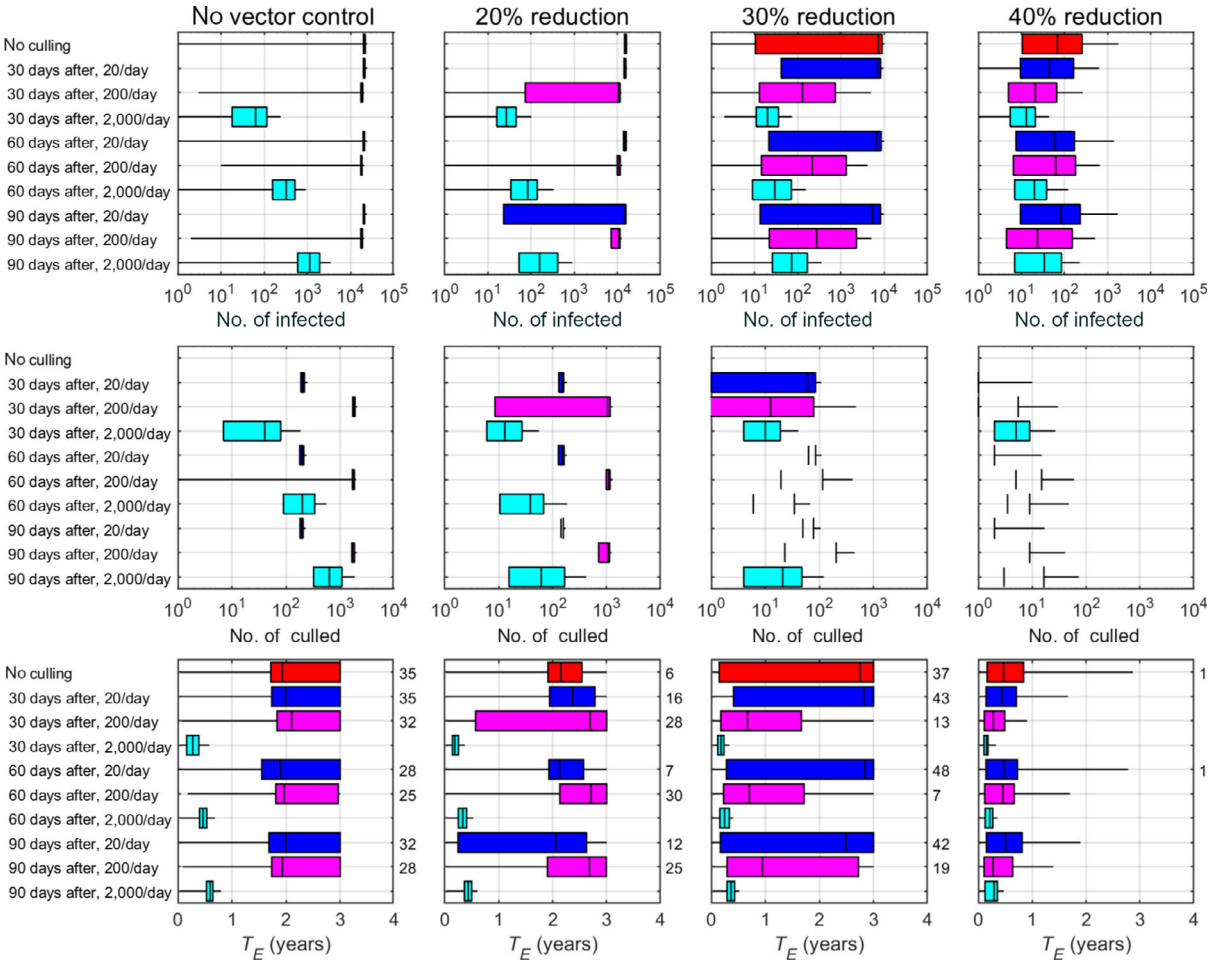
- Vaccination and reduced mosquito abundance through vector control measures,
- Test-and-culling and reduced mosquito abundance through vector control measures.

When combined with either vaccination or testing and culling, vector control measures sufficient to reduce abundance by 10% have limited additional impact (Figures 10 and 11). When they are sufficient to reduce abundance by 20–30% vector control measures have some impact in reducing both the number of infected animals and time to extinction, particularly where vaccination or testing and culling have only a limited impact (i.e. vaccinating 20 animals per day or testing and culling 20 or 200 animals per day) (Figures 10 and 11).



The top row shows the cumulative number of infected animals and the bottom row shows the time to extinction (the numbers indicate the number of replicates for which RVFV had not been eliminated by the end of the third year of the simulation). Incursions were simulated in January and assumed a completely naive population (except for any pre-emptive vaccination). Vaccination was implemented 60 or 30 days prior to or 30, 60 or 90 days after the incursion at a rate of 20, 200 or 2000 animals per day and assumed a vaccine efficacy of 60%. Vector control measures were assumed to reduce abundance by 10, 20 or 30%. Box-and-whisker plots show the median (black line), interquartile range (box) and 2.5th and 97.5th percentiles (whiskers) for 100 replicates of the model.

Figure 10: Impact of vaccination in combination with vector control measures on an incursion of Rift Valley fever to Mayotte



The top row shows the cumulative number of infected animals (including those which were not detected and those which were detected and culled), the middle row shows the cumulative number of infected animals detected and culled, and the bottom row shows the time to extinction (the numbers indicate the number of replicates for which RVFV had not been eliminated by the end of the third year of the simulation). Incursions were simulated in January, April, July and October and assumed a completely naive population. Culling was implemented as part of a test and cull strategy starting 30, 60 or 90 days after the incursion, with 20, 200 or 2,000 animals tested per day. Vector control measures were assumed to reduce abundance by 10, 20 or 30%. Box-and-whisker plots show the median (black line), interquartile range (box) and 2.5th and 97.5th percentiles (whiskers) for 100 replicates of the model.

Figure 11: Impact of testing and culling in combination with vector control measures on an incursion of Rift Valley fever to Mayotte

Key messages

- When a vaccination strategy is considered in combination with the application of vector control measures, null or small combined effects can be seen for reduction of mosquito population less than 40%.
- When testing and culling strategy is considered in combination with vector control measures, the latter, for mosquito reductions of 40% or above, increase the efficacy of the culling strategy.

3.4. Surveillance strategy for early detection in case of risk of introduction of RVF into continental EU

In case of high risk of RVFV introduction in EU, the surveillance measures necessary to ensure early detection are assessed below. Currently, there is no current EU legislation or diagnostic manual for the early detection or surveillance with respect to RVF, and the sampling procedures and diagnostics for all category A disease according to Regulation (EU) 2016/429 (among those also RVF) will be also assessed in next opinions by EFSA.

3.4.1. Objective of the surveillance

The objective of any surveillance in the EU would be to detect the incursion of the RVFV as early as possible to put in place proper control measures to limit the spread and the impact of the infection on the EU territory.

3.4.2. Geographical areas for surveillance

To have the highest chance of detecting the RVFV in case of entry, the surveillance should be focused in those areas at major risk of RVFV introduction only. In the previous EFSA Opinion (EFSA AHAW Panel, 2020a), an assessment of possible RVFV introduction pathways into the EU has been made. While the probability of introduction through infected animals was considered 'very low', due to the rigorous measures hampering the import of live animals from infected countries, the entry of infected vectors when shipped by flight or sea containers was assessed as 'low'. In the same EFSA Opinion, it has been recommended, considering that higher risk values estimated for the introduction of infected vectors, to integrate the surveillance systems already in place in the EU for invasive mosquitoes, with particular attention to those points of entry receiving major air and sea traffic from RVF affected countries. Under this scenario for RVFV introduction, cattle and small ruminant establishments located in the proximity of these points of entry (ports, airports, cargo, container yards) should be included in the surveillance.

In addition, in the recommendations of the previous EFSA Opinion (EFSA AHAW Panel, 2020a), it was stated that: 'Considering the possible future source of risk represented by the spread of infection into new areas closer to the EU borders, it is of paramount importance for the EU to establish and maintain a close collaboration with North African and Middle Eastern countries in the surveillance of possible introduction of RVF from currently infected areas, as well as to carefully monitor the evolution of the epidemics in African countries'. This should be especially monitored along the southern borders of the EU, which would be the area more exposed in case of the presence of RVFV infections in North African and Middle Eastern countries. To date, apart from Libya and Egypt, all other countries of these two regions are considered free from RVF. Although the presence of a RVF epidemic would not pass unnoticed, the social detriment situation due to the war in Libya and the contemporaneous presence of SARS-CoV-2 infection could substantially delay the recognition of a RVF spread in human and animal populations. For these reasons, the EU territory closer to Libya, like Sicily, Malta and southern Greek islands, could be considered eligible to be included into a surveillance scheme in order to ensure early detection and timely implementation of control in case of introduction into EU.

3.4.3. Type of surveillance

3.4.3.1. Passive surveillance

The introduction of RVFV into a fully susceptible ruminant population, such as in the Europe, would result in a significant number of clinical cases, with high mortality in young animals and abortion storms. For this reason, passive surveillance can be considered the most effective for the early

detection of the infection under these circumstances. An enhanced passive surveillance of abortions, stillbirths and neonatal mortality in cattle, sheep and goats, therefore, should be applied during summer and autumn (during the peak of and end of vector season) in the areas at major risk of introduction. In case of abnormal abortion or mortality rates, all aborted fetuses and dead animals should be investigated also for the presence of RVFV during the vector season.

3.4.3.2. Active surveillance

In the lack of any credible assessment of the RVF epidemic dynamic under the EU conditions (see outputs of model results, Section 3.5.1.3), it is difficult to hypothesise the level of infection that should be the target of an active surveillance strategy at the beginning of an RVF epidemic.

The only documented experience of RVFV introduction into a naïve territory is the RVFV incursion into the Kingdom of Saudi Arabia and Yemen in 2000–2001. From the end of August 2000 to September 2001, a total of 886 human cases and thousands of affected animals were reported in the southwestern region of Jazan in Saudi Arabia (Madani et al., 2003). Two-thirds (64.7%) of the animal cases occurred in September and October 2000 and the apparent prevalence at the end of this epidemic wave was 9.7% in sheep, 7.9% in goats, 1.2% in cattle and 1.3% in camels (Elfadil et al., 2006). Difference between these values may depend on several variables: test sensitivity, animal density, type of husbandry, sample size etc. Control measures, including the mass vaccination of livestock (primarily sheep and goats) with the live-attenuated RVF Smithburn strain vaccine, were implemented immediately after the outbreak was detected (Elfadil et al., 2006). A serological study conducted from August to October 2004 on non-vaccinated animals belonging to 17 small ruminant flocks (n = 6,143) in which death, abortion and/or diarrhoea were observed, resulted in the detection of 0.36% IgM-positive animals (Elfadil et al., 2006), which may suggest a possible reference value for estimating a design prevalence in EU.

Although the epidemiological conditions of the RVF epidemic in Saudi Arabia must be considered largely different from those that would be encountered in the EU in terms of the ecological/climatic conditions, the type of animal breeds and the vector species involved, this is the only known and documented case of introduction of RVF into a free territory. If the level of infections observed in Saudi Arabia is taken into consideration for an active surveillance for early detection in the EU based on antibody detection, then a target prevalence around 0.3% should be at least considered. For comparison, this would correspond to the target prevalence value estimated for Mayotte at 90 days post introduction (see Section 3.3.2.2), while the target prevalence value estimated for Mayotte at earliest time post introduction (30 days) would correspond to 0.04%. Real-time RT-PCR against two target genes should be used for virus detection although serology tests using commercial ELISA kits could be used for screening large numbers of animals.

Key messages:

- In the scenario of RVFV introduction into EU by introduced vectors as previously described (EFSA AHAW Panel, 2020a), it is recommended cattle and small ruminant establishments located in the proximity of the points of disease entry (ports, airports, cargo, container yards) should be included in the surveillance
- Passive surveillance can be considered the most effective for the early detection of the infection in continental EU when a risk of introduction would emerge. An enhanced surveillance on abortions, stillbirths and neonatal mortality, therefore, should be applied during summer and autumn (during the peak of and end of vector season) in the areas at major risk of introduction.
- Based on the only known and documented case of introduction of RVF into a free territory (Saudi Arabia), a target prevalence based on antibody detection of around 0.3% or lower for designing an active surveillance for early detection of RVF in the EU should be considered.

3.5. Assessment of feasibility, availability and effectiveness of prevention and control measures in the event of RVF occurring in the EU

The general measures for the prevention and control of listed diseases are set out in the enacting terms of Parts I and II of the Commission Delegated Regulation 2020/687[13], and the epidemiological

[13] COMMISSION DELEGATED REGULATION (EU) 2020/687 supplementing Regulation (EU) 2016/429 of the European Parliament and the Council, as regards rules for the prevention and control of certain listed diseases.

specificities set out in Annexes I–X of the same Regulation. Parts I and II of this Regulation describe the measures to be applied in case of suspicion of an outbreak of category A disease and in case of confirmation of an outbreak, the measures to be applied in the restricted zone (protection and surveillance zones) and the related derogations. The Annexes include (i) sampling procedures (clinical and laboratory) for confirming disease and carrying out surveillance to demonstrate disease freedom or evidence to allow derogations from movement restrictions, (ii) the monitoring period for which measures in the restriction zones should be maintained and the time used in epidemiological investigations, (iii) the minimum size and duration of the restriction zones, (iv) all the prohibitions of activities concerning animals of listed species and their products and (v) risk mitigating treatments of the products.

In terms of detecting and confirming disease, given the livestock population in the EU and the small number of wild or captive animals of other susceptible species in comparison, early warning passive or active surveillance using laboratory tests would be most effective in cattle and domestic small ruminants.

In the event of an outbreak of RVF being confirmed, the competent authority prescribes the culling of all animals in the farm, the proper disposal of carcasses, products and materials, cleaning and disinfection and all biosecurity measures to avoid further spread. Derogations from immediate culling of all animals on the infected establishment are only allowed for animals kept in confined establishments, animals in research establishments, rare breeds and animals of high genetic, cultural and educational value. In addition, in establishments keeping animals of listed species in two or more epidemiological units, the competent authority may grant a derogation from killing for the epidemiological units in which the disease has not been confirmed. Different culling strategies are assessed in Section 3.5.2.2 of this opinion. Testing and culling alongside mosquito surveillance is recommended to assess whether the disease further spreads as well as to increase the surveillance of livestock: this will be part of the assessment in the EFSA Scientific Opinion on the control measures for all category A diseases. In terms of derogating from culling listed species in certain circumstances, this presents a very low risk of spread, providing that the animals have been in vector-proof or -protected housing and are tested negative regularly during the monitoring period (i.e. every 4–5 days). Clinical examination alone will not give sufficient confidence as these species may experience occult infections.

Furthermore, the competent authority must establish restriction zones around the infected establishment, which comprises a Protection Zone (PZ) and a Surveillance Zone (SZ) with the possibility to establish further restricted zones according to epidemiological criteria (set out in Article 64 of Regulation (EU) 2016/429). The size of the restriction zone is assessed in Section 3.5.2.5.

The Delegated Regulation (EU) 2020/687 requires certain measures in the restriction zones, which must be in place for a minimum period, set as 30 days for RVF (plus additional period of 15 days for surveillance measures), for which the assessment will be carried out in the EFSA Scientific Opinion on the control measures for all Category A diseases. These measures include no movements of live animals of listed species out of the PZ, unless directly to slaughter; no movement of live animals within or through the zone except under specific conditions to minimise the risk; tracing of animal by-products. In addition, monitoring for clinical signs in listed species should be in place and insect control in and around establishments carried out. The in-depth analysis of these measures will be part of the EFSA Scientific Opinion on the control measures for Category A diseases.

A clinical examination of all listed species in the PZ should be carried out as quickly as possible along with suitable testing sufficient to detect disease if necessary. As RVF can cause occult infection in older, non-pregnant animals, laboratory sampling will be necessary to demonstrate less than 5% prevalence with 95% confidence in each flock or herd. There is no indication in the legislation on what level of surveillance (design prevalence) should be carried out. As the PZ is greater than 3 km radius, the authorities may decide to require only a visit to a representative number of premises, and in this case, a risk factor sampling strategy would be used, where those establishments with a higher density of livestock and suitable vector habitat would be targeted.

Certain derogations for moving animals directly to slaughter within the PZ or moving animals to pasture in the SZ may be considered and these will be assessed in details in the EFSA Scientific Opinion on the control measures for all Category A diseases. This will include statistical sampling of animals to provide evidence of disease freedom for which there is currently no guidance. Derogations for moving animals to slaughter within the monitoring period require pre-movement testing for each individual animal, as the potential public health concerns of slaughtering infected animals must take priority.

In the SZ, although the Delegated Regulation allows for clinical examination only for surveillance, given the possibility of occult infection, laboratory sampling for a statistical sample targeting those establishments with certain risk factors can be used to rule out the infection with a certain level of confidence. There are derogations for the movement of live animals directly to slaughter or to grazing pastures within the SZ or to a slaughterhouse or processing plant outside the Restriction Zone.

