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REVIEW

Eco-Epidemiological Uncertainties of Emerging Plant Diseases: The Challenge of Predicting *Xylella fastidiosa* Dynamics in Novel Environments

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ABSTRACT

In order to prevent and control the emergence of biosecurity threats such as vector-borne diseases of plants, it is vital to understand drivers of entry, establishment, and spatiotemporal spread, as well as the form, timing, and effectiveness of disease management strategies. An inherent challenge for policy in combatting emerging disease is the uncertainty associated with intervention planning in areas not yet affected, based on models and data from current outbreaks. Following the recent high-profile emergence of the bacterium *Xylella fastidiosa* in a number of European countries, we review the most pertinent epidemiological uncertainties concerning the dynamics of this bacterium in novel environments. To reduce the considerable ecological and socio-economic impacts of these outbreaks, eco-epidemiological research in a broader range of environmental conditions needs to be conducted and used to inform policy to enhance disease risk assessment, and support successful policy-making decisions. By characterizing infection pathways, we can highlight the uncertainties that surround our knowledge of this disease, drawing attention to how these are amplified when trying to predict and manage outbreaks in currently unaffected locations. To help guide future research and decision-making processes, we invited experts in different fields of plant pathology to identify data to prioritize when developing pest risk assessments. Our analysis revealed that epidemiological uncertainty is mainly driven by the large variety of hosts, vectors, and bacterial strains, leading to a range of different epidemiological characteristics further magnified by novel environmental conditions. These results offer new insights on how eco-epidemiological analyses can enhance understanding of plant disease spread and support management recommendations.

Keywords: bacterial pathogens, disease control and pest management, ecology, emerging infectious plant disease, epidemiology, epidemiological model, pest risk assessment, plant health, *Xylella fastidiosa*

Rapid environmental changes and human activities have been linked to disease emergence and reemergence in humans, animals, and plants, mainly due to the creation of new pathways of contact among hosts, vectors, and pathogens. In particular, vector-borne diseases represent a major challenge for epidemiologists as their complex dynamics often entails multihost multivector transmission, the exact details of which tend to vary in different pathosystems (Hollingsworth et al. 2015). To prevent and control the spread of these diseases, it is crucial to understand drivers of entry and establishment, spatiotemporal disease progress, and effectiveness of control strategies (Cunniffe et al. 2015). However, data on the epidemiology of plant pathogens is often limited, host and vector population structure can be difficult to characterize, and human-mediated movements of plants and vectors can exhibit considerable stochasticity over time and space. Additionally,

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infection rates are strongly controlled by environmental conditions, and disease is frequently cryptic and/or poorly reported, particularly in noncrop hosts (such as wild hosts) (Cunniffe et al. 2015). Thus, a better understanding of these drivers is paramount to reduce the level of uncertainty in pest risk assessments and disease management strategies. This is particularly important in addressing the inherent policy challenge associated with emerging disease, where policy makers must make projections from data-rich areas to data poor areas (Yates et al. 2018).

Xylella fastidiosa is a widespread vector-borne pathogen considered one of the most complex threats to plant health worldwide (Sicard et al. 2018) (Box 1). First described in California in 1892 as the cause of the devastating Pierce's disease (PD) of grapevines, it is no longer restricted to the Americas (EPPO 2020). Currently, it threatens natural areas and horticultural, agricultural, and forestry sectors as the recognized agent of numerous severe and economically important diseases of crops and landscape plants (Almeida and Nunney 2015). In 2013, *X. fastidiosa* was discovered in Europe in the ancient olive groves of Puglia (Italy) and subsequently recognized as the causative agent of the olive quick decline syndrome (OQDS) outbreak (or in Italian CoDiRO-Complesso del Disseccamento Rapido dell'Olivo), where it is still killing millions of olive trees (Saponari et al. 2019). After the first detection in Europe, the bacterium has been isolated in outbreaks in Corsica (France), the southern region of Côte d'Azur (France), the Balearic Islands (Spain), the Norte Region (Portugal), and the autonomous community of Valencia (Spain) (EFSA PLH 2019), but single detection events are also reported from elsewhere (EPPO 2020).

Following these first detections of *X. fastidiosa* in Europe, emergency measures were instigated by the European Commission in order to reduce further spread (Decision EU 2015/789 and updates). These measures were driven by the fact that although relatively little is known of the full potential geographical range of *X. fastidiosa* in Europe, there is a risk of further establishment and human pathways might facilitate introduction into new locations (EFSA PLH 2019). Such decisions must be grounded in scientific understanding, and therefore policy-makers have been relying upon scientists to provide the epidemiological knowledge required to develop effective surveillance and control measures, reliable pest risk assessments, and appropriate disease management plans and mitigation strategies (EFSA PLH 2019). Increasing the effectiveness of plant health regulations is imperative, particularly due to the current intensification of recognized risk factors for the introduction and spread of *X. fastidiosa* (e.g., human-mediated environmental modifications, expansion of bacterium/host/vector range, high volumes of plant trade) (Pautasso et al. 2015), and yet, many fundamental epidemiological questions remain unanswered. Moreover, policy based on current epidemiological knowledge might not be suitable for current *Xylella*-free countries, where environmental and human-related conditions may be significantly different from the locations of existing outbreaks. Indeed, introduction, establishment and spread of *X. fastidiosa* in a novel environment is the result of new combinations of biotic interactions, abiotic conditions, and human-mediated processes, underlining the substantial value of epidemiological data from multiple settings (Yates et al. 2018). Although modeling and evidence-based approaches have been commonly used to support policy decisions, the predictive and explanatory abilities of models are highly dependent on the accuracy of spatiotemporal epidemiological data and directly measured parameters, which are typically lacking in the case of emerging diseases (Parnell et al. 2015). This emphasizes the importance of identifying and targeting current *X. fastidiosa* eco-epidemiological knowledge gaps. Similarly, designing and implementing effective predictive, monitoring, and control measures in different environmental and legislative settings also poses new challenges for scientists and regulators who are urged to prevent potential yield loss and restriction of trade of important crops (e.g., grapevines in California, Tumber et al. 2014; *Citrus* spp. in Brazil, Gonçalves et al. 2014; olives in Italy, Schneider et al. 2020).

In this paper, we illustrate the major eco-epidemiological uncertainties and knowledge gaps to be filled in order to characterize the dynamics of *X. fastidiosa* in novel environments. We elicit expert knowledge and opinion from a range of scientists, industry representatives, and regulators with experience of plant diseases and use the results to rank the uncertainties in terms of their importance to eco-epidemiology and to plant procurement and disease management strategies. The aim is to identify the most important factors affecting *X. fastidiosa* transmission and emergence risk, which can provide a direction to future research in order to understand, prevent, and manage *X. fastidiosa* outbreaks in current locations and novel environments.

FACTORS INFLUENCING UNCERTAINTIES IN PREDICTING *X. FASTIDIOSA* INTRODUCTION, ESTABLISHMENT, AND SPREAD

In order to understand *X. fastidiosa* eco-epidemiology, we display the epidemiological factors in Figure 1A, which symbolizes not only the basic factors associated with disease causation for *X. fastidiosa*—namely, the bacterium–host–vector triad, but also the other eco-epidemiological elements affecting disease dynamics with their mutual connections. In *X. fastidiosa* pathosystems,

BOX 1

SUMMARY OF *XYLELLA FASTIDIOSA* BIOLOGY AND ECOLOGY

X. fastidiosa is a gammaproteobacterium (Xanthomonadaceae) that colonizes plant xylem vessels. Transmitted exclusively by xylem sap feeding insects (Hemiptera, Auchenorryncha), it multiplies in host's xylem vessels, often leading to desiccation of the plant (Rapicavoli et al. 2018). The pathogen has a semipersistent relationship with the vector, meaning that it colonizes and persists in the foregut but is not transmitted between insect life stages (Purcell and Finlay 1979). The potential host plant pool comprises more than 500 species, of which it can be a harmless endophyte, or cause severe disease (EFSA PLH 2019). The variability of host plants matches the high genetic diversity of this pathogen, of which different subspecies and strains display a loose host specificity (Rapicavoli et al. 2018). Symptoms caused by *X. fastidiosa* infection are nonspecific, mostly generic indications of hydric stress, such as drying of leaf margins, scorched leaves, and wilting, and vary in intensity depending on host species, pathogen genotype, environmental conditions, and host–bacterium association (Rapicavoli et al. 2018). However, after inoculation, infected plants can remain asymptomatic for a highly variable period of time—from 2 to 3 months in Pierce's disease to more than 12 months in other cases, such as 14 months in olive quick decline—depending on biotic and abiotic conditions (EFSA PLH 2019). Symptoms seem to be caused by the production of biofilm by the bacterium and defense structures by the plant so that water movement in the vessels is restricted and the plant progressively desiccates (Roper et al. 2019). Duration and severity of symptoms, and time to host death also vary depending on multiple factors, determining variable ecological end economic impacts in different ecosystems and agro-ecosystems (Almeida and Nunney 2015).

transmission is driven by bacterium–host–vector interactions with a significant, yet not fully understood, influence of abiotic conditions, landscape features, and human activities. Therefore, any attempt to shed light on epidemiological dynamics such as introduction routes, spread patterns, and disease management efficacy requires a deep insight into these elements. In the following subsections, we will discuss the eco-epidemiological factors and present a comprehensive review of the related uncertainties (also summarized in Supplementary Table S1), with the focus on how these affect prevention and control of potential outbreaks in novel locations. An example of the variability of the eco-epidemiological aspects is graphically illustrated in Figure 1B and C, which constitute a conceptual model of two hypothetical eco-epidemiological scenarios characterized by different combinations of variables for each pathosystem level in Figure 1A. Figure 1B represents a fictional pathosystem where *X. fastidiosa* is occurring, while Figure 1C illustrates a novel environment where *X. fastidiosa* has not been introduced yet, and presents significant environmental differences compared with Figure 1B. The figure represents the complexity of translating eco-epidemiological knowledge from known outbreak locations to very different environments, where *X. fastidiosa* does not occur yet. The sheer amount of eco-epidemiological uncertainties have a remarkable impact on the accuracy of epidemiological predictions for disease prevention and control strategies, thus, this review aims to provide a tool to identify knowledge gaps that need to be filled in order to offer additional supporting evidence and context for decision makers.

