Heuristic optimisation of the management strategy of a plant epidemic using sequential sensitivity analyses

Short title: Optimisation of plant disease management strategies

Loup Rimbaud\textsuperscript{1,2}, Sylvie Dallot\textsuperscript{1}, Claude Bruchou\textsuperscript{3}, Sophie Thoyer\textsuperscript{4}, Emmanuel Jacquot\textsuperscript{1}, Samuel Soubeyrand\textsuperscript{3} and Gaël Thébaud\textsuperscript{1*}

\textsuperscript{1} BGPI, INRA, Montpellier SupAgro, Univ. Montpellier, CIRAD, TA A-54/K, Campus de Baillarguet, 34398, Montpellier Cedex 5, France.
\textsuperscript{2} Present address: CSIRO Agriculture and Food, GPO Box 1700, Canberra, ACT 2601, Australia.
\textsuperscript{3} BioSP, INRA, 84914, Avignon, France.
\textsuperscript{4} CEEM, Montpellier SupAgro, INRA, CNRS, Univ. Montpellier, France

* Corresponding author: Gaël Thébaud
Phone: +33 4 99 62 48 55
Email: gael.thebaud@inra.fr
Abstract

- Optimisation of management strategies of epidemics is often limited by constraints on experiments at large spatiotemporal scales. A promising approach consists in modelling the biological epidemic process and human interventions, which both impact disease spread. However, few methods enable the simultaneous optimisation of the numerous parameters of sophisticated control strategies. To do so, we propose a heuristic approach based on sequential use of sensitivity analysis. This work is motivated by sharka (caused by *Plum pox virus*), a vector-borne disease of prunus trees (especially apricot, peach and plum), and its management in orchards, mainly based on surveillance and tree removal.

- Our approach is based on three sensitivity analyses which respectively aim to: i) identify the key parameters of a spatiotemporal model simulating disease spread and control; ii) approach optimal values for the key parameters; iii) refine the optimisation.

- We highlight the importance of carefully designing the removal procedure, and propose improved strategies with regard to an economic criterion accounting for both the cost of the different control measures and the benefit generated by productive trees.

- We expect that our general approach will help policymakers to design sustainable and cost-effective strategies for the management of infectious diseases.

Keywords: cost-effectiveness, culling, PPV, roguing, SEIR, Sobol.

Introduction

Optimising large-scale disease management constitutes a major challenge. Faced with the urgent need to deal with emerging epidemics, one often relies on expert opinions to design management strategies for infectious diseases, but they are not necessarily based on quantitative data. Some specific control methods can be tested through field trials, but they constitute only part of a global management strategy, which must be assessed at large spatiotemporal scales. However, at such scales field trials are considerably limited by tractability issues arising from ethical, regulatory, or logistical constraints. Epidemiological models represent one promising approach to overcome these obstacles and to account for the numerous interactions between biological processes and human interventions that jointly impact disease spread. The key epidemiological parameters of these models constitute prime targets for control measures. As shown for plant viruses (Chan & Jeger, 1994; Jeger & Chan,
1995; Holt et al., 1999; Rimbaud et al., 2018a), plant fungi (Xu & Ridout, 1998; Papaïx et al., 2014) and invasive plants (Coutts et al., 2011), these parameters can be identified using global sensitivity analysis. By varying input parameters of a simulation model within their respective variation ranges, this statistical method allows the computation of ‘sensitivity indices’ which represent the influence of the variability of each input parameter on a given output variable (Saltelli et al., 2008). The same approach may be used for simulation models that explicitly account for control actions and their potential interactions with epidemiological processes.

Some epidemiological models aim to assess the potential of different control actions in various epidemic scenarios (simulated using different combinations of epidemiological parameters). In this context, studies dealing with the management of perennial plant diseases have addressed management strategies based on roguing and possibly replanting (Parnell et al., 2009; Parnell et al., 2010; Filipe et al., 2012; Sisterson & Stenger, 2013; Cunniffe et al., 2014; Cunniffe et al., 2015; Cunniffe et al., 2016; Hyatt-Twynam et al., 2017), planting with different densities (Chan & Jeger, 1994; Jeger & Chan, 1995; Cunniffe et al., 2014; Cunniffe et al., 2015), planting at distances that are isolated from contaminated areas (Chan & Jeger, 1994; Jeger & Chan, 1995; Filipe et al., 2012), or spraying with insecticides (Filipe et al., 2012). These studies proposed some optimal control parameters under various epidemiological scenarios, but mostly for one or two control parameters—the other parameters being fixed at their reference value.

An alternative approach is to use global sensitivity analysis to jointly explore numerous combinations of control parameters and identify a combination which maximise (or minimise) a criterion. In the present study, we perform a set of global sensitivity analyses of a model which jointly simulates an epidemic process and a flexible management (meta-)strategy. For this, we use Sobol’s method, which is a reference method to compute sensitivity indices of model parameters and their interactions (Saltelli et al., 2008). This method proved able to account for model stochasticity by replicating the simulations for all parameter combinations (e.g. Rimbaud et al., 2018a).

The selection of a relevant criterion is a crucial task in an optimisation procedure. Epidemiological criteria that have been minimised for management optimisation include disease incidence (Xu & Ridout, 1998; Holt et al., 1999), prevalence (Lurette et al., 2009; Courcoul et al., 2011), severity (Xu & Ridout, 1998), propagation rate (Coutts et al., 2011; Filipe et al., 2012), basic reproduction number (Chan & Jeger, 1994), proportion of infected plants...
at the end of the simulation (Sisterson & Stenger, 2013), probability of pathogen establishment (Papaïx et al., 2014), time until eradication (Jeger & Chan, 1995; Parnell et al., 2009; Parnell et al., 2010; Barclay & Vreysen, 2011; Courcoul et al., 2011), or proportion/number of removed trees required to achieve eradication (Parnell et al., 2009; Hyatt-Twynam et al., 2017). Interestingly, the two last criteria aim to reduce the cost of the management strategy, which may be huge if disease eradication is intended. Nevertheless, to be feasible and sustainable, the choice of a management strategy must be guided by the balance between the costs induced by control actions and the economic benefits of the reduction of epidemic damage (Fraser et al., 2004; Forster & Gilligan, 2007). Here, we solve this issue by proposing: i) an epidemiological criterion based on the number of productive hosts, and ii) an economic criterion based on the present value of the flow of benefits generated by productive hosts (i.e. harvest sales), minus the costs induced by different control actions.

Our approach is applied to sharka, the most damaging disease of prunus trees (Cambra et al., 2006). Its causal agent, Plum pox virus (PPV, genus Potyvirus), is naturally transmitted by more than 20 aphid species in a non-persistent manner (Labonne et al., 1995) and has spread worldwide due to human shipping and planting of infected material (Cambra et al., 2006). Faced with the threat posed by sharka, various management strategies have been adopted in different countries (for a review, see Rimbaud et al., 2015). In countries targeting disease limitation (e.g. France) or eradication (e.g. United States), a key element of the management strategy is the appropriate surveillance of nurseries and orchards, followed by tree removals. Surveillance methods rely on leaf sampling followed by serological or molecular diagnostics, or, alternatively, visual inspection of prunus trees to detect sharka symptoms (mostly on leaves and fruits). When infected trees are detected, they are culled to remove viral sources contributing to epidemics. Regardless of the surveillance method, the infection may be detected only several months or years after inoculation (Sutic, 1971; Quiot et al., 1995). This delay hampers the detection of infected hosts and explains, combined with evidence of short-distance transmission of PPV (Dallot et al., 2003; Gottwald et al., 2013; Pleydell et al., 2018), why non-symptomatic trees surrounding detected trees may need to be removed as well. In France, sharka management is compulsory and a national decree specifies the control actions mentioned above (JORF, 2011). In particular, this decree describes a complex procedure defining the frequency of visual inspections of orchards depending on
their distance to the nearest detected infection, the removal of whole orchards if their annual contamination rate exceeds a given threshold, and the conditions for replanting. Since this strategy is complex and based on expert opinions, it is crucial to conduct a cost-benefit analysis and identify potential improved management rules.

