Risk of Crimean Congo haemorrhagic fever virus (CCHFV) introduction and spread in CCHF-free countries in southern and Western Europe: A semi-quantitative risk assessment

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ABSTRACT

Crimean-Congo hemorrhagic fever (CCHF) is a severe tick-borne viral zoonotic disease caused by Crimean-Congo hemorrhagic fever virus (CCHFV). The disease is usually asymptomatic in domestic and wild animals, both of which may act as reservoirs of the virus. CCHF is endemic in parts of Africa, Asia, the Middle East and Eastern Europe. During the last decade, the emergence or re-emergence of CCHF was described in several countries in the Eastern Mediterranean Region, with an increasing risk of extension into new areas. Given the public health importance, this study undertakes a semi-quantitative risk assessment to analyse the likelihood of entry and exposure of CCHFV into 9 CCHF-free countries in Southern and Western Europe. Based on a framework outlining the probability of the virus entry and exposure, the risk estimates were assessed for each individual country. The risk assessment was performed using information from public databases and the available scientific literature. The likelihood of entry was conducted considering 3 main pathways: infected tick vectors, wildlife and livestock. The likelihood of exposure was assessed considering the probability of survival of the infected ticks once introduced in CCHF-free countries (depending on abiotic and biotic factors), and the exposure of resident un-infected susceptible ticks to infected imported wildlife and livestock. The risk estimates (combined CCHFV introduction and exposure) were low for the majority of the countries (Austria, Belgium, Germany, Luxembourg, Netherlands, Slovenia and Switzerland) and medium for France and Italy, if accounting only for animal health consequences. Considering the public health consequences only, the risks were rated low for all the countries, except for Italy where it was assessed to be medium.

1. Introduction

Crimean–Congo hemorrhagic fever virus (CCHFV) (family *Nairoviridae,* genus *Orthonairovirus*) is the causative agent of a tick-borne zoonosis disease (Crimean–Congo hemorrhagic fever - CCHF) which is endemic in Africa, the Balkans, the Middle East, and Asian countries [1].

The virus is transmitted to humans and animals by Ixodid ticks, mainly belonging to *Hyalomma* genus, with *H. marginatum* as the most relevant vector in Europe [2]. The geographic distribution of the disease is directly linked with the distribution of *Hyalomma* ticks, having a 50° North latitude limit [3]. Another transmission route to humans is through direct contact with blood and other body fluids of viraemic patients and animals. Therefore, people working in the agro-pastoral or animal husbandry fields and in contact with fresh flesh and blood from animals are most at risk of infection [4].

The disease presents a high fatality rate in humans (approximately 30%) [5], and significant difficulties in treatment, prevention, and control [6]. Clinical symptoms include fever, myalgia, nausea, vomiting, diarrhoea, hepatomegaly with abdominal pain, and agitation. These are generally followed by sleepiness, depression, and lassitude. Other signs are tachycardia, lymphadenopathy, petechial rash, and other haemorrhagic phenomena. In case of severe form, patients may experience kidney deterioration, sudden liver failure or pulmonary failure. The presence of such nonspecific prodromal symptoms makes it difficult to clinically distinguish CCHF infection from other undifferentiated febrile illness or viral haemorrhagic fevers (VHFs) [7].