These measures are lifted once the monitoring period has elapsed and preliminary cleaning and disinfection on the infected establishment are completed and all establishments have had favourable clinical and/or laboratory examinations. In the case of a vector-borne disease, the duration of measures can take into account other factors relevant for disease spread. After 30 days (for RVF), these measures are lifted but instead the measures applied in the SZ will continue for the PZ for an additional period of 15 days.

Vaccination against Category A diseases is not foreseen by the Regulation, although it has been requested to be assessed for RVF in the present opinion. Lessons learnt from other exotic vector-borne diseases (e.g. LSD epidemics in Europe in 2015–2018) suggest that vaccination is often a key measure, and sometimes the only effective one, to contain the spread of certain diseases. Vaccination strategies are assessed in Section 3.5.2.1 of this opinion.

According to the Implementing Regulation (EU) 2018/1882, RVF belongs to Category A of listed diseases that do not normally occur in the Union and for which immediate eradication measures must be taken as soon as they are detected, as referred to in Article 9(1)(a) of the Regulation (EU) 2016/429(EFSA AHAW Panel, 2020a).

The disease prevention and control rules for RVF referred to in Article 9(1) of Regulation (EU) 2016/429 shall apply for the listed species referred to in the table set out in the Annex of Regulation (EU) 2018/1889, namely Perissodactyla, Antilocapridae, Bovidae, Camelidae, Cervidae, Giraffidae, Hippopotamidae, Moschidae and Proboscidae and vector species belonging to Culicidae.

The following points are dealt in the present assessment, i.e. the use of vaccination, the culling strategies, the size of the restriction zones, the requirement to test wild animals. The other prohibitions, mitigations and derogations will be assessed in details in a separate EFSA scientific opinion on disease control measures for category A diseases.

3.5.1. Assessment of potential RVF spread in EU

In order to assess the effectiveness of the prevention and control measures against RVF in case of incursion into the EU, one case study has been carried out where simulations of RVF spread are run by a mathematical model. The case study is the RVF spread following incursion into the Netherlands.

3.5.1.1. Ruminant population

The density of farms of large and small ruminants in the Netherlands is plotted in a grid 2 $\times$ 2 km in Figure 12 and Figure 13. In the Netherlands, there are around 70,000 farms with large or small ruminants (30,000 with only cattle, 30,000 with small ruminants and 10,000 mixed).

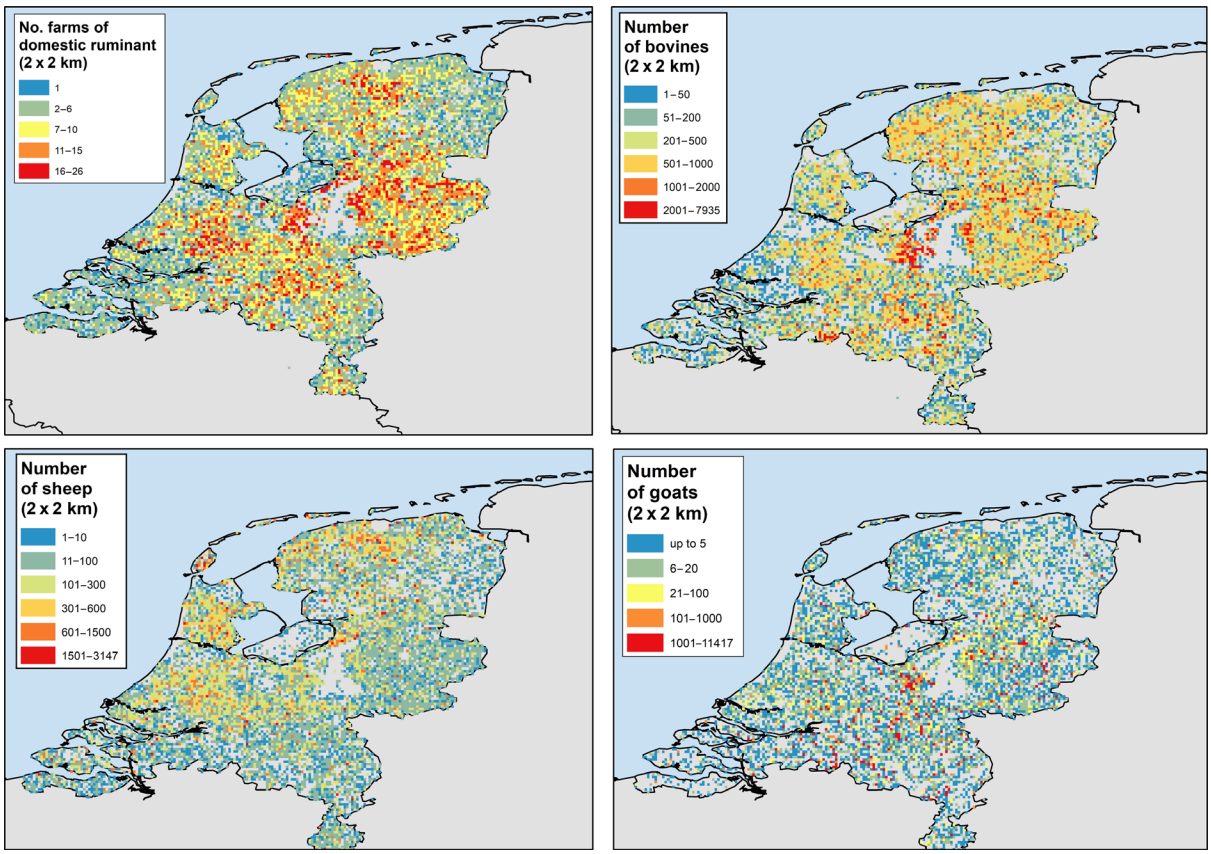


Figure 12: Distribution of farms and bovines, sheep and goats at 2 × 2 km grid in the Netherlands

The distributions of farm sizes of cattle and small ruminants in the Netherlands are displayed in Figure 13.

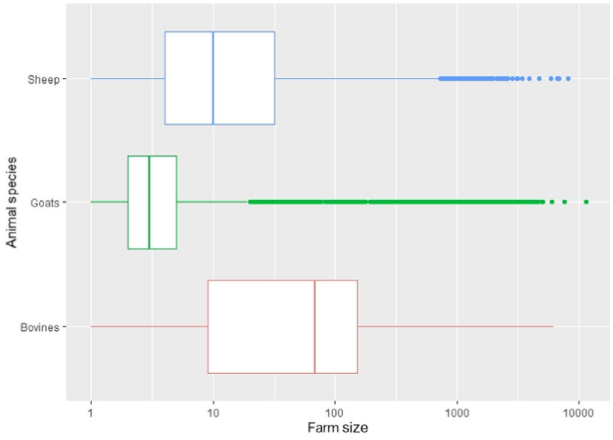


Figure 13: Distributions of herd sizes of cattle and small ruminants in the Netherlands

3.5.1.2. Vectors

Potential vectors of RVFV in the Netherlands

The mosquito fauna in the Netherlands comprises 35 native mosquito species and two invasive mosquito species, *Ae. japonicus japonicus* that is considered established and *Ae. albopictus* which establishment is uncertain (ECDC mosquito maps[14]); (Beuk, 2002; Ibañez-Justicia et al., 2015). In addition, several imported species mainly via aircrafts have been detected in the Netherlands but are

[14] https://ecdc.europa.eu/en/disease-vectors/surveillance-and-disease-data/mosquito-maps

not currently established such as *Ae. aegypti*, *Ae. atropalpus*, *Cx. quinquefasciatus*, *Cx. antennatus*, *Ae. mcintoshi* and *An. algeriensis*. Some of these species are considered important vectors for RVFV and the risk of introduction into Europe via international means of transports was assessed previously (EFSA AHAW Panel, 2020a).

In a surveillance conducted by the Centre for Monitoring of Vectors in the Netherlands from 2010 to 2013 under the framework of the National Vector Survey in urban, rural-agriculture and natural environments (Ibañez-Justicia et al., 2015), 778 random locations were sampled twice every year. The seasonality of mosquitoes was recorded from mid-April to second half of October. From this work, 27 species of mosquitoes were recorded.

The most diverse genus in the Netherlands was found to be *Aedes*, while the most widespread species was *Cx. pipiens/torrentium*, and the most abundant species were *Ae. vexans*, *Cx. pipiens/torrentium*, *Culiseta annulata*, *Ae. cinereus* and *Coquillettidia richiardii*. These species were present in all types of environments, with similar mosquito fauna in urban and agricultural areas. The Netherlands is considered to have fragmented landscape structure, where urban and rural area predominate and are highly connected to natural areas. Therefore, mosquito species can actively or passively move easily from one environment to another. Among the species which are native to the Netherlands, only *Ae. vexans* and *Cx. pipiens* can be considered as proven RVFV vectors, based on virus isolation from field specimens in Africa (Reference). In Africa, *Aedes* species are considered to have a role in the persistence of the virus via vertical transmission, and also to initiate transmission events. *Culex* species, on the other hand, are considered to increase the magnitude of transmission and thus the risk of transmission to humans. For most of the proven and/or potential vector species, the role of vertical transmission of RVFV within the vector is uncertain, since it has been recorded only in *Ae. macintoshi*, *Ae. vexans* and *Cx. quinquefasciatus* (EFSA AHAW Panel, 2020b).

In regards to seasonality, *Cx. pipiens/torrentium* were active during the whole mosquito season in the Netherlands (April to October), having a peak of abundance in mid-July, while other species such as *Ae. vexans* were active from June.

From all the species present in the Netherlands and considering the current status of the potential competent vectors for RVFV in Europe, only *Ae. vexans* and *Cx. pipiens* can be considered as candidates for RVFV transmission. In fact, natural European populations of *Ae. vexans* have been confirmed to be competent vectors for RVFV transmission in laboratory trials (Birnberg et al., 2019) In addition, both species are abundant and widespread in the Netherlands favouring its vector capacity (Figure 14). The vector role of *Ae. albopictus* remains uncertain, since evidences of RVFV transmission come mainly from laboratory trials only and its presence in the Netherlands is currently also uncertain.

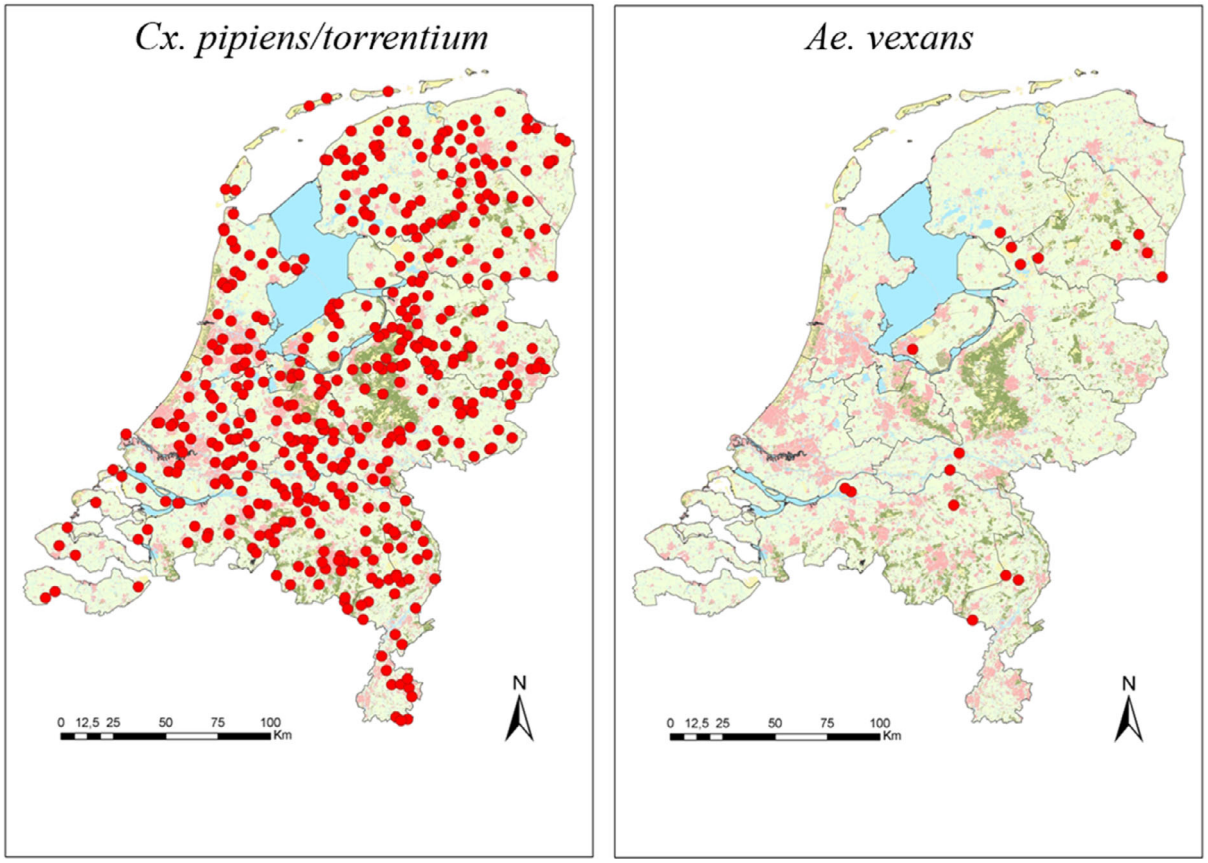


Figure 14: Distribution of *Cx. pipiens/torrentium* and *Ae. vexans* in the Netherlands recorded from 2010 to 2013 (Source: Ibañez-Justicia et al., 2015. By permission of Oxford University Press on behalf of Entomological Society of America)

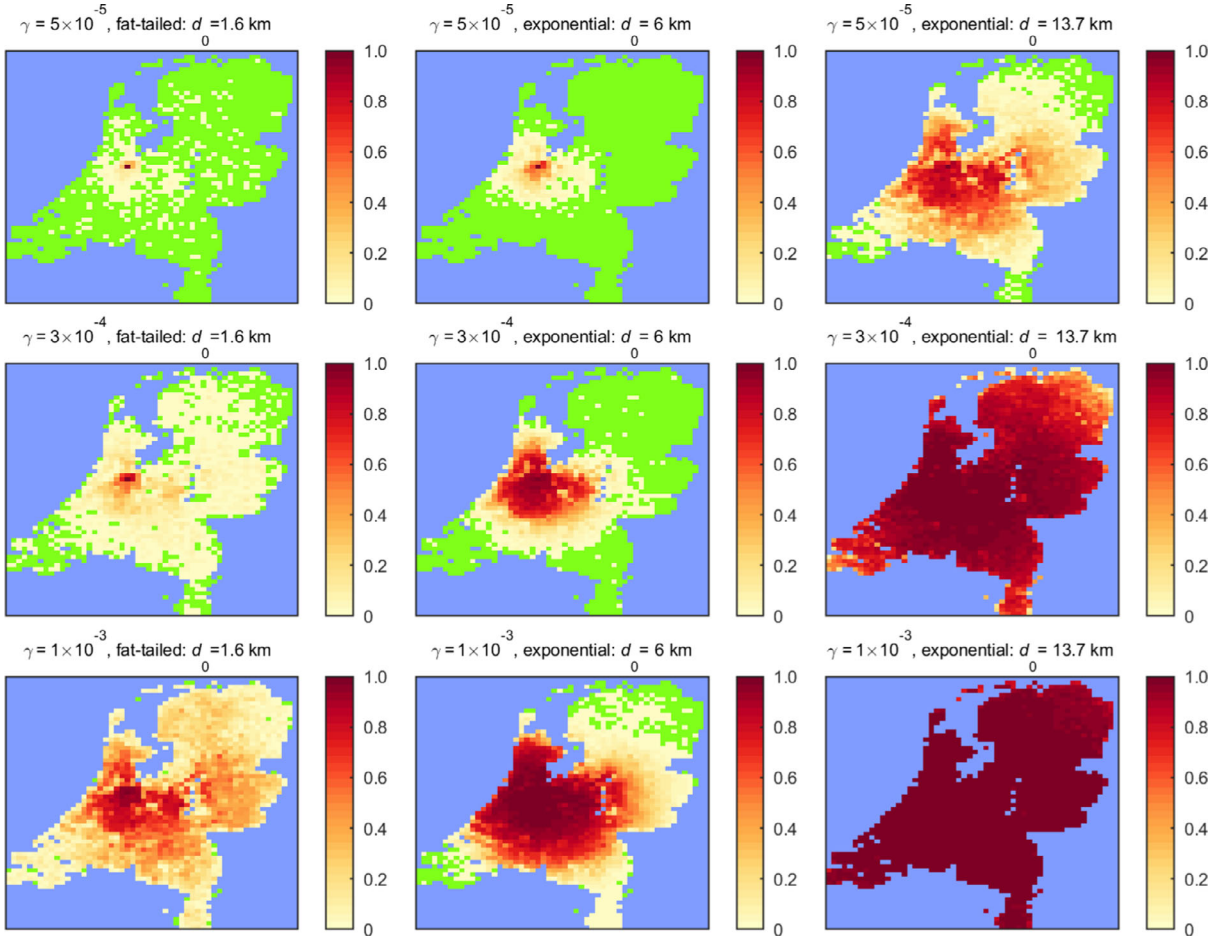
Aedes vexans, Culex pipiens occur also in other European countries, together with other relevant RVF vectors such as *Aedes caspius, Aedes detritus, Aedes japonicus and Culex theileri*, and have been described in EFSA AHAW Panel (2020a) and their presence modelled in Wint et al. (2020).