To identify improved alternatives to the current French management strategy, we propose a heuristic approach based on sequential sensitivity analyses of a stochastic spatiotemporal simulation model. This model simulates prunus cultivation in a real agricultural landscape (553 patches, representing a total area of 524 ha) with recurrent introductions of the pathogen through orchard plantings and its subsequent spread via aphid vectors, and its management with a flexible strategy. This strategy is defined by 24 parameters (14 for surveillance, 6 for removals and 4 for replanting restrictions; see Fig. 1 and Table 1 for details) and encompasses the management strategies of several countries, including France. Consequently, the identified strategies should be of interest for many countries targeting area-wide management of sharka and more generally perennial plant diseases.

Results

In a first step, we identified the most promising control measures to manage sharka, by ranking the control parameters by influence on both our epidemiological criterion (average number of fully productive trees per hectare and per year, \( \mu Y \)) and our economic criterion (average net present value over a period of 30 years, \( \mu NPV \), measuring the discounted difference between benefits of fruit sales and costs generated by the management of all orchards of the landscape). In a second step, only the most influential control measures were retained and sensitivity analysis was used to approach an optimal combination of control parameters with regard to the economic criterion. In the last step, this optimisation was further refined using another sensitivity analysis. The identified management strategies were evaluated on simulated epidemics, in order to assess their epidemiological and economic performance relative to the current French strategy, as well as their robustness to stronger epidemics.

Step 1: identifying the most promising control parameters

The first sensitivity analysis showed that the predicted economic impact strongly depends on the contamination threshold of the ‘epicentre for removal’ (\( \chi_R \), above which
orchards in the removal zone are culled; with a total sensitivity index ($SI_{tot}$) of 0.54; CI95: 0.39-0.65) and the contamination threshold in orchards of the neighbourhood of a previously culled orchard ($\chi_{n}$, above which replanting is forbidden; $SI_{tot}$ of 0.36; CI95: 0.25-0.45) (Fig. 2). These parameters were also the main contributors to model stochasticity (Fig. S1). Next came the radius of the removal zone ($\zeta_R$, $SI_{tot}$ of 0.15; CI95: 0.08-0.20), then a Boolean variable indicating whether whole orchards are removed immediately or at the end of the year ($\Upsilon_R$, $SI_{tot}$ of 0.13, CI95: 0.06-0.18), followed by the detection probability ($\rho$; $SI_{tot}$ of 0.09; CI95: 0.07-0.12) and the size of the removal epicentre—where the contamination rate is measured to assess if orchards in the removal zone must be culled—($r_{eR}$; $SI_{tot}$ of 0.09; CI95: 0.05-0.12). The effect of all of these parameters seems to be mostly due to interactions with other parameters, since their total Sobol indices were much higher than their 1st-order indices. This probably explains why it was difficult to predict the net present value ($NPV$) from the values of $\zeta_R$, $\Upsilon_R$ or $r_{eR}$ only (Fig. 2, insets). The strong impact of removal and planting measures is likely due to excessive tree removals or orchard planting bans, when the respective contamination thresholds are low (below 5% for removals and below 10% for planting bans; Fig. 2, insets). However, for higher thresholds, $\mu_{NPV}$ remained stable, suggesting that these parameters no longer have an effect. This may be the sign of an absence (or rarity) of high contamination events in orchards or in removal epicentres (and thus of extremely rare planting bans or removal of whole zones). Finally, the quadratic effect of $\rho$ reveals the existence of a trade-off between detection efficiency and the costs induced by orchard surveillance.

Interestingly, the 11 least influential parameters (5 epidemiological parameters and 6 control parameters) had very low total sensitivity indices (less than 0.03), which indicates a negligible effect of their variation on the mean output. Control actions governed by these parameters have little effect on the economic impact of epidemics, compared to the parameters discussed above. Similar conclusions emerged from the analysis of the epidemiological output of the model (Fig. S2). Consequently, the 6 least influential control parameters, governing the control measures with the highest degree of complexity (surveillance and planting ban reinforcement in locally highly contaminated areas), $r_{x,y}$, $\eta^x$, $\chi^0$, $r_{c0}$, $\eta^p$ and $\chi^y$, were removed in the next step in order to simplify the model in the context of sharka management.
Step 2: approaching optimal values of control parameters

A second sensitivity analysis was performed on the control parameters only, except for the 6 parameters discarded in step 1. Optimal values of the 17 control parameters were approached either by using the parameter combination leading to the best $\mu_{NPV}$ ('best-value strategy'), or the combinations leading to the best percentile of $\mu_{NPV}$ ('best-percent strategy'). In both approaches, management is improved when detected trees are removed immediately (i.e. after an average of 10 days, rather than at the end of the year; see $Y_R^T$ in Fig. 3). The obtained values for the removal threshold ($\chi^R$), and the radius of the removal zone ($\zeta^R$) and its epicentre ($r_{\zeta^e R}$, where contamination rate is measured) were so high that no removal of whole orchards may occur in the associated simulations (see $\chi^R$ in Fig. 3 and all other parameters in Fig. S3). In addition, small values for these parameters ($\chi^R < 5\%$; $\zeta^R < 2$ km; $r_{\zeta^e R} < 20\%$) were associated with the worst epidemics (last percentile of $\mu_{NPV}$). These results suggest that in our model, removal of healthy hosts induces higher costs than the maintenance of undetected or latently infected hosts. With regard to observations, either the focal area matched approximately the security area ($r_{\zeta^f}$, ‘best-value strategy’), or the observation frequencies in these zones were the same ($\eta_f$ and $\eta_s$, ‘best-percent strategy’). This indicates that the distinction of two different zones may not be necessary. Thus the control actions governed by parameters $\chi^R$, $\zeta^R$, $r_{\zeta^e R}$, $Y_R$, $r_{\zeta^f}$ and $\eta_f$ were discarded in the next step.

Step 3: refining the optimisation

A third sensitivity analysis was performed on the 10 remaining control parameters to further refine their optimisation. In this analysis, variation ranges of the target parameters were restricted to the most probable optimal values (see $\rho$ in Fig. 3 and all other parameters in Fig. S3). Then, the optimisation procedure was exactly the same as in step 2 (Fig. 3 and Fig. S4). The resulting ‘best-value’ and ‘best-percent’ strategies are significantly simpler than the current French strategy (Fig. 4). To summarise the best-value strategy, every time a symptomatic tree is detected in an orchard, this orchard is surveyed three times per year for the three following years (Table 2, reference epidemic context). Whole orchards are removed only if the proportion of living trees falls below $\chi_{SEHD}=0.66$ (for profitability reasons, see Methods and Table S1), and in this case they can be replanted without delay. Nevertheless, replanting is forbidden within a radius of 2.8 km if the contamination rate of an orchard...
exceeds 60% (i.e. in case of a massive introduction, in our simulations). In areas where no infected tree has been detected in the three previous years, orchards are surveyed once every four years. The detection probability is 36%, meaning that orchard are surveyed in approximately one every two rows under our assumptions.