In contrast to the disease in humans, CCHFV can circulate unnoticed in numerous wild and domestic animals as the infection does not cause significant clinical signs. In particular, high prevalence of antibodies against CCHFV has been detected in the sera of domestic animals such as
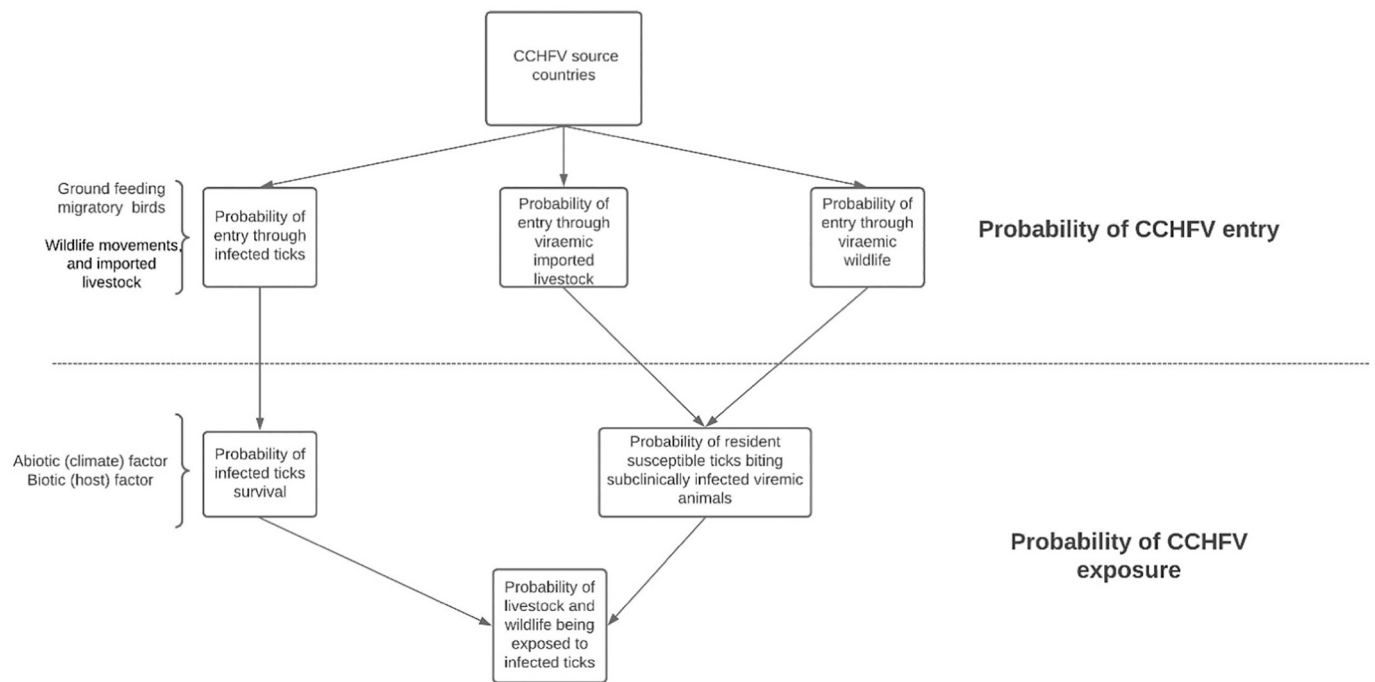
Fig. 1. Schematic flow chart showing the events considered in each step of the risk assessment.

cattle, horse, goat and sheep as well as in the sera of hares in Europe. This suggests that these animals play an important role in the epidemiology of CCHF [8,9].

H. marginatum is a two-host tick, with larvae and nymphs feeding on small mammals (e.g. hares) and ground-feeding birds, while adults on larger mammals (e.g. livestock and wild ungulates) [10,11].

Ground-feeding birds play an important role in the dispersal of ticks over long distances, and there are several records of *H. marginatum* being imported into Europe with migratory birds [10]. Despite their importance as mechanical vectors for ticks, the majority of the studies reported no evidence of CCHFV infection in birds [8].

Livestock (horses included) also have an important role in transporting large numbers of ticks into new areas. Contrary to birds, they develop viraemia and thus they may have an important role in the maintenance of CCHFV circulation and as sources of human exposure [8].

Among wildlife, hares are important hosts for immature *Hyalomma* ticks, as well as proficient amplifiers of the virus. In Eastern Europe, the increase in hare populations, as a result of changes in land use and hunting practices, seem to be linked to high levels of CCHFV circulation [12]. Other animals playing a considerable role in the epidemiology of the disease are large mammals, such as wild boar and red deer. Unpublished data from Turkey suggests that the areas where most of the CCHF human cases have occurred had a significant increase in wild boar density [1]. Likewise, a large proportion of red deer have proven to be exposed to CCHFV in Spain, where CCHF has been recently reported [13,14].

The rise in the population densities of wild boars and deer could facilitate the spread of CCHFV through a parallel increase in tick numbers and dispersion across Europe [11]. Migration of animals is recognized to be especially sensitive to climate warming, and changes in host migratory patterns have important consequences for infectious diseases. During the last decade, climate change exerted an important role on the change of wildlife ranges into new areas, this in turn increased significantly the risk of introduction and spread of pathogens into previously unexposed host populations. [15–19]. Climate change has also a direct influence on tick survival, activity, and development, as well as on the vegetation structure, where ticks may find their ecological optima [20].