Bacterium. *X. fastidiosa* shows high genetic variability, with three supported subspecies (*fastidiosa*, *multiplex*, and *pauca*) and two which are still debatable (*morus* and *sandyi*) (Potnis et al. 2019; Vanhove et al. 2019). Genetic analyses are progressively uncovering new nonrecombinant and recombinant strains, which differ in terms of infectivity, growth rate, within-host movement rate, and symptom severity. Bacterial populations undergo extensive homologous recombination, allowing adaptation to new hosts and ecological niches (Vanhove et al. 2019). Human-mediated movements of infected plant material have favored the long-range dispersal of *X. fastidiosa* and an increase in new recombination events (Landa et al. 2019). This means that disease risk in a specific area might be represented by the introduction of new genotypes combined with the recombination potential of sympatric genotypes independently introduced, as recently discovered in European outbreaks (Potnis et al. 2019). Hence, it is difficult to predict the genotype likely to invade new locations, as this may depend not only on proximity and connection with affected areas, but also on introduction routes of potentially infected plants and new recombination events.

Some degree of host specialization has been demonstrated, as individual sequence types seem to be associated with a limited number of hosts, and this information can be used to predict susceptible host plants in new areas following an introduction (Nunney et al. 2019). However, recent experiments on nonrecombinant strains of subsp. *multiplex* showed a general lack of infection of nonhomologous hosts (Nunney et al. 2019). Therefore, in areas where the flora is thought not to have been previously

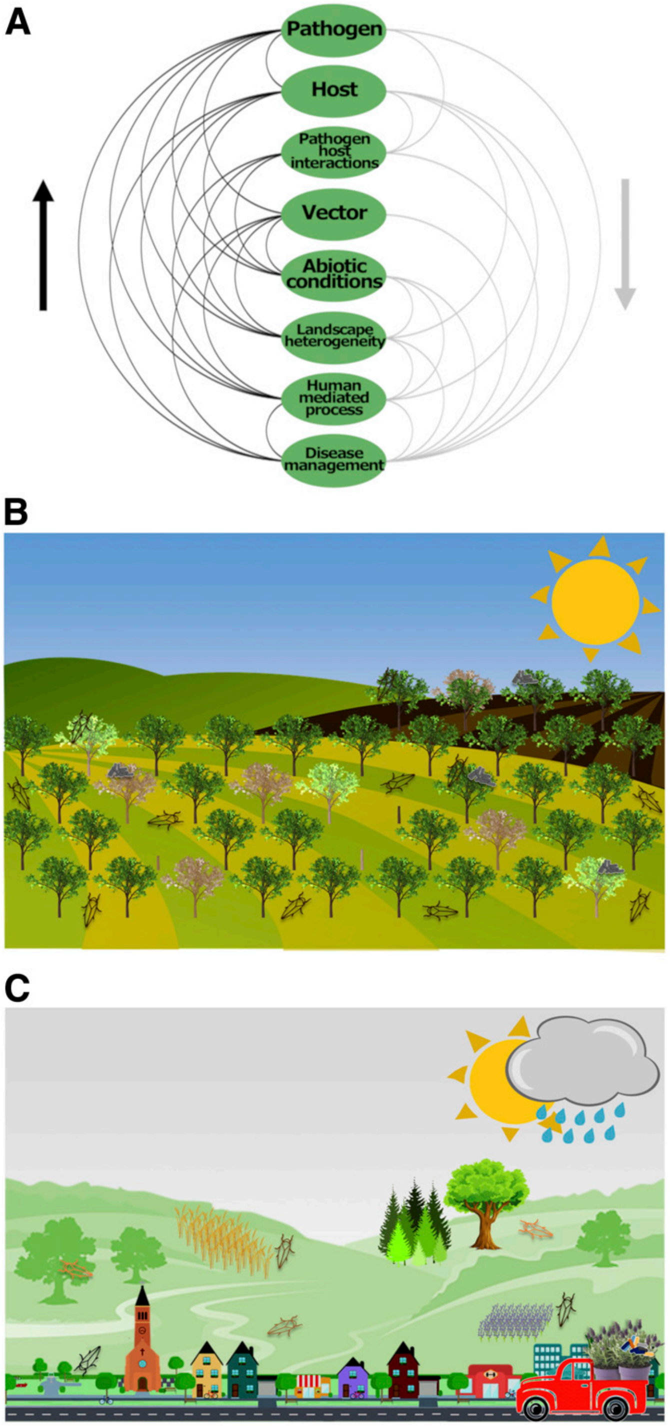

FIGURE 1

A, Conceptual diagram of factors affecting *Xylella fastidiosa* epidemiology displayed by pathosystem level with related uncertainties and nexus to be considered in predicting its establishment and spread in a novel environment. Considering a theoretic *X. fastidiosa* pathosystem, each node corresponds to an epidemiological component involved in disease dynamics, while arches represent the interactions of the components with each other. Gray connections are directed downward (right), black connections are directed upward (left). **B and C,** Conceptual model of two hypothetical eco-epidemiological scenarios characterized by different combinations of variables for each pathosystem level in **A**. **B** represents a low-diversity susceptible crop system with a Mediterranean-like climate, a dominant vector species, and a control strategy based on infected plant removal, where the outbreak is caused by a single pathogen genotype (e.g., similar to outbreak of olive quick decline in Puglia, Italy). In contrast, **C** illustrates a completely novel environment where a potential *X. fastidiosa* introduction (different genotypes) has not occurred yet: mix of natural and agricultural land with unknown host susceptibility, numerous potential vector species, temperate climate, different human-related processes (e.g., plant trade network), and policy framework.

exposed to *X. fastidiosa*, the potential host range remains unclear, as well as the potential emergence risk and the potential socioeconomic and ecological impacts (genotypic diversity seems to also affect pathogenicity and transmission rates) (Almeida and Nunney 2015).

Evidence of bacterial genetic variability is represented by variability in host specificity, spatiotemporal dynamics, and environmental impact among the current European outbreaks (Landa et al. 2019). In Puglia (Italy), the pathogen introduction likely occurred via infected plants from Central America carrying a single *X. fastidiosa* genotype (Saponari et al. 2019). The resultant epidemic largely affected olive trees, although other hosts in the vicinity of olive groves were also found to be infected (Saponari et al. 2019). In other cases, such as Corsica (France), multiple independent introduction events are the most likely scenario, with different genotypes affecting different hosts and habitats, with more subtle expression of symptoms and patchy distribution (Landa et al. 2019). This may have caused the infections to be undetected for longer than previously thought (Soubeyrand et al. 2018). In areas where *X. fastidiosa* does not currently occur, it is therefore extremely difficult to predict which genotypes of the bacterium are most likely to invade. Commonly this has been based only on climatic suitability models (Godefroid et al. 2019) and how these genotypes might adapt to the available hosts/habitats. In this regard, whole-genome studies are providing promising insights into ecological and epidemiological traits of *X. fastidiosa*, such as dispersal pathways or relationships among strains that are of biological and quarantine relevance, which might be useful in developing disease management strategies (Landa et al. 2019).

Host plant. The potential host pool of *X. fastidiosa* is extremely broad, from herbaceous plants to trees, including valuable crops and ornamentals (Delbianco et al. 2019). As its distribution expands, other susceptible species are progressively being discovered (e.g., adaptations to new hosts, plants not yet tested, etc.) (EFSA PLH 2019). In a new environment, identifying the potential host community, and more importantly the reservoir community, is challenging. Numerous *X. fastidiosa* strains do not spread evenly in the host, especially in asymptomatic hosts, so that these plants represent a particularly obscure reservoir pool (Purcell and Saunders 1999). Hence, the identification of specific focal species for epidemiological investigations, or for targeted disease management strategies, can be challenging. As a result, it has been suggested that several plausible scenarios are considered when undertaking pest risk assessment and planning detection surveys (EFSA 2019). These might include all the recognized susceptible species (EFSA PLH 2019) widely occurring in the area of interest; all susceptible species where infection can have major economic impacts; hosts of known major outbreaks; or all host species preferred by the available vectors (if known). In addition, plant phylogenetic relatedness analyses might be an alternative approach to forecast potential hosts in a new location (Parker et al. 2015).