Key messages:

- In the Netherlands, *Ae. vexans* and *Cx. pipiens* can be considered as candidates for RVFV transmission. Both species are abundant and widespread in the Netherlands favouring its vector capacity. The vector role of *Ae. albopictus* remains uncertain, since evidences of RVFV transmission come mainly from laboratory trials only and its presence in the Netherlands is currently also uncertain.

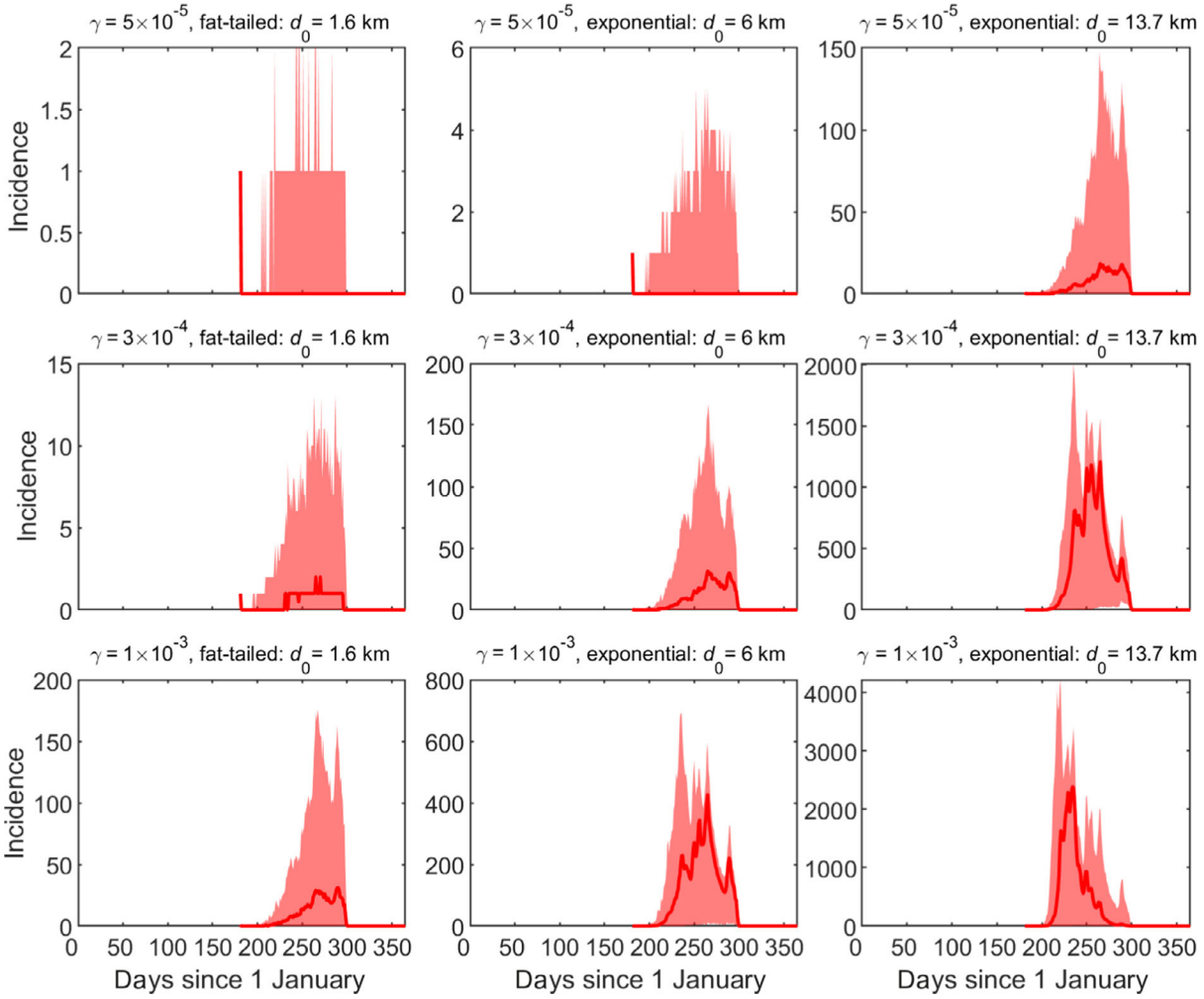
3.5.1.3. Simulations of RVF spread in NL

The simulated spread of RVF following incursion into the Netherlands and related time course of epidemics in the absence of control measures is displayed in Figures 15 and 16. Time course of RVF epidemics simulated by different model settings after incursion in the Netherlands in the absence of control measures: median (line) and 95% prediction interval (ribbon) for the incidence (number of new infected farms per day) based on 100 replicates of the model. Incursion is on 1 July, respectively. Different model settings for the between-herd transmission, as explained in Section 2.3.5, are used to produce the simulated spread and the outputs discussed.



Between-herd transmission parameter (gamma) varies by row: (top) inferred from within-farm model parameters (excluding the vector to host ratio); (middle) estimated from Tanzania data; (bottom) inferred from within-farm model parameters (including the vector to host ratio). The kernel varies by column: (left) fat-tailed, Tanzania distance parameter (d); (middle) exponential, half mean dispersal of Tanzania (d); (right) exponential, Tanzania mean dispersal (d). Each map shows the proportion of replicates for which at least one farm becomes infected in each 5 km grid square (as indicated by the colour bar). For each scenario, 100 simulations were run from the time of incursion (1 July) to the end of the year (31 December).

Figure 15: RVF spread scenarios by different model settings simulated after incursion in the Netherlands in the area of Amsterdam in the absence of control measures



Between-herd transmission parameter (gamma) varies by row: (top) inferred from within-farm model parameters (excluding the vector to host ratio); (middle) estimated from Tanzania data; (bottom) inferred from within-farm model parameters (including the vector to host ratio). The kernel varies by column: (left) fat-tailed, Tanzania distance parameter (d); (middle) exponential, half mean dispersal of Tanzania (d); (right) exponential, Tanzania mean dispersal (d).

Figure 16: Time course of RVF epidemics simulated by different model settings after incursion in the Netherlands in the absence of control measures: median (line) and 95% prediction interval (ribbon) for the incidence (number of new infected farms per day) based on 100 replicates of the model. Incursion is on 1 July

As explained in Section 2.3.3, the limited data available on transmission of RVFV between herds in endemic countries and none directly applicable to Europe increase the uncertainty of the parameter values that have to be considered when setting an RVF spread model. This is the reason why in the above-reported figures, a range of scenarios for the transmission parameter (γ) and kernel distance scaling (d_0) are explored and, consequently, the model outputs of the model differ substantially. The estimation of between herd transmission may be driven either by the estimation from real epidemiological data or similar to the within farm transmission and then further scaled by distance.

Nevertheless, for the scope of this opinion, the important aspect is the comparison of the relative effect of the control measures, which is comparable across the scenarios, and not the absolute value of the probability of RVF spread for each scenario. The relative effect of different control measures is discussed in the next section.

3.5.2. Assessment of possible RVF control measures in EU

3.5.2.1. Assessment of possible vaccination strategies to control RVF

The most probable scenario for the use of vaccines in the EU (except overseas regions) is as a reaction to the detection of RVF in the EU territory. It is difficult, in fact, to hypothesise a preventive use of vaccination, unless a slow progression of the RVF infection in the countries surrounding the EU is considered, which is, to date, a remote possibility.

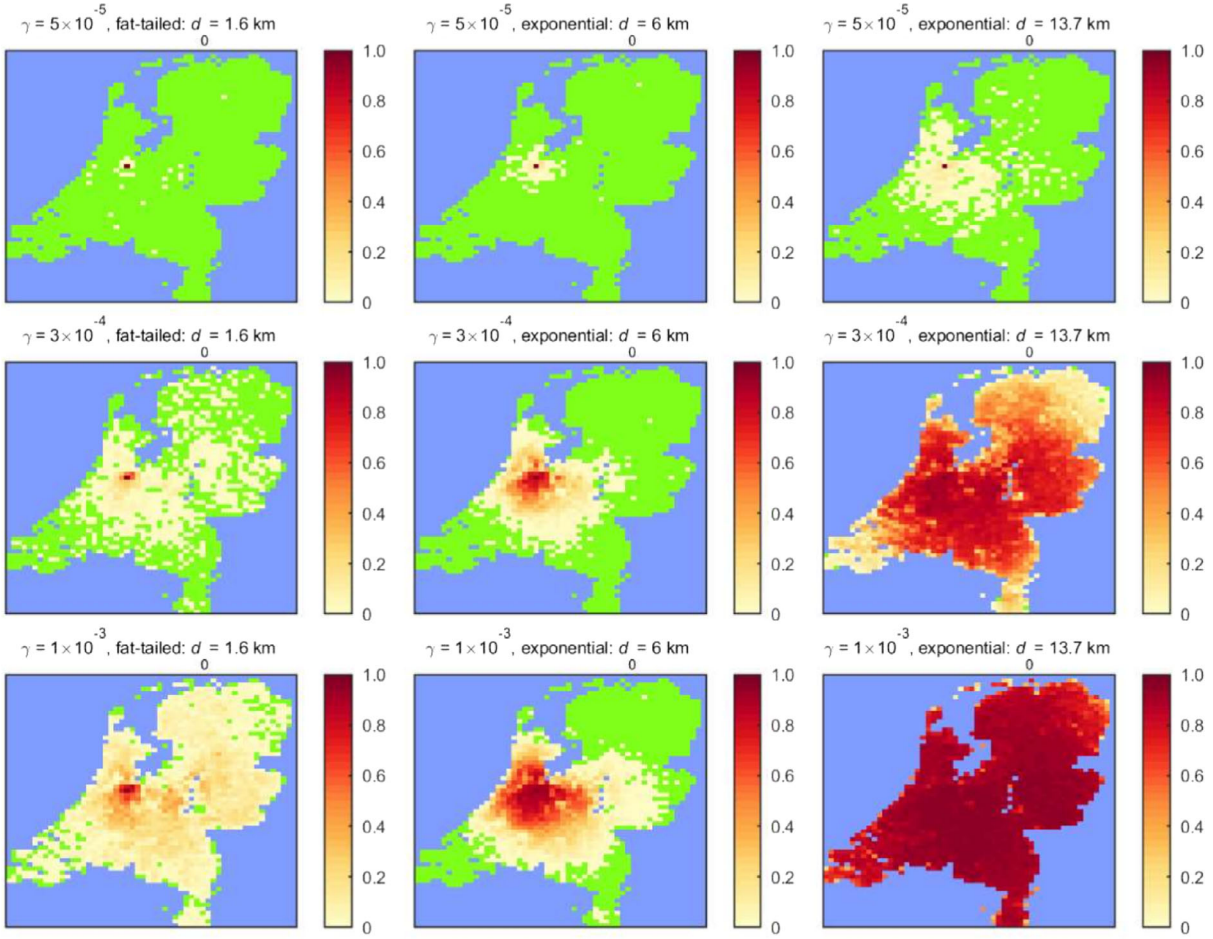
Therefore, under a scenario of reactive vaccination, as a response to the introduction of RVF in any part of the EU territory, the sole vaccine eligible for such emergency vaccination would be the inactivated vaccine, because of the safety limitations affecting the live-attenuated vaccines and the risks that mosquitoes transmit actively the vaccine strain due its use during the vector season.

Because the inactivated vaccines are the only ones plausibly usable, it must be considered that two injections at 3- to 4-week interval are required to immunise the animals. Considering the time needed for the establishment of a solid immunity in vaccinated animals, it should be considered that animals are only immune at least 4–5 weeks from the first injection.

A further aspect to be considered in case of an emergency vaccination against RVF under the scenario of its introduction into the EU is related to the vaccine availability on the market. Both inactivated and live-attenuated vaccines are available in the market, but in case a very high number of doses is required, it must be considered that a certain number of months are needed to produce millions of doses in case of an inactivated vaccine.

As follows, two different types of interventions of vaccination against RVF are simulated: vaccination in a 50 km area around detected farms, and ring vaccination with 20 km inner radius and 50 km outer radius. The results should be compared with the no control scenario as shown in Figure 15.

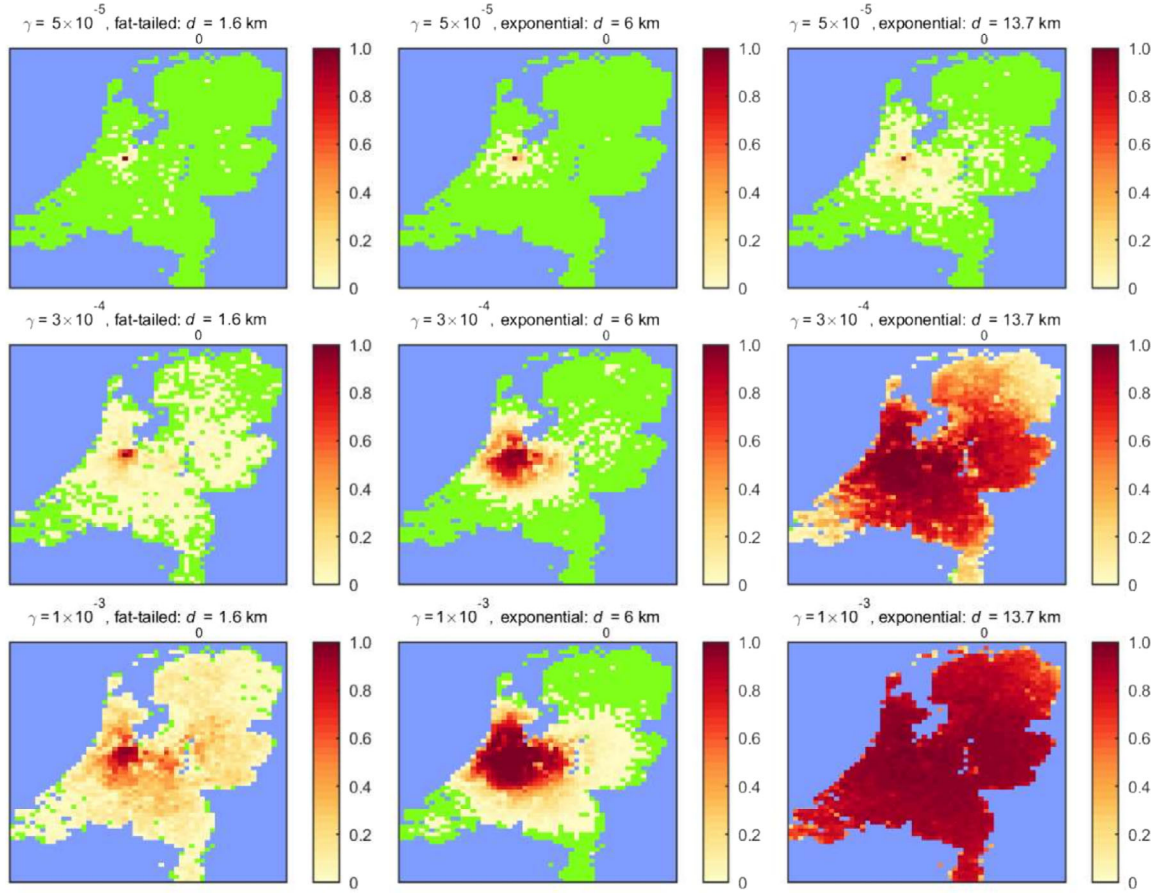
The first one is a reactive vaccination (vaccination following introduction of disease) in a 50 km radius and all farms and animals within the zone are vaccinated over the 14 days after the central farm was detected (Figure 17). Farms were assumed to be detected if an animal died of RVF or if the farmer reported disease (which happened with daily probability of 0.05). Vaccine efficacy is assumed to be 90% and the time to full protection is 21 days.



Between-herd transmission parameter (gamma) varies by row: (top) inferred from within-farm model parameters (excluding the vector to host ratio); (middle) estimated from Tanzania data; (bottom) inferred from within-farm model parameters (including the vector to host ratio). The kernel varies by column: (left) fat-tailed, Tanzania distance parameter (d); (middle) exponential, half mean dispersal of Tanzania (d); (right) exponential, Tanzania mean dispersal (d). Each map shows the proportion of replicates (indicated by the colour bar) for which at least one farm was infected in each 5 km grid square. For each scenario, 100 simulations were run from the time of incursion (1 July) to the end of the year (31 December).