For all these reasons, CCHF has been identified as a priority disease for the EU [6]. Several experts have expressed their concerns on the spread of the virus outside its current geographic range through the introduction of infected ticks by migratory birds, wild mammals or the international livestock trade [21,22].

Given the public health importance of the disease, the objective of this study is to perform a semi-quantitative risk assessment on the risk of CCHFV introduction and spread in CCHF-free countries in Southern and Western Europe using the most updated information available.

2. Materials and methods

2.1. Risk question

The risk question to be addressed was:

- What is the current risk of CCHFV introduction and spread in CCHF-free countries in Southern and Western Europe?

In this study, the risk question was addressed using the most updated information available (2018–2020). An exception was done for data on: i) European hare (*Lepus europaeus*) occurrence for which the period 2010–2021 was used due to the limited information and large variability among years [23], ii) biotic factor influencing *H.marginatum* suitability for which the output of the model developed by Estrada-Peña et al. 2015 was used as reference [24], iii) expenditure on health as a percentage of gross domestic product for which the latest data available was 2013 [25].

2.2. Risk framework

The risk assessment methodology developed by the World Organization for Animal Health (OIE) for the import of animals and animal products was adopted [26]. The risk assessment is characterized by 4 inter-related steps: i) entry assessment, ii) exposure assessment, iii) consequences assessment, and iv) risk estimation (Supplementary material A-FigS1). For the purpose of this study, the countries which could

act as sources of the virus were retrieved from the Global CCHF Risk map, showing the areas with active CCHFV circulation (virological and serological evidence) (Supplementary material D) [3]. With regards to the countries considered to be free of CCHFV, the authors focused on the nine CCHF-free countries in Southern and Western Europe (Austria, Belgium, France, Germany, Italy, Luxembourg, Netherlands, Slovenia and Switzerland). The target countries were selected as they are classified within the geographical sub-regions of interests by the UN Statistics Division [27], and they have no virological or serological evidence of CCHFV circulation [3]. The risk assessment was performed separately for each country.

For this assessment, "entry" or release corresponds to the entry of the hazard (i.e. CCHFV) into CCHF-free countries through infected ticks, viraemic wildlife or imported livestock. The exposure assessment evaluates the parameters that determine the establishment and spread of the virus depending on i) survival of the infected tick once introduced into the CCHF-free countries, and ii) the exposure of resident uninfected susceptible ticks to infected imported wildlife and livestock. The authors focused only on *H. marginatum* species, due to the epidemiological importance of this species in CCHFV transmission in Eurasia [28].

The framework of the risk assessment for this analysis is provided in Fig. 1.

2.3. Risk pathway

The theoretical probability of each event in the pathway was assessed using data from scientific literature and public databases. All the factors considered in the assessment were quantified with a basic scoring system from 0 (minimum impact) to 3 (maximum impact). This process was done with consultation and consensus of two international

Table 1
Factors used to assess the likelihood of entry of CCHFV into EU free-countries.

Factor	Explanation	Data Source
Number of CCHFV source countries within the main birds flyways (Supplementary material-Fig.S2)	Given the shapefile of the main flyways including the countries of interest, the number of source countries was evaluated using the geoprocessing tools in QGIS software [28]. These are used to establish the potential connections with CCHFV source countries.	The CMS Flyways Working Group [29]
Number of species of ground-feeding migratory birds[a] shared with CCHFV source countries	The ground-feeding migratory birds species shared with CCHFV source countries were extracted from Bird species distribution maps of the world using the geoprocessing tools in QGIS software [28]	http://datazone.birdlife.org/species/requestdis [30]
Number of neighbouring CCHFV source countries	The number of neighbouring CCHFV source countries were counted to assess the risk of wildlife cross-border movement.	
Number of live animals imported from CCHFV source countries	Total number of livestock and horses imported in 2019 (most recent information available) from CCHFV source countries	https://comtrade.un.org/ [31]
Number of CCHFV source countries as exporting trading partners	Total number of CCHFV source countries as exporting trading partners of live animals (livestock and horses) in 2019 (most recent information available)	https://comtrade.un.org/ [31]