Alternatively, in the best-percent strategy (Table 2), each time a symptomatic tree is detected, the orchard is surveyed once in the following year. Similar to the best-value strategy, whole orchards may only be removed for profitability reasons, and can be replanted without delay (except in the unlikely event of a contamination rate higher than 92% in an orchard within a radius of 962 m). In the first year after planting, young orchards are surveyed once. Older orchards in non-contaminated areas are routinely surveyed every four years. The detection probability is 60% (i.e. close to the reference value).

Simulation of the improved strategies

Repeated simulations of the identified improved strategies were carried out in order to compare their epidemiological ($Y$) and economic ($NPV$) outcomes with those obtained in disease-free and management-free scenarios, and with the reference management (i.e. the current strategy for managing sharka in France). Firstly, these simulations show that managing the disease is vital, since the median number of productive trees per hectare and per year is only 513 and is highly variable [2.5%; 97.5% quantiles: 462; 551] compared to the disease-free scenario (median number of 560 trees [551; 569]) (Fig. 5a). This results in a 59% decrease in the median $NPV$ (6.03 million euros [-4.06; 13.0] in the absence of management, vs 14.6 million euros [13.5; 15.7] in the absence of disease), and possibly huge economic losses in the worst-case scenarios (Fig. 5b). It is interesting to note that, in our model, the reference strategy is very efficient with respect to the reduction of direct losses to sharka (median of 559 productive trees per ha and per year [550; 569]). Nevertheless, the costs associated to disease management considerably reduce the $NPV$ (12.1 million euros [10.7; 13.4]). This $NPV$ is 17% lower than in the disease-free scenario, but still much higher than in the absence of management. The improved best-value and best-percent strategies are nearly as efficient as the reference strategy with regard to the number of productive trees, but resulted in similar reduced costs, with a median $NPV$ of 13.7 [12.2; 15.0] and 13.7 [11.7; 15.0] million euros, respectively. These management strategies are associated with slightly higher disease incidence and prevalence than for the current French strategy (Fig. S5, top line). This results
in more individual tree removal, but is overly compensated by the smaller number of observations in orchards (Fig. S6, top line). Consequently, both of these strategies are more cost-effective.

When tested in harsher epidemiological contexts with half expected duration of the latent period of the pathogen ($\theta_{exp}$), the identified management strategies were still efficient with respect to both the epidemiological ($Y$) and economic ($NPV$) criteria (Fig. S7a,b). However, with doubled transmission coefficient ($\beta$), the improved management strategies (in particular the best-percent strategy) were not as efficient as the reference scenario (Fig. S7c,d). This resulted in higher levels of disease prevalence and incidence (Fig. S6, bottom line) and consequently more tree removals (Fig. S7, bottom line). In contrast, the reference management strategy was robust to the simulated changes in epidemic severity (Figs. S5, S6, S7). We re-ran the whole heuristic optimisation approach with shorter latent period or stronger transmission coefficient. The new identified strategies, indicated in Table 2, mainly differ from the previous ones by the increased surveillance frequency of contaminated and non-contaminated orchards, as well as by the introduction of a delay before orchard replanting. These new strategies satisfy both epidemiological and economic performance criteria (Figs. S8, S9).

**Discussion**

**Optimising management strategies of epidemics**

In this article, we propose an innovative heuristic approach based on the sequential use of global sensitivity analysis of a simulation model to improve management strategies of plant disease epidemics. Following the identification of the most promising control measures (step 1), the exploration of parameter space, initially large (step 2) and then more restricted (step 3), enables a simplification of the strategy and the joint improvement of the control parameters by progressively approaching an optimal combination. One can note that further sensitivity analyses could be performed if more accuracy is required for some parameters. In contrast with previous studies focussing on a restricted number of control parameters (e.g. Parnell et al., 2010; Cunniffe et al., 2015; Hyatt-Twynam et al., 2017), our approach includes a wide range of management strategies and enables to jointly improve the entire set of control parameters.
Accounting for the long-term costs and benefits of disease control is crucial to the design of feasible, durable, and cost-effective management strategies (Fraser et al., 2004; Forster & Gilligan, 2007), which in turn, will increase the likelihood of adoption by growers. Some recent studies proposed approaches to prioritise surveillance or removal options under limited resources (Cunniffe et al., 2016; Faulkner et al., 2016). Other studies proposed optimised management of different perennial plant diseases using a composite criterion which includes the number of disease-induced deaths and removals of trees (i.e. proxies for intrinsic costs of the epidemic and the management, respectively) and the time to eradication (Cunniffe et al., 2015), or accounting for the cost of observation of a single tree relative to the net profit generated by the cultivation of this tree (Cunniffe et al., 2014). Here, we developed an economic criterion which explicitly accounts for the benefits generated by the cultivation of productive hosts (i.e. fruit sales), and the costs induced by orchard cultivation plus different control actions comprising observations, removals, replantings and planting bans. By doing so, the different components of the management strategy can be optimised with explicit consideration of their cost relative to the benefit due to the reduction of epidemic damage. Although this criterion was specifically parameterised for peach orchards, it could easily be employed for other crops by reassessing the costs and benefits associated with their cultivation and disease management. Finally, we also used an epidemiological criterion to assess the epidemiological efficiency of the identified optimised strategies. This metric integrated the number of productive hosts across the whole landscape and the whole simulation period, and is therefore comparable to the ‘healthy area duration’ used in many epidemiological models (e.g. Lo Iacono et al., 2013; Rimbaud et al., 2018b; Papaïx et al., early view).

Managing perennial plant epidemics and especially sharka

This work was motivated by the management of sharka, a viral disease of prunus trees against which a complex management strategy is currently applied in France. Once implemented in our simulation model, this strategy provided a particularly relevant reference point because it represents management strategies for numerous perennial plant diseases, based on surveillance, removals and replanting restrictions (Fig. 1). We note, however, that some control actions (for which we had no cost/benefit values) were not investigated in our model, like nursery protection measures or planting at different densities. In addition, vector
control by pesticides, shown to be efficient against some diseases like citrus huanglongbing (Lee et al., 2015), was not studied here because pesticides generally fail with non-persistent viruses such as PPV (Perring et al., 1999; Rimbaud et al., 2015).

**Identifying promising control measures.** The first sensitivity analysis highlighted the most influential control parameters on sharka epidemics in French peach orchards. These were associated with the removal of orchards, the ban on plantings and the probability of detection (Fig. 2). These elements highlight the importance of modelling studies designed to optimise detection efficiency (e.g. using hierarchical sampling, Hughes et al., 1997), and removal actions (e.g. by identifying an optimal cull-radius, Parnell et al., 2009; Parnell et al., 2010; Cunniffe et al., 2015; Cunniffe et al., 2016).