Figure 17: Simulated impact of reactive vaccination in 50 km circular zones around detected farms on the spread of Rift Valley fever virus in the Netherlands

The second scenario of control is ring vaccination around detected farms Figure 18). Farms were assumed to be detected if an animal died of RVF or if the farmer reported disease (which happened with daily probability of 0.05). Vaccination zones have an inner radius of 20 km and an outer radius of 50 km and all farms and animals within the ring zone are vaccinated over the 14 days after the central farm was detected. Vaccine efficacy is assumed to be 90% and the time to full protection is 21 days.



Between-herd transmission parameter (gamma) varies by row: (top) inferred from within-farm model parameters (excluding the vector to host ratio); (middle) estimated from Tanzania data; (bottom) inferred from within-farm model parameters (including the vector to host ratio). The kernel varies by column: (left) fat-tailed, Tanzania distance parameter (d); (middle) exponential, half mean dispersal of Tanzania (d); (right) exponential, Tanzania mean dispersal (d). Each map shows the proportion of replicates (indicated by the colour bar) for which at least one farm was infected in each 5-km grid square. For each scenario, 100 simulations were run from the time of incursion (1 July) to the end of the year (31 December).

Figure 18: Simulated impact of reactive ring vaccination around detected farms on the spread of Rift

The number of farms and animals vaccinated in each of the scenarios is shown in Tables 11 and 12 below. In all cases, the vaccination strategies require > 20% of farms and animals (cattle, sheep and goats) to be vaccinated.

Table 11: Number of farms vaccinated (thousands) as part of vaccination strategies

Transmission scenario	Median no. farms vaccinated (95% prediction interval) (thousands)	
	Vaccination in PZ and SZ	Vaccination in SZ only
$\gamma = 1 \times 10^{-5}$, fat-tailed kernel, $d_0 = 1.6$ km	13.3 (13.3, 24.7)	11.4 (0, 26.1)
$\gamma = 1 \times 10^{-5}$, exponential kernel, $d_0 = 6.0$ km	13.3 (0, 18.7)	13.4 (0, 24.4)
$\gamma = 1 \times 10^{-5}$, exponential kernel, $d_0 = 13.7$ km	21.8 (0, 47.4)	24.3 (11.4, 44.3)
$\gamma = 3 \times 10^{-4}$, fat-tailed kernel, $d_0 = 1.6$ km	37.7 (13.3, 61.2)	39.1 (11.4, 63.8)
$\gamma = 3 \times 10^{-4}$, exponential kernel, $d_0 = 6.0$ km	25.5 (13.3, 43.0)	30.4 (15.6, 47.0)
$\gamma = 3 \times 10^{-4}$, exponential kernel, $d_0 = 13.7$ km	65.7 (13.3, 65.7)	65.7 (45.9, 65.7)
$\gamma = 1 \times 10^{-3}$, fat-tailed kernel, $d_0 = 1.6$ km	62.4 (13.3, 65.7)	64.1 (11.4, 65.7)
$\gamma = 1 \times 10^{-3}$, exponential kernel, $d_0 = 6.0$ km	37.5 (13.3, 53.8)	43.1 (29.2, 58.1)
$\gamma = 1 \times 10^{-3}$, exponential kernel, $d_0 = 13.7$ km	65.7 (13.3, 65.7)	65.7 (11.4, 65.7)

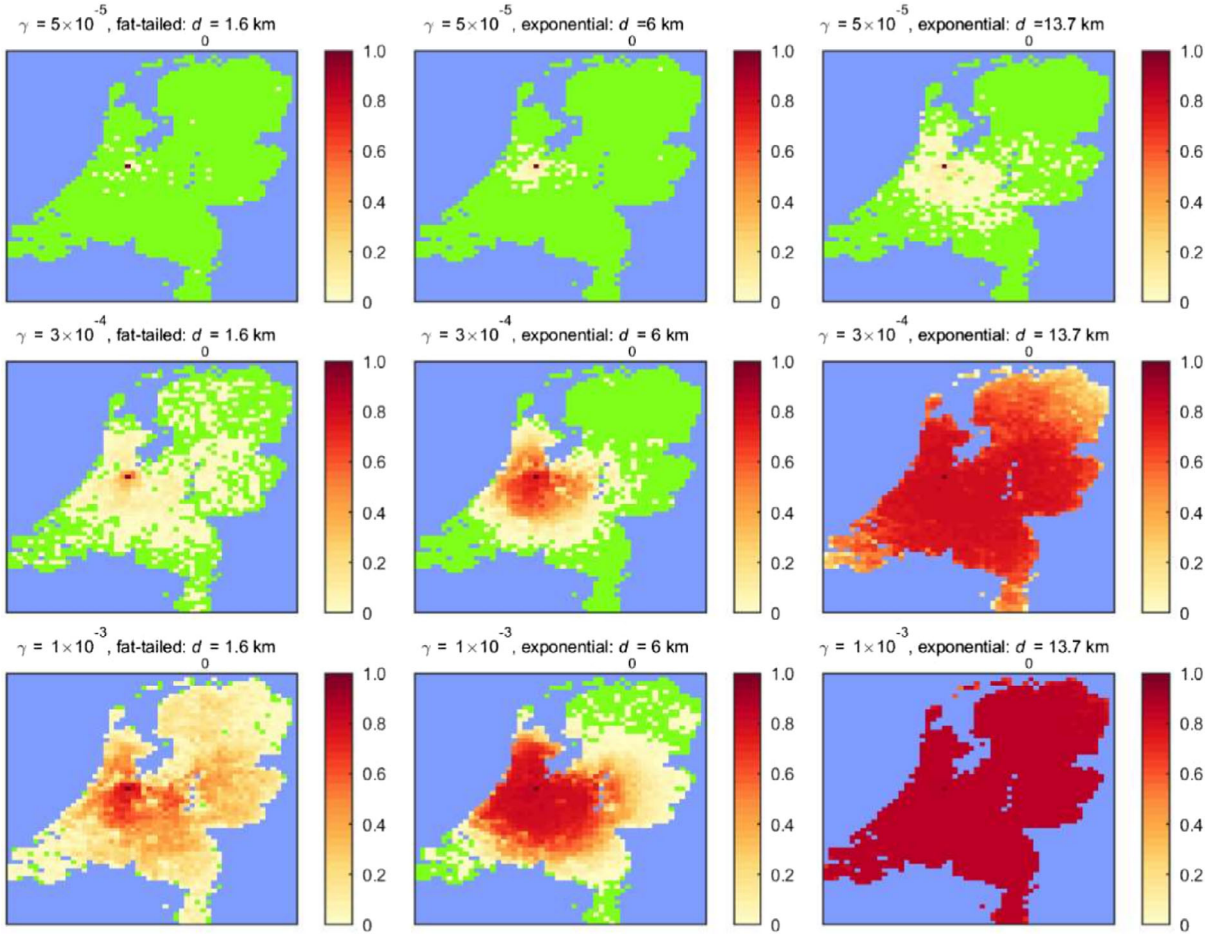
Table 12: Number of animals vaccinated (millions) as part of vaccination strategies

Transmission scenario	Median no. animals vaccinated (95% prediction interval) (millions)	
	Vaccination in PZ and SZ	Vaccination in SZ only
$\gamma = 1 \times 10^{-5}$, fat-tailed kernel, $d_0 = 1.6$ km	1.32 (1.32, 2.36)	1.18 (0, 2.45)
$\gamma = 1 \times 10^{-5}$, exponential kernel, $d_0 = 6.0$ km	1.32 (0, 1.88)	1.37 (0, 2.29)
$\gamma = 1 \times 10^{-5}$, exponential kernel, $d_0 = 13.7$ km	2.13 (0, 4.68)	2.38 (1.18, 4.23)
$\gamma = 3 \times 10^{-4}$, fat-tailed kernel, $d_0 = 1.6$ km	3.74 (1.32, 5.86)	3.72 (1.18, 6.10)
$\gamma = 3 \times 10^{-4}$, exponential kernel, $d_0 = 6.0$ km	2.46 (1.32, 4.12)	2.93 (1.55, 4.51)
$\gamma = 3 \times 10^{-4}$, exponential kernel, $d_0 = 13.7$ km	6.24 (1.32, 6.24)	6.24 (4.36, 6.24)
$\gamma = 1 \times 10^{-3}$, fat-tailed kernel, $d_0 = 1.6$ km	6.00 (1.32, 6.24)	6.13 (1.18, 6.24)
$\gamma = 1 \times 10^{-3}$, exponential kernel, $d_0 = 6.0$ km	3.59 (1.32, 5.10)	4.13 (2.79, 5.56)
$\gamma = 1 \times 10^{-3}$, exponential kernel, $d_0 = 13.7$ km	6.24 (1.32, 6.24)	6.24 (1.18, 6.24)

3.5.2.2. Assessment of possible culling strategies to control RVF

Two different types of interventions of stamping out against RVF are simulated: stamping out of detected farms and stamping out of farms in a 20 km circular zone around detected farms. The results should be compared with the no control scenario as shown in Figure 15.

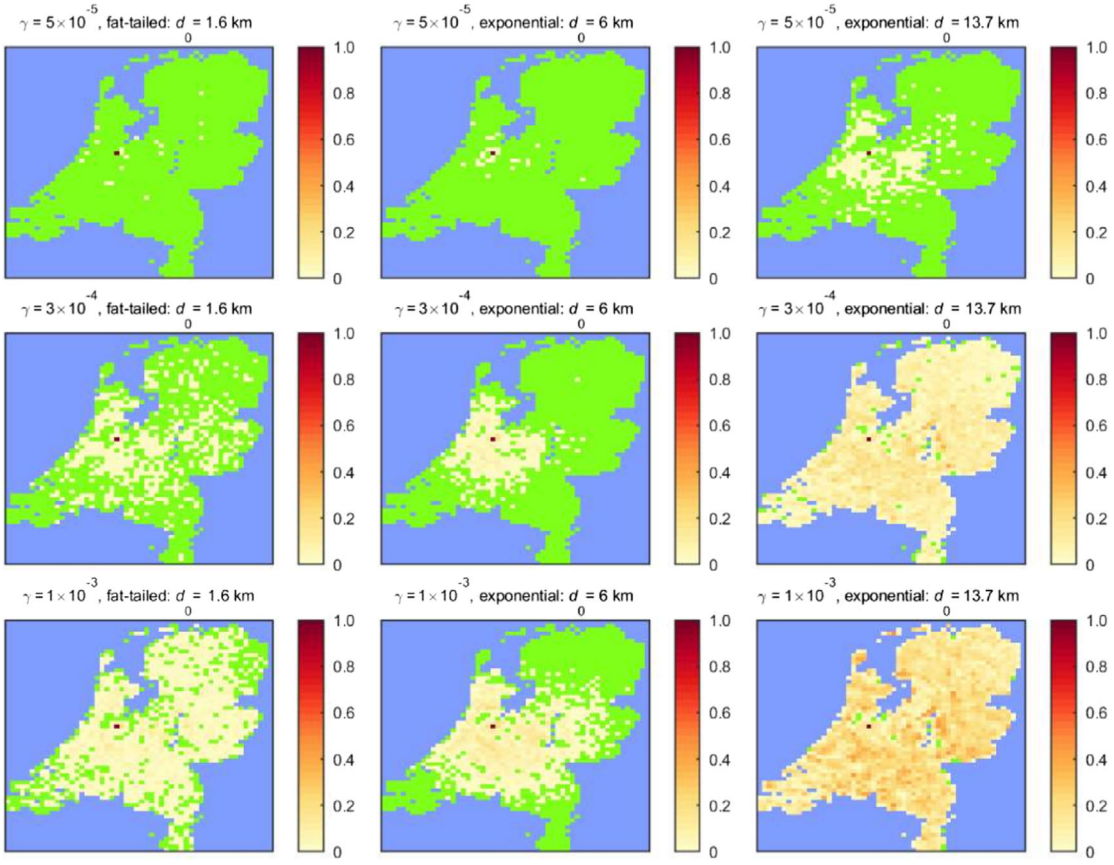
The first stamping out scenario is the culling of only detected farms Figure 19). Farms were assumed to be detected if an animal died of RVF or if the farmer reported disease (which happened with daily probability of 0.05).



Between-herd transmission parameter (gamma) varies by row: (top) inferred from within-farm model parameters (excluding the vector to host ratio); (middle) estimated from Tanzania data; (bottom) inferred from within-farm model parameters (including the vector to host ratio). The kernel varies by column: (left) fat-tailed, Tanzania distance parameter (d); (middle) exponential, half mean dispersal of Tanzania (d); (right) exponential, Tanzania mean dispersal (d). Each map shows the proportion of replicates (indicated by the colour bar) for which at least one farm was infected in each 5-km grid square. For each scenario, 100 simulations were run from the time of incursion (1 July) to the end of the year (31 December).

Figure 19: Simulated impact of stamping out of detected farms on the spread of Rift Valley fever virus in the Netherlands

The second stamping out scenario is the culling of farms in a 20-km circular zone around detected farms Figure 20). Farms were assumed to be detected if an animal died of RVF or if the farmer reported disease (which happened with daily probability of 0.05). All farms and animals within the zone were culled over the 14 days after the central farm was detected.



Between-herd transmission parameter (gamma) varies by row: (top) inferred from within-farm model parameters (excluding the vector to host ratio); (middle) estimated from Tanzania data; (bottom) inferred from within-farm model parameters (including the vector to host ratio). The kernel varies by column: (left) fat-tailed, Tanzania distance parameter (d); (middle) exponential, half mean dispersal of Tanzania (d); (right) exponential, Tanzania mean dispersal (d). Each map shows the proportion of replicates (indicated by the colour bar) for which at least one farm was infected in each 5-km grid square. For each scenario 100 simulations were run from the time of incursion (1 July) to the end of the year (31 December).

Figure 20: Simulated impact of reactive stamping out of farms in a 20-km circular zone around detected farms on the spread of Rift Valley fever virus in the Netherlands

The number of farms and animals culled in each of the scenarios is shown in Table 14.

Table 13: Number of farms culled[15] (thousands) as part of stamping out strategies

Transmission scenario	Median no. farms culled (95% prediction interval) (thousands)	
	Detected farms only	20 km zone
$\gamma = 1 \times 10^{-5}$, fat-tailed kernel, d0 = 1.6 km	0.001 (0.001, 0.004)	1.89 (1.89, 5.35)
$\gamma = 1 \times 10^{-5}$, exponential kernel, d0 = 6.0 km	0.001 (0.001, 0.013)	1.89 (1.89, 5.48)
$\gamma = 1 \times 10^{-5}$, exponential kernel, d0 = 13.7 km	0.004 (0.001, 0.035)	4.59 (1.89, 20.98)
$\gamma = 3 \times 10^{-4}$, fat-tailed kernel, d0 = 1.6 km	0.014 (0.001, 0.22)	6.13 (1.89, 37.1)
$\gamma = 3 \times 10^{-4}$, exponential kernel, d0 = 6.0 km	0.38 (0.001, 2.37)	7.43 (1.89, 20.7)
$\gamma = 3 \times 10^{-4}$, exponential kernel, d0 = 13.7 km	18.4 (0.001, 37.5)	61.9 (1.89, 65.5)
$\gamma = 1 \times 10^{-3}$, fat-tailed kernel, d0 = 1.6 km	0.31 (0.001, 3.5)	26.7 (0, 60.9)
$\gamma = 1 \times 10^{-3}$, exponential kernel, d0 = 6.0 km	5.66 (0.001, 13.5)	19.4 (1.89, 39.6)
$\gamma = 1 \times 10^{-3}$, exponential kernel, d0 = 13.7 km	45.1 (0.001, 47.8)	65.7 (1.89, 65.7)

[15] There are 65,740 farms and 6,244,938 animals in the population used for the Netherlands simulations.