Even in known susceptible taxa, such as grapevines and olives, where the pathogen causes distinctive outbreaks, there can be significant variation in symptom expression and transmissibility between host species/cultivars (Sabella et al. 2019). As a result, anticipating the course of an epidemic in a novel environment, with particular biotic and abiotic conditions, is fraught with uncertainties. In particular, host tolerance and resistance to infection may need to be considered. Whereas tolerance can be considered a reduction in the impacts of infection on the health of a host, resistance is associated with lower bacterial loads and lower proportions of colonized vessels (Roper et al. 2019). Further, pathogen establishment or disease severity depend also on other factors such as plant age (Roper et al. 2019).

Thus, in an environment where the flora has not previously been exposed to *X. fastidiosa*, the pool of potential hosts, their relative susceptibility to infection and disease, and the symptoms of disease, are unknown. This variability occurs among different genotypes of the same species (e.g., olive cultivars) as well as among different species in the same genus (e.g., *Prunus* spp.) (Rapicavoli et al. 2018). For example, different olive cultivars show significantly different bacterial loads and other bacterium-associated responses that determine different symptoms expression and resistance of some cultivars (Sabella et al. 2019). In addition, the bacterium can be irregularly distributed in the host, making detection through sampling not always reliable (Purcell and Saunders 1999). Detection based on visual inspection for symptoms of disease is further complicated by the nonspecific nature of symptoms and a long and variable asymptomatic period (likely to be influenced by climatic conditions) (Rapicavoli et al. 2018). Host assemblages might not only vary in terms of spatial scale (and time scale if considering crop growth and planting rotation) but also in terms of host abundance and host density, which is information rarely available in noncrop settings. As a result, epidemiological predictions unsupported by empirical testing are unlikely to be accurate, especially considering the remarkably high number of potential combinations between hosts (>560) (EFSA PLH 2019) and *X. fastidiosa* genotypes (>80, described by multilocus sequence typing) (Landa et al. 2019; Potnis et al. 2019; Vanhove et al. 2019).

Nonetheless, predicting the risk posed by *X. fastidiosa* to specific areas may be essential to minimize potential economic losses due to an outbreak. Depending on the combination host–pathogen strain–environment, among other factors such as agricultural practices, there is a great variability in the risk of yield loss (Rapicavoli et al. 2018). In California, estimated grape-growing industry losses due to PD are approximately $104 million per year (Tumber et al. 2014). In Europe, an analysis of the occurring genotypes, suggested that olive is the most sensitive crop to this pathogen (subsp. *pauca*), with very high estimated yield losses, especially concerning areas where the trees are older than 30 years, which represent the majority of the areas of olive production in EU (EFSA PLH 2019), whereas almond and *Citrus* spp. are considered to be at lower risk compared with olive (subsp. *multiplex* and *fastidiosa*) (EFSA PLH 2019), although outside Europe, in different environmental conditions, where cultivation practices, host, and pathogen genotypes are different, these crops are seriously affected by *X. fastidiosa* infection (Coletta-Filho et al. 2020).

In Italy, analyses of economic impact of OQDS forecasted losses between 1.9 to 5.2 billion Euros in the worst-case scenario, in which production ceases after orchards without replanting resistant cultivars, while the availability of resistant cultivars significantly reduced the estimated impact (0.6 to 1.6 billion Euros) (Schneider et al. 2020). This analysis demonstrates the importance of strengthen the ongoing research on host and cultivar resistance, which constitutes a significant element of eco-epidemiological uncertainty. However, economic predictions are likely to be inaccurate when epidemiological knowledge is lacking. Estimation of key disease progression parameters may be crucial to achieve informed policy and adapt agricultural practices to reduce economic impact. However, these parameters, which vary for different hosts (and likely for different pathogen strain and environmental conditions), are not generally available, with few exceptions, e.g., olives in Puglia (White et al. 2020). Similar information, including the timescale of the different phases of the infection, concerning other pathosystems would greatly reduce the amount of eco-epidemiological uncertainty around *X. fastidiosa*.

Insect vector. Worldwide, all insect species feeding on xylem-sap are potentially able to transmit *X. fastidiosa*. These belong to the superfamily Cercopoidea (froghoppers and spittlebugs), the superfamily Cicadoidea (cicadas), and the subfamily Cicadellidae Cicadellinae (sharpshooters): with approximately 100 species in Europe (Cornara et al. 2019). In Europe, the most widespread potential vectors are native spittlebugs, in particular the meadow spittlebug *Philaenus spumarius* (Saponari et al. 2019). Other species have been found not to be competent transmitters of the bacterium or are not considered epidemiologically relevant due to their biology and ecology (Cavalieri et al. 2019; Morente et al. 2018), although more research is currently underway to evaluate the potential role of some of these taxa. Interestingly, cicadas and leafhoppers, which are also found in olive groves in Puglia, do not seem to be able to transmit *X. fastidiosa* in this setting (Cornara et al. 2020). Conversely, in North and South America, froghoppers, cicadas, and sharpshooters (Cercopoidea, Cicadoidea, and Cicadellidae Cicadellinae) are considered the key vectors for the pathogen (Krugner et al. 2019). In particular, the invasive *Homalodisca vitripennis* (glassy-winged sharpshooter) is one of the most important vectors of PD in California, suggesting differences in terms of vector dynamics and vector control strategies between American and European pathosystems (Krugner et al. 2019).

X. fastidiosa is the first case of a pathogen transmitted by spittlebugs in Europe, with *P. spumarius* the main vector of the Italian OQDS outbreak (Bodino et al. 2019). These insects were not considered plant pests and were only studied for their striking elytral polymorphisms (Stewart 1996); thus, relatively little was known of their biology and ecology at the time of first detection of *X. fastidiosa* in the continent. Transmission studies with *P. spumarius* have only been carried out in the South of Italy after the OQDS outbreak, whereas more information is available for *H. vitripennis* due to its long association with the epidemics of PD in North America. Two more spittlebugs, *P. italosignus* and *Neophilaenus campestris*, have been demonstrated to be competent vectors of the strain ST53 associated with OQDS, but in southern Puglia olive groves, these have a lower abundance, a lower affinity to olive trees, and lower transmission efficiency compared with *P. spumarius*, which remains the major OQDS vector (Cavalieri et al. 2019). Nevertheless, in other ecosystems, these species may be more abundant than *P. spumarius*, as demonstrated by Panzavolta et al. (2019), in which *P. italosignus* was found to be more abundant than *P. spumarius* in olive groves in Tuscany. This suggests that other xylem-sap feeder insects might have a transmission role in different pathosystems and in other environments than olive groves (which have been studied in less detail). Indeed, *P. spumarius* has been found to infect only in Italy and Corsica (France), confirming that additional xylem-feeding insects may play a role in transmitting the bacterium elsewhere (Cornara et al. 2019).

With the exception of *P. spumarius* in Puglia, data are scarce regarding distribution, abundance, phenology, seasonality, host preference, and dispersal capabilities of potential vectors (but see Bodino et al. 2019). In Italy, field experiments showed that *P. spumarius* nymphs preferred herbaceous plants, while adults shifted to woody hosts, in particular olive trees or *Quercus* species, at the beginning of the summer probably because of the dryness of the herbaceous cover, before returning to herbaceous plants at the end of summer (Bodino et al. 2019). However, it is unclear whether this is an innate pattern, or whether it might not be observed where the herbaceous plants do not dry out, such as in colder/wetter climates or in case of different vegetation assemblages. Host preference mediates host–vector interactions and vector seasonal dynamics, and knowledge of this can therefore be useful when designing vector control strategies or when predicting the course of epidemics in different climatic scenarios (Gruber and Daugherty 2013). Vector behavior in different environmental conditions is difficult to predict, as demonstrated by the complex behavioral response triggered by warmer temperatures in the case of *Graphocephala atropunctata* transmitting *X. fastidiosa* to grapevines. The interaction between climate and vector behavior, which affects disease dynamics such as onset of host infectiousness and onset of symptoms, is likely to depend on the pathosystem (Daugherty et al. 2017). For instance, in northern Italian olive groves, adult meadow spittlebugs persist in the olive canopy until October (while in Puglia these disappear after July) and occur on a wider range of alternative hosts compared with southern areas (Bodino et al. 2019). Whether this represents the impact of biotic or abiotic conditions will be an interesting area of investigation, as less suitable abiotic conditions for the vector may result in a higher host diversity and longer adult persistence.