Ranking model parameters by their influence on a given output variable also allows the identification of weak contributors. Among the implemented control parameters, those associated with the modification of surveillance in response to observed local prevalence had a negligible impact on both epidemiological and economic outcomes (Fig. 2). Therefore, in the scenarios we investigated, reinforcing surveillance in highly contaminated areas may not result in improved management. Thus, the associated parameters could be discarded from the modelled management strategy without altering its efficiency. It is important to note that we assumed that each symptomatic tree had the same detection probability, regardless of its age, cultivar and time elapsed since symptom expression. Nevertheless, field experience shows that all these factors impact symptom expression and consequently visual detection. Moreover, detection events were considered independent, which enabled an excellent global detection rate after a few observation rounds. These elements could partly explain why reinforcing surveillance in highly contaminated areas had a negligible impact.

In previous studies, the connectivity of the patch of first introduction was the most influential epidemiological parameter on sharka spread in the absence of management (Rimbaud et al., 2018a). It is still the case here, in presence of management (Fig. 2, parameter $q_v$). This result suggests that reinforced baseline surveillance of highly connected patches could be a promising control measure. This result also supports the need to match management efforts with the risk index of different patches (Nelson et al., 1994; Barnes et al., 1999; Parnell et al., 2014) or individual hosts (Hyatt-Twynam et al., 2017) and to prioritise such management under limited resources (Cunniffe et al., 2016; Faulkner et al., 2016). Favouring
the planting of resistant cultivars in patches with high risk indices could also be a promising approach for disease management.

**Improving the management strategy.** Our results suggest that removing whole orchards triggers higher costs than potential losses associated with maintaining cryptically infected hosts. The identified improved strategies are thus based on a ‘symptomatic hosts hunt’ (Fig. 4). However, orchard surveillance to identify these symptomatic hosts also induces high costs. Thus, in contaminated orchards, improved strategies relied either on few surveillance rounds with a good probability of detection (close to the reference value), or a greater number of surveillance rounds with a low probability of detection (half the reference value, which may correspond to the orchard surveillance of every other row only, and was assumed here to trigger smaller costs per surveillance round). Overall, while surveying an orchard more than once a year multiplies the cost, it favours the detection of trees which may be cryptically infected at the time of the first round of surveillance.

These surveillance procedures, and the absence of removal zones, make these strategies simpler and less expensive than the current French management of sharka (Fig. 5). Nevertheless, in the improved strategies, the basic frequency of orchard surveillance is increased to once every four years (instead of once every six years for the reference frequency). This indicates that better management should be obtained by more frequently surveying all orchards in a region. Indeed, costs of management can be considerably decreased by prompt implementation of control measures after new introductions (Cunniffe et al., 2016).

With respect to the improved strategies identified here, we note several assumptions which may influence our recommendations. In particular, the ability to detect symptomatic hosts may have been overestimated, as explained above. Consequently, in the field and under certain conditions, it might still be interesting to rogue whole orchards (or even nearby orchards if eradication is intended) in order to remove hardly detectable diseased trees. Additionally, it may be interesting to investigate the potential of alternative detection protocols, like serological or molecular methods, which are used for the management of several perennial plant epidemics (including sharka) in the United States (Gougherty et al., 2015). Such investigation could be performed with our model by changing the relationship between the probability of detection and the cost of surveillance. Furthermore, we assumed...
that all orchards had the same susceptibility to PPV. However, evidence suggests that young plants may be more susceptible to viral infection than older ones (Astier et al., 2007). Thus, in our results, surveillance of young orchards was probably not as crucial as it should be.

Despite these considerations, the best-value and best-percent strategies deserve to be investigated in order to improve cost-efficiency of sharka management. Globally, these options are based on the simplification of surveillance and removal measures to reduce management costs while maintaining good epidemiological performance. However, our results show that these strategies may fail to control disease in harsh epidemic contexts. For these situations, the flexibility of our approach allowed us to identify new strategies, illustrating its general ability to find improved combinations of control parameters in a given epidemic context.

Methods

Model description

Model overview. A stochastic, spatially-explicit, SEIR (susceptible-exposed-infectious-removed) model was previously developed to simulate sharka epidemics in a cultivated landscape (Pleydell et al., 2018; Rimbaud et al., 2018a). The model is orchard-based, with a discrete time step of 1 week. Each host is in one of five different health states (Fig. 1a). The epidemic process and the transitions between states are described in previous articles (Pleydell et al., 2018; Rimbaud et al., 2018a), and summarised in Method S1. Briefly, healthy trees (state S) become infected (state E) when successfully inoculated by infectious aphid vectors. After a latent period, infected trees become infectious and symptomatic (state H), from where they may be detected (state D) and subsequently culled (state R). It is assumed that infectious trees are no longer productive, due to either diseased-induced reduction of fruit yield, or a sales ban on fruit from symptomatic trees. However, the disease is not supposed to affect host lifespan (no available data reported any increase in prunus mortality due to PPV), thus hosts can move to state R only if removed. Due to orchard turnover (independent from the disease), whole orchards can be replaced by trees in state S (or possibly H). Table 1 summarises all the model parameters.

A management strategy, based on orchard surveillance and tree removal, is applied after $a_m=6$ years of epidemic during 30 years, which is twice the mean lifespan of the hosts.
and consequently a reasonable duration in which to assess the efficiency of a management strategy. The reference management strategy is based on the French management of sharka in prunus orchards (JORF, 2011). Nevertheless, our model allows a multitude of variations on each control measure, which makes it possible to include some aspects of sharka management in other countries (e.g. removal radius around detected trees, as done in the United States, Gottwald et al., 2013).

**Orchard surveillance.** All orchards in a region are effectively surveyed for disease at least once every \( \frac{1}{\eta_0} \) years, and at each survey symptomatic hosts (state H) are independently detected with probability \( \rho \). Detected trees trigger the definition of two nested zones around their orchard: a security zone whose radius is \( \zeta_s \) and a focal zone whose radius is \( \zeta_f \) (Fig. 1b). Within security and focal zones, orchards are surveyed \( \eta_s \) and \( \eta_f \) times per year, respectively, during \( \gamma_o \) years. Furthermore, in the focal zone the surveillance frequency is changed to \( \eta_f^* \) if the contamination rate of the epicentre exceeds a threshold value \( \chi_o \) (see Method S2 for calculation of the contamination rate). The ‘observation epicentre’, whose radius is \( \zeta_{eo} \), corresponds to a fraction of the focal area where the contamination rate (noted \( q_{eo} \)) is calculated. Additionally, young orchards are surveyed \( \eta_y \) times per year during \( \gamma_y \) years, but this frequency is changed to \( \gamma_y^* \) if the contamination rate of the environment around the patch to be planted exceeds a threshold value \( \chi_{yo} \) (Fig. 1c). The environment is a zone around the patch to be planted; its radius is \( \zeta_{eo} \) (i.e. the same as the observation epicentre).

When an orchard falls simultaneously within several surveillance zones, the maximal surveillance frequency is applied. The observation dates are drawn from a uniform distribution between the 92th and the 207th day of the year, i.e. the earliest and the latest observation dates in the database collected in southeastern France, respectively. If the cultivar produces flowers with petals (on which symptoms may be observed), the observation period is extended from the 59th to the 207th day (Fig. S10).