[a] The ground-feeding migratory birds species were retrieved from List of birds of the European Union available at https://ec.europa.eu/environment/nature/conservation/wildbirds/eu_species/index_en.htm

experts. The experts were selected based on their expertise on CCHF epidemiology as well as on risk assessment methodology. The experts were met once per week over four weeks to discuss the information on every event in the pathway. A table summarizing the gathered data was prepared and scores were assigned during the discussion (Supplementary material B). The final sum was then translated into adjectives to describe the levels of probabilities (respectively entry and exposure) and the magnitude of consequences (Supplementary material A-table S1). To do so the values were categorized into intervals linked to qualitative outputs following an ordinal scale of ranges (Supplementary material B). The qualitative probability scale used in this risk assessment is described in table S2 (Supplementary material A). The final estimate of risk was obtained by combining the probability of occurrence and the magnitude of consequences. The probability matrix was built applying the following concept: when combining two probabilities, the resulting probability is not greater than the lower probability scale of the two (conditional matrix adapted from Wieland et al. 2011 [29]-Supplementary material A- table S3). The uncertainty associated with assigning a probability was expressed in qualitative terms (adapted from Hartley et al. [30]-Supplementary material A- table S4).

2.4. Consequences assessment methodology

The consequences were assessed for both animal and human populations following the method proposed by Dufour et al. [31]:
for animal health consequences:

 i) Health and economic consequences for a particular holding
 ii) Likelihood of disease spread in livestock and wildlife
 iii) National and international economic consequences

for public health consequences:

 i) Individual gravity (burden of CCHFV infection in humans)
 ii) Likelihood of disease spread in human populations
 iii) Overall health and economic consequences

Animal and public health consequences were assessed separately.

2.5. Data sources

Information used to estimate the pathway probabilities are summarised hereunder.

2.5.1. Probability of entry
The factors considered for the entry assessment are listed in Table 1. Specifically, the probability of entry through infected ticks on migratory birds was assessed considering the number of CCHFV source countries within the main birds flyways and the number of ground-feeding migratory birds species shared with CCHFV source countries. The list of migratory birds was retrieved from the EU Bird List (Supplementary material C). The risk posed by waterbirds was considered negligible and was not included in the assessment. The number of neighbouring CCHFV source countries was used as a proxy to assess the probability of entry through infected ticks on wildlife and the probability of entry through viraemic wildlife. Finally, the probability of entry through infected ticks on imported livestock and the probability of entry through viraemic livestock was considered to be proportionate to the quantity of livestock imported from CCHF affected countries and the number of CCHF affected exporting trading partners.

2.5.2. Probability of exposure
The probability of infected ticks survival once introduced was

evaluated consulting the output[1] of the spatial model developed by Estrada-Peña et al. [24] for the abiotic (climate) factor. Additionally, the reported distribution of indigenous *H. marginatum* [32] was used as an index of favourable conditions for the spread of ticks and the probability of resident susceptible ticks biting viraemic animals. Countries at higher risk of exposure were considered the ones where *H. marginatum* is widely distributed. The biotic factor (host availability) influencing the probability of infected ticks survival and the probability of livestock and wildlife being exposed to infected ticks were evaluated using data from 2 public databases: i) information on the European hares, considered as the main wildlife reservoir for the virus, occurrence over the last 10 years was retrieved from GIBIF [23], ii) figures on density of cattle, sheep, goats and horses (expressed as livestock units) was derived from FAOSTAT (most updated information 2018) [33].

2.5.3. Consequence assessment

Information retrieved from scientific publications and public databases was used to assess the consequences Specifically, for each item (in bracket) the following questions were considered.

For animal health consequences:

  i) What is the degree of livestock suffering from CCHFV infection? Does CCFHV infection in livestock lead to reduced income for farmers? (Health and economic consequences for a particular holding):
 ii) Is the competent vector widely distributed in the country? (Likelihood of disease spread in livestock and wildlife)
iii) Are CCHF contingency plans implemented in the country? Does CCHF impact on free exchange on animals and animal products? (National and international economic consequences)

For public health consequences:

  i) What is the burden of CCHFV infection in humans? (Individual gravity)
 ii) Can CCHFV spread easily in human populations? (Likelihood of disease spread in human populations)
iii) What is the level of efficiency of the country health system? (Overall health and economic consequences)

For the last item, the expenditure on health as a percentage of gross domestic product was used as an indicator of the health system efficiency [25].