Little is known about vector dispersal, which will influence how far an infectious vector can spread the pathogen. Meadow spittlebug dispersal is characterized by short-distance flights, traveling an average of 30 m in a single flight, and up to 100 m within 24 h (Cornara et al. 2019). Passive wind-mediated movements and “hitchhiking” on vehicles have also been reported as mechanisms of long-distance dispersal for this species, although this has yet to be quantified (Cornara et al. 2019). In California, *Homalodisca* species (sharpshooters) were found to travel 30 to 150 m in 72 h, depending on the wind speed and the landscape configuration (including host plants, structural complexity of hosts, host matrix, and topography) (Krugner et al. 2019). However, these measures are extremely difficult to translate into an accurate and realistic estimate of movement distances, which may help to infer disease spread. In addition, these studies are restricted in terms of species, habitat, and abiotic conditions, so the extrapolation of these results to different areas may be problematic. Thus, field studies and experiments are required in order to accurately estimate vector dispersal capabilities in different conditions.

Spread of insect-transmitted plant pathogens has been assumed to be mainly a function of vector abundance, nonetheless vector phenology is one of the less known aspects of vector–plant pathogen systems (Sisterson and Stenger 2016), and the areas at risk of *X. fastidiosa* introduction are no exception. Further, variability has been found among the relative importance of vector numbers and feeding periods with regards to *X. fastidiosa* transmission, with lower competence potentially being offset by higher abundance, polyphagy, mobility, or lack of biological control organisms (Daugherty and Almeida 2009). Experimental and empirical data collected in several pathosystems will shed light on the different components of vector transmission affecting *X. fastidiosa* infection. Indeed, the likelihood of transmission is the result of vector phenology, representing host–vector contact rate, vector dispersal, distance covered by a potentially infectious individual, vector competence, and efficiency in acquiring and transmitting the pathogen, which varies with bacterial genotype–host–vector species combinations (Gruber and Daugherty 2013).

Abiotic conditions. Temperature is a major determinant of transmission in vector-borne diseases as both the infectious agent and the vectors may be temperature-sensitive (Kamiya et al. 2019). Similarly, abiotic conditions seem to have a major impact on *X. fastidiosa* (Feil and Purcell 2001). Climate affects bacterium survival and growth rate, as well as host–vector distribution and abundance (Daugherty et al. 2017). Abiotic conditions are tightly linked to multiple epidemiological factors (Fig. 1), and transmission is driven by the interactions among these, which have rarely been evaluated when assessing *X. fastidiosa* risk in novel environments. Additionally, in the context of climate change, abiotic conditions can vary in unpredictable ways (Trębicki et al. 2017), representing a significant source of uncertainty to take into account when considering epidemiological dynamics in novel locations for present and future scenarios. Nonetheless, the effect of temperature or other abiotic factors on *X. fastidiosa* pathosystems are largely unexplored, especially in climatic conditions and bacterial genotype–host–vector combinations dissimilar from known outbreaks.

Modeling studies indicated that, in the United States, areas with milder winter temperatures were at higher risk of emergence of *X. fastidiosa*-related diseases because they are more favorable to the survival of the bacterium and the vector (Cornara et al. 2019; Feil and Purcell 2001). Whereas in Europe, species distribution models, which currently represent the main available method of estimating the potential distribution of *X. fastidiosa*, found that several climatic variables are likely to affect the distribution of *X. fastidiosa* (e.g., average summer temperature, seasonality of precipitation), and predict that all coastal areas of the Mediterranean, the Atlantic coast of France, Portugal, and Spain, and other lowland areas are suitable for establishment of the bacterium (EFSA PLH 2019; Godefroid et al. 2019). However, this approach is biased toward actual occurrences (or areas with similar features) and does not take into account bacterial genotype variability, bacterial and vector host preference, bacterial nonequilibrium distribution, or any other variables driving the potential environmental range expansion of *X. fastidiosa*. For example, variation in the effects of temperature and culture media on bacterial growth and biofilm formation was identified between different *X. fastidiosa* genotypes in vitro experiments (J. A. Navas-Cortés, *personal communication*). Hence, the suitable range of expansion of the pathogen remains uncertain until further empirical data are available. Currently, the evidence suggest that higher temperatures favor greater vector feeding rates and vector survival (Cornara et al. 2019), higher *X. fastidiosa* growth rate (Feil and Purcell 2001), higher transmission efficiency and shorter latency period in hosts (Daugherty et al. 2017), and greater infectivity in plants (Lieth et al. 2011).

In areas with lower temperatures, such as oceanic/continental climates, there is little or no empirical knowledge about how (and if) the bacterium may spread, although there are records as far north as southeastern Canada. There, *X. fastidiosa* subsp. *multiplex* has been observed to cause leaf scorch in shade trees and shrubs (e.g., *Ulmus*, *Acer*, and *Quercus*). In those cases, colder temperatures have been hypothesized to reduce the rates of spread and symptom development (Gould and Lashomb 2005). Cold curing experiments (in which low temperatures have resulted in recovery from infection) have demonstrated that below a temperature threshold the within-host growth rate of the bacterium may become negative, or at least does not systemically spread. However, this threshold is dependent upon multiple factors such as pathogen genotype, host species/cultivar, experimental conditions, and length of exposure to suboptimal temperatures (Lieth et al. 2011; Rathé et al. 2012). As a result, extrapolating any given temperature threshold to other pathosystems is likely to be fraught with uncertainty.

Epidemiological data in Mediterranean and subtropical climates are more readily available, as the outbreaks of PD in Californian grapevine, citrus variegated chlorosis in Brazilian citrus, and OQDS in Puglian olive boosted research in these areas. Climatic conditions in these areas are characterized by high summer and winter temperatures and high seasonality in precipitation (resulting in periods of hydric stress in plants). Yet, the effect of temperature or dryness on transmission has not been systematically analyzed and available empirical or modeling studies exhibit a variety of outcomes. Daugherty et al. (2017) experimentally demonstrated that at higher temperatures sharpshooter vectors preferred to feed on healthy hosts because of the exacerbated symptom expression, reducing *X. fastidiosa* spread. Nevertheless, there are pathosystems where vectors are attracted to infected hosts, and earlier symptom onset might therefore favor greater disease incidence (Eigenbrode et al. 2017). Better understanding of the interplay among climate and other epidemiological factors and a more systematic approach to test the effect of abiotic conditions on transmission dynamics are needed to comprehend and predict specific responses in a given pathosystem.

Landscape heterogeneity. Landscape heterogeneity (in terms of landscape scale, configuration, and type of vegetation assemblages) has been observed to influence spread for a variety of plant pathogens (Papaïx et al. 2015). In the case of *X. fastidiosa*, these factors will therefore affect the epidemiological framework used to predict transmission dynamics. For example, different epidemiological behaviors may depend on diversity, density, and spatial arrangement of host plants in the landscape (Caraco et al. 2001). Landscape composition affects *X. fastidiosa* inoculum pressure as well as spatiotemporal spread dynamics by influencing vector behavior (Santoiemma et al. 2019). In novel environments, the interactions between landscape heterogeneity and the bacterium–host–vector triad (Fig. 1) are likely to influence epidemiological processes, as occurs in other pathosystems (Papaïx et al. 2015). Assuming different degrees of plant susceptibility, it can be hypothesized that the response of *X. fastidiosa* to a highly diverse landscape (such as the natural environment as opposed to a monoculture) might be to limit adaptation to any given host, so that selection pressure is in favor of a more diverse and less pathogenic bacterial population (Sicard et al. 2018). Furthermore, the vector, which is generally polyphagous, would feed on a wider variety of host plants, thereby decreasing the probability of encountering the most susceptible host and thus spreading the most pathogenic genotype (Ostfeld and Keesing 2012). Conversely, in crop systems, with a high dominance of phylogenetically related hosts, *X. fastidiosa* might quickly adapt to easily spread between hosts (or the bacterial strain introduced may be already highly specialized for that host) and express higher virulence (Sicard et al. 2018). The phenomenon that less or noncompetent host-species dilute transmission potential, providing alternative routes for the pathogen/vector, has often been observed, especially in vector-borne diseases (Ostfeld and Keesing 2012). However, due to the variability of *X. fastidiosa* pathosystems, the generality of the dilution effect cannot be assumed in absence of further experimental data on transmission dynamics in a wider range of hosts/landscapes. Indeed, in some areas, a high diversity of susceptible but symptomless plants were found to be a source of constant *X. fastidiosa* inoculum (a “hidden reservoir” of infection) (Soubeyrand et al. 2018).

In terms of landscape scale, epidemiological dynamics might be considered over a large area (e.g., national scale pest risk assessments) or with a focus on specific areas with high density of host species, such as highly susceptible or high valuable crops (e.g., preparedness measures specific to the horticultural sector). In both cases, it would be complex to predict and characterize *X. fastidiosa* transmission potential of host plants in a location where data are not available. Even for the second approach, it will be challenging to estimate the susceptibility of a crop in a new location, as the susceptibility of a single crop has been found to vary in different locations due to climatic conditions, cultivation practices, spatial configuration, surrounding matrix, and host–bacterium association (Lopes et al. 2010). The spatial configuration of the plants, distance between plants, and shape of the patch, directly and indirectly affects *X. fastidiosa* vector dispersal capabilities (Krugner et al. 2019). In central Italy, the land use type surrounding olive groves has been found to affect *P. spumarius* abundance and dispersal patterns (with vineyards negatively correlated to spittlebug abundance in olive groves), affecting the risk of *X. fastidiosa* transmission (Santoiemma et al. 2019). In Puglia, olive grove distribution and tree density were found to influence *X. fastidiosa* dynamics at a landscape level (White et al. 2017). However, no correlation was found between land-use and *X. fastidiosa* occurrence in Corsica, most likely because of the capability of proliferation on a great variety of plants widely distributed in several land-cover classes (Martinetti and Soubeyrand 2019). However, generally the information regarding host species distribution/abundance at landscape scale, host spatial configuration, and distribution of vegetation assemblages are not available.