**Removals and replantings.** Detected trees are removed individually and are not supposed to be replanted, because it would lead to orchard desynchronization in terms of phenology and fruit maturation. Moreover, if contamination rate \( q_{er} \) in the ‘removal epicentre’ (defined by a radius \( \zeta_{er} \)) exceeds a threshold value \( \chi_r \), all orchards inside the removal zone (whose radius distance is \( \zeta_{r} \)) are removed as well (Fig. 1d). Two Boolean variables, \( \Upsilon_{RT} \) and \( \Upsilon_{R} \), indicate whether individual detected trees or whole orchards, respectively, are to be removed after a mean delay of \( \delta \), or at the end of the year. To avoid...
excessive fragmentation of orchards due to individual removals, orchards are totally removed if the proportion of living trees (i.e. trees in all health states except R) falls below $\chi_{SEHD}$, which is a threshold for economic profitability (see details in Table S1).

Orchards can be replanted after a delay of $\gamma$ years. However, planting is forbidden if the contamination rate of the environment exceeds a threshold value $\chi_y$, or if an orchard located at a distance below $\zeta$ has a contamination rate above a threshold value $\chi_n$ (Fig. 1c).

**Output variables.** The model generates two output variables. The epidemiological output, noted $Y$, is the mean equivalent number of fully productive trees per hectare per year, from the first ($a_m$=6) to the last ($a_f$=35) year of management. In this criterion, fully described in (Rimbaud et al., 2018a), mature trees count for 1 whereas diseased and newly planted trees count for 0.

The economic output (used as an optimisation criterion in our approach based on sensitivity analyses) is based on the net present value (in euros) of prunus cultivation over the same time period (years 6 to 35). Considering the whole landscape as a single 'farm' with all the benefits and costs associated with prunus cultivation and sharka management, the gross margin, noted $GM_a$, of this farm can be calculated for year $a$ ($a=a_m, \ldots, a_f$) as the benefit generated by fruit production and sale ($p$), minus fixed cultivation costs ($c_F$), orchard planting cost ($c_S$), orchard observation cost ($c_O$), and the cost of removal of a tree ($c_{RT}$) or a whole orchard ($c_{R}$).

Reference values for these economic parameters were estimated (Table S1) based on expert opinions, as well as data on French peach production (Agreste, 2013, 2014, 2015), selling price (FranceAgriMer, 2015), and consumer price index (INSEE, 2015). The cost of one orchard observation is described by a simple linear function of the detection probability: $c_O = 40 + 182 \times \rho$, to account for the effect of partial observation of orchards (e.g. surveillance of every other row only), which reduces both the probability of detection and the cost of observation. Thus, $GM_a$ is calculated as follows:

$$GM_a = \sum_{i=1}^{I} \left\{ y_{i,a} \cdot p \cdot \frac{S_{i,a} + E_{i,a}}{N_{i,a}} \cdot A_i - c_F \cdot A_i - \frac{R}{a_{i,a}} \cdot c_R \cdot A_i - \frac{S}{a_{i,a}} \cdot c_S \cdot A_i - \frac{R}{a_{i,a}} \cdot c_{RT} \cdot R_{i,a} - c_o \cdot O_{i,a} \cdot A_i \right\}$$

with, for orchard $i$ in $\{1, \ldots, I\}$ during year $a$:

- $y_{i,a}$ the relative age-dependent fruit yield of the hosts in S and E states;
- $A_i$ the orchard area (ha);
- $\frac{S_{i,a} + E_{i,a}}{N_{i,a}}$ the proportion of the orchard that produces fruits;
the number of observations; 
the number of newly (individually) removed trees due to PPV detection; 
a Boolean which equals 1 if the orchard is removed, and 0 otherwise; 
a Boolean which equals 1 if the orchard is planted, and 0 otherwise.

Using a discount rate $\tau_a=4\%$ (Quinet, 2013), the net present value (NPV) for the landscape from $a_m$ to $a_f$ is:

$$NPV = \sum_{a=a_m}^{a_f} \frac{GM_a}{(1+\tau_a)(a-a_m)}.$$ 

**Management improvement through sequential sensitivity analyses**

Improvement of the management strategy was performed using three sensitivity analyses. For these analyses, we used Sobol’s method, which consists of: i) defining the target parameters, their respective variation ranges and probability distributions (uniform, in this work); ii) generating a design to explore the parameter space; iii) running simulations; and iv) computing Sobol’s sensitivity indices which quantify the influence of the variation of each target parameter on the output variable (Saltelli et al., 2008). The 1st-order sensitivity index of a parameter, noted $SI_i$, measures the main effect of this parameter whereas the total sensitivity index, noted $SI_{tot}$, accounts for its interactions with other parameters. These indices are bounded by 0 and 1, thus a total index close to 0 means that the parameter has a negligible effect on the output variable.

Sobol’s method requires that exploration of the parameter space be performed using independent distributions to sample the target parameters. Thus, since the focal zone, the epicentre for observation and the epicentre for removal are nested in the security zone, the focal zone and the removal zone, respectively, these zones were re-parameterised using the following area ratios:

$$r_{\zeta_f} = \frac{\pi \times \zeta_f^2}{\pi \times \zeta_s^2} = \left(\frac{\zeta_f}{\zeta_s}\right)^2, \quad r_{\zeta_y} = \left(\frac{\zeta_y}{\zeta_f}\right)^2, \quad \text{and} \quad r_{\zeta_R} = \left(\frac{\zeta_R}{\zeta_f}\right)^2.$$ 

In addition, the contamination threshold, above which the observation frequency in young orchards is modified, was re-parameterised using its ratio relative to the contamination threshold above which replanting is forbidden: $r_{\chi_y^*} = \frac{\chi_y^*}{\chi_y}$. 

**Step 1: assessing the relative influence of model parameters.** The 23 control parameters defined in the implemented management strategy were targeted in this first step,
in addition to 6 parameters associated with the main epidemiological processes (introduction: $q_\kappa$, $\Phi$, and $p_{MI}$; dispersal: $W_{exp}$; transmission coefficient: $\beta$; and latent period duration: $\theta_{exp}$).

Except for $q_\kappa$ and $p_{MI}$, variation ranges were defined as the 99% credibility intervals of the parameter estimates provided by a Bayesian inference model applied to PPV-M epidemics in southeastern France (Pleydell et al., 2018). In contrast, variation ranges of $q_\kappa$, $p_{MI}$ and the 23 control parameters were defined as their respective domain of definition, possibly restricted using expert opinions when this domain was infinite (Table 1).

Simulations were performed for 310,155 different parameter combinations generated with Sobol sequences (Sobol, 1976). To account for stochasticity, each combination was replicated 30 times (this number was found to be largely sufficient to generate robust estimates of the mean and standard deviation associated with each combination; Fig. S11). Then, the indices were calculated as in (Rimbaud et al., 2018a) on the standardised means and standard deviations of the epidemiological ($\mu_Y$ and $\sigma_Y$) and economic ($\mu_{NPV}$ and $\sigma_{NPV}$) criteria.

**Step 2: approaching optimal values of the most influential parameters.** In the second step, only the most influential control parameters (i.e. those with the highest $SI_{tot}$) identified in the first step were retained. The 17 remaining parameters were varied within the same variation ranges as previously (Table 1), using 310,156 different parameter combinations and 30 stochastic replicates. In this sensitivity analysis, the 6 epidemiological parameters were not targeted, but for each simulation they were drawn from uniform distributions using the same bounds as in the previous step, in order to optimise the management strategy for variable epidemics.

A heuristic joint optimisation of the 17 control parameters was obtained by isolating the parameter combination associated with the highest $\mu_{NPV}$ (‘best-value strategy’). Additionally, a marginal optimisation of the same parameters was achieved using the mode of the distribution of each parameter within the combinations associated with the best 1% values of $\mu_{NPV}$ (‘best-percent strategy’). A similar approach allowed identification of the parameters associated with the worst 1% values of $\mu_{NPV}$. It is important to note that the first method accounted for possible interactions between parameters, since a whole parameter combination was retained.