3. Results

Table 2 shows the probability of occurrence for each country, considering the probability of entry and exposure of CCHFV. The probability of entry is medium for the majority of the countries, low for 3 countries and high for 1 country (France). The level of uncertainty is medium for all the countries. The probability of exposure is low for 6 out of 9 countries, medium for 2, and high for 1 country (Italy). The level of uncertainty is low for all the countries with the exception of Slovenia, for which the uncertainty is estimated to be medium as information on *H. marginatum* presence is lacking [32]. Applying the probability matrix, the authors conclude that the likelihood of occurrence is low for all the EU free-countries, except for France, Germany and Italy where it is estimated to be medium.

As shown in Table 3 the magnitude of the consequences for animal health were considered high for Italy, medium for France and Switzerland, and low for the remaining countries. The consequences for public health are low and medium, for two-thirds and one-thirds of the countries respectively.

The assessed risk for animal and human population is depicted in Fig. 2. Considering only the animal health consequences, the combination of the probability of occurrence and the consequences of occurrence is low for every country, excluding France and Italy where the risk is estimated to be medium (Fig. 2, a). The risk is medium only for Italy if evaluating the Public Health consequences, whereas the rest of the countries have a low risk (Fig. 2, b).

4. Discussion

In this study, we conducted a semi-quantitative assessment of the risk of introduction and spread of CCHFV into 9 CCHF free-countries in Southern and Western Europe. Prior to this work, the risk prediction of CCHFV incursion in Europe was made based on expert opinion only at regional level [34], not addressing country characteristics that might increase the risk of introduction and spread.

A GIS- based approach has been proposed by Gale et al. [35] to account for the complexity of vector borne diseases epidemiology. In line with this, Messina et al. [36] created a map of environmental suitability for CCHF occurrence. Also Esser et al. [36] used geostatistical analyses to identify the areas at higher risk of CCHFV occurrence in Netherlands. Although spatial modelling has increasingly been employed as a support for decision makers and diseases surveillance [37–42], it requires quantitative (spatial) information, which is very rarely available, especially if large areas need to be covered. Considering this constrain, this study used a semi-quantitative risk assessment framework, which allows to incorporate not only environmental factors, influencing mainly vector suitability, but also data on livestock trade and proxy for wildlife cross-border movements. This is of particular importance as ticks are constantly introduced into new areas through movement and transport of wildlife and livestock [35]. Additionally, in contrast with the spatial approach, the risk assessment methodology specifically assesses the consequences for animal and public health, which are an essential step to estimate the risk [31].

Table 2
Likelihood of occurrence of CCHF into EU free-countries.

Country	Likelihood of entry (Uncertainty)	Likelihood of exposure (Uncertainty)	Likelihood of occurrence
Austria	Medium (Medium)	Low (Low)	Low
Belgium	Low (Medium)	Low (Low)	Low
France	High (Medium)	Medium (Low)	Medium
Germany	Medium (Medium)	Medium (Low)	Medium
Italy	Medium (Medium)	High (Low)	Medium
Luxembourg	Low (Medium)	Low (Low)	Low
Netherlands	Medium (Medium)	Low (Low)	Low
Slovenia	Medium (Medium)	Low (Medium)	Low
Switzerland	Low (Medium)	Low (Low)	Low

Table 3
Assessment of animal and public health consequences.

Countries	Animal health consequences	Public health consequences
Austria	Low	Low
Belgium	Low	Low
France	Medium	Low
Germany	Low	Low
Italy	High	Medium
Luxembourg	Low	Medium
Netherlands	Low	Low
Slovenia	Low	Medium
Switzerland	Medium	Low