Table 14: Number of animals culled (millions) as part of stamping out strategies

Transmission scenario	Median no. animals culled (95% prediction interval) (millions)	
	Detected farms only	20-km zone
$\gamma = 1 \times 10^{-5}$, fat-tailed kernel, d0 = 1.6 km	0.0012 (0.0012, 0.0017)	0.14 (0.14, 0.46)
$\gamma = 1 \times 10^{-5}$, exponential kernel, d0 = 6.0 km	0.0012 (0.0012, 0.0022)	0.14 (0.14, 0.54)
$\gamma = 1 \times 10^{-5}$, exponential kernel, d0 = 13.7 km	0.0015 (0.0012, 0.0058)	0.37 (0.14, 2.05)
$\gamma = 3 \times 10^{-4}$, fat-tailed kernel, d0 = 1.6 km	0.0026 (0.0012, 0.022)	0.58 (0.14, 3.58)
$\gamma = 3 \times 10^{-4}$, exponential kernel, d0 = 6.0 km	0.034 (0.0012, 0.24)	0.59 (0.14, 2.04)
$\gamma = 3 \times 10^{-4}$, exponential kernel, d0 = 13.7 km	2.05 (0.0012, 4.26)	5.90 (0.14, 6.22)
$\gamma = 1 \times 10^{-3}$, fat-tailed kernel, d0 = 1.6 km	0.034 (0.0012, 0.41)	2.64 (0, 5.80)
$\gamma = 1 \times 10^{-3}$, exponential kernel, d0 = 6.0 km	0.60 (0.0012, 1.57)	1.93 (0.14, 3.75)
$\gamma = 1 \times 10^{-3}$, exponential kernel, d0 = 13.7 km	5.22 (0.0012, 5.67)	6.24 (0.14, 6.24)

3.5.2.3. Vector control

Mosquito control methods are well developed in the EU. Breeding sites can be controlled either by physical or biocide methods (e.g. *Bacillus thuringiensis*). For mosquitoes present in freshwater flooding areas, salt marshes and irrigation channels (e.g. *Cx. pipiens*, *Ae. vexans* and *Ae. caspius*), larvicides are commonly used, such as *B. thuringiensis israelensis* (*Bti*) and *Lysinibacillus sphaericus (Ls)*, insect growth regulators (IGR diflubenzuron, pyriproxyfen, S-methoprene) (Becker and Zgomba, 2007).

Adulticides are used in very specific scenarios, usually when local transmission of human diseases related to arboviruses occurs (i.e. WNV, DENV), because of the environmental concerns and the risk to induce insecticide resistance in the local populations. All these methods can be applied in the EU in case RVFV is introduced and transmitted by local vector species (e.g. *Cx. pipiens*), but there is no information about the effect of those control measures in the rate of transmission of the virus. Vector control using both larvicides and adulticides is probable to be applied in the case of transmission of RVFV to humans, similar to the current situation when West Nile, dengue and chikungunya outbreaks are detected in the EU (Becker and Zgomba, 2007; Bellini et al., 2014). Because of that, WNV can be used as a proxy to estimate the efficacy of vector control on decreasing vector population and therefore, potentially also the rate of transmission (Chaskopoulou et al., 2016). Outbreaks of WNV are detected each year in the EU (Haussig et al. 2018) and is mainly transmitted by *Cx. pipiens.* In addition, this mosquito species is found to be predominant in farms in Europe, such as horse, bird and cattle farms (Boukraa et al., 2016; Brugman et al., 2018).

Regular control of floodwater mosquitoes, including potential vectors of RVFV in Europe such as *Cx. pipiens* and *Ae. vexans* (Brustolin et al., 2017; Ducheyne et al., 2013), is conducted in the MS by using mostly larvicides. For example, in Germany (Becker and Zgomba, 2007), the use of *Bt*i and *Ls* has resulted in 95% annual reduction of floodwater mosquitoes, such as *Ae. vexans* and *Culex* mosquitoes over 2,500 km^2 of breeding areas. In Greece, the control procedures (mainly larvicides) conducted in 50 departments (100.000 ha) since 1996 has reduced by 97% the biting rate of floodwater mosquitoes in 2001. In Italy, the region of Comacchio started a mosquito control programme in 1991 (including larvicides and adulticides), reducing biting densities by 95% compared to pre-intervention densities. In Poland, large-scale control activities were developed after catastrophic floods in 1997. Since 2001, regular larvicide treatments in floodwater irrigated areas resulted in a reduction of mosquito populations of 95%.

Main preventive measures are based in source reduction strategies, while adulticide ground and/or aerial insecticide treatments are recommended just in the case of outbreaks involving human cases (Bellini et al. 2014). For adulticides, usually pyrethroid is the first option. For example, Chaskopoulou et al. (2011) showed that ultra-low volume applications of deltamethrin and d-phenothrin decreased mean population of wild mosquito populations (*Ae. caspius*, *Cx. modestus* and *Anopheles sacharovi*) by 76.5% and 78%, respectively, in rice field areas in Greece.

In regard to the effect of vector control on the transmission of WNV, there are studies from four places in the USA (urban and peri-urban areas) and one in Greece showing positive results. These results have been recently reviewed by ECDC with the aim of developing control strategies against WNV (Chaskopoulou et al., 2020). In general, repeated aerial ultra-low volume (ULV) treatments (e.g. over three sequential nights) reduced vector abundance and decreased transmission; however, there

are also reports showing no success in transmission reduction due to vector control measures (reviewed in Bellini et al. 2014). All studies reporting successful reduction of WNV transmission showed this through reduction of WNV prevalence in sentinel animals or vectors due to adult population control. For example, Elnaiem et al. (2008) showed 75% reduction of *Cx. pipiens* in Sacramento decreasing the risk of WNV infection, while Clifton et al. (2019) showed that pyrethroid ULV treatments decreased host seeking females 24 h after treatment by 65.3% but not gravid females in Chicago (USA), possibly not affecting infection rate of the population.

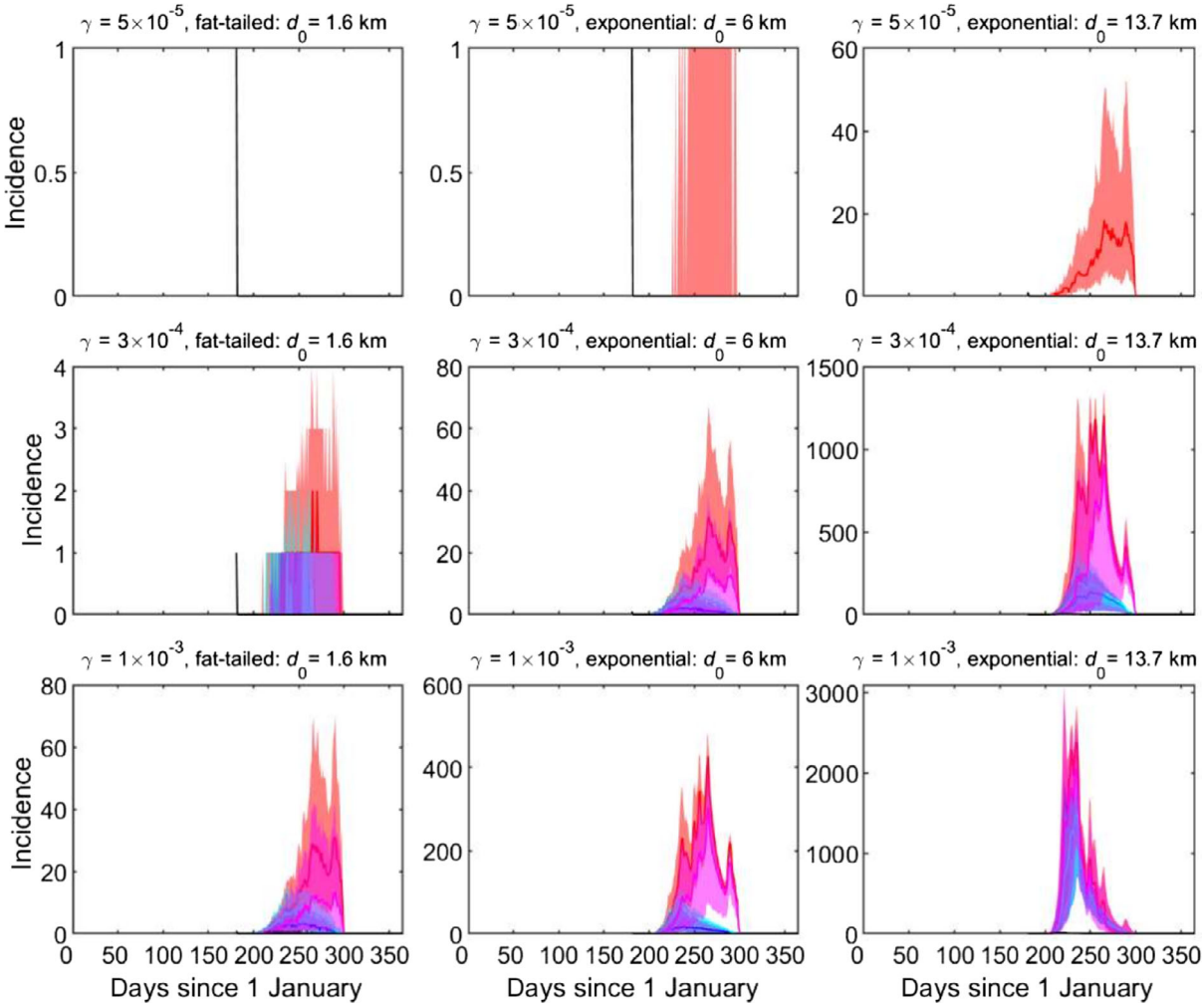
In case of RVFV introduction in Europe, vector control, such as adulticide treatments, would be in place if transmission in human cases is detected, similar to WNV scenario. It is uncertain what would be the effect of the regular current control measures, mainly larvicides, of floodwater mosquitoes on RVFV transmission among domestic animals. The use of adulticides by ground/aerial treatments, a part of those intended around human cases, would probably not be applied in general in farm environments and surroundings due to environmental concerns that depend on the status of protection of the habitat and surface to be treated. There is uncertainty as well on the efficacy of those adulticide control measures at farm level for decreasing transmission rate of RVFV. It is also uncertain what would be the effect of vector control by using larvicides in and around farms, compared to the WNV scenario where flooded areas, peri-urban and urban areas are the main target. The most plausible scenario for vector control in the case of introduction of RFV in the EU would be the use of biological larvicides (i.e. *Bti*) in floodwater areas around farms and possibly, the use of repellents to avoid mosquito feeding activity on animals. These measures can be applied independently to other RFV control strategies, such as vaccination and stamping out. For this assessment, it is assumed that there would be no difference on the efficacy of vector control either considering a scenario of vaccination or stamping out.

Key messages:

- Floodwater potential vectors of RVFV in Europe, such as *Cx. pipiens* and *Ae. vexans,* are regularly controlled in European MS.
- Most of the vector control strategies in Europe are based on the use of larvicides, mainly *Bti*, while adulticides are used just in case of human outbreaks of arboviral diseases, such as West Nile, dengue or chikungunya.
- Efficacy of vector control measures is highly variable. In general, long-term vector control programmes by using larvicides achieve higher rates (up to 95%) of vector control.
- Decrease of transmission of WNV, transmitted by the same vector species as RVFV, in urban and peri-urban areas has been achieved by decreasing adult population of vectors, mainly by using adulticides.
- On average, adulticide control in WNV scenarios achieves around 70% of efficacy.
- It is uncertain what would be the effect of the current regular floodwater mosquito control measures of MS, mainly larvicides, on the RVFV transmission among domestic animals.
- There is an uncertainty about RVFV vector control in and around farms compared to the WNV scenario where flooded areas, peri-urban and urban areas are the main target.

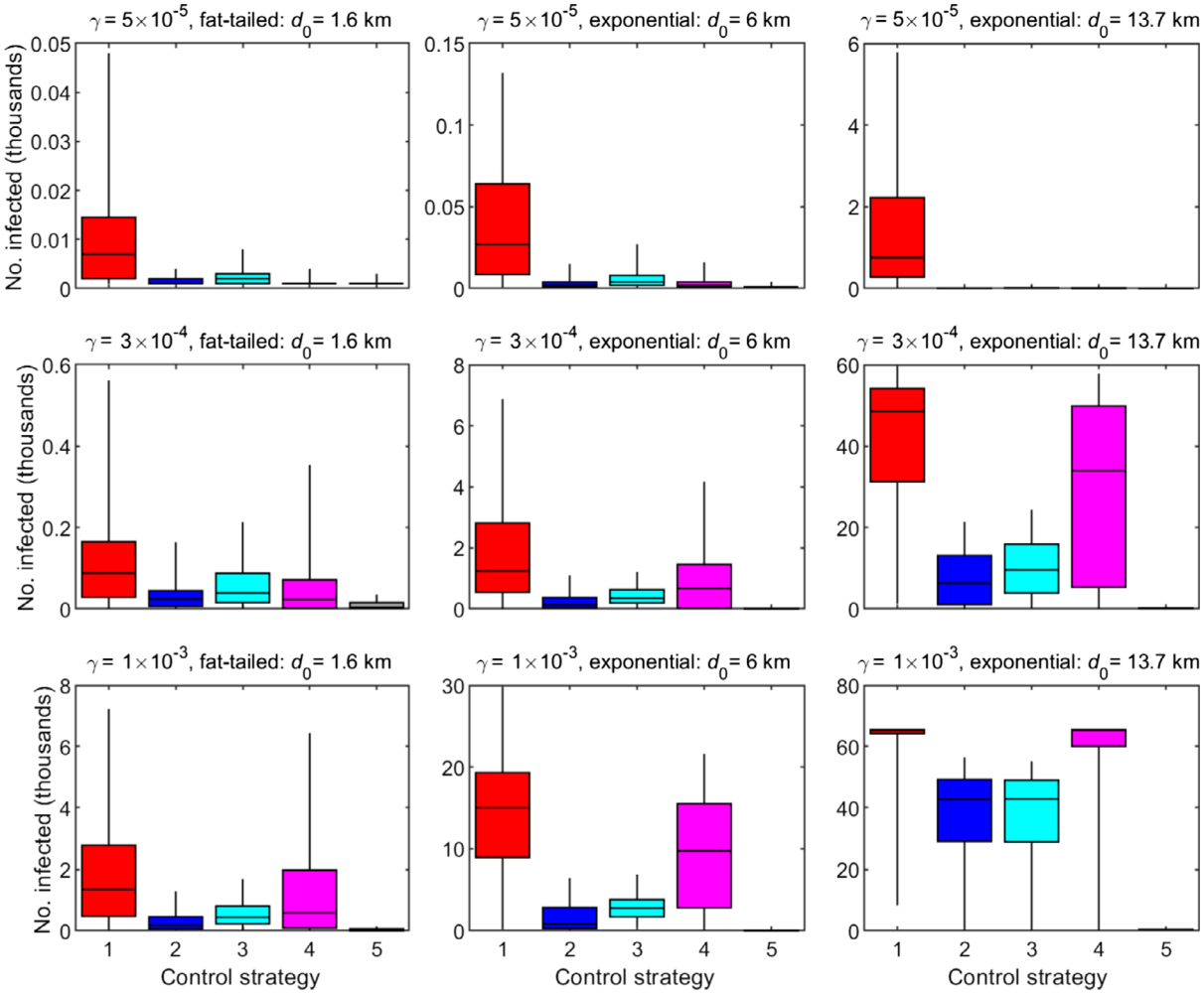
3.5.2.4. Comparison of control strategies

For the purpose of comparison, in the following graphs, the comparison of the effect of the four types of control measures is displayed for each transmission scenario (Figures 21 and 22). Vector control would be applied in all cases (spraying around infected farms); this would reduce the force of infection in all scenarios, so the effect of vector control would be comparable across all the measures applied.



Each plot shows the median RVF incidence (line) and interquartile range (shading) for a control strategy assuming nine different scenarios for the spread of RVFV between farms in terms of the transmission parameter (γ), kernel shape and distance scaling (d0) (indicated above the plot). Five control strategies were considered: no control (red); vaccination in a circular zone of 50-km radius around detected farms (blue); vaccination in a ring of inner radius 20 km and outer radius 50 km around detected farms (cyan); stamping out of detected farms (magenta); and stamping out of farms in a circular zone of 20-km radius around detected farms (black). Farms were assumed to be detected if an animal died of RVF or if the farmer reported disease (which happened with daily probability of 0.05). All farms and animals within a zone were vaccinated or culled over the 14 days after the central farm was detected. Vaccine efficacy is assumed to be 90% and the time to full protection is 21 days. For each scenario, 100 simulations were run from the time of incursion (1 July) to the end of the year (31 December).

Figure 21: Simulated time course for the number of farms newly infected with Rift Valley fever virus each day in the Netherlands under different control measures



Each plot shows the median incidence (line) and interquartile range (shading) for a control strategy assuming nine different scenarios for the spread of RVFV between farms in terms of the transmission parameter (γ), kernel shape and distance scaling (d0) (indicated above the plot). Five control strategies were considered: no control (1, red); vaccination in a circular zone of 50-km radius around detected farms (2, blue); vaccination in a ring of inner radius 20 km and outer radius 50 km around detected farms (3, cyan); stamping out of detected farms (4, magenta); and stamping out of farms in a circular zone of 20-km radius around detected farms (5, black). Farms were assumed to be detected if an animal died of RVF or if the farmer reported disease (which happened with daily probability of 0.05). All farms and animals within a zone were vaccinated or culled over the 14 days after the central farm was detected. Vaccine efficacy is assumed to be 90% and the time to full protection is 21 days. For each scenario, 100 simulations were run from the time of incursion (1 July) to the end of the year (31 December).

Figure 22: Simulated number of farms ever infected with Rift Valley fever virus in the Netherlands under different control measures

For a better comparison among the type of interventions, in Figure 23, one scenario is chosen where the four types of control measures are applied, compared to no control. In terms of reducing the spread probability, the stamping out in 20-km radius around infected farms appear the most effective measures, while the stamping out of only infected farms the least effective.