**Step 3: refining the optimisation.** Based on the results of the previous step, six control parameters were found unnecessary (see Results section), one control parameter was
improved with certainty, and the estimated values of the 10 remaining control parameters were still imprecise. These 10 parameters were further improved using a dedicated sensitivity analysis and variation ranges restricted to the most probable optimal values (Table 1). This sensitivity analysis was performed as in previous steps, using 310,152 different parameter combinations and 30 replicates.

**Simulation of the improved management strategies**

To test the performance of the identified management strategies, 10,000 simulation replicates were performed with parameters corresponding to different scenarios: (A) “Disease-free” (PPV is not introduced in the landscape); (B) “Management-free” (PPV is introduced and not managed); (C) “Reference management” (PPV is introduced and managed according to the current French strategy, defined in (JORF, 2011)); (D) “best-value strategy”; and (E) “best-percent strategy”. In scenarios B to E, the six epidemiological parameters were varied inside their respective specific ranges (Table 1). The impact of the epidemic was assessed by the distribution of the epidemiological criterion ($Y$), the economic criterion ($NPV$), as well as the dynamics of annual prevalence and incidence, and the dynamics of observations and removals. Furthermore, similar simulations were performed using doubled values for the pathogen transmission coefficient ($\beta$) and halved values for the latent period duration ($\theta_{exp}$), in order to test the robustness of the identified management strategies to harsher epidemic contexts.

**Computing tools**

The model was written in R and C languages. Sobol’s sequences and Sobol’s indices were respectively generated and calculated using the packages *fOptions*, v3010.83 ([Wuertz et al., 2017](https://cran.r-project.org/web/packages/fOptions/index.html)) and *sensitivity*, v1.11 ([Pujol et al., 2017](https://cran.r-project.org/web/packages/sensitivity/index.html)) of the R software, v3.0.3 ([R Core Team, 2012](https://www.r-project.org/)). A simulation takes approximately 8 seconds with a regular desktop (Intel® Core™ i7-4600M).

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platforms and L. Houde and S. Ravel for providing support. LR was supported by a DGA-MRIS scholarship, and this work was partly funded by the EU (SharCo project, FP7 programme) and FranceAgriMer (Sharka project).

Author Contributions

Designed research: LR, SD, EJ, SS, GT. Performed research: LR. Analysed data: LR, SD, CB, ST, EJ, SS, GT. Wrote the paper: LR, EJ, SS, GT. Secured funding for project’s execution: SD, EJ, SS, GT.

References


Coulltts SR, van Klinken RD, Yokomizo H, Buckley YM. 2011. What are the key drivers of spread in invasive plants: dispersal, demography or landscape: and how can we use this knowledge to aid management? Biological Invasions 13(7): 1649-1661.


Table 1. Parameters of the model: description, reference values for sharka epidemics in French peach orchards, and variation ranges in the sensitivity analyses. The first sensitivity analysis (step 1) targeted 23 control parameters and 6 epidemiological parameters to assess their relative influence on model outputs. In the second step, only the 17 most influential control parameters (bounds in bold) were kept and improved. In the third step, 6 unnecessary parameters were removed, 1 parameter was fixed, and the remaining 10 parameters (in bold) were further improved.

<table>
<thead>
<tr>
<th>Parameter and description</th>
<th>Reference value</th>
<th>Steps 1 and 2</th>
<th>Step 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Min</td>
<td>Max</td>
</tr>
<tr>
<td><strong>Temporal and landscape parameters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$a_0$ First year of epidemic</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>$a_m$ First year of management</td>
<td>6</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>$a_f$ Last year of simulation</td>
<td>35</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>$\psi$ Expected orchard duration (years)</td>
<td>15 $^a$</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Epidemiological parameters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$q_x$ Quantile of the connectivity of the patch of first introduction</td>
<td>0.50</td>
<td>0.00 $^b$</td>
<td>1.00 $^b$</td>
</tr>
<tr>
<td>$\phi$ Probability of introduction at planting</td>
<td>0.007 $^a$</td>
<td>0.0046 $^a$</td>
<td>0.0107 $^a$</td>
</tr>
<tr>
<td>$p_{mi}$ Relative probability of massive introduction</td>
<td>0 $^a$</td>
<td>0.00 $^a$</td>
<td>0.10 $^a$</td>
</tr>
<tr>
<td>$W_{exp}$ Expected value of the dispersal weighting variable</td>
<td>0.486 $^c$</td>
<td>0.469 $^c$</td>
<td>0.504 $^c$</td>
</tr>
<tr>
<td>$W_{var}$ Variance of the dispersal weighting variable</td>
<td>0.0434 $^c$</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>$\beta$ Transmission coefficient</td>
<td>1.32 $^c$</td>
<td>1.25 $^c$</td>
<td>1.39 $^c$</td>
</tr>
<tr>
<td>$\theta_{exp}$ Expected duration of the latent period (years)</td>
<td>1.92 $^c$</td>
<td>1.71 $^c$</td>
<td>2.14 $^c$</td>
</tr>
<tr>
<td>$\theta_{var}$ Variance of the latent period duration (years)</td>
<td>0.44 $^c$</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Surveillance parameters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\rho$ Probability of detection of a symptomatic tree</td>
<td>0.66 $^c$</td>
<td>0 $^b$</td>
<td>0.66 $^h$</td>
</tr>
<tr>
<td>$\gamma_o$ Duration of observation zones (years)</td>
<td>3 $^d$</td>
<td>0 $^b$</td>
<td>10 $^i$</td>
</tr>
<tr>
<td>$\gamma_y$ Duration of young orchards (years)</td>
<td>3 $^d$</td>
<td>0 $^b$</td>
<td>10 $^i$</td>
</tr>
<tr>
<td>$\zeta_s$ Radius-distance of security zones (m)</td>
<td>2,500 $^d$</td>
<td>0 $^b$</td>
<td>5,800 $^j$</td>
</tr>
<tr>
<td>$r_{\zeta_f}$ Ratio of the focal area over the security area</td>
<td>0.36 $^d$</td>
<td>0 $^b$</td>
<td>1 $^b$</td>
</tr>
<tr>
<td>Parameter</td>
<td>Description</td>
<td>Value</td>
<td></td>
</tr>
<tr>
<td>-----------</td>
<td>-----------------------------------------------------------------------------</td>
<td>-------</td>
<td></td>
</tr>
<tr>
<td>$r_{\xi o}$</td>
<td>Ratio of the observation epicentre area over the focal area</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>$1/\eta_o$</td>
<td>Maximal period between 2 observations (year)</td>
<td>6 d</td>
<td></td>
</tr>
<tr>
<td>$\eta_s$</td>
<td>Observation frequency in security zones (year$^{-1}$)</td>
<td>1 d</td>
<td></td>
</tr>
<tr>
<td>$\eta_f$</td>
<td>Observation frequency in focal zones (year$^{-1}$)</td>
<td>2 d</td>
<td></td>
</tr>
<tr>
<td>$\eta_f^o$</td>
<td>Modified observation frequency in focal zones (year$^{-1}$)</td>
<td>3 d</td>
<td></td>
</tr>
<tr>
<td>$\eta_y$</td>
<td>Observation frequency in young orchards (year$^{-1}$)</td>
<td>2 d</td>
<td></td>
</tr>
<tr>
<td>$\eta_y^o$</td>
<td>Modified observation frequency in young orchards (year$^{-1}$)</td>
<td>3 d</td>
<td></td>
</tr>
<tr>
<td>$\chi_o$</td>
<td>Contamination threshold in the observation epicentre, above which</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td></td>
<td>the observation frequency in focal zone is modified</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$r_{\chi y^o}$</td>
<td>Ratio (over $\chi y$) of the contamination threshold in the environment,</td>
<td>0.50</td>
<td></td>
</tr>
<tr>
<td></td>
<td>above which the observation frequency in young orchards is modified</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\delta$</td>
<td>Mean delay before removal of a detected tree (days)</td>
<td>10 d</td>
<td></td>
</tr>
<tr>
<td>$Y_R^T$</td>
<td>(Boolean) Individual trees are removed:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0: after a mean delay $\delta$</td>
<td>0 d</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1: at the end of the year</td>
<td>0 b,m</td>
<td></td>
</tr>
<tr>
<td></td>
<td>$Y_R$</td>
<td>(Boolean) Whole orchards are removed:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0: after a mean delay $\delta$</td>
<td>1 d</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1: at the end of the year</td>
<td>0 b,m</td>
<td></td>
</tr>
<tr>
<td></td>
<td>$\zeta_R$</td>
<td>Radius-distance of the removal zone (m)</td>
<td>0 d</td>
</tr>
<tr>
<td></td>
<td>$T_{\xi oR}$</td>
<td>Ratio of the removal epicentre area over the removal area</td>
<td>0 d</td>
</tr>
<tr>
<td></td>
<td>$\chi_R$</td>
<td>Contamination threshold in the removal epicentre, above which</td>
<td>0.10</td>
</tr>
<tr>
<td></td>
<td>orchards inside the removal zone are removed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\gamma_S$</td>
<td>Delay before replanting of a removed orchard (years)</td>
<td>0 d</td>
<td></td>
</tr>
<tr>
<td>$\zeta_n$</td>
<td>Radius-distance of the neighbourhood (m)</td>
<td>200 d</td>
<td></td>
</tr>
<tr>
<td>$\chi_y$</td>
<td>Contamination threshold in the environment around young orchards, above</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td></td>
<td>which the planting of orchards is forbidden</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\chi_n$</td>
<td>Contamination threshold in the neighbourhood, above which the planting of</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td></td>
<td>orchards is forbidden</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Removal parameters