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[1] See figure 4 "Classification of the target territory into categories of suitability for *H. marginatum*" presented in the work of Estrada-Peña et al. (2015)
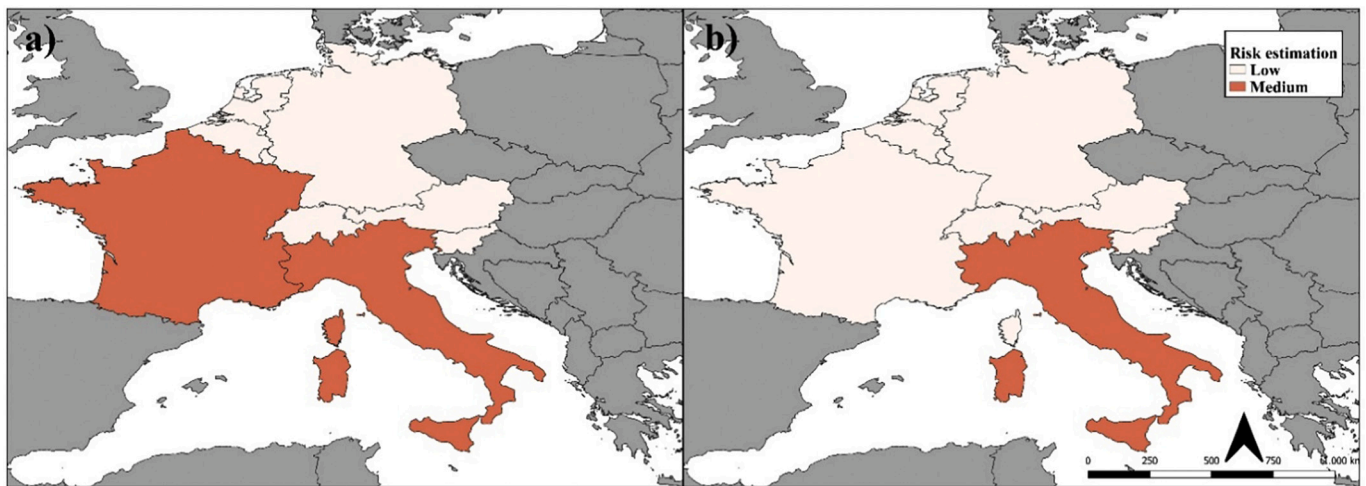
Fig. 2. CCHFV Risk estimation considering animal health (a) and public health (b) consequences. *Countries excluded are grey marked in the map.*

In this study, the final risk estimates were low for the majority of the countries (Austria, Belgium, Germany, Luxembourg, Netherlands, Slovenia and Switzerland) and medium for France and Italy when considering the animal health consequence. Likewise, the risks were rated medium for Italy and low for the remaining countries if accounting for the public health consequences. The low risk of CCHFV entry and exposure in most of the countries for both animal and public health is influenced by the low probability of spread of the virus. This depends mainly from the countries characteristics for the successful establishment of permanent tick populations [24].

In this study, the risk assessment was conducted considering only three pathways: infected tick vectors, wildlife, and livestock. These routes have been estimated to be non-negligible through the elicitation of expert opinion [43]. Other routes of CCHFV introduction are possible; including human mobility, trade in animal products and pet movements [34]. These have been considered in a recent review on the epidemiological aspects of CCHF in Western Europe, highlighting that the introduction of *H. marginatum* associated to human and pets travel cannot always be ruled out [44]. However, the risk of CCHFV introduction through these routes is thought to be rare and thus, they were not accounted in this study.

The probability of infected ticks entering into CCHF-free EU countries should be evaluated considering the frequency of occurrence of ticks on migratory birds, mammals movements, and imported livestock (including horses), as well as the origin of those ticks and their hosts [34]. Obtaining accurate information on these factors is complex. This is especially true for the risk of introduction by migratory birds, for which surveillance should be improved. Because of the gaps in such data, the uncertainty around the likelihood of CCHFV entry into CCHF-free Southern and Western EU-countries is estimated medium. Indirect factors can be used as surrogate for a semi-quantitative assessment in case of lack of data. In this sense, the authors evaluated the number of migratory ground-feeding bird species shared with CCHFV source countries, which suggest a greater richness in Southern Europe [45]. Indeed, although the number of connections with the CCHFV source countries through flyways is higher for the Western countries (Belgium, France, Germany, Luxemburg and Netherlands) that are included in the two main European migratory routes (the East Atlantic Flyway and the Mediterranean/Black Sea Flyway) (Supplementary material A-Figure S2), the number of ground-feeding migratory birds species is almost twice in Italy ($n = 84$) than Germany ($n = 55$), and even 3 times higher than Luxemburg ($n = 27$). The richness of migratory birds follows a latitudinal gradient, with Mediterranean countries showing higher values than central and northern Europe.