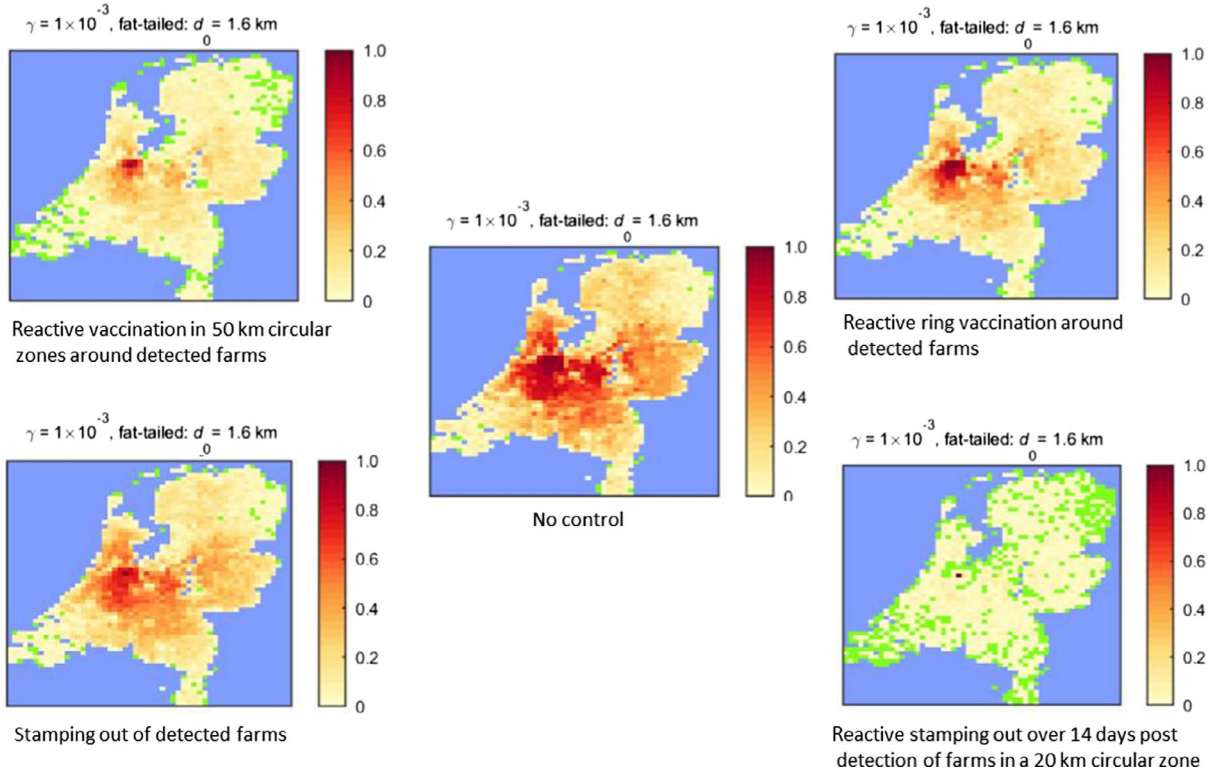


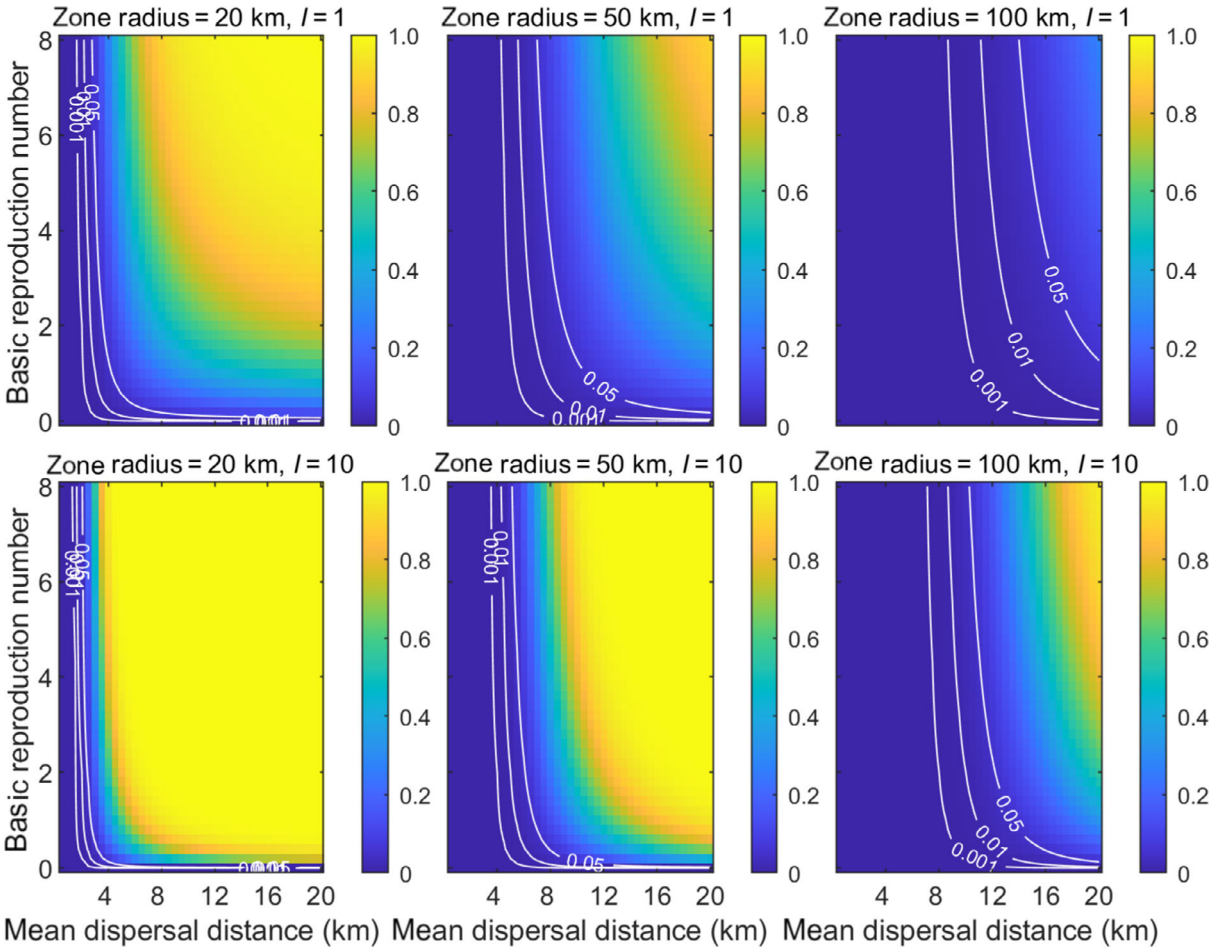
Figure 23: Comparison of control strategies considering the spread scenario based on transmission parameter gamma $= 1 \times 10^{-3}$, fat-tailed kernel and distance scaling of 1.6 km

Key messages:

- According to the model used, stamping out of farms in a 20-km radius around detected farms appears as the most effective measure to control RVF spread after introduction in the Netherlands, although its feasibility and acceptability in terms of large number of animals to be culled should be evaluated.
- The following most effective measures are vaccination in a 50-km radius around detected farms, ring vaccination between 20 and 50 km and culling of only detected farms.

3.5.2.5. Size of restriction zones

The radius of a restriction zone for RVFV (the area where preventive and control measures should be applied following the detection of the disease, in order to prevent the further spread) and its dependence on the between-herd reproduction number, the mean dispersal distance, the number of infected herds in the zone when it is implemented and the probability of escape (probability of herds infected with Rift Valley fever virus being found outside a surveillance zone) is reported in Figure 24.



Plots are shown for different zone radii and numbers of infected farms (I) within the zone when implemented. Computation of the probability of escape assumes an exponential dispersal kernel K(r) = exp(−r/L), where L is the mean dispersal distance. The colour bar indicates the probability of escape and the contours probabilities of escape of 0.001, 0.01 or 0.05.

Figure 24: Probability of herds infected with Rift Valley fever virus being found outside a surveillance zone of a specified radius and its dependence on the between-farm reproduction number and mean dispersal distance

Some examples of above-mentioned probability values are indicated in Table 15.

Table 15: Example of probability of herds infected with Rift Valley fever virus being found outside a surveillance zone of a specified radius and its dependence on the between-farm reproduction number and mean dispersal distance

Restriction zone		**20 km**		**50 km**		**100 km**	
Mean vector dispersal	**Numbers of infected farms detected within the zone when implemented**	**R0 = 2**	**R0 = 6**	**R0 = 2**	**R0 = 6**	**R0 = 2**	**R0 = 6**
5 km	1	0.17	0.42	0.001	0.003	8.6×10^{-8}	2.6×10^{-7}
	10	0.84	1.0	0.01	0.03	8.6×10^{-7}	2.6×10^{-6}
10 km	1	0.56	0.91	0.08	0.22	0.001	0.003
	10	1.0	1.0	**0.55**	0.91	**0.099**	0.03

Key messages:

- According to the model, following RVFV introduction and considering an R0 = 2, mean dispersal of vectors of 10 km and 10 infected farms detected inside the restriction zones, the RVFV would spread beyond a radius of up to 100 km from the infected area with a probability of 10%. Under the same conditions, if the radius was 50 km, the probability of RVF spreading beyond this zone would be 55%.
- What most influences the probability of spread beyond a certain radius of restriction zone is mostly the mean dispersal distance of vectors and the number of infected farms detected inside the restriction zones, rather than R0. This suggests that the number of infected farms detected inside the restriction zones should be kept as small as possible; thus, early detection and early implementation of restriction zones are key measures to contain the spread.
- The dispersal distance of vectors is largely varying according to the biology of each mosquito species and the climatic (e.g. winds) and geographic (e.g. the presence of mountains or other barriers) conditions which can modulate the dispersal of mosquitoes, even to long distances.

3.5.3. Possible role of wildlife in RVF spread in EU

In Africa, RVFV is able to persist in the environment for long periods between epidemics probably through two main mechanisms:

- Through transovarial transmission in some mosquito species (Linthicum et al., 1985), or
- by low level transmission cycles in wild species populations (Evans et al., 2008; Olive et al., 2012; Capobianco Dondona et al., 2016).

Wild ruminants have been investigated in some African countries about their possible role in the RVFV transmission. Serological positive findings and abortion have been observed in African buffaloes (*Syncerus caffer*) in South Africa (Olive et al., 2012) and Kenya (Evans et al., 2008). Antibodies against RVFV at high prevalence, varying from 20% to 35%, were detected in springbok (*Antidorcas marsupialis*), wildebeest (*Connochaetes taurinus*) and black-faced impala (*Aepyceros melampus petersi*) in Namibia (Capobianco Dondona et al., 2016), as well as in Thomson's gazelle (*Gazella thomsonii*), lesser kudu (*Tragelaphus strepsiceros*) and impala (*Aepyceros melampus*) in Kenya (Evans et al., 2008). In Namibia, viral RNA was detected in 9% of tested springbok in 2011 (Capobianco Dondona et al., 2016).

Other wild mammal species have been studied for their possible susceptibility to the infection and antibodies against RVFV were detected in black rhino (*Diceros bicornis*), giraffe (*Giraffa camelopardalis*), African elephant (*Loxodonta africana*) and warthog (*Phacochoerus aethiopicus*) (Lubisi et al., 2020). Even some bats have been found serologically positive and RVFV strains were isolated from pooled organs of three bat species (*Micropteropus pusillus*, *Hipposideros abae* and *Hipposideros caffer*) in Guinea (Olive et al., 2012).

The epidemiological role of these animal species is not fully understood in the African context, albeit wild ruminants are considered to play a role in the maintenance of the infection during the inter-epizootic periods in some areas of southern Africa due to their significant density.

No data are available about the susceptibility of European wild ruminant species to RVFV, or the capacity of the virus of causing a detectable viraemia in these animals. The sole indication outside the African continent is related to white-tailed deer (*Odocoileus virginianus*) in North America (Wilson et al., 2018).

Concerning the possible role of wild ruminants in case of RVFV introduction into Europe, it must be considered that the density of these animal species in Europe is in general much lower than domestic ruminants. However, a possible involvement of some European wild ruminant species on RVFV transmission cannot be excluded, especially for those species and geographical areas with highest density, such as Central Europe (Figures 25 and 26. Map of cumulated density of main wild ruminants (all species merged as from Figure 9) in Europe.).

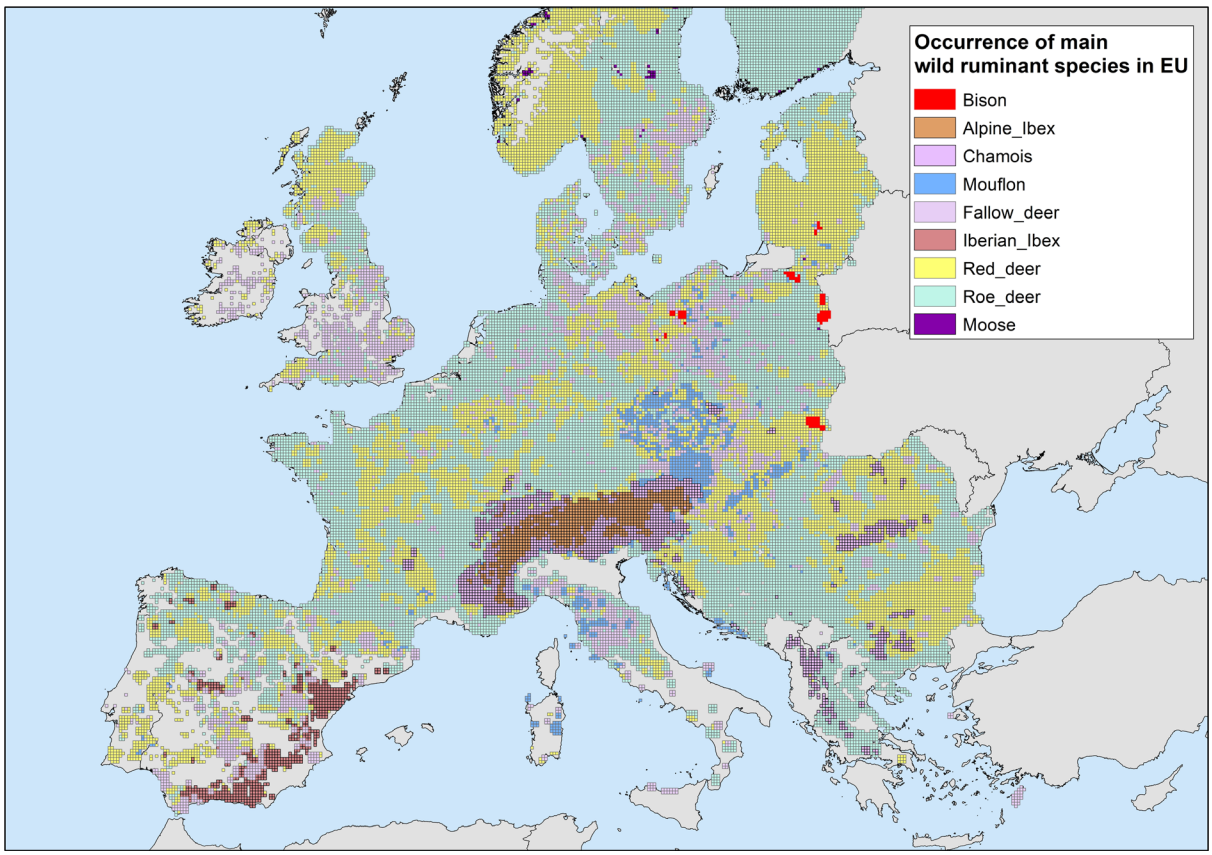


Figure 25: Map of occurrence of main wild ruminants in Europe (Data source: Linnell et al. 2020) Data source: Apollonio et al. (2010) and Linnell et al. (2020).