- $r_{\xi o}$: Ratio of the observation epicentre area over the focal area
- $1/\eta_o$: Maximal period between 2 observations (year)
- $\eta_s$: Observation frequency in security zones (year$^{-1}$)
- $\eta_f$: Observation frequency in focal zones (year$^{-1}$)
- $\eta_f^o$: Modified observation frequency in focal zones (year$^{-1}$)
- $\eta_y$: Observation frequency in young orchards (year$^{-1}$)
- $\eta_y^o$: Modified observation frequency in young orchards (year$^{-1}$)
- $\chi_o$: Contamination threshold in the observation epicentre, above which the observation frequency in focal zone is modified
- $r_{\chi y^o}$: Ratio (over $\chi y$) of the contamination threshold in the environment, above which the observation frequency in young orchards is modified
- $\delta$: Mean delay before removal of a detected tree (days)
- $Y_R^T$: (Boolean) Individual trees are removed: 0: after a mean delay $\delta$ 1: at the end of the year
- $Y_R$: (Boolean) Whole orchards are removed: 0: after a mean delay $\delta$ 1: at the end of the year
- $\zeta_R$: Radius-distance of the removal zone (m)
- $T_{\xi oR}$: Ratio of the removal epicentre area over the removal area
- $\chi_R$: Contamination threshold in the removal epicentre, above which orchards inside the removal zone are removed

Replanting parameters

- $\gamma_S$: Delay before replanting of a removed orchard (years)
- $\zeta_n$: Radius-distance of the neighbourhood (m)
- $\chi_y$: Contamination threshold in the environment around young orchards, above which the planting of orchards is forbidden
- $\chi_n$: Contamination threshold in the neighbourhood, above which the planting of orchards is forbidden
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Economic parameters</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\gamma$</td>
<td>Relative age-dependent yield of hosts in S or E states</td>
<td>0.00 until 2 years&lt;sup&gt;a&lt;/sup&gt;, 0.50 at 3 years&lt;sup&gt;a&lt;/sup&gt;, 0.65 at 4 years&lt;sup&gt;a&lt;/sup&gt;, 0.85 at 5 years&lt;sup&gt;a&lt;/sup&gt;, 1.00 from 6 to 15 years&lt;sup&gt;a&lt;/sup&gt;, 0.80 from 16 years&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>$c_S$</td>
<td>Planting cost of one orchard (€.ha&lt;sup&gt;-1&lt;/sup&gt;)</td>
<td>14,000&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>$c_R$</td>
<td>Removal cost of one orchard (€.ha&lt;sup&gt;-1&lt;/sup&gt;)</td>
<td>1,000&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>$c_T$</td>
<td>Removal cost of one individual tree (€)</td>
<td>15&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>$c_F$</td>
<td>Yearly fixed cost associated with prunus cultivation (€.ha&lt;sup&gt;-1&lt;/sup&gt;)</td>
<td>13,600&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>$c_O$</td>
<td>Cost of one observation (€.ha&lt;sup&gt;-1&lt;/sup&gt;)</td>
<td>160&lt;sup&gt;a,f&lt;/sup&gt;</td>
</tr>
<tr>
<td>$p$</td>
<td>Maximal yearly benefit generated by fruit harvest (€.ha&lt;sup&gt;-1&lt;/sup&gt;)</td>
<td>37,250&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>$\tau_o$</td>
<td>Discount rate</td>
<td>0.04&lt;sup&gt;g&lt;/sup&gt;</td>
</tr>
<tr>
<td>$\chi_{SEHD}$</td>
<td>Minimum proportion of living trees, below which the orchard is not profitable and thus removed</td>
<td>0.66&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> estimated through expert opinion.
<sup>b</sup> domain of definition.
<sup>c</sup> estimated in (Pleydell et al., 2018).
<sup>d</sup> fixed by (JORF, 2011). With regard to $\zeta_R$ and $\tau_{cR}$, when fixed at 0, the removal zone or the removal epicentre correspond to the contaminated orchard only.
<sup>e</sup> estimated from the economic analysis of prunus cultivation (Table S1).
<sup>f</sup> with $\rho=0.66$.
<sup>g</sup> (Quinet, 2013).
<sup>h</sup> we assumed that the detection probability could not go further because of technical limitations.
<sup>i</sup> these durations aim at detecting latent infections, and 10 years is well beyond the expected duration of the latent period ($\theta_{exp}$).
<sup>j</sup> 5,800 m is the maximal distance between the centroids of 2 orchards in the landscape; 5,475 m is the maximal distance between the closest points of 2 orchards.
<sup>k</sup> 15 years is the expected duration ($\psi$) of an orchard.
<sup>l</sup> given the time window to survey prunus leaves in orchards, 8 observations/year is equivalent to 1 observation/fortnight. We supposed that higher observation frequencies were not economically viable (Table S1), which has been confirmed by the results of the sensitivity analyses.
<sup>m</sup> either 0 or 1 (Boolean variable).
<sup>n</sup> the management process of the model does not change any more for $\chi_R$ above 0.34, since any orchard with a proportion below $\chi_{SEHD}=0.66$ of living trees is removed for profitability reasons (Table S1).
Table 2. Summary of the economically improved management strategies in different epidemic contexts. Values of the control parameters estimated using the combination leading to the best value (1), or the best percentile (1%) of $\mu_{NPV}$, and outputs of 10,000 simulations, in the reference epidemic context or in harsh epidemic contexts (halved values for the expected duration of the latent period, $\theta_{exp}$; or doubled values for the transmission coefficient, $\beta$).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Management strategy</th>
<th>Reference</th>
<th>Shorter latency</th>
<th>Stronger transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\rho$</td>
<td>Detection prob.</td>
<td>0.36</td>
<td>0.60</td>
<td>0.47</td>
</tr>
<tr>
<td>$\zeta_s$</td>
<td>Radius-dist. of security zones (m)</td>
<td>61</td>
<td>54</td>
<td>27</td>
</tr>
<tr>
<td>$\zeta_n$</td>
<td>Radius-dist. of neighbourhood (m)</td>
<td>2787</td>
<td>962</td>
<td>4157</td>
</tr>
<tr>
<td>$\chi_n$</td>
<td>Neighbourhood conta. thres. above which orchard planting is forbidden</td>
<td>0.60</td>
<td>0.92</td>
<td>0.73</td>
</tr>
<tr>
<td>$1/\eta_0$</td>
<td>Maximal period between 2 obs. (years)</td>
<td>4</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>$\eta_s$</td>
<td>Obs. freq. in security zones (year$^{-1}$)</td>
<td>3</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>$\eta_y$</td>
<td>Obs. freq. in young orchards (year$^{-1}$)</td>
<td>-</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>$\gamma_o$</td>
<td>Duration of obs. zones (years)</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>$\gamma_y$</td>
<td>Duration of young orchards (years)</td>
<td>-</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>$\gamma_S$</td>
<td>Delay before replanting (years)</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>