Human influences on dispersal, infection, and management. Since biosecurity threats have been strongly linked to the expansion of human activities such as trade and tourism, understanding human-mediated processes in the various stages of disease transmission, surveillance, monitoring, and control of plant pathogens to predict and prevent disease spread is essential to reduce epidemiological uncertainties (Marzano et al. 2017). Human actions affect the type and numbers of plant pathogens and pests being dispersed, as well as the potential dispersal distances, which therefore influence the risk of spread (human-mediated transmission). However, they also influence the ability to counteract disease through movement restrictions, surveillance, and control efforts. These "human management actions" require behavioral change, which can be achieved using a variety of approaches, including policy, economics, and engagement (Marzano et al. 2017). Human activities also influence host distribution and landscape configuration, which can subsequently influence vector introduction and spread (Fig. 1) (Potter and Urquhart 2017). Hence, the consideration of human mediated processes in eco-epidemiological research includes how humans influence transmission directly or indirectly via the movement and placement of host plants (such as procurement practices), but also includes human knowledge of potential plant diseases and responses to the pathogen through regulatory and management systems established to constrain spread following discovery of the pathogen (Laxminarayan et al. 2014). Public acceptability of control measures put into place following discovery of *X. fastidiosa* will also be key to successful management, as was demonstrated during the OQDS outbreak in Puglia, where lack of early scientific communication and stakeholder engagement exacerbated pathogen transmission (Colella et al. 2019).

The plant trade network has been identified as a key pathway for the introduction of plant pests and pathogens into nonendemic countries, and has also been shown to strongly influence transmission patterns following entry (Pautasso et al. 2015). Nevertheless, the structures of national and international plant trade networks and the flows within these are still insufficiently documented. Detailed data (e.g., host species level) on plant trade are scarce for a variety of reasons (e.g., the sheer volume of data, unwillingness of trading companies to disclose information, difficulties collecting human behavioral data, existence of illegal behaviors that generate markets) (Marzano et al. 2017). Yet, research on *Phytophthora* demonstrated a significant increase in transmission potential when commercial movement of plants was considered (Harwood et al. 2009). This is highly likely to occur in the case of *X. fastidiosa*, the main outbreaks of which arose in human-modified pathosystems and where the main hosts are heavily traded as crops or ornamentals, for which trading routes and detailed distribution are poorly understood (Almeida and Nunney 2015). Although estimating the movements of crops and ornamental plants would require much more investigation effort into human activities, it would also be beneficial to better characterize long-distance dispersal routes, introduction pathways, and the landscape distribution of susceptible hosts.

Stakeholders' actions are dependent on various factors that are particularly difficult to predict and investigate such as values and motivations, risk perceptions, ability, and willingness to act and exist within a landscape of regulatory and economic considerations and education and awareness programs (Marzano et al. 2017). For example, scientists have advocated for greater trade restrictions (Hantula et al. 2014) and EU legislation has restricted the trade of *X. fastidiosa* hosts from known affected areas. However, global trade rules, largely determined by the World Trade Organization (WTO), strongly favor free trade, as its main concern is safeguarding economies rather than plant health. As a result, any trade restrictions must be justified by evidence-based pest risk assessments (WTO Sanitary and Phytosanitary Agreement) or penalties are imposed. Due to the considerable epidemiological uncertainties early in a new epidemic (as may happen in the case of new diseases caused by *X. fastidiosa*), risks may not be accurately characterized, and there may be delays in the implementation of effective trade restrictions (Marzano et al. 2017). For situations with high epidemiological uncertainties, different pest risk assessments may lead to different conclusions. This might affect the selection of preventive measures, which can cause disruption of trade, generating international disputes and stakeholders' discontent, as occurred when the EU banned citrus imports from South Africa due to the risk of spread of citrus black spot disease (Laurenza and Montanari 2014). Stakeholder responses to disease management strategies therefore pose another source of uncertainty, and yet have a great influence on the progression of a potential outbreak (Marzano et al. 2017; Saponari et al. 2019).

In *X. fastidiosa* pathosystems, a key complexity for the implementation of disease management is represented by host distribution in heavily human modified environments, such as isolated and discontinuous host distribution in private gardens, or orchards with a high host density. Analogous conditions have been recognized in citrus Huanglongbing outbreaks (Gottwald 2010). In these cases, stakeholder compliance may represent a limiting factor to successful disease control, and therefore human response highly affects the intensity and distribution of risk. Human behavior is difficult to characterize and predict, and thus represents a great source of epidemiological uncertainty. For example, roguing (i.e., plant removal), which is a common approach to disease management, may be difficult to apply to in the case of *X. fastidiosa* due to the sensitive nature of removing asymptomatically infected host plants from private land, as the implications may be political and economic, as well as ecological (Marzano et al. 2017). Nonetheless, in other pathosystems, such as Huanglongbing and plant mosaic disease, collaboration between growers applying roguing and vector control seemed to be essential in controlling the infection at landscape scale while preventing yield loss (Craig et al. 2018; Rakshit et al. 2019). Successful disease management strategies necessarily include a high degree of stakeholder engagement, in particular, recent research on Huanglongbing in Florida, showed that informing stakeholders about the effectiveness of control methods was of much greater importance than increasing disease risk perceptions (Milne et al. 2020).

Thus, including information on human-related factors in eco-epidemiological research will give further insights on potential pathogen entry pathways and on the human pathways to target for surveillance and control purposes, as well as on how to preserve livelihoods and food security (Milne et al. 2020; Parnell et al. 2015). Such insights are critical to ensure cost-effective disease management strategies and stakeholder awareness and compliance. In addition, stakeholder engagement provides key support to scientific research, such as disease reporting, the lack of which pose a major constraint to any surveillance protocol (White et al. 2018).

PRIORITIZATION OF ECO-EPIDEMIOLOGICAL UNCERTAINTIES: SURVEY

The uncertainties highlighted in the sections above are also listed and summarized in Supplementary Table S1, where we also point out the potential sources of data that could help to fill the knowledge gaps. To help prioritize these uncertainties, we asked an interdisciplinary group of experts in different fields of plant pathology, ecology and plant health to rank each uncertainty in terms of their perceived importance for the development of accurate pest risk assessments, and to identify which were most challenging. The survey was conducted following the Code of Ethics of the Social and Economic Research Group (SERG) at Forest Research, Roslin, U.K. It included 28 academics from universities (9) and research institutes (17), mainly based in the United Kingdom (15), but also in Italy (6), France (2), Spain (1), The Netherlands (1), and the United States (1), with two respondents preferring not to disclose their affiliation and country. Their disciplinary context ranged from epidemiological and ecological modeling to crop genetics, plant pathology, plant disease epidemiology, entomology, social science, and microbiology. In particular, according to the description they provided of their field of research, eight were modelers involved in *X. fastidiosa* projects, seven specialized in different aspects of molecular phytopathology and microbiology, five were entomologists with expertise in the insect vectors of *X. fastidiosa*, five were plant epidemiologists, two were ecologists, and one was a social scientist who specializes in stakeholder engagement in the field of plant health. These experts were presented with the list of data types in Supplementary Table S1 and were asked to rank the data types in terms of both "urgency" and "difficulty" to prioritize them for each pathosystem level and to propose an overall ranking for the most urgent and the most difficult data to collect. The experts' answers were then analyzed by averaging their ranking value assigned and arranging the data according to the new ranking values.

There was no evidence of an effect of the academic discipline of the expert on the ranking proposed, as assessed by the Kruskal-Wallis H test. Considering each pathosystem level separately, the priorities identified were (in order from most to least important): bacterial genotype–host specialization, host distribution, temperature-dependent infection rates, vector distribution, climatic suitability for the bacterium, effect of susceptible host diversity on transmission rates, and impact of plant trade network (Supplementary Table S1 provides full ranking). However, the results from the overall ranking showed that, across all levels, the most urgent knowledge gaps to be filled were: host distribution (identification of susceptible host(s) at different taxonomic levels across different spatial scales); vector dispersal (distance traveled by vector species locally and nonlocally); temperature-dependent infection rates in different host–bacterium genotype combinations; vector abundance (local density of vectors in different habitats, which represent host–vector contact rate); bacterial genotype–host specialization; and vector distribution (presence of vector species at different spatial scales). Interestingly, these results are in alignment with epidemiological studies investigating the impact of different epidemiological components on *X. fastidiosa* transmission dynamics. For example, Kyrkou et al. (2018), using a mechanistic modeling approach, performed a sensitivity analysis of all parameters to find the ones most affecting PD transmission in Southern California. They found that host–vector contact rate, host and vector density, and asymptomatic lag (also considered temperature-dependent) most affected transmission.