Infectious diseases, including tick-borne diseases, are constantly

introduced into new areas through short and long distance movement of wild mammals [32]. Countries where there is active CCHFV circulation may pose a high risk for the virus introduction in neighbouring countries through cross border circulation of wild animals. In this sense, the risk of entry through wild mammals movements increases for Slovenia, which shares more than one border with CCHFV source countries. Nevertheless, large mammals (e.g. deer and wild boar) have usually wide home-range, and tend to roam over large distances in search of new territories, resources or food [47]. Thus, the risk of introduction through infected ticks on wildlife and viraemic wildlife cannot be excluded in areas which are distant from CCHFV source countries. Importantly, the risk of introduction through wild mammals movement is also influenced by the environmental features of the border (e.g. presence of mountains, lakes, hills) and the ecological pattern of the species. This requires a detailed evaluation of the countries characteristics and the species considered. In this study, we used a simplified approach accounting only for the number of borders shared with CCHFV source countries. This should be considered when evaluating the results obtained.

In Southern and Western Europe, the trade of domestic animals with countries outside and within EU is well regulated, with animals subjected to strict border inspection [48]. However, CCHFV is not screened regularly, and does not cause any clinical symptoms in animals, thus the detection of viraemia in the imported livestock is highly improbable. Similarly, the detection of ticks on imported animals is unlikely. Considering the reasons above, the introduction of CCHFV through the trade of infected livestock (together with adult ticks) may easily pass unnoticed. The prevalence of CCHF infection in the exporting countries is a determinant of the probability of the virus entry. Several authors published surveys on CCHFV infection in various countries and species. However, most of them were performed decades ago, and there is a high variability in the number of studies available and species sampled for each country [8]. Given the lack of comparable data, the authors decided not to weight the probability of entry with the prevalence of CCHF in the exporting countries. Instead, the number of trading partners serving as CCHFV source, together with the total number of live animals imported were considered. France, Germany and Netherlands resulted to trade with the greatest number of CCHFV source countries, importing the highest number of domestic animals ($>$100,000 heads) in 2019 [49].

Central to the exposure assessment are the tick adaptation to the new environments and the presence of resident ticks which might be infected with CCHFV. For the first factor, the success of colonization is influenced by the spatial and temporal overlap between the environmental conditions suitable for tick survival and the vulnerability of the territory, intended as the availability of suitable hosts. With the exception of Italy and France, which are characterized respectively by an optimal and

suboptimal climate suitability, the risk of *H. marginatum* to successfully establish is estimated to be still low, even if adequate climatic conditions for the life-cycle of *Hyalomma* improved over the last decades [24]. It is important to bear in mind that this assessment is a general evaluation at the country level, without accounting for the fact that ticks suitability vary greatly within countries. Additionally, a geographical variation of *H. marginatum* distribution exists. Italy is the only CCHF free countries with a widely distributed *H. marginatum* resident population, whereas local heterogeneity is present in France with a hotspot in the Southern part of the country. The presence of imported ticks is also reported in several zones of Western Europe [32].

The host availability is an important factor influencing the probability of exposure. In this assessment, the authors focused only on domestic animals and European hare populations, due to the important role of lagomorphs in the disease epidemiology. With regards to domestic animals, the countries at higher risk are Italy and France where the high densities of livestock (> 500,000 LSU) may facilitate the disease spread. Interestingly, these are also the countries with the most suitable climate for *Hyalomma* life cycle.

Hare is considered to be one of the main wildlife reservoir for CCHFV [1], playing a pivotal role in the epidemiology of the disease [50]. The European hare is the most common hare species in Europe, and it has one of the largest range of any mammal species [51]. For this reason, if CCHFV enters into an EU free country, the potential risk for the virus spreading may be quite high. Specifically, the occurrence of the European hare is higher in France, Germany and Netherlands than the other countries included in this study [23].

The assessment of consequences is a key step in the risk assessment method that requires a One Health approach, heeding of both animal and human populations [31]. Using the available literature to estimate the magnitude of the consequences for animal health, the authors concluded that the magnitude is low for the majority of the countries. In fact, CCHFV infection does not cause severe clinical signs in livestock, and infection is generally subclinical [1]. Thus, generally, there are no negative micro-economic consequences at farm level (e.g. reduction in the productive capacity of the animals). Nevertheless, the macro-economic consequences are estimated to be very high. Indeed, CCHF is an OIE–listed diseases, and it may impact on free exchange on animals and animal products.