Median output of 10,000 replicates

- $Y$ Nb. of productive hosts (trees.ha$^{-1}$.year$^{-1}$) | 559 | 558 | 559 | 558 | 559 | 558
- $NPV$ Net present value (million euros) | 13.7 | 13.7 | 13.7 | 13.6 | 12.7 | 13.1

*a when $\zeta_s$ is so small, the security zone corresponds to the contaminated orchard.
Fig. 1 Schematic representation of the spatiotemporal stochastic model simulating shank spread and its management. (a) Flow diagram of the SEHDR architecture. S: susceptible (i.e. healthy); E: exposed (i.e. infected but neither infectious nor diseased); I: infectious and symptomatic; H: hidden (i.e. not detected); D: detected; R: removed. Productive and non-productive (diseased) hosts are in green and red, respectively. Healthy hosts incur the infectious potential ($\lambda$) applied by infectious hosts at various distances. Infected hosts become infectious after a mean latent period $\theta_{exp}$. Symptomatic hosts can be detected with probability $\rho$, and next removed after a mean delay $\delta$. Regardless of their sanitary state, hosts can be removed due to orchard turnover (with mean orchard lifespan $\psi$). Each orchard planting has a mean risk of introduction ($\phi$) of infectious trees (whose mean proportion is $E(\tau)$ in the orchard). (b) Orchard surveillance, depending on their location relative to previously infected
trees and contamination rate of the epicentre. (c) Planting restrictions and surveillance for young orchards, depending on the contamination rates of the environment and neighbourhood. (d) Removal of orchards depending on the contamination rate of the epicentre. In the French strategy to manage sharka, the removal zone and its epicentre correspond to the orchard only (i.e. \( \zeta_{eR} = \zeta_R = 0 \)). All model parameters are defined in Table 1.

Fig. 2 Step 1: Sobol's sensitivity indices of the 23 control parameters and 6 epidemiological parameters on the mean output of the stochastic replicates (\( \mu_{NPV} \), average net present value). \( \sum SI_1 = 0.64 \). Parameters in black are kept in step 2; parameters in red are removed; parameters in green are the epidemiological parameters. Insets: value of the output variable (\( \mu_{NPV} \), in million €) obtained with the different values of the six most influential parameters (grey colouration: density). All model parameters are defined in Table 1.
Fig. 3 Heuristic optimisation of control parameters through sequential sensitivity analyses: example on three parameters. The improved combination of control parameters is approached by isolating the combination associated with the highest value of $\mu_{NPV}$, or using the mode of the distribution of each parameter within the combinations associated with the best percentile of $\mu_{NPV}$. In step 2, an improved value (red circle) is found for $\Upsilon_{RT}$, and $\chi_R$ can be removed from further analyses (dashed blue line: improved values for removal parameters are so high that removals may never occur). The improvement of $\rho$ is refined in step 3, using a restricted variation range (blue arrows). See the results with all control parameters in Figs. S10 and S11.
Fig. 4 Improved management strategies. Surveillance, plantings and removals according to the combination of control parameters associated with the best value (a) or the best percentile (b) of $\mu_{NPV}$. Given its radius, the security zone may consist of the contaminated orchard only. Whole orchards may only be removed if the proportion of remaining trees falls below a profitability threshold ($\chi_{SEHD}=0.66$).
Fig. 5 Distribution of \( Y \) (equivalent number of fully productive trees per hectare and per year, a), and \( NPV \) (net present value of all orchards of the landscape, b) after 30 years of management. Different scenarios are simulated: absence of disease, absence of management, disease managed with the reference strategy (French management in orchards), or with economically improved management strategies identified through two different methods (combination associated with the best value or the best percentile of \( \mu_{NPV} \)).
Supporting information

The following supporting information is available for this article:

**Fig. S1.** Step 1: Sobol’s sensitivity indices of the 23 control parameters and 6 epidemiological parameters on the standard deviation of the stochastic replicates.

**Fig. S2.** Step 1: Sobol’s sensitivity indices of the 23 control parameters and 6 epidemiological parameters on the mean epidemiological output of the stochastic replicates.

**Fig. S3.** Step 2: Five best values, and distributions of the best and worst percentiles of each parameter with regard to the mean economic criterion in the second sensitivity analysis.

**Fig. S4.** Step 3: Five best values, and distribution of the best and worst percentiles of each parameter with regard to the mean economic criterion in the third sensitivity analysis.

**Fig. S5.** Distribution of $Y$ and $NPV$ after 30 years of management in harsher epidemic contexts.

**Fig. S6.** Dynamics of annual prevalence and incidence under different management strategies and epidemic contexts.

**Fig. S7.** Dynamics of observations, tree and orchard removals under different management strategies and epidemic contexts.

**Fig. S8.** Distribution of $Y$ and $NPV$ after 30 years of management in harsh epidemic contexts, with strategies specifically improved in these contexts.

**Fig. S9.** Dynamics of annual prevalence and incidence under management strategies specifically improved in harsh epidemic contexts.

**Fig. S10.** Distribution of the observation dates, depending on the observed plant organ.

**Fig. S11.** Convergence of the mean and standard deviation of $NPV$ with the number of replicates.

**Table S1.** Economic analysis of prunus cultivation in France.

**Method S1.** Description of the epidemic model.

**Method S2.** Calculation of the contamination rate.