The epidemiological aspects for which comprehensive understanding was considered most difficult to achieve, were identified as follows: duration of transmission lag for different combinations of host–bacterial genotypes; duration of asymptomatic lag for different combinations of host–bacterial genotypes; seasonality in symptom onset in different abiotic conditions for different combinations of host–bacterial genotypes; recombination potential of different bacterial strains (significance of recombination in the (co)evolutionary, host-adaptation, and epidemiological context); effect of temperature on infection rates in different host–bacterial genotype combinations; and vector dispersal distance (natural and human-mediated routes). It is notable that these are mostly related to the host–pathogen interaction, demonstrating relative lack of information in this field. Although research on this is currently undergoing, the combination of bacterial genetic variability in conjunction with the great number of host species in different climatic conditions leads to a very large number of potential combinations, making it very challenging to estimate these crucial epidemiological features in most cases. The effect of temperature on infection rates and the distance of vector dispersal occurred in both top-five lists, emphasizing the importance of exploring *X. fastidiosa* transmission dynamics in climatic conditions other than the current outbreak locations, and on identifying the processes underlying the natural and human-mediated movement of vector species in these different environments. Although vector movement is often not explicitly understood due to the lack of data, several modeling studies have shown that vector dispersal patterns can have very significant effects on *X. fastidiosa* spread (Strona et al. 2020; White et al. 2017).

Considering the average rank at pathosystem level, data relative to the vectors were considered the most urgent, although there was high variability in responses among experts and data types (Supplementary Fig. S1 and Supplementary Table S1). This variability occurred also for host data (second most urgent pathosystem level). Yet, the range of ranks assigned to these two data types included mostly higher values than other pathosystem levels, with the exception of pathogen–host interactions (which displayed the lowest ranking variability) and pathogen in third and fourth place, respectively (Supplementary Table S1 and Supplementary Fig. S1). Interestingly, the experts agreed that abiotic conditions and landscape heterogeneity were the least important data to collect in new environments to improve pest risk assessments (Supplementary Fig. S1). Nonetheless, the data types ranking higher in the most urgent pathosystem levels were highly connected to and dependent upon climate and landscape variability (e.g., temperature-dependent infection rate, host distribution, and vector dispersal). By contrast, the levels considered most difficult to explore were pathogen–host interactions, pathogen, and host, reflecting the high level of uncertainty discussed in the previous sections. Surprisingly, vectors and abiotic factors were judged the most straightforward to investigate (Supplementary Table S1). Pathogen, host, pathogen–host interactions, and vector levels showed great divergence between urgency and difficulty rank, appearing to be remarkably more urgent (Supplementary Fig. S1b), whereas abiotic conditions and landscape were recognized to be largely more challenging than urgent to investigate (Supplementary Fig. S1b).

FINAL CONSIDERATIONS

Diseases caused by *X. fastidiosa* are of great concern in both endemic and unaffected areas, especially considering the major economic impact this pathogen had and still has in endemic and emerging contexts (Schneider et al. 2020; Tumber et al. 2014). Prevention and control of these diseases requires a good understanding of how *X. fastidiosa* spreads in different environments and regions. However, the variety of bacterial strains, potential vectors, and potential hosts makes this difficult to characterize in all settings. These complexities are further accentuated when we consider how epidemiological characteristics are impacted by different ecological, social, and economic considerations. Given the sheer scale of potential data needs and the difficulties inherent in obtaining these, careful consideration needs to be given to which data are most desirable if we are to develop clear and robust evidence-based control strategies, especially in areas currently though to be free from the pathogen. We consider this issue by first highlighting a number of different factors of significance to the eco-epidemiology of *X. fastidiosa*, and demonstrate the interconnections between these with particular focus on how this knowledge can be applied in novel environments (Fig. 1). Although the eco-epidemiological complexity and harmful impact on valuable crops make *X. fastidiosa* an emblematic case, these kinds of issues are common for many other emerging and reemerging phytopathogens. Confronting epidemiological uncertainties through focused data collection will allow us to improve our ability to accurately estimate disease risk and implement effective prevention and control strategies while also improving engagement with stakeholders.

Considering the eco-epidemiological uncertainties highlighted here, it may not be possible to design management strategies for areas at risk which are as accurate as the guidelines recommended by agencies such as EFSA (European Food Safety Authority), EPPO (European and Mediterranean Plant Protection Organization), or NAPPO (North American Plant Protection Organization), which advise the identification of local host populations, epidemiological units, and take into account relevant epidemiological factors. In novel environments, where no information on local host susceptibility is available, plant species known to be potentially susceptible to multiple bacterial subspecies might be prioritized (EFSA 2019). In data-poor environments, abiotic conditions in the area of interest might be considered to set the main study objectives; in areas with oceanic/continental climates, the focus may be on prevention or early detection of new incursions, with a focus on preincursion and human pathways (EFSA PLH 2019); and in environmental conditions similar to those in areas of existing outbreaks, the main concern might be to use epidemiological understanding from existing outbreaks to design effective mitigation strategies (EFSA PLH 2019). Models can also be used to perform sensitivity analyses to identify key uncertainties affecting success of management strategies, such as the effect of short-range vector dispersal distances on the size of cull radius around individual infected plants, or the effect of long-distance vector dispersal on buffer zone size (White et al. 2017). As well as spatial considerations, the temporal dynamics of spread and disease are of importance—with uncertainty surrounding the length of the latent and asymptomatic phases affecting the ability to accurately simulate spread, evaluate the effectiveness of biosecurity measures such as surveillance and quarantine, and interpret results of diagnostic tests (EFSA PLH 2019).

The evidence base to predict *X. fastidiosa* potential suitable distribution and spread is currently mainly based on modeling approaches that do not explicitly account for the effect of abiotic conditions on epidemiological dynamics, or are biased toward areas where the pathogen already occurs. Thus, the collection of evidence-based data in a wider set of eco-epidemiological conditions, across different spatial and temporal scales, will be the key to overcome uncertainties that exists to assess *X. fastidiosa* emergence risk in novel environments, and favor the development of models offering more robust predictions. The outcome of our expert elicitation suggests that there are specific eco-epidemiological areas to prioritize. Information on the fundamental bacterium–host–vector triad (and their interactions) was recognized as both the most urgent and the most difficult form of data to obtain. This is likely due to the variability of the three elements, and so to the enormous number of potential combinations between bacterial strains, host species, and vector species. Unfortunately, no data are available regarding awareness or risk perception of public and stakeholders, which may be potentially key vectors for the pathogen, although examples from other plant pests revealed low to modest levels of awareness even among key stakeholders in the horticultural and forestry sector (Marzano et al. 2015, 2016).

Some of the aspects highlighted in the expert elicitation show high levels of agreement, with experts from different academic backgrounds jointly recognizing that a more detailed characterization of pathogen, susceptible host, and vector dynamics was paramount to support accurate pest risk assessments and improve biosecurity policy and practice. In particular, data on vector dispersal patterns, recognized as a top priority as well as one of the most difficult information to gather, will be extremely relevant to the implementation of novel control strategies focused on reducing long distance movements (Strona et al. 2020). Similarly, temperature-dependent infection rate scored highly among the most desirable and most challenging data, confirming that investigating *X. fastidiosa* dynamics in a wider range of climatic conditions is crucial, although the effect of abiotic conditions on transmission might remain one of the greatest sources of uncertainty. Moreover, it seems clear that the increasing numbers of *X. fastidiosa* whole-genome studies (Landa et al. 2019) have the potential to reveal knowledge on bacterial genetic variability and paths of dispersal, which are crucial in assessing the potential risks of introduction and establishment in a new location.

In conclusion, the eco-epidemiological uncertainties highlighted here constrain our capacity to effectively assess disease risk and develop and implement successful policy and management strategies, especially given the severity of the threat that *X. fastidiosa* represents. Concerted efforts must be made to fill the knowledge gaps surrounding the ecological and evolutionary drivers of *X. fastidiosa*-associated disease emergence, especially in relation to the priorities highlighted by our expert elicitation. Ideally, these should be complemented by exploration of the effects of human-mediated transmission and of human actions in relation to policy, management, and awareness in order to prevent the disease from spreading more widely, support decision making, and enhance biosecurity.

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LITERATURE CITED

Almeida, R. P. P., and Nunney, L. 2015. How do plant diseases caused by *Xylella fastidiosa* emerge? Plant Dis. 99:1457-1467.

Bodino, N., Cavalieri, V., Dongiovanni, C., Plazio, E., Saladini, M. A., Volani, S., Simonetto, A., Fumarola, G., Di Carolo, M., Porcelli, F., Gilioli, G., and Bosco, D. 2019. Phenology, seasonal abundance and stage-structure of spittlebug (Hemiptera: Aphrophoridae) populations in olive groves in Italy. Sci. Rep. 9:17725.

Caraco, T., Duryea, M. C., Glavanakov, S., Maniatty, W., and Szymanski, B. K. 2001. Host spatial heterogeneity and the spread of vector-borne infection. Theor. Popul. Biol. 59:185-206.

Cavalieri, V., Altamura, G., Fumarola, G., di Carolo, M., Saponari, M., Cornara, D., Bosco, D., and Dongiovanni, C. 2019. Transmission of *Xylella fastidiosa* subspecies *pauca* sequence type 53 by different insect species. Insects 10:324.