Further costs related to the disease may include the eradication and surveillance activities, comprising extra precautions on slaughter-houses. Considering the approach suggested by Dufour et al. [31], the magnitude of consequences for animal health are estimated to be high only in Italy as the spread of the virus can be facilitated by the presence of indigenous *Hyalomma* population.

When assessing the consequences for human health, two items are particularly important: the consequences at individual and at the community level. In the case of CCHF, the disease burden, defined as loss of QALY's (quality adjusted life years), is estimated to be high for infected people. The direct healthcare costs for patients hospitalized may vary according to the severity of the illness [52], but they are overall estimated to be high. Furthermore, there are other costs to be considered, which are related to the provision of adequate infection control materials, the labour and investigational costs, as well as the travel costs to hospital for the patient and family for relatives visiting.

The 'spreading abilities' of the disease are of pivotal importance when considering the consequences of the disease at a community level [31]. In contrast to other emerging viruses, human-to-human transmission of CCHFV is typically limited occurring in a household or nosocomial setting when no proper personal protective equipment is worn [53]. Therefore, cases of CCHF in Western and Southern Europe are likely to be sporadic and limited to those who are in frequent contact with livestock, wildlife or those who lives in areas where ticks are present.

With regards to the mortality rate, the WHO estimated that it is approximately 30% [5], however, this can drop drastically thanks to a rapid diagnosis and a trained medical staff. Indeed, the case fatality rate of CCHF depends on the available health-care system infrastructure [54]. In the countries included in this study, the expenditure on health as a percentage of gross domestic product (proxy of the health system efficiency) is quite high, ranging from 6.94% in Luxemburg to 11.66% in Switzerland [25], therefore, the authors concluded that the overall health and economic consequences are minimal.

For the above-mentioned reasons, the public health consequences are estimated to be low or medium depending on the individual country. Nevertheless, an important factor which might negatively influence the economy of a country in case of CCHFV introduction is the public perception of the disease. For instance, people may start to avoid certain animal products leading to drop in market prices, as well as there can be a negative impact on the tourism industry.

In this risk assessment, the presence of uncertainty and lack of data for some factors were the major challenges to establish the risk estimates. Considering this, the authors decided not to use the uncertainty levels for the calculation of risks. Instead, the uncertainty levels were provided separately for the likelihood of entry and the likelihood of exposure in order to make the risk assessment more transparent and understandable. In particular, the likelihood of introduction needs to be interpreted with attention, given the medium uncertainty related to the lack of data on the frequency of occurrence of CCHFV infected ticks on migratory birds. This is believed to be the most likely route of introduction of the virus, and further researches are needed to better assess this component.

Another limitation was represented by the absence of accurate estimations on wildlife density. Such knowledge would have allowed improving the exposure assessment, reducing the uncertainty of the exposure likelihood.

Finally, when evaluating the livestock density, we did not account for the farming system (extensive vs intensive) in place in each country due to the lack of information. This should be considered since it may also play a role in shaping the risk exposure probability.

5. Conclusion

This study presents the first semi-quantitative risk assessment of CCHFV introduction and spread in CCHF-free countries in Southern and Western Europe. Qualitative and semi-quantitative risk assessment may provide a useful tool when data is not statistically powerful to perform a quantitative assessment. This methodology presents the available evidence in a transparent manner, allowing for uncertainty to be considered. The findings from this study can inform risk managers about the risk of CCHFV, helping them to identify the most effective risk mitigation options. Considering the lack of updated information on CCHFV circulation and prevalences in animals, the authors suggest that further studies should be carried out in order to improve the accuracy of future risk assessments. The finding of low and medium risk will need continual updating as the risk may be higher or lower depending on the time-windows evaluated. This is particularly true given the potential for climate change to alter the current status. Indeed, it is expected that the climate and environmental changes may affect CCHFV epidemiology, influencing the migration behaviour strategy and routes of the ground-feeding birds, as well as impacting on hares abundance, which may increase through milder winters and enhanced heavy rainfall [43]. Of particular interest to the introduction of *H. marginatum* ticks are the models of bird migratory behaviour and tick cycling [55]. These may be useful for predicting the emergence of CCHF in Southern and Western Europe. Considering these reasons, the authors highlight the importance of update the present risk assessment and refine the risk prediction under future scenario.

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Declaration of Competing Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the manuscript and there is no financial interest to report. We certify that the submission is original work and is not under review at any other publication.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.onehlt.2021.100290.

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