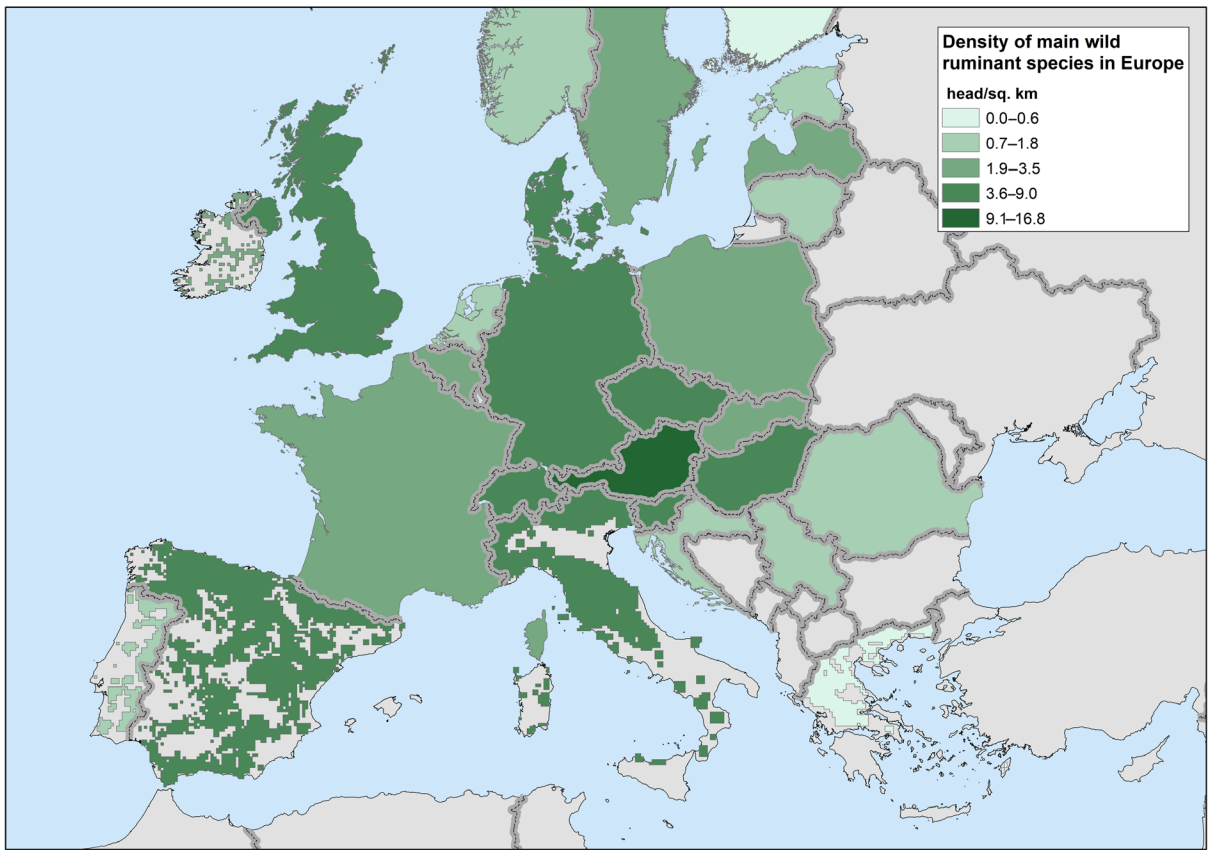


Figure 26: Map of cumulated density of main wild ruminants (all species merged as from Figure 9) in Europe

Key messages:

- In some southern African countries, wild ruminants are considered to play a role in the maintenance of RVFV infection during the inter-epizootic periods.
- No data are available about the susceptibility of European wild ruminant species to RVFV, or the capacity of the virus of causing a detectable viraemia in these animals.
- The density of wild ruminants species in Europe is much lower than domestic ruminants, but even with large uncertainty due to lack of data from ad hoc trials, it cannot be excluded a possible involvement of these animals in RVFV transmission in specific geographical areas or epidemiological contexts.

3.6. Uncertainty analysis

The sources of uncertainty identified during the scientific assessment related with the data available for the different parts of the assessment are displayed in the table below (Table 16).

Table 16: Sources of uncertainty in the different parts of the assessment

Part of the assessment	Sources of uncertainty
Effectiveness of restriction zones	• The mean dispersal distance of vectors is unknown since it can vary according to the biology of each mosquito species and the climatic (e.g. winds) and geographic (e.g. the presence of mountains or other barriers) conditions, which can modulate the dispersal of mosquitoes, even to long distances.

Part of the assessment	Sources of uncertainty
RVF spread model in Mayotte and related surveillance and control methods	• No data are available about the current level of immunity in the ruminant population in Mayotte. • The sensitivity of passive surveillance under Mayotte conditions is unknown. • Data on impact of vector control measures on RVF transmission in Mayotte are lacking. • Data on vaccination effectiveness under Mayotte conditions for the major available vaccine products are not available.
RVF spread model in the EU and related surveillance and control measures	• Lack of data to estimate the force of infection of RVF transmission between farms in the continental EU, due to the absence of historical episodes of RVF in Europe and the poor quality of the current available data on RVF outbreaks in Africa. • Lack of solid data on vaccination effectiveness under the European conditions for the major available vaccine products • Lack of available data for the estimation of the design prevalence at early stage of RVFV incursion into a free area. • Vector competence of various EU mosquito species is not available. • Lack of detailed mosquito abundance data for major species in the EU. • The effect on the RVFV transmission of the current regular floodwater mosquito control measures, mainly larvicides, applied by the EU MS is unknown.
Possible role of wildlife in the EU	• No data are available about the susceptibility of European wild ruminant species to RVFV, or the capacity of the virus of causing a detectable viraemia in these animals.

4. Conclusions

Availability, safety and effectiveness of vaccines and diagnostic tests for RVF:

- Commercially available live-attenuated vaccines lack both safety (especially in pregnant animals) and DIVA.
- The commercially available inactivated vaccine requires multiple doses or annual revaccination to provide protection, which renders the use of this vaccine not feasible in endemic zones, such as Mayotte, due to high costs, and especially in remote areas, where it is difficult to track animals, but suitable for emergency vaccination in not at-risk areas or at least in valuable breeding animals.
- Vaccine availability in the short term may be an issue in case of need of high number of vaccine doses, due to the limited stocks available and to the production on demand of the manufacturers.

Control measures in place in Mayotte against RVF in 2018–2019**:**

- Priority was put on protection measures for animal to human transmission, because the spread of infection in animals was very fast, involving the whole island in short time.
- No stamping out, no protection zones, no vaccination were implemented, because the disease spread too fast compared to the available veterinary resources in Mayotte.
- The measures applied in the farms focussed on increasing the biosecurity and vector control.

Assessment of possible control measures in Mayotte:

Restriction zone:

- Due to the small geographical size of Mayotte and the potential dispersal of mosquitoes over long distances (e.g. > 6 km), the whole island can be considered a single protection zone; thus, the use of restriction zones was not considered further.

Surveillance:

- Considering that the rainy season in Mayotte is from December to March and this is the period at higher risk for the establishment of an RVF epidemic, two main objectives for active surveillance can be considered:

  - early detection of RVFV circulation, ideally before the occurrence of a significant number of human and/or animal cases. This implies a design prevalence values so low that a high (up to 3500) number of animals must be tested, which may not be readily feasible.
  - Verification of RVFV circulation during previous rainy season, which can be achieved testing a limited number of animals, due the higher design prevalence.

- Monitoring the seroprevalence will provide estimates of the spatial and temporal distribution and suggest areas of higher risk of re-occurrence of RVF infections.
- Passive surveillance, based on the notification and testing of aborted fetuses and animals showing clinical signs suggestive of RVFs, is the pillar of any early warning system and at present the only feasible surveillance option, given the high percentage of animals naturally immunised after the 2018–2019 epidemic.

Vaccination:

- The results of the analysis of the impact of vaccination on reducing RVF infections suggest that the vaccination is more effective when applied before the start of the epidemic and quickly implemented throughout the population. Different levels of vaccine effectiveness, either 60% or 90%, have a relatively minor impact on the reduction of the expected number of infected animals.
- In particular with a rate of 200 or 2,000 animals vaccinated per day, the epidemics is halted within one year, regardless whether the vaccination is applied before or after the RVF incursion. Moreover, the number of infections is kept under 3% if the vaccination is conducted at least 30 days prior to incursion with at least 200 animals vaccinated per day (20% coverage achieved at time of incursion, 100% coverage achieved 120 days post incursion). The same effect is achieved if the vaccination is conducted at 2,000 animals vaccinated per days, started at 60 days post incursion at the latest (100% vaccination coverage would be achieved 75 days after RVF incursion).
- On the contrary, with 20 animals vaccinated per day, the epidemics continue for more than 2 years and the whole population would get infected.

Culling:

- A test-and-cull strategy does not seem a useful alternative for the control of RVF in Mayotte unless high number (ca. 2,000 per day) of animals are tested every day and the infected quickly culled.

Vector control:

- There are few examples of control of RVFV vectors in endemic African countries, but none of them showed an effective control of all mosquito species involved in RVFV transmission.
- Vector control activities are in place in Mayotte, mainly focused to protect humans, but with probably a limited impact on the RVFV transmission.
- Vector control alone does not seem to be a useful alternative for the control of RVF in Mayotte. Only a reduction of 40% or more of mosquito abundance (which is achievable for short time, e.g. 2 weeks, according to experience from Kenya using larvicides against *Aedes* spp.) can have a measurable effect on the transmission and re-occurrence of the infection.
- Effective vector control, mostly by using larvicides, will require long-term use considering the mosquito habitat and climatology of Mayotte. General use of adulticides is unachievable due to the potential impact on the environment.
- Lower rates of mosquito reduction (10–30%, which may also be very challenging to achieve) may reduce the total number of animals infected during its course but also flatten the epidemic curve, thus increasing the duration of the whole epidemic.

Combined control measures:

- When a vaccination strategy is considered in combination with the application of vector control measures, no or small combined effects can be seen for reduction of mosquito population less than 40%.
- When a test and cull strategy is considered in combination with vector control measures, the latter, for mosquito reductions of 40% or above, increase the efficacy of the culling strategy.

Assessment of possible control measures in the continental EU in case of RVF incursion or risk of:

Surveillance:

- Under the scenario for risk of RVFV introduction, cattle and small ruminant establishments located in the proximity of the possible points of disease incursion by vector import (ports, airports, cargo, container yards) should be included in the surveillance.
- Passive surveillance can be considered the most effective for the early detection of the infection under these circumstances. An enhanced surveillance on abortions, stillbirths and neonatal mortality, therefore, should be applied during summer and autumn (during the peak of and end of vector season) in the areas at major risk of introduction for cattle and small ruminants.
- Based on the only known and documented case of introduction of RVF into a free territory (Saudi Arabia), a target seroprevalence of 0.3% or less should be considered for active surveillance based on serology.

RVF vectors relevant in continental EU:

- In the Netherlands, the case study used for simulating RVF control, *Ae. vexans* and *Cx. pipiens* can be considered as candidates for RVFV transmission. Both species are abundant and widespread in the Netherlands favouring its vector capacity. The vector role of *Ae. albopictus* remains uncertain, since evidences of RVFV transmission come mainly from laboratory trials only and its presence in the Netherlands is currently also uncertain.
- The above-mentioned vector species are widespread also in other European countries together with other relevant RVF vectors in EU such as *Ae. caspius, Ae. detritus, Ae. japonicus and Cx. theileri.*

Control measures:

- The assessment of the spread of RVF in the EU and efficacy of the various control measures has been conducted by choosing the Netherlands as a case study, due to the results of the previous EFSA Opinion about the risk of RVF introduction in the EU. Therefore, the results presented in this Opinion are related to the epidemiological conditions that can be observed in that country only.
- A range of simulated scenarios of RVF spread are presented, which differ in terms of magnitude of number of infected animals and extension of geographical spread. This is due to the very limited data available on transmission of RVFV between herds in endemic countries and no data directly applicable to Europe. This makes it difficult to identify a single set of parameters describing the force of infection and so produce a single spread scenario.
- According to the model used, stamping out of farms in 20-km radius around detected farms appears as the most effective measure to control RVF spread after introduction in the Netherlands, although its feasibility and acceptability in terms of number of animals to be culled should be evaluated.
- The following most effective control measures are vaccination in a 50-km radius around detected farms, ring vaccination between 20 and 50 km and culling of only detected farms.
- The time to protection depends on the type of vaccine used (live or inactivated), and therefore, the results of the model should be evaluated in the light of this aspect as well.

Vector control:

- Floodwater potential vectors of RVFV in Europe, such as *Cx. pipiens* and *Ae. vexans,* are regularly controlled in European MS.
- Most of the vector control strategies in Europe are based on the use of larvicides, mainly *Bti*, while adulticides are used just in case of human outbreaks of arboviral diseases, such as West Nile, dengue or chikungunya.
- Efficacy of vector control measures is highly variable. In general, long-term vector control programmes by using larvicides achieve higher rates (up to 95%) of vector control.
- Decrease of transmission of WNV, transmitted by the same vector species as RVFV, in urban and peri-urban areas has been achieved by decreasing adult population of vectors, mainly by using adulticides.
- In average, adulticide control in WNV scenarios achieve around 70% of efficacy.

- It is uncertain what would be the effect of the current regular floodwater mosquito control measures of MS, mainly larvicides, on the RVFV transmission among domestic animals.
- There is an uncertainty about RVFV vector control in and around farms compared to the WNV scenario where flooded areas, peri-urban and urban areas are the main target.

Restriction zones:

- According to the model developed, following RVFV introduction and considering an R_0 = 2 (value of basic reproduction number of RVF estimated from the literature), a mean dispersal of vectors of 10 km and 10 infected farms detected inside the restriction zones, the RVFV would spread beyond a radius of up to 100 km from the infected area with a probability of 10%. Under the same conditions, if the radius is 50 km, the probability of RVF spreading beyond this zone would be 55%.
- What most influences the probability of spread beyond a certain radius of restriction zone is mostly the mean dispersal distance of vectors and the number of infected farms detected inside the restriction zones, rather than R0. This suggests that the number of infected farms detected inside the restriction zones should be kept as small as possible, implying that the early detection and early set of restriction zones are one of the key measures to contain the spread.
- The dispersal distance of vectors is largely varying according to the biology of each mosquito species and the climatic (e.g. winds) and geographic (e.g. the presence of mountains or other barriers) conditions which can modulate the dispersal of mosquitoes, even to long distances.

Role of wildlife in the spread of RVF in EU:

- In some southern African countries, wild ruminants are considered to play a role in the maintenance of RVFV infection during the inter-epizootic periods. Although the density of wild ruminant species in Europe is much lower than domestic ruminants and no data are available about the susceptibility of European wild ruminant species to RVFV, or the capacity of the virus of causing a detectable viraemia in these animals, it cannot be excluded a possible involvement of these animals in RVFV transmission in specific geographical areas or epidemiological contexts.

Uncertainty

- The panel identified several limitations in the data available for performing the scientific assessment, mainly related to the current infection and immunological status of the livestock population in Mayotte, the spread dynamics of RVF in newly infected countries in general and in Europe in particular. Given the uncertainty generated by these limitations, results should be interpreted carefully.

5. Recommendations

- The biggest impact on the efficacy of any vaccination programme against RVF in Mayotte is given by the number of animals that can be vaccinated per day; therefore, efforts should be focused on vaccinating as many animals per day. The logistics to organise this should be properly planned.
- Considering the importance of an early detection of the RVF infection in case of introduction into the EU, enhanced passive surveillance during the peak to the end of vector season should be implemented in the geographical areas at major risk of introduction, such as in the proximity of the possible points of disease incursion by infected vector import (ports, airports, cargo, container yards) and in those territories closer to infected countries.
- Considering the possibility, under certain circumstances, of RVFV spreading beyond a radius of up to 100 km from the infected area, in the absence of vaccination, the possibility of increasing the radius of surveillance zone currently proposed by the EU legislation (50 km) should be considered.
- In case of RVF incursion into EU, if vaccination policy is adopted, a large number of doses would be needed and the quick vaccine availability would have to be considered.
- The already mentioned drawbacks of currently available vaccines indicate the need for further researches to develop vaccines safer and more immunogenic, as well as based on DIVA approaches. Since the RVF simulated spread may cover long distance in at least some

scenarios, those countries bordering the infected one should be alerted and ready to take appropriate measures.
- A precise estimate of RVF force of infection would be needed to simulate control measures. In the absence of outbreaks in the EU, where real data can be collected, the research should focus on better assessment of vector dispersal.
- Moreover, more robust and informative outbreak data from African context are needed in order to better estimate force of infection.
- More research on the efficacy and developed protocols about vector control at farm level under the scenario of hypothetical RVF incursion into EU should be conducted.

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Abbreviations

ADNS	Animal Disease Notification System
EIP	Extrinsic incubation period
ELISA	Enzyme-linked immunosorbent assay
MSs	Member States
OIE	World Organisation for Animal Health
RT-PCR	real time PCR
RVF	Rift Valley Fever
ULV	ultra-low volume
VBD	Vector-borne diseases
WNV	West Nile virus

Annex A – Impact of RVFV control measures on Mayotte with pre-existing immunity

Here, we show the impact of the control strategies when there is pre-existing immunity (equal to levels expected after the 2018–2019 epidemic).