Colella, C., Carradore, R., and Cerroni, A. 2019. Problem setting and problem solving in the case of olive quick decline syndrome in Apulia, Italy: A sociological approach. Phytopathology 109:187-199.

Coletta-Filho, H. D., Castillo, A. I., Laranjeira, F. F., Chumbinho de Andrade, E., Teixeira Silva, N., Alves de Souza, A., Esteves Bossi, M., Almeida, R. P. P., and Lopes, J. R. S. 2020. Citrus variegated chlorosis: An overview of 30 years of research and disease management. Trop. Plant Pathol. 45: 175-191.

Cornara, D., Marra, M., Tedone, B., Cavalieri, V., Porcelli, F., Fereres, A., Purcell, A., and Saponari, M. 2020. No evidence for cicadas' implication in *Xylella fastidiosa* epidemiology. Entomol. Gen. 40:125-132.

Cornara, D., Morente, M., Markheiser, A., Bodino, N., Tsai, C.-T., Fereres, A., Redak, R. A., Perring, T. M., and Spotti Lopes, J. R. 2019. An overview on the worldwide vectors of *Xylella fastidiosa*. Entomol. Gen. 39:157-181.

Craig, A. P., Cunniffe, N. J., Parry, M., Laranjeira, F. F., and Gilligan, C. A. 2018. Grower and regulator conflict in management of the citrus disease Huanglongbing in Brazil: A modelling study. J. Appl. Ecol. 55:1956-1965.

Cunniffe, N. J., Koskella, B., Metcalf, C. J. E., Parnell, S., Gottwald, T. R., and Gilligan, C. A. 2015. Thirteen challenges in modelling plant diseases. Epidemics 10:6-10.

Daugherty, M. P., and Almeida, R. P. P. 2009. Estimating *Xylella fastidiosa* transmission parameters: Decoupling sharpshooter number and feeding period. Entomol. Exp. Appl. 132:84-92.

Daugherty, M. P., Zeilinger, A. R., and Almeida, R. P. P. 2017. Conflicting effects of climate and vector behavior on the spread of a plant pathogen. Phytobiomes J. 1:46-53.

Delbianco, A., Czwienczek, E., Pautasso, M., Kozelska, S., Monguidi, M., and Stancanelli, G. 2019. A new resource for research and risk analysis: The updated European Food Safety Authority Database of *Xylella* spp. host plant species. Phytopathology 109:213-215.

EFSA (European Food Safety Agency). 2019. Pest survey card on *Xylella fastidiosa.* EFSA Supporting Publications EN-1667:53.

EFSA Panel on Plant Health (PLH), Bragard, C., Dehnen-Schmutz, K., Di Serio, F., Gonthier, P., Jacques, M.-A., Jaques Miret, J. A., Justesen, A. F., MacLeod, A., Magnusson, C. S., Milonas, P., Navas-Cortés, J. A., Potting, R, Reignault, P. L., Thulke, H.-H., van der Werf, W., Vicent Civera, A., Yuen, J., Zappalà, L., Boscia, D., Chapman, D., Gilioli, G., Krugner, R., Mastin, A., Simonetto, A., Spotti Lopes, J. R., White, S., Abrahantes, J. C., Delbianco, A, Maiorano, A., Mosbach-Schulz, O., Stancanelli, G., Guzzo, M., and Parnell, S. 2019. Update of the scientific opinion on the risks to plant health posed by *Xylella fastidiosa* in the EU territory. EFSA J. 17: 5665.

Eigenbrode, S. D., Bosque-Pérez, N. A., and Davis, T. S. 2017. Insect-borne plant pathogens and their vectors: Ecology, evolution, and complex interactions. Annu. Rev. Entomol. 63:169-191.

EPPO (European Plant protection Organisation). 2020. Global Database. https://gd.eppo.int/taxon/XYLEFA/distribution

Feil, H., and Purcell, A. H. 2001. Temperature-dependent growth and survival of *Xylella fastidiosa* in vitro and in potted grapevines. Plant Dis. 85: 1230-1234.

Godefroid, M., Cruaud, A., Streito, J. C., Rasplus, J. Y., and Rossi, J. P. 2019. *Xylella fastidiosa*: Climate suitability of European continent. Sci. Rep. 9: 8844.

Gonçalves, F. P., Stuchi, E. S., Lourenço, S. A., Kriss, A. B., Gottwald, T. R., and Amorim, L. 2014. The effect of irrigation on development of citrus variegated chlorosis symptoms. Crop Prot. 57:8-14.

Gottwald, T. R. 2010. Current epidemiological understanding of citrus huanglongbing. Annu. Rev. Phytopathol. 48:119-139.

Gould, A. B., and Lashomb, J. H. 2005. Bacterial leaf scorch of shade trees. APS*net* Features. doi:10.1094/APSnetFeature/2005-1105

Gruber, B. R., and Daugherty, M. P. 2013. Understanding the effects of multiple sources of seasonality on the risk of pathogen spread to vineyards: Vector pressure, natural infectivity, and host recovery. Plant Pathol. 62: 194-204.

Hantula, J., Müller, M. M., and Uusivuori, J. 2014. International plant trade associated risks: Laissez-faire or novel solutions. Environ. Sci. Policy 37: 158-160.

Harwood, T. D., Xu, X., Pautasso, M., Jeger, M. J., and Shaw, M. W. 2009. Epidemiological risk assessment using linked network and grid based modelling: *Phytophthora ramorum* and *Phytophthora kernoviae* in the UK. Ecol. Modell. 220:3353-3361.

Hollingsworth, T. D., Pulliam, J. R. C., Funk, S., Truscott, J. E., Isham, V., and Lloyd, A. L. 2015. Seven challenges for modelling indirect transmission: Vector-borne diseases, macroparasites and neglected tropical diseases. Epidemics 10:16-20.

Kamiya, T., Greischar, M. A., Wadhawan, K., Gilbert, B., Paaijmans, K., and Mideo, N. 2019. Temperature-dependent variation in the extrinsic incubation period elevates the risk of vector-borne disease emergence. Epidemics 30:100382.

Krugner, R., Sisterson, M. S., Backus, E. A., Burbank, L. P., and Redak, R. A. 2019. Sharpshooters: A review of what moves *Xylella fastidiosa*. Austral Entomol. 58:248-267.

Kyrkou, I., Pusa, T., Ellegaard-Jensen, L., Sagot, M. F., and Hansen, L. H. 2018. Pierce's disease of grapevines: A review of control strategies and an outline of an epidemiological model. Front. Microbiol. 9:2141.

Landa, B. B., Castillo, A. I., Giampetruzzi, A., Kahn, A., Román-Écija, M., Velasco-Amo, M. P., Navas-Cortés, J. A., Marco-Noales, E., Barbé, S., Moralejo, E., Coletta-Filho, H. D., Saldarelli, P., Saponari, M., and Almeida, R. P. P. 2019. Emergence of a plant pathogen in Europe associated with multiple intercontinental introductions. Appl. Environ. Microbiol. 86: e01521-e19.

Laurenza, E. C., and Montanari, F. 2014. Pest risk analysis–Recent trends in the EU and its trade implications: The citrus black spot case. Eur. J. Risk Regul. 5:201-207.

Laxminarayan, R., Reif, J., and Malani, A. 2014. Incentives for reporting disease outbreaks. PLoS One 9:e90290.

Lieth, J. H., Meyer, M. M., Yeo, K. H., and Kirkpatrick, B. C. 2011. Modeling cold curing of Pierce's disease in *Vitis vinifera* 'Pinot Noir' and 'Cabernet Sauvignon' grapevines in California. Phytopathology 101:1492-1500.

Lopes, J. R. S., Daugherty, M. P., and Almeida, R. P. P. 2010. Strain origin drives virulence and persistence of *Xylella fastidiosa* in alfalfa. Plant Pathol. 59:963-971.

Martinetti, D., and Soubeyrand, S. 2019. Identifying lookouts for epidemiosurveillance: Application to the emergence of *Xylella fastidiosa* in France. Phytopathology 109:265-276.

Marzano, M., Allen, W., Haight, R. G., Holems, T. P., Keskitalo, E. C. H., Langer, E. R., Shadbolt, M., Urquhart, J., and Dandy, N. 2017. The role of the social sciences and economics in understanding and informing tree biosecurity policy and planning: A global summary and synthesis. Biol. Invasions 19:3317-3332.

Marzano, M., Dandy, N., Bayliss, H. R., Porth, E., and Potter, C. 2015. Part of the solution? Stakeholder awareness, information and engagement in tree health issues. Biol. Invasions 17:1961-1977.

Marzano, M., Dandy, N., Papazova-Anakieva, I., Avtzis, D., Connolly, T., Eschen, R., Glavendekić, M., Hurley, B., Lindelöw, Å., Matošević, D., Tomov, R., and Vettraino, A. M. 2016. Assessing awareness of tree pests and pathogens amongst tree professionals: A pan-European perspective. For. Policy Econ. 70:164-171.

Milne, A. E., Gottwald, T., Parnell, S. R., Alonso Chavez, V., and van den Bosch, F. 2020. What makes or breaks a campaign to stop an invading plant pathogen? PLOS Comput. Biol. 16:e1007570.

Morente, M., Cornara, D., Plaza, M., Durán, J. M., Capiscol, C., Trillo, R., Ruiz, M., Ruz, C., Sanjuan, S., Pereira, J. A., Moreno, A., and Fereres, A. 2018. Distribution and relative abundance of insect vectors of *Xylella fastidiosa* in olive groves of the Iberian peninsula. Insects 9:175.

Nunney, L., Azad, H., and Stouthamer, R. 2019. An experimental test of the host-plant range of nonrecombinant strains of North American *Xylella fastidiosa* subsp. *multiplex*. Phytopathology 109:294-300.

Ostfeld, R. S., and Keesing, F. 2012. Effects of host diversity on infectious disease. Annu. Rev. Ecol. Evol. Syst. 43:157-182.

Panzavolta, T., Bracalini, M., Croci, F., Ghelardini, L., Luti, S., Campigli, S., Goti, E., Marchi, R., Tiberi, R., and Marchi, G. 2019. *Philaenus italosignus* a potential vector of *Xylella fastidiosa*: Occurrence of the spittlebug on olive trees in Tuscany (Italy). Bull. Insectol. 72:317-320.

Papaïx, J., Burdon, J. J., Zhan, J., and Thrall, P. H. 2015. Crop pathogen emergence and evolution in agro-ecological landscapes. Evol. Appl. 8: 385-402.

Parker, I. M., Saunders, M., Bontrager, M., Weitz, A. P., Hendricks, R., Magarey, R., Suiter, K., and Gilbert, G. S. 2015. Phylogenetic structure and host abundance drive disease pressure in communities. Nature 520:542-544.

Parnell, S., Gottwald, T. R., Cunniffe, N. J., Alonso Chavez, V., and van den Bosch, F. 2015. Early detection surveillance for an emerging plant pathogen: A rule of thumb to predict prevalence at first discovery. Proc. R. Soc. B 282:20151478.

Pautasso, M., Petter, F., Rortais, A., and Roy, A. S. 2015. Emerging risks to plant health: A European perspective. CAB Rev. 10.

Potnis, N., Kandel, P. P., Merfa, M. V., Retchless, A. C., Parker, J. K., Stenger, D. C., Almeida, R. P. P., Bergsma-Vlami, M., Westenberg, M., Cobine, P. A., and De La Fuente, L. 2019. Patterns of inter- and intrasubspecific homologous recombination inform eco-evolutionary dynamics of *Xylella fastidiosa*. ISME J. 13:2319-2333.

Potter, C., and Urquhart, J. 2017. Tree disease and pest epidemics in the Anthropocene: A review of the drivers, impacts and policy responses in the UK. For. Policy Econ. 79:61-68.

Purcell, A. H., and Finlay, A. 1979. Evidence for noncirculative transmission of Pierce's disease bacterium by sharpshooter leafhoppers. Phytopathology 69:393-395.

Purcell, A. H., and Saunders, S. R. 1999. Fate of Pierce's disease strains of *Xylella fastidiosa* in common riparian plants in California. Plant Dis. 83: 825-830.

Rakshit, N., Al Basir, F., Banerjee, A., and Ray, S. 2019. Dynamics of plant mosaic disease propagation and the usefulness of roguing as an alternative biological control. Ecol. Complex. 38:15-23.

Rapicavoli, J., Ingel, B., Blanco-Ulate, B., Cantu, D., and Roper, C. 2018. *Xylella fastidiosa*: An examination of a re-emerging plant pathogen. Mol. Plant Pathol. 19:786-800.

Rathé, A. A., Pilkington, L. J., Gurr, G. M., and Daugherty, M. P. 2012. Potential for persistence and within-plant movement of *Xylella fastidiosa* in Australian native plants. Australas. Plant Pathol. 41:405-412.

Roper, C., Castro, C., and Ingel, B. 2019. *Xylella fastidiosa*: Bacterial parasitism with hallmarks of commensalism. Curr. Opin. Plant Biol. 50: 140-147.

Sabella, E., Aprile, A., Genga, A., Siciliano, T., Nutricati, E., Nicolì, F., Vergine, M., Negro, C., De Bellis, L., and Luvisi, A. 2019. Xylem cavitation susceptibility and refilling mechanisms in olive trees infected by *Xylella fastidiosa*. Sci. Rep. 9:9602.

Santoiemma, G., Tamburini, G., Sanna, F., Mori, N., and Marini, L. 2019. Landscape composition predicts distribution of *Philaenus spumarius*, vector of *Xylella fastidiosa*, in olive groves. J. Pest Sci. 92:1101-1109.

Saponari, M., Giampetruzzi, A., Loconsole, G., Boscia, D., and Saldarelli, P. 2019. *Xylella fastidiosa* in olive in Apulia: Where we stand. Phytopathology 109:175-186.

Schneider, K., van der Werf, W., Cendoya, M., Mourits, M., Navas-Cortés, J. A., Vicent, A., and Oude Lansink, A. 2020. Impact of *Xylella fastidiosa* subspecies *pauca* in European olives. Proc. Natl. Acad. Sci. USA 117: 9250-9259.

Sicard, A., Zeilinger, A. R., Vanhove, M., Schartel, T. E., Beal, D. J., Daugherty, M. P., and Almeida, R. P. P. 2018. *Xylella fastidiosa*: Insights into an emerging plant pathogen. Annu. Rev. Phytopathol. 56:181-202.

Sisterson, M. S., and Stenger, D. C. 2016. Disentangling effects of vector birth rate, mortality rate, and abundance on spread of plant pathogens. J. Econ. Entomol. 109:487-501.

Soubeyrand, S., de Jerphanion, P., Martin, O., Saussac, M., Manceau, C., Hendrikx, P., and Lannou, C. 2018. Inferring pathogen dynamics from temporal count data: The emergence of *Xylella fastidiosa* in France is probably not recent. New Phytol. 219:824-836.

Stewart, A. J. A. 1996. The colour/pattern polymorphism of *Philaenus spumarius* (L.) (Homoptera: Cercopidae) in England and Wales. Philos. Trans. R. Soc. Lond. B Biol. Sci. 351:69-89.

Strona, G., Castellano, C., Fattorini, S., Ponti, L., Gutierrez, A. P., and Beck, P. S. A. 2020. Small world in the real world: Long distance dispersal governs epidemic dynamics in agricultural landscapes. Epidemics 30:100384.

Trębicki, P., Dáder, B., Vassiliadis, S., and Fereres, A. 2017. Insect–plant–pathogen interactions as shaped by future climate: Effects on biology, distribution, and implications for agriculture. Insect Sci. 24:975-989.

Tumber, K. P., Alston, J. M., and Fuller, K. 2014. Pierce's disease costs California $104 million per year. Calif. Agric. 68:20-29.

Vanhove, M., Retchless, A. C., Sicard, A., Rieux, A., Coletta-Filho, H. D., De La Fuente, L., Stenger, D. C., and Almeida, R. P. P. 2019. Genomic diversity and recombination among *Xylella fastidiosa* subspecies. Appl. Environ. Microbiol. 85:e02972-e18.

White, R. M., Young, J., Marzano, M., and Leahy, S. 2018. Prioritizing stakeholder engagement for forest health, across spatial, temporal and governance scales, in an era of austerity. For. Ecol. Manage. 417: 313-322.

White, S. M., Bullock, J. M., Hooftman, D. A. P., and Chapman, D. S. 2017. Modelling the spread and control of *Xylella fastidiosa* in the early stages of invasion in Apulia, Italy. Biol. Invasions 19:1825-1837.

White, S. M., Navas-Cortés, J. A., Bullock, J. M., Boscia, D., and Chapman, D. S. 2020. Estimating the epidemiology of emerging *Xylella fastidiosa* outbreaks in olives. Plant Pathol. 00:1-11.

Yates, K. L., Bouchet, P. J., Caley, M. J., Mengersen, K., Randin, C. F., Parnell, S., Fielding, A. H., Bamford, A. J., Ban, S., Barbosa, A. M., Dormann, C. F., Elith, J., Embling, C. B., Ervin, G. N., Fisher, R., Gould, S., Graf, R. F., Gregr, E. J., Halpin, P. N., Heikkinen, R. K., Heinänen, S., Jones, A. R., Krishnakumar, P. K., Lauria, V., Lozano-Montes, H., Mannocci, L., Mellin, C., Mesgaran, M. B., Moreno-Amat, E., Mormede, S., Novaczek, E., Oppel, S., Ortuño Crespo, G., Peterson, A. T., Rapacciuolo, G., Roberts, J. J., Ross, R. E., Scales, K. L., Schoeman, D., Snelgrove, P., Sundblad, G., Thuiller, W., Torres, L. G., Verbruggen, H., Wang, L., Wenger, S., Whittingham, M. J., Zharikov, Y., Zurell, D., and Sequeira, A. M. M. 2018. Outstanding challenges in the transferability of ecological models. Trends Ecol. Evol. 33:790-802.