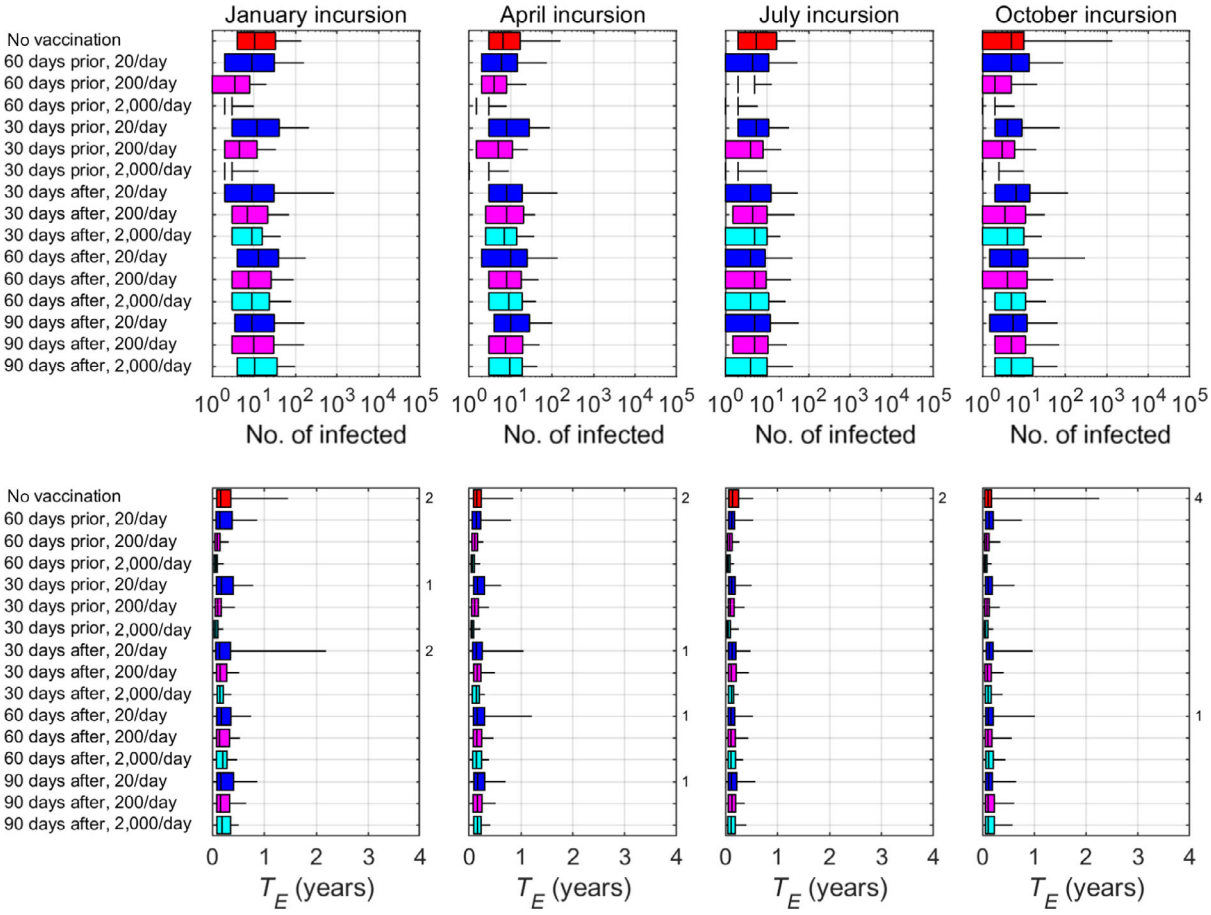

Figure A.1: Impact of vaccination on incursions of Rift Valley fever to Mayotte assuming a vaccine efficacy of 60%. The top row shows the cumulative number of infected animals and the bottom row shows the time to extinction (the numbers indicate the number of replicates for which RVFV had not been eliminated by the end of the third year of the simulation). Incursions were simulated in January, April, July and October and assumed a population with immunity equal to that after the 2018–2019 epidemic. Vaccination was implemented 60 or 30 days prior to or 30, 60 or 90 days after the incursion at a rate of 20, 200 or 2,000 animals per day. Box-and-whisker plots show the median (black line), interquartile range (box) and 2.5th and 97.5th percentiles (whiskers) for 100 replicates of the model

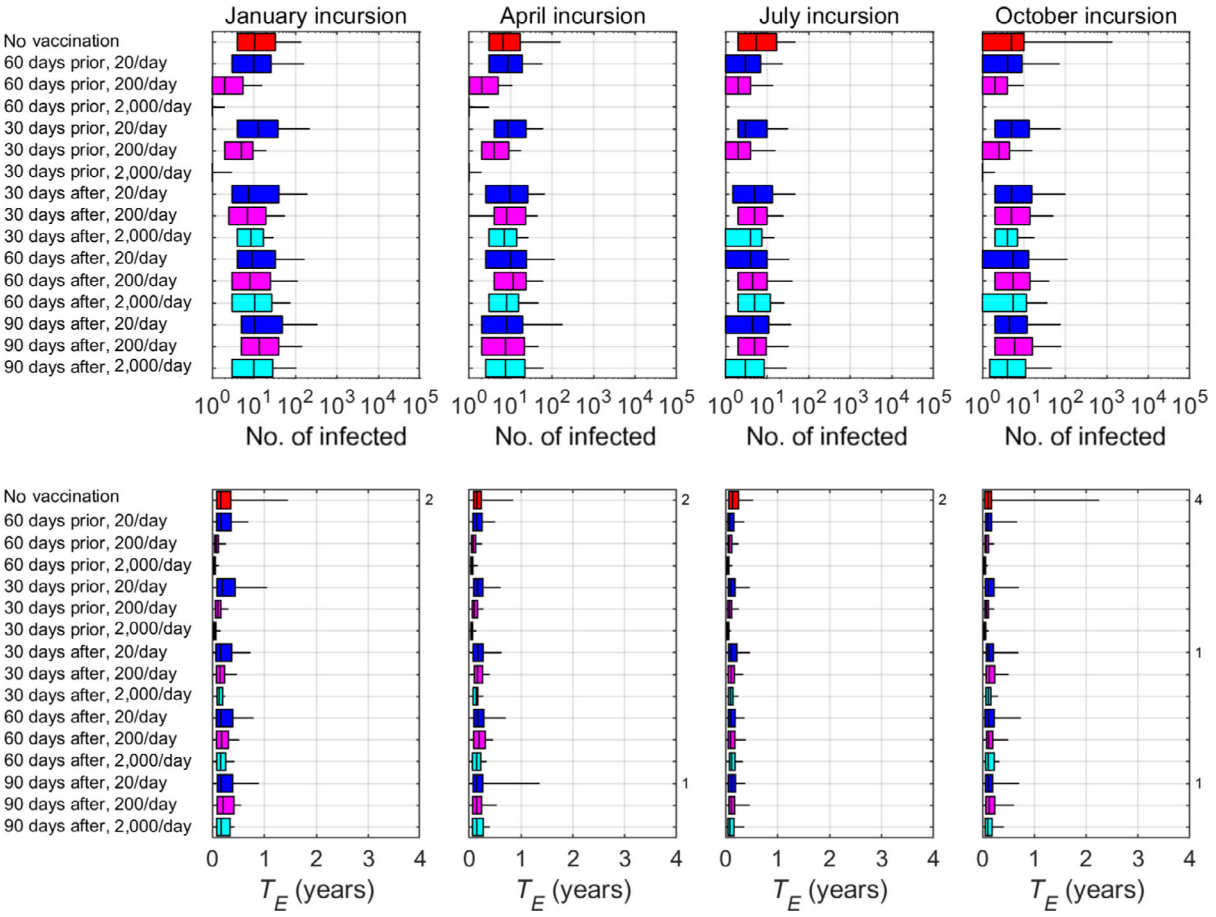

Figure A.2: Impact of vaccination on incursions of Rift Valley fever to Mayotte assuming a vaccine efficacy of 90%. The top row shows the cumulative number of infected animals and the bottom row shows the time to extinction (the numbers indicate the number of replicates for which RVFV had not been eliminated by the end of the third year of the simulation). Incursions were simulated in January, April, July and October and assumed a population with immunity equal to that after the 2018–2019 epidemic. Vaccination was implemented 60 or 30 days prior to or 30, 60 or 90 days after the incursion at a rate of 20, 200 or 2,000 animals per day. Box-and-whisker plots show the median (black line), interquartile range (box) and 2.5th and 97.5th percentiles (whiskers) for 100 replicates of the model

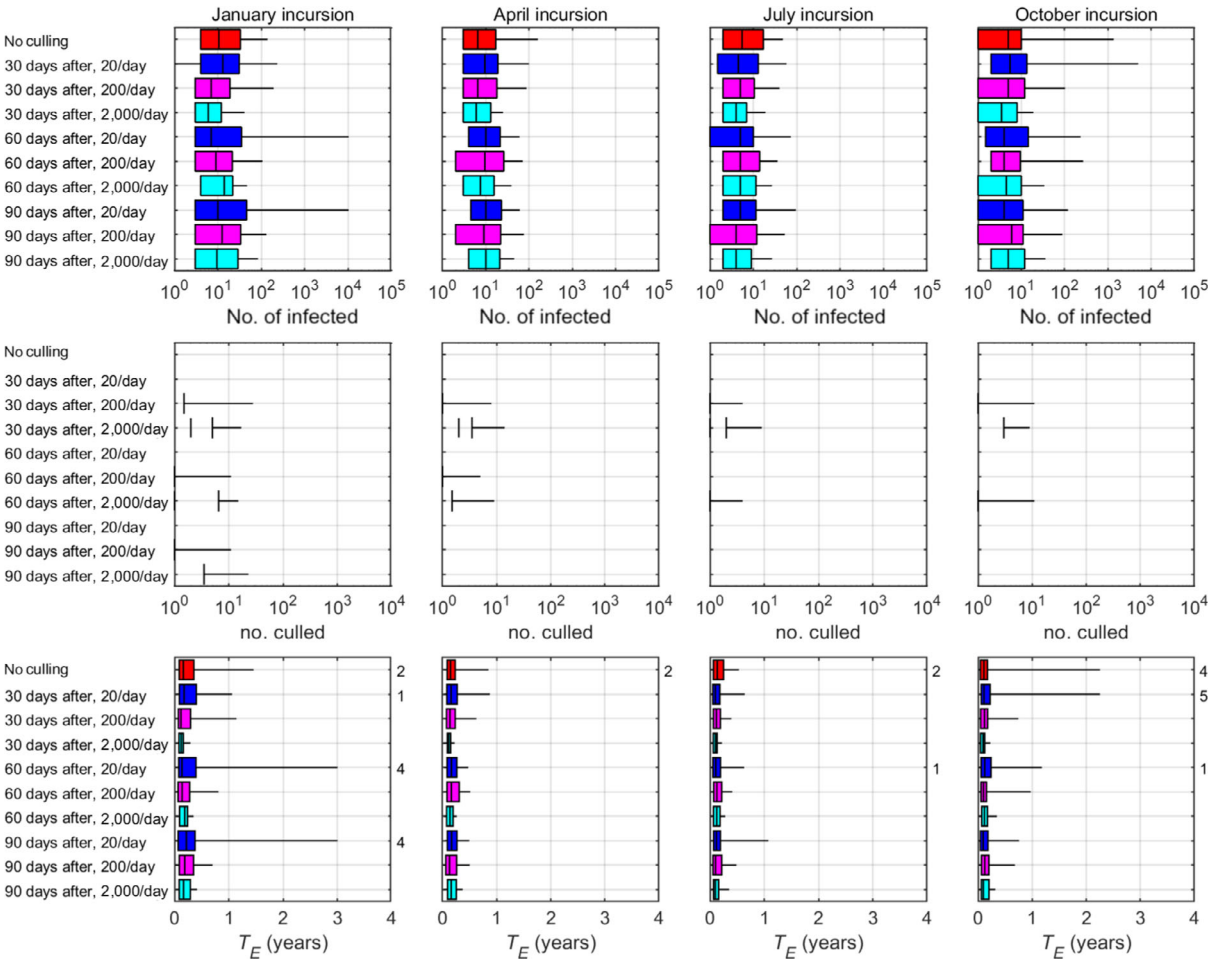

Figure A.3: Impact of culling on incursions of Rift Valley fever to Mayotte. The top row shows the cumulative number of infected animals (including those which were not detected and those which were detected and culled), the middle row shows the cumulative number of infected animals detected and culled, and the bottom row shows the time to extinction (the numbers indicate the number of replicates for which RVFV had not been eliminated by the end of the third year of the simulation). Incursions were simulated in January, April, July and October and assumed a population with immunity equal to that after the 2018–2019 epidemic. Culling was implemented as part of a test and cull strategy starting 30, 60 or 90 days after the incursion, with 20, 200 or 2,000 animals tested per day. Box-and-whisker plots show the median (black line), interquartile range (box) and 2.5th and 97.5th percentiles (whiskers) for 100 replicates of the model

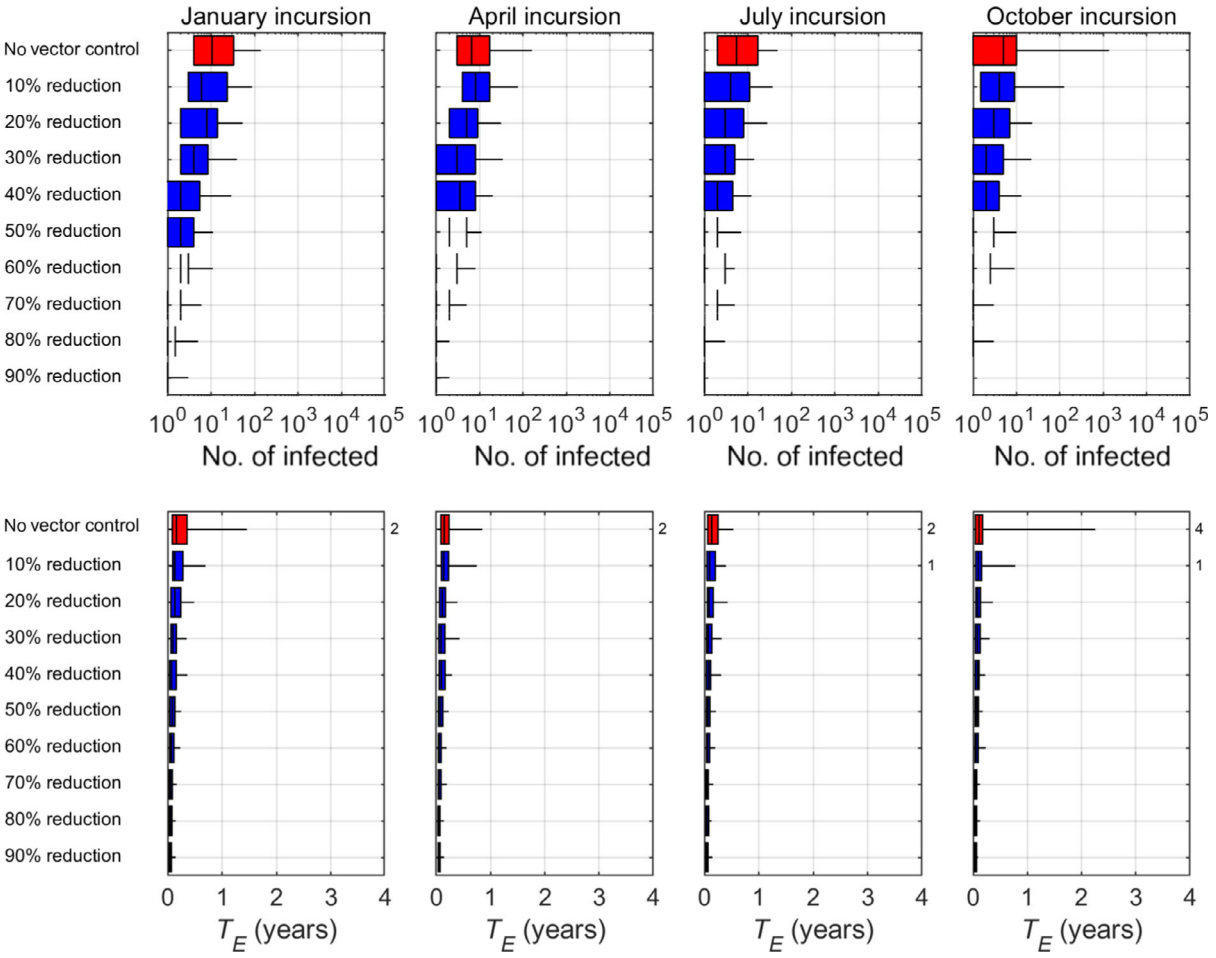

Figure A.4: Impact of reduced mosquito abundance through vector control measures on incursions of Rift Valley fever to Mayotte. The top row shows the cumulative number of infected animals and the bottom row shows the time to extinction (the numbers indicate the number of replicates for which RVFV had not been eliminated by the end of the third year of the simulation). Incursions were simulated in January, April, July and October and assumed a population with immunity equal to that after the 2018–2019 epidemic. Vector control measures were assumed to reduce abundance by 10–90%. Box-and-whisker plots show the median (black line), interquartile range (box) and 2.5th and 97.5th percentiles (whiskers) for 100 replicates